Clinical and Experimental Health Sciences

Contents

RESEARCH ARTICLES

Contents

REVIEW

CASE REPORT

Clinical and Experimental Health Sciences

Naringenin Reduces Hepatic Inflammation and Apoptosis Induced by Vancomycin in Rats

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ABSTRACT

Objective: This investigation aimed to detect the possible protective impacts of naringenin (NAR) on vancomycin (VCM)-induced liver toxicity through measuring caspase-3, – 8 and – 9 activities as markers of apoptosis and the levels of tumor necrosis factor-alpha, cyclooxygenase-2 and vascular endothelial growth factor as inflammation markers and assessing the histopathological alterations in rats.

Methods: The rats were allocated into seven groups as, the control group (saline, intraperitoneally (i.p.)), VCM group (400 mg/kg/day, i.p.), carboxymethyl cellulose (CMC) group (0.5%, orally), NAR100 group (100 mg/kg/day, orally), VCM+NAR25 group (25 mg/kg/day, orally), VCM+NAR50 group (50 mg/kg/day, orally), VCM+NAR100 group (100 mg/kg/day, orally). The caspase enzyme activities and inflammation markers were measured using colorimetric methods and ELISA, respectively. Histopathological examinations were performed.

Results: The caspase activities and levels of inflammation markers were significantly higher in the VCM group as opposed to the other groups. The caspase activities were significantly ameliorated in the VCM+NAR25 group compared to the VCM+NAR50 and VCM+NAR100 groups, but the levels of inflammation markers were significantly reduced in the VCM+NAR50 group and, especially, the VCM+NAR100 group compared to the VCM+NAR25 group.

Conclusion: NAR has potential protective impact on liver injury caused by VCM, and the protective impacts of NAR at distinct doses may occur via different molecular mechanisms.

Keywords: Vancomycin, naringenin, liver, apoptosis, inflammation

1. INTRODUCTION

Drug-induced hepatotoxicity is the most frequent reason for acute liver failure. It constitutes approximately 10% of acute liver failure worldwide and approximately 40-50% of all cases of liver damage (1). Furthermore, antibiotic-induced hepatotoxicity accounts for 25-45% of drug-induced liver injuries (2). Vancomycin (VCM) is a glycopeptide antibiotic which is mostly employed to cure aerobic and anaerobic gram-positive bacteria, which include methicillin-resistant *Staphylococcus aureus* infections (3). Approximately 90% of VCM is eliminated with glomerular filtration (4), thus, its major side effect is nephrotoxicity (5). Also, VCM has been reported to have side effects on the liver that restrict its therapeutic use in patients with impaired liver function (6), and sufficient evidence has been found that potential VCM causes idiosyncratic hepatotoxicity and a type of hepatocellular lesion (7).

VCM–induced nephrotoxicity has been reported extensively, but its mechanism is still not exactly known (5). Lately, studies on animal model have revealed that apoptotic cell death, oxidative stress and inflammation can conduce to the pathogenesis of VCM-induced nephrotoxicity (3,5). Inflammation and oxidative stress are important factors that affect the progression of renal injury. These factors also play a significant part in the progression of liver injury. The liver is the most frequently targeted organ in drugs-induced damages (2) and is an organ that is majorly attacked by reactive oxygen species (ROS) (8). In the event of the excessive formation of ROS by various factors, redox homeostasis is impaired which leads to oxidative stress. Oxidative stress and inflammation in hepatocyte cause mitochondrial dysfunction and permeability and induce cell death via necrotic and/or apoptotic mechanisms, which in turn leads to cellular and tissue injuries (8,9). Little is known on the mechanism of VCM-induced hepatotoxicity, however, it is thought that these factors might play a role in liver injuries.

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Flavonoids, which are naturally occurring substances, have various therapeutic uses and pharmacological impacts and are significant sources of medicine worldwide. Some flavonoids owing to their phenolic structures have antioxidant activity and prevent processes related to free radical, and thus flavonoids, which are antioxidants, have the properties that can improve apoptosis (5). Naringenin (4',5,7-trihydroxyflavanone, NAR) is a flavonoid that is present in vegetables, flowers, leaves, seeds, fruits, plants bark etc. (10). NAR has biological properties such as pharmacologically potent antioxidant, anti-inflammatory, nephroprotective, antimutagenic, antinitrosative, antifibrogenic, neuroprotective, antiatherogenic, anticarcinogenic and antitumor activities (5,11). NAR has also very specific hepatoprotective properties (12). NAR has been reported to have protective effects against liver damage resulting from cadmium (5), ethanol (11), carbon tetrachloride (CCl_4) (13), arsenic (14), lead (15) in rats and acetaminophen (16) in mice. Previous studies have shown that NAR has a preventive effect against apoptosis, inflammation and oxidative stress caused by drugs or chemicals in liver tissues (9-11,13). Therefore, it can be stated that NAR may have potential protective effect on VCM-induced liver injuries. Nonetheless, as far as we know, there are no prior studies conducted on the protective impact of NAR on apoptosis and inflammation caused by VCM in the livers of rats.

This study aimed to clarify whether VCM induced apoptosis and inflammation in the livers of rats and to detect possible protective impact of NAR on VCM-induced liver toxicity through measuring caspase-3, – 8 and – 9 activities as markers of apoptosis and the levels of cyclooxygenase-2 (COX-2), vascular endothelial growth factor (VEGF) and tumor necrosis factor-alpha (TNF-α) as inflammation markers and assessing histopathological alterations.

2. METHODS

2.1. Animals

Animals were purchased from the Laboratory of the Animal Production Unit of Mersin University, Mersin, Turkey. Forty-nine adult male Wistar albino rats that weighed between 180 and 250 g were employed for the experiment. The rats were maintained at standard laboratory conditions, under cycles of 12 hours of light and 12 hours of dark with relative humidity 55±8 % and temperature of 25±2 °C. The animals had a standard diet and access to drinking water ad libitum. The current investigation was endorsed by the Animal Experiments Local Ethics Committee of Mersin University, Turkey with the ethical approval number of 2016/HADYEK/E.98180, 2016/21.

2.2. Chemicals

NAR was supplied from Sigma-Aldrich Chemistry (St. Louis, MO, USA) and VCM was obtained from Kocak Farma (Istanbul, Turkey). All other chemicals were of analytical grade. The chemicals used in the experiment were prepared fresh daily.

2.3. Experimental Design

NAR and VCM doses were chosen according to previous studies (9,10,17-19). 49 rats were randomly assigned to one of the seven groups, each of the group consisted of seven rats. The experimental plan of the investigation is schematized in Figure 1 and illustrated in Table 1. The control and VCM groups were taken from our previous study (20).

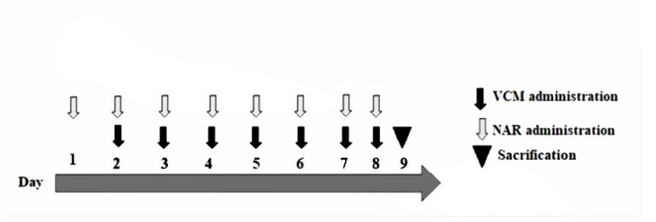

Figure 1. *Schematic presentation of the experimental plan of the study*

Table 1. *The experimental plan of the study*

Group	n	Treatment regimen
Control[a]	7	Saline administration was applied intraperitoneally (i.p.) once a day along 8 days
CMC	7	Carboxymethyl cellulose (0.5%) was administered via gavage once a day along 8 days
VCM[a]	7	VCM administration was applied at a dose of 400 mg/kg/day i.p. once a day at 24 hours intervals along 7 days
NAR100	7	NAR dispersed in CMC was applied orally at dose of 100 mg/kg once a day along 8-day
VCM+NAR25[b]	7	NAR25 administration was applied orally at a dose of 25 mg/kg once a day along 8-day. One day after the initial administration of NAR, administration of VCM (400 mg/kg/day) was initiated and proceeded along 7 days.
VCM+NAR50[b]	7	NAR50 administration was applied orally at a dose of 50 mg/kg once a day along 8-day. A day after the initial administration of NAR, VCM administration (400 mg/kg/day) was initiated and proceeded along 7 days.
VCM+NAR100[b]	7	NAR100 administration was applied orally at a dose of 100 mg/kg once a day along 8-day. A day after the initial administration of NAR, VCM administration (400 mg/kg/day) was initiated and proceeded along 7 days.

[a]*Control and VCM group were taken from our previous study (20);* [b]*VCM was administered 1 h after NAR administration; VCM: vancomycin; CMC: carboxymethyl cellulose; NAR: naringenin; VCM+NAR: VCM+NAR administered group.*

On the 9th day of the experiment and 24 hours after receiving the last dose, all of the rats were sacrificed under xylazine hydrochloride (10 mg/kg i.p.) and ketamine hydrochloride (30 mg/kg i.p.) anesthesia. The liver tissues were promptly excised and stored at –20 ^{0}C for the biochemical analyses and histopathological examinations.

2.4. Biochemical Studies

2.4.1. Tissue homogenization

The homogenization of rat livers was performed in an ice-cold lysis buffer. The centrifugation of homogenates was made for 10 minutes at 14 000 g at 4 °C, and the resulting supernatants were used to study the selected biochemical parameters.

2.4.2. Determination of the activities of the caspase-3, – 8, and – 9 enzymes

The activities of caspase-3, – 8 and – 9 enzymes were assessed using Colorimetric Test Kits (BioVision Research Product, Mountain View, CA, USA) in line with manufacturer's directions. The protein levels were detected by Lowry test (21). Accordingly, the appropriate volume of dilution buffer was added to 50 µg of protein and the protein was diluted to 50 µL. Caspase – 3, – 8 and – 9 assay kits were used for colorimetric analysis to determine chromophore *p*-nitroanilide (*p*NA) after separation from the labeled substrate. The caspase – 3, – 8 and – 9 enzymes' substrates were Asp-Glu-Val-Asp (DEVD)-*p*NA, Ile–Glu–Thr–Asp (IETD)-*p*NA and Leu–Glu–His–Asp (LEHD)-*p*NA, respectively. A microplate reader at 405 nm was used to measure pNA light emission.

2.4.3. Determination of hepatic TNF-α, COX-2 and VEGF levels

Measurement of COX-2, TNF-α and VEGF levels were done using enzyme-linked immunosorbent assay kits (ELISA kits, Sunred Biological Technology, Shanghai, China) in line with the manufacturer's directions. The intensity of the color of the samples was determined for TNF-α, COX-2, and VEGF at 450 nm with the ELISA plate reader. The values were demonstrated as ng/mg protein.

2.5. Histopathological Study

Liver tissues from each rat were removed and weighted. The tissues were cut into 1 cm^3 pieces and fixed in a 10% neutral buffered formalin solution for 48 hrs. Upon fixation, the samples were employed routinely, embedded in paraffin and cut at 5 µm on a rotary microtome. The cut sections were then mounted on glass slides, stained with hematoxylin and eosin (H&E) and Masson's Trichrome, and visualized under the light microscope (Olympus BX50, Olympus GmBH Tokyo, JAPAN) for histopathological evaluations. The histopathological studies were conducted by two histopathologists and the grading was done according to a semiquantitative scale: (–) no significant histopathological injury, (+) mild degree of injury, (++) moderate degree of injury and (+++) severe degree of injury. The gradings were done according to the following parameters: nuclear pleomorphism, inflammation, pyknosis, capsule thickening, fibrosis, necrosis, vacuolization, and sinusoidal dilation (22,23).

2.6. Statistical Analysis

Statistical analyses were done using SPSS Version 25.0 statistical software package. The values were represented as means ± standard deviation (SD). Comparisons of the caspase activities and the levels of inflammation markers among the groups were made using One-way analysis of variance (ANOVA) with Tukey's *post hoc* test and Mann Whitney U test or Kruskal Wallis H test, respectively. Statistically significant was considered when a *p* value was below 0.05.

3. RESULTS

3.1. Caspase Enzyme Activities

The alterations in the hepatic caspase enzymes activities were shown in Figure 2. The caspase-3 and – 9 enzyme activities were detected to be significantly more elevated in the NAR100, VCM, VCM+NAR (50 and 100) groups as opposed the control group ($p<0.05$). The caspase-3 and – 9 activities in the CMC and VCM+NAR25 groups were detected to be significantly more reduced than those in the VCM group ($p<0.05$). Furthermore, statistically reduced caspase-3 and – 9 activities were detected in the VCM+NAR25 group when compared with the NAR100 and VCM+NAR (50 and 100) groups ($p<0.05$). Caspase-8 activity was significantly more elevated in the VCM group as opposed to the control, CMC, NAR100, VCM+NAR25 groups ($p<0.05$). Caspase-3, – 8 and – 9 activities were significantly more reduced in the CMC group versus the VCM and VCM+NAR (50 and 100) groups. These findings revealed that the hepatic activities of caspase-3, – 8, and – 9 caused by VCM were significantly reduced by NAR25 administration.

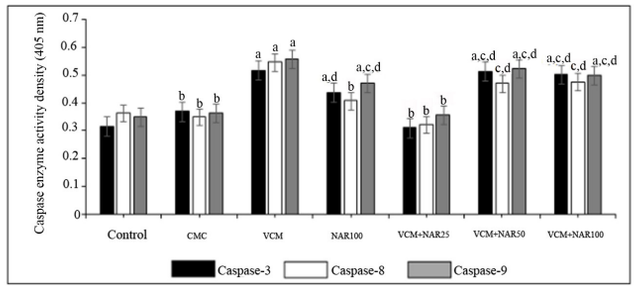

Figure 2. *Impact of NAR against hepatic activities of caspase-3, – 8, and – 9 caused by VCM. Values are mean ± SD; [a]p< 0.05 vs. control group; [b] p< 0.05 vs. VCM group;, [c]p< 0.05 vs. CMC group; [d]p<0.05 vs. VCM+NAR25 group; NAR: naringenin; VCM: vancomycin; SD: standard deviation; CMC: carboxymethyl cellulose.*

3.2. Hepatic TNF-α, COX-2 and VEGF Levels

As seen in Figure 3, the hepatic COX-2, TNF-α and VEGF levels were significantly more elevated in the VCM group as opposed to the control group (p<0.05). The hepatic levels of TNF-α were significantly more elevated in the VCM group than in the CMC, NAR100, VCM+NAR (25, 50 and 100) groups (p<0.05). However, no significant difference was noted among the VCM+NAR groups (p>0.05). Also, the COX-2 levels in the

VCM group were also significantly more elevated compared to the CMC, NAR100 and VCM+NAR (50 and 100) groups ($p<0.05$). The levels of COX-2 were significantly lower in the VCM+NAR100 group as opposed to the VCM and VCM+NAR25 groups ($p<0.05$). Interestingly, no significant difference was noted between the VCM+NAR50 and both the VCM+NAR25 and VCM+NAR100 groups in terms of COX-2 levels. The hepatic VEGF levels were significantly higher in the VCM group as opposed to the CMC, NAR100 and VCM+NAR100 groups ($p<0.05$). Among the VCM+NAR groups, the VEGF levels in the VCM+NAR100 were significantly lower in comparison to the VCM+NAR25 and VCM+NAR50 groups ($p<0.05$). No important difference was noted between the VCM+NAR25 and VCM+NAR50 groups in terms of VEGF levels ($p>0.05$). These results indicated that increased hepatic TNF-α, COX-2 and VEGF levels caused by VCM were significantly decreased by NAR treatments, particularly NAR100 mg.

3.3. Histopathological Examination

The liver tissues were evaluated according to the determined histopathological parameters, namely vacuolization, nuclear pleomorphism, sinusoidal dilatation, pyknosis, inflammation, necrosis, capsule thickening and fibrosis (22,23). As shown in Table 2 and Figures 4-6, vacuolization, pyknosis, nuclear pleomorphism, and sinusoidal dilatation were not observed in the study groups. Furthermore, no histopathological changes were determined in the control and CMC groups. However, fibrosis was mildly observed in the VCM, VCM+NAR (25, 50, and 100) and NAR100 groups. Necrosis and capsule thickening were mildly detected in the VCM, VCM+NAR50 and VCM+NAR100 groups, while mild inflammation was detected in the VCM and VCM+NAR50 groups. These findings showed that VCM caused histopathological damages, even if they were not severe in rat liver, and that the damages were ameliorated by the administration of NAR25 mg.

Table 2. *Scores of histopathological alterations observed in study groups*

Histopathological parameters	Mean Score						
	Control	CMC	VCM	NAR100	VCM+NAR25	VCM+NAR50	VCM+NAR100
Vacuolization	-	-	-	-	-	-	-
Nuclear pleomorphism	-	-	-	-	-	-	-
Sinusoidal dilatation	-	-	-	-	-	-	-
Pyknosis	-	-	-	-	-	-	-
Inflammation	-	-	+	-	-	+	-
Necrosis	-	-	+	-	-	+	+
Capsule thickening	-	-	+	-	-	+	+
Fibrosis	-	-	+	+	+	+	+

+++: severe; ++: moderate; +: mild; – : none. VCM: vancomycin, CMC: carboxymethyl cellulose, NAR: naringenin, VCM+NAR: VCM+NAR administered group.

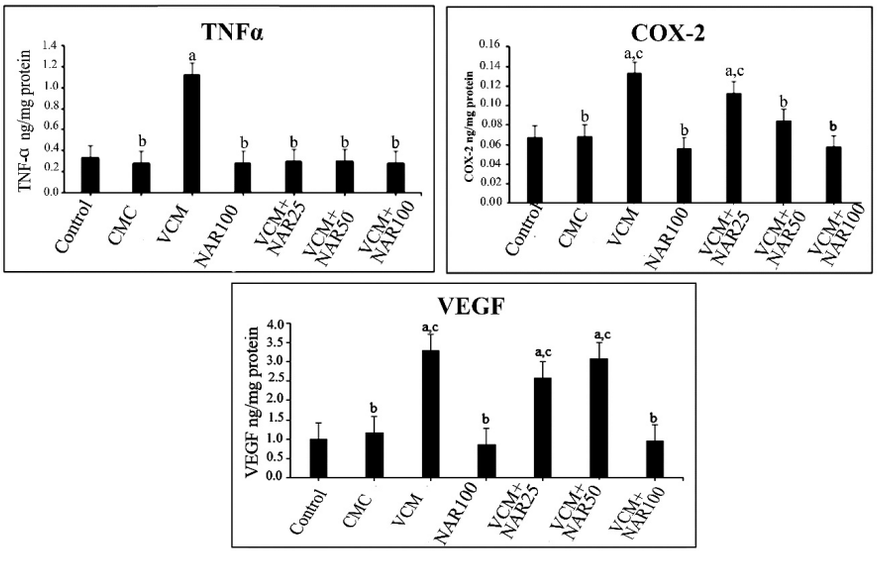

Figure 3. *Impact of NAR against hepatic TNF-α, COX-2 and VEGF levels induced by VCM. Values are mean ± SD; [a]p<0.05 vs. control group; [b]p<0.05 vs. VCM group; [c]p<0.05 vs. VCM+NAR100 group; NAR: naringenin; TNF-α: tumor necrosis factor-alpha; COX-2: cyclooxygenase-2; VEGF: vascular endothelial growth factor; VCM: vancomycin; SD: standard deviation.*

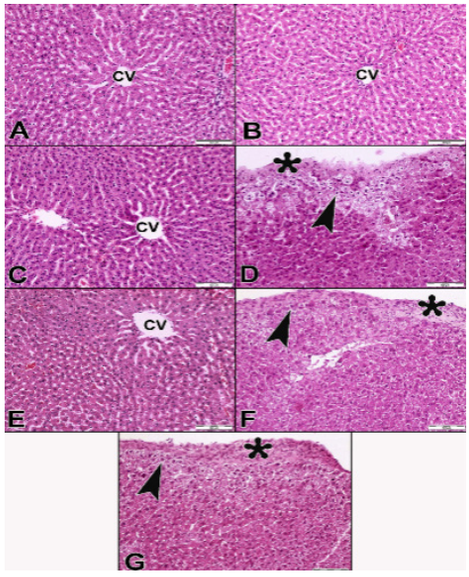

Figure 4. *Representative photomicrographs of H&E-stained liver sections. Control group (A), CMC group (B), NAR100 group (C), VCM group (D), VCM+NAR25 group (E), VCM+NAR50 group (F), VCM+NAR100 group (G); central vein (CV), necrotic cells with cytoplasmic vacuoles (black arrowhead), capsule thickening (black asterisk) (X100, scale bar 100 µm); CMC: carboxymethyl cellulose; NAR: naringenin; VCM: vancomycin.*

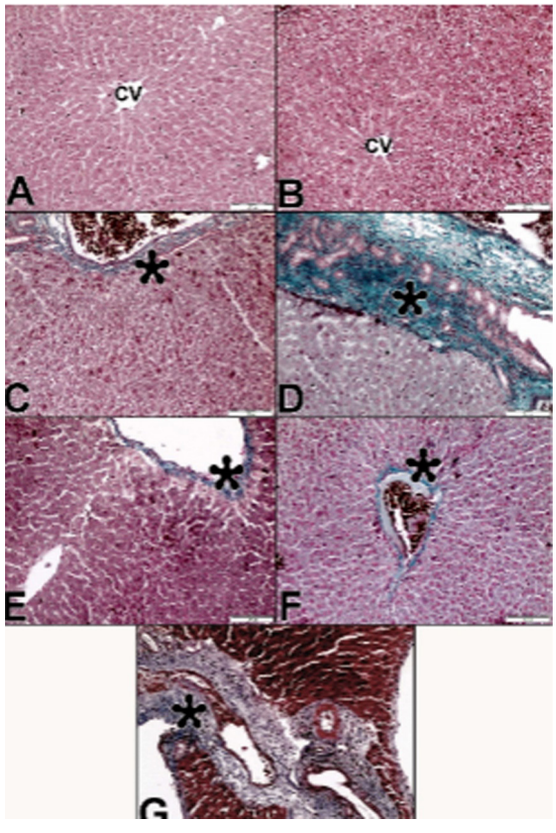

Figure 5. *Representative photomicrographs of Masson's trichrome-stained liver sections. Control group (A), CMC group (B), NAR100 group (C), VCM group (D), VCM+NAR25 group (E), VCM+NAR50 group (F), VCM+NAR100 group (G); central vein (CV), fibrosis (asterisk) (X100, scale bar 100 µm); CMC: carboxymethyl cellulose; NAR: naringenin; VCM: vancomycin.*

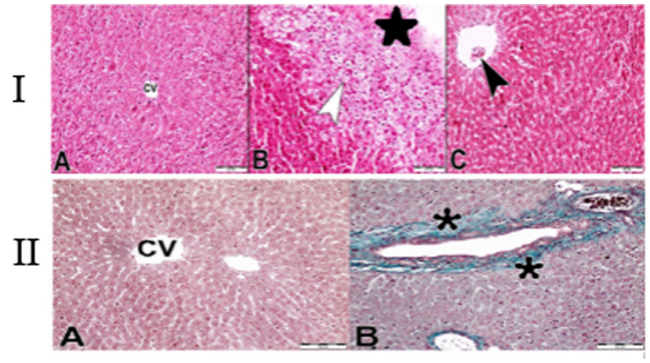

Figure 6. *H&E (I) and Masson's trichrome (II) staining in control and VCM groups. Control group (A), VCM group (B and C); central vein (CV), necrotic cells with cytoplasmic vacuoles (white arrowhead), capsule thickening (black star), cell debris spilling into vein lumen (black arrowhead), fibrosis (asterisk). A, B and C X100; VCM: vancomycin.*

4. DISCUSSION

The possible protective impacts of NAR were surveyed by measuring caspase-3, – 8 and – 9 activities as markers of apoptosis and levels of COX-2, TNF-α and VEGF as inflammation markers, and by examining the histopathological alterations. In this study, it was determined that the protective impact of NAR on apoptosis and inflammation occurred at its different doses. This investigation is the first study to show the potential protective impacts of NAR on VCM-induced apoptosis and inflammation in the livers of rats. This study is important as it provided valuable data on the protective mechanism of NAR.

A variety of inflammatory, toxic and metabolic insults lead to liver injury and disease through the activation of apoptotic and/or necrotic cell death (24). Apoptosis is a primary factor in numerous liver diseases and injuries (24) and is induced via two pathways, which are the extrinsic (death receptor pathway) and the intrinsic (mitochondrial pathway) pathways, and the increased activities of caspase-8 and – 9, which are initiator caspases, stimulate the extrinsic and intrinsic pathways of apoptosis, respectively and activate caspase-3 that is a primary executioner caspase in apoptosis (5). Very little is known about the mechanism of VCM-induced liver injuries and caspase-dependent apoptosis caused by VCM in the liver tissue. In this study, it was determined that the hepatic activities of caspase-3, – 8, and-9 were significantly more elevated in the VCM group as opposed to the control group ($p<0.05$). Additionally, the activities of caspase-3, – 8 and – 9 enzymes in the VCM+NAR25 group were significantly lower compared to the VCM group ($p<0.05$). Therefore, it can be concluded that NAR25 significantly inhibits the activities of caspase-3, – 8 and – 9 enzymes induced by VCM.

Flavonoids are known to indicate both pro-oxidant and antioxidant activity based on their high concentrations, polyphenolic structure and type of cell and exhibit cytotoxic activities at comparatively high doses in the micromolar concentration range (25). Flavonoids at high concentrations

have been shown to able to be produced ROS via auto-oxidation. ROS are the main signaling molecules that modulate cell death. The findings of the current study revealed that a 25 mg dose of NAR had more potential inhibitory impacts on VCM-induced caspase activity in liver tissue compared to 50 and 100 mg doses of NAR. This might be due to NAR at high concentration displaying cytotoxic activity and the generation of ROS as a result of their pro-oxidant activity. NAR25 significantly reduced the increase in caspase activities in the liver tissues.

Inflammation plays a significant part in the progression of liver injury. There is little information about how VCM causes inflammation in the liver tissue. TNF-α is an extremely pleiotropic cytokine that induces diverse biological effects, such as necrotic and/or apoptotic cell death, inflammatory responses, metabolic activation and cell proliferation (26). It plays a significant part in toxic liver damage. In this study, it was revealed that TNF-α levels were significantly more elevated in the VCM group versus the control group, while TNF-α levels in the VCM+NAR (25, 50 and 100) groups were significantly lower compared to the VCM group. No statistically significant difference was noted between the VCM+NAR25, VCM+NAR50 and VCM+NAR100 groups. Depending on the results, it can be concluded that NAR can reduce the levels of TNF-α. Similar to the results of this study, several studies have also reported that NAR can decrease proinflammatory cytokines like IL-6, IL-1β and TNF-α with the suppression of NF-κB, which is a signal transduction pathway promoting the transcription of gene coding for proinflammatory proteins (27,28).

COX-2 is another significant inflammatory mediator due to its rate-limiting synthesis of the precursors of thromboxanes and prostaglandins (29). Increased COX-2 levels cause eicosanoid production in high concentrations by initiating the COX-prostanoid pathway leading to necrosis and cellular inflammation (29). The COX-2 gene, which is mostly expressed in Kupffer cells, is expressed in response to various cytokines and proinflammatory agents. Also, COX-2 has a relationship with liver pathogenesis that includes cancer and fibrosis (30). In this study, it was revealed that the levels of COX-2 were significantly more elevated in the VCM group as opposed to the control group (p<0.05). COX-2 levels were significantly more reduced in the VCM+NAR50 and VCM+NAR100 groups as opposed to the VCM group (p<0.05). However, in terms of COX-2 levels, there was no significant distinction between the VCM+NAR50 group (36.1% reduction) and VCM+NAR100 (56.4% reduction) or VCM+NAR25 (15% reduction), but a significant distinction was between the VCM+NAR100 and VCM+NAR25 groups. Therefore, it can be concluded that dosages of 50 mg and, especially, 100 mg NAR effectively reduce the levels of COX-2 induced by VCM (Figure 3). In the study by Jayaraman *et al.* (31), by virtue of its anti-inflammatory effects, NAR (50 mg/kg) was reported to inhibit several inflammatory mediators such as COX-2, TNF-α and NF-κB, thereby contributing to the treatment of liver damage caused by exposure to ethanol. Esmaeili and Alilou (13) also reported that NAR (50 mg/kg) attenuated liver inflammation by downregulating the CCl_4-induced activation of nitric oxide synthase (iNOS), TNF-α and COX-2 at protein and mRNA levels in rats. Besides, Dong *et al.* (32) also administered 30, 60 and 120 mg/kg of naringin, the aglycone of which is naringenin, doses to CCI4-treated mice and revealed that NAR at a dose of 120 mg/kg sharply downregulated the expressions of TNF-α, COX-2, NF-κB, IL-6, IL-1β, HMGB-1, AP-1, iNOS and TLR4. These previous results are in agreement with the findings of this study.

VEGF, which is a signal protein stimulating angiogenesis, acts as a proinflammatory cytokine by improving endothelial permeability in vivo at nanomolar concentrations, inducing the expression of endothelial cell adhesion molecules and by acting as a monocyte chemoattractant (33). Liver VEGF is mostly present in hepatocytes and endothelial cells with the VEGF receptors (34) and the production of VEGF can also be induced by COX-2. The findings of this report revealed that the levels of VEGF were significantly higher in the VCM group as opposed to the control group (p<0.05). However, the VEGF levels are significantly lower in the VCM+NAR100 group versus the VCM group and also the VCM+NAR (25, 50 and 100) groups (p<0.05). Therefore, it can be concluded that a dose of 100 mg of NAR was more effective in increasing the levels of VEGF caused by VCM than lower doses (25, 50 mg).

In this study, it was determined that a dose of 25 mg of NAR was more effective for caspase-dependent apoptosis than higher doses (50 and 100 mg) while 50 mg and, especially, 100 mg of NAR was more effective for inflammation than lower dose (25 mg). The preventive effects of NAR on apoptosis and inflammation occurred at different doses. This is an extremely interesting result, and it may suggest that caspase-dependent apoptosis and inflammation are caused by the different mechanisms in distinct doses of NAR.

The extrinsic pathway of apoptosis is activated by the binding of the death ligand to death receptors on the plasma membrane. Death ligands belong to the TNF superfamily, involving TNF-related apoptosis that induce ligand (TRAIL), TNF-α and Fas ligand (FasL) (35) and the most well-known death receptors are TNFR-1 and Fas (CD95), which are abundant in the liver. For the extrinsic pathway of NAR, it can be stated that Fas is activated by FasL, which subsequently binds to Fas-associated protein with death domain (FADD), and that the Fas-FADD complex activates procaspase 8, which subsequently activates other caspases, causing apoptosis (12). The Fas/FasL interaction is already known to be a significant initiator of apoptosis via the extrinsic pathway, which can trigger the caspase cascades in liver damage (32). Therefore, in this study, although a dose of 25 mg of NAR had potential prevention effects on caspase activities, it might be suggested that higher NAR doses (50 and 100 mg) induce the extrinsic pathway of apoptosis via FasL instead of TNF-α.

In the intrinsic pathway of apoptosis, the administration of VCM leads to ROS generation, and higher doses of NAR can act as pro-oxidants. This may also increase cells' oxidative status. ROS are the main signal molecules modulating cell death and increased ROS can induce apoptosis. The

antioxidant and/or pro-oxidant effects of NAR may vary depending on the flavonoid concentration, the model used and the radical formed (12). For the reason, higher doses of NAR, unlike lower dose, may have induced apoptosis.

However, higher doses of NAR may have inhibited inflammation by different mechanisms. NAR is known to suppress diverse NF-kB-regulated gene products involving COX-2, VEGF, matrix metalloproteinase-2 and – 9 (36). Hernández-Aquino *et al.* (37) examined the molecular mechanisms involved in the hepatoprotective impacts of NAR (100 mg/kg body weight, p.o. per day) on liver fibrosis induced by CCl_4. They reported that CCl_4-treated rats performed elevated IL-1, IL-10 and NF-κB protein levels, yet concomitant administration of NAR and CCl_4 precluded these increases. NAR suppresses NF-κB through the downregulation of toll-like receptor 2 (TLR2) and TLR4 protein and mRNA levels and the reduced translocation and DNA binding of NF-κB. This causes the suppression of the expression of NF-κB dependent interleukins, like IL-1 and IL-10, and accordingly, prevents necrosis. In a study carried out by Yilma *et al.* (38), NAR was demonstrated to suppress TLR2 and 4 signaling, giving rise to the attenuation of neuroinflammation induced by pathogen.

The activated TLRs are known to trigger various liver cells and lead to the release of cytokines facilitating the progression of liver disease (39). Polyphenols have been reported to decrease inflammation by TLR4 signaling pathway modulation (40). NAR is a polyphenol, and it could be stated that NAR at higher doses can reduce inflammation by inhibiting the signaling pathway of TLRs.

Histopathological examinations revealed mild necrosis, inflammation, capsule thickening, and fibrosis were observed in the VCM group. In the study by Bruniera *et al.* (4), the effect of distinct VCM dilutions on liver, kidney and endothelial damage was investigated by histopathological analysis and biochemical parameters. They reported changes in alanine aminotransferase (ALT) that featured hepatotoxicity and reported that the animal groups that were treated for 3 days (infusion of VCM – 10mg/kg/day – in dilutions of saline 5 mg/ml and 10 mg/ml) demonstrated minor changes in the histopathological examinations, which are similar to the results of this study. Also, they suggested that morphological changes might be observed in some cases, and that but the commonly used and proposed markers did not aid in the monitoring of toxic effects of VCM. The main elimination pathway of VCM is the kidney, on which VCM has a major side effect as it tends to accumulate there (41). Therefore, biochemical and histopathological damages caused by VCM can easily be observed in renal tissues. However, approximately 5 to 8.5% of VCM clearance is extra-renal, possibly through hepatic conjugation, leading to VCM crystalline degeneration products (42). Accordingly, the biochemical effects may be clearly observed rather than histopathological effects of VCM in liver tissue. Thus, routine continuous monitoring of hepatic events among patients receiving VCM is recommended (43).

5. CONCLUSION

This study performed that the administration of VCM was able to cause caspase-dependent apoptosis by increasing the activities of caspase – 3, – 8 and – 9 and inflammation by inducing TNF-a, COX-2 and VEGF. Furthermore, the results demonstrated that the administration of NAR at different doses attenuated the liver injuries induced by VCM by decreasing the activities of caspases and the levels of inflammation markers. Consequently, NAR has potential protective impacts on liver injury caused by VCM, and the protective impacts of NAR at distinct doses may occur via different molecular mechanisms.

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Conflicts of interest

The authors declare that they have no conflict of interest.

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Clinical and Experimental Health Sciences

Nicotine Dependence Levels of Individuals Applying to a Family Health Center and Their Status of Being Affected by Warnings on Cigarette Packs

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ABSTRACT

Objective: The aim of this study is to determine the frequency of smoking and the status of being affected by the textual and pictorial warnings on cigarette packs in individuals who apply to a family health center for any reason.

Methods: This is a descriptive study. After the sample size calculation, 320 individuals were included in the study. A questionnaire prepared by the researchers upon the literature review and Fagerström test for nicotine dependence were used to collect the data. In the study, the data were analyzed using SPSS 22.0 packaged software and the significance level was accepted as $p<0.05$.

Results: It was found that the average age of the participants was 38.53±14.21. 40.9% of the participants were smokers. 19.8% had a high level of nicotine dependence. 35.9% stated that they were affected by warnings on cigarette packs. In the study, all the participants' statuses of being affected by pictorial and textual messages on cigarette packs were compared in terms of their gender and it was found that while men found the textual message of "Smoking damages sperms and reduces fertility" more effective, women found the textual message of "Smoking during pregnancy is harmful to your baby" more effective. On the other hand, the picture showing the couple sitting side by side in bed among the pictures was effective.

Conclusion: Smoking cessation interventions, priority can be given to young people and those with low education. In addition, warnings about baby/child and sexuality can be involved more on cigarette packs.

Keywords: cigarette, dependence, effect, family health center, public health nurse.

1.INTRODUCTION

Cigarette causes dependence due to high rate of nicotine it contains, and thus leading to death of more than eight million people every year (1). In 2016, the smoking rate was 15.5% among American adults, 17.5% in men, and 13.5% in women (2). Smoking rate was found as 39.1% in a study conducted in the People's Republic of China (3), 35.1% in a study conducted with healthcare professionals in Croatia (4), 24.8% in a study conducted in Montenegro (5). A study conducted in Turkey reported that the smoking rate was 25.7% among participants, 39.2% for men, and 12.6% for women (6). According to result of Global Adult Tobacco Survey, the smoking rate is 27.1% in Turkey. While this rate is 41.5% in men, it is 13.1% in women (7). When data of OECD 2019 for Turkey are examined, it is seen that the rate of smokers aged 15 years and over is 26.5% (8).

Tobacco kills approximately half of its users. One-fifth of deaths in the United States of America are associated with the health problems caused by smoking (cancer, respiratory and cardiovascular diseases) (9). The American Center for Disease Control and Prevention estimates that averagely 430.700 people die each year due to smoking. Dependence, which occurs within months for alcohol and within days for heroin, is seen within hours for nicotine (10). Being one of the most important health problems in the world, nicotine dependence is responsible for one of every ten deaths in the world each year (11). A person dies every six seconds in the world due to tobacco use. It is predicted that the smoking-related deaths would reach to 8.4 million by 2030 (12).

The warnings on cigarette packs are important for informing the users about health risks in long-term smoking (13). A person who smoke one pack of cigarettes a day has to face these warnings on cigarette packs at least 7000 times a year. Therefore, one can resist against smoking whenever he/she wants to smoke (14). After seeing the warnings on the cigarette packs, the number of people thinking to quit smoking by considering them between 2008-2012 increased at the rate of 14.4% (7). Due to its positive effects, the use of textual and pictorial warnings on cigarette packs against smoking, fighting

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with tobacco use, and making various interventions to prevent smoking are very important (14). In their study, Ozkaya & Edinsel (15) investigated the effect of textual warnings on cigarette packs on high school students and determined that the students evaluated all warning texts as *important and very important*. While the rate of those who thought that these warning texts would create positive effects was 38.9%, the rate of those who believed that they would not create any positive effect was 61.1%. 22.5% of the students quitted smoking after reading these warnings. 44.4% were affected by the warnings but could not stop smoking, 33.1% were not affected at all and continued to smoke.

In another study conducted in Turkey concerning the opinions of university students about the warnings on cigarette packs, it was determined that while "*smoking can cause the fetal death*" expression ranked the first (64.1%), the second one was the expression of *"smoking occludes the veins and causes heart attacks and strokes"* (16). Again, in a study conducted with the ninth, tenth, and eleventh-grade high school students in Turkey, it was observed that while male students paid attention mostly to the picture pointing out impotence, female students paid attention to the picture pointing out the negative effects of smoking during pregnancy on babies. More than half of the male students and one-fourth of female counterparts considered the picture of impotence as effective (17). In their study, Mazlum and Mazlum (18) determined that the most effective picture was "*Smoking during pregnancy is harmful to your baby*" and the second effective one was "*smoking occludes the veins and causes heart attacks and strokes*".In a qualitative study investigating the awareness about warnings on cigarette packs in Saudi Arabia, most of the participants emphasized that they were aware of warnings on packs, more discouraging written expressions should be included on packs, and these warnings should be addressed in terms of cultural ethnic/religious perspectives and renewed periodically (19). In a study conducted in the United States of America, it was concluded that the pictures on cigarette packs recommended by the U.S. Food and Drug Administration were effective in reducing smoking but individuals with low self-efficacy were not affected by these pictures (20). In another study conducted with 5439 participants from Australia, USA, Canada and Mexico, they saw pictures on cigarette packs used in their country. It was found that the pictures led them to exhibit negative emotional reactions such as disgust and fear and these negative emotions increased the smoking cessation attempts by encouraging the behavioral changes (21).

Based on these facts, the purpose of this study designed on smoking affecting human health is to determine smoking frequency and status of being affected by the textual and pictorial warnings on cigarette packs in individuals who applied to a family health center for any reason. In the study, the answers to the following questions were sought;

-What is the smoking frequency of the participants?

-What are the dependence levels of the participants?

-What are the variables affecting smoking frequency?

-What are the variables affecting the dependence levels of individuals?

-How is the individuals' status of being affected by pictorial and textual warnings on cigarette packs?

2.METHODS

2.1.Purpose of the Study: This study was conducted to determine smoking frequency, dependence levels, and status of being affected by textual/pictorial warnings on cigarette packs in individuals who applied to a family health for any reason as well as the influencing factors.

2.2.Study Type: The study was conducted with descriptive design.

2.3.Place of the Study and Its Characteristics: The study was conducted in Kale Family Health Center (FHC) determined using simple random sample method among 21 FHCs located in city center of Kırşehir. Three family physicians, a midwife and a nurse work at the related FHC. The professionals in this FHC provide healthcare services to approximately 8000 people. An average of 2600 individuals are enrolled per physician.

2.4.Population and Sample of the Study: The sample size was calculated based on the study conducted by Uysal, Sonmez (22) reporting that the smoking frequency was 26.7%. In the case of known population, sample size was calculated according to the sample calculation formula at significance level of 0.05 and confidence interval of 95% by accepting the population as 8000 and the number of people to be included in the sample was found as 292. Due to possibility of data losses, 320 participants were included in the study.

2.5.Dependent Variable: Smoking status, dependence level, and status of being affected by pictorial and textual warnings on cigarette packs.

2.6.Independent Variable**:** *Sociodemographic characteristics* (age, gender, educational status, and marital status) and smoking-related characteristics (previous attempts to quit smoking and presence of a smoking family member).

2.7.Data collection technique and tools: The researcher collected the data by using face-to-face interview technique. Individuals, who applied to the related FHC for any reason between November 2018 and April 2019 and agreed to participate in the study, were included in the study. In the study, a questionnaire with three parts prepared by the researcher based on the literature was used. The first part of the questionnaire includes sociodemographic and smoking – related characteristics, the second part includes features related to textual and pictorial warnings on cigarette packs, and the third part includes nicotine dependence test which was reviewed by Fagerstrom et al., (23) and whose Turkish validity and reliability study was conducted by Uysal et al., (24). In the its reliability analysis, Cronbach's alpha value of the scale was calculated as 0.56. Each item of the test with six items is scored between 0 – 3 points and score interval of the test varied between 0-10 points. According to total scores taken from the scale, nicotine dependence is rated under

three groups as low (0-3 points), moderate (4-6 points), and high (≥7 points).

2.8.Preliminary application: Before the study, a preliminary application was conducted with ten smokers enrolled in another FHC in terms of the content, comprehensibility, and time of the questions.

2.9.Data Analysis: In the statistical analyses, the chi-square test was used to compare percentage differences between the groups along with the descriptive statistics such as number, percentage and mean. Statistical significance level was accepted as p<0.05.

2.10.Ethical considerations: Before starting the study, the institutional permission from Kırsehir Provincial Directorate of Health (number: 13389610-806.99, date: 02.11.2018), Ethics committee approval from Kırsehir Ahi Evran University Non-invasive Ethics Committee (2018-18/164, 09.10.2018), and informed consents from the participants were obtained.

3.RESULTS

A total of 320 people who applied to Kale FHC for any reason were included in the study. Their mean age was 38.53±14.21. Table 1 shows some descriptive characteristics, smoking-related characteristics and dependence levels of the participants. Of the participants, 54.7% were male, 41.6% had secondary school or lower education level, and 55.3% were married. 37.2% of the participants were working and 67.8% had a moderate income.

It was found that 40.9% of the participants were smokers including 49.1% of male participants and 31% of female counterparts. The rate of having a smoking family member was 48.4%. The mean age of starting smoking was 17.71±5.13 (min.7, max.42). 19.8% of the participants had a high level of nicotine dependence.

Pictorial warnings on cigarette packs attracted the attention of 58.8% of the participants and 35.9% stated that they were affected by the warnings on cigarette packs.

The participants' some descriptive characteristics, smoking status and status of being affected by the warnings on cigarette packs were compared (Table 2). It was determined that there was a statistically significant difference between smoking status (p<0.004), the presence of previous attempts to quit smoking (p<0.025), the status of drawing attention by pictorial warnings (p<0.000) and the status of being affected by the warnings on cigarette packs.(Table 2)

It was determined in the study that 19.8% of the participants were highly dependent on nicotine. Some descriptive characteristics and Fagerström nicotine dependence levels of the participants were compared and given in Table 3. There was a significant difference between the dependence level and age (p<0.001). Although the rate of being highly dependent was higher in men (23.3%) than women (13.3%), there was no statistically significant difference between genders in terms of dependence level (p=0.176). When the dependence level was evaluated in terms of education level, those with secondary school and lower education level (71.9%) and those with high school and higher education levels (86.5%) had mostly low and moderate dependence levels. There was a significant difference between education level and dependence degree (p<0.038). The dependence level of single participants (23.7%) was higher than the level of the married counterparts (16.7%). While one-third of the respondents (29.8%) who stated "not effective at all" for the warnings on cigarette packs were highly dependent, 89.5% of those who stated "effective" option were lowly and moderately dependent. There was a statistically significant difference between the status of being affected by the warnings on cigarette packs and the nicotine dependence level (p<0.040). Dependence level and status of paying attention to pictorial warnings (p=0.147), previous attempts to quit smoking (p=0.456) and the presence of a smoking family members (p=0.435) were similar and there was no statistically significant difference between them. (Table 3)

Table 1 *The distribution of some descriptive characteristics of the participants (N=320)*

Age	**Mean±S.D**	**38.53±14.21**
	Number (n)	Percentage (%)
Gender		
Male	175	54.7
Female	145	45.3
Education level		
Secondary school and below	133	41.6
High school and above	187	58.4
Marital status		
Married	177	55.3
Single	143	44.7
Smoking status		
Smoker	131	40.9
Non-smoker	189	59.1
Individual smoking in the family		
Yes	155	48.4
No	165	51.6
Dependence Levels of Smokers*		
Low	65	49.6
Moderate	40	30.5
High	26	19.8
Affected by textual and pictorial warnings		
Affected	115	35.9
Slightly affected	99	30.9
Never affected	106	33.2
Previous attempt to quit smoking**		
Yes	115	65.3
No	61	34.7
Attention to pictorial warnings		
Get your attention	188	58.8
Unobtrusive	132	41.2
Total	320	100

**A total of 131 places are indicated with *. Totally 176 in the places indicated with **.*

In the study, the participants' status of being affected by textual and pictorial warnings on cigarette packs was compared according to genders and given in Tables 4 and 5.

The expression of "*Smoking damages sperms and reduces fertility"* was found to be more effective in men (59.4%) than women (41.4%) and the difference between them was statistically significant (p=0.005). Although this textual warning was more effective in men, pictorial warnings did not differ between genders. The expression of *"Smoking during pregnancy is harmful to your baby"* was considered as more effective by women (69.1%) compared to men (66.9%) and the difference between them was statistically significant (p=0.038). It was found that the picture of this textual warning did not make an effective difference between the genders.

When the status of the images to affect the participants were examined in the study, it was determined that the picture showing the couple sitting side by side in bed (no.9) was more effective in men (65.7%) than women (47.6%) and the difference between the genders was statistically significant (p=0.004), but there was no statistically significant difference between the genders since the written message on the same picture ("*Smoking slows the blood flow and causes sexual impotence*") was effective.

Table 2 *Comparison of some descriptive characteristics of the participants with smoking status and the warnings on cigarette packs*

	Effective		Less effective		Non-effective		Total		
Variables	n	%	n	%	n	%	n	%	p
Age									
40 age and under	62	33.0	57	30.3	69	36.7	188	100	0.231
Over 40 years	53	40.2	42	31.8	37	28.0	132	100	
Gender									
Male	58	33.1	55	31.4	62	35.4	175	100	0.475
Female	57	39.4	44	30.3	44	30.3	145	100	
Education level									
Secondary school and below	48	36.1	37	27.8	48	36.1	133	100	0.517
High school and above	67	35.8	62	33.2	58	31.0	187	100	
Marital status									
Married	60	33.9	60	33.9	57	32.2	177	100	0.431
Single	55	38.5	39	27.3	49	34.3	143	100	
Smoking status									
Smokers	38	29.0	36	27.5	57	43.5	131	100	0.004
Non-smokers	77	40.7	63	33.3	49	25.9	189	100	
Individuals smoking in the family									
Yes	53	34.2	48	31.0	54	34.8	155	100	0.771
No	62	37.6	51	30.9	52	31.5	165	100	
Dependency level**									
Less	19	29.2	21	32.3	25	38.5	65	100	0.111
Medium	15	37.5	10	25.0	15	37.5	40	100	
High	4	15.4	5	19.2	17	65.4	26	100	
Previous attempt to quit smoking *									
Yes	40	34.8	37	32.2	38	33.0	115	100	0.025
No	14	23.0	14	23.0	33	54.1	61	100	
Attention to pictorial warnings									
Get your attention	81	43.1	66	35.1	41	21.8	188	100	0.000
Unobtrusive	34	25.8	33	25.0	65	49.2	132	100	
Total							320	100	

** is 176 in total. ** is 131 in the places indicated with.*

Table 3 *Comparison of some descriptive characteristics of the participants with their Fagerström nicotine dependence levels*

	Fagerström Test for Nicotine Dependence						
	Low and Medium grade		High grade		Total		
Variables	n	%	n	%	n	%	p
Age							
40 age and under	72	88.9	9	11.1	81	100	0.001
40 age and over	33	66.0	17	34.0	50	100	
Gender							
Male	66	76.7	20	23.3	86	100	0.176
Female	39	86.7	6	13.3	45	100	
Education status							
Secondary school and below	41	71.9	16	28.1	57	100	0.038
High school and above	64	86.5	10	13.5	74	100	
Marital status							
Married	60	83.3	12	16.7	72	100	0.313
Single	45	76.3	14	23.7	59	100	
Attention to pictorial warnings							
Get your attention	53	85.5	9	14.5	62	100	0.147
Unobtrusive	52	75.4	17	24.6	69	100	
Affected by textual and pictorial warnings							
Affected	34	89.5	4	10.5	38	100	0.040
Slightly affected	31	86.1	5	13.9	36	100	
Never affected	40	70.2	17	29.8	57	100	
Previous attempt to quit smoking							
Yes	61	82.4	13	77.2	74	100	0.456
No	44	17.6	13	22.8	57	100	
Individual smoking in the family							
Yes	64	78.0	18	22.0	82	100	0.435
No	41	83.7	8	16.3	49	100	
Total					131	100	

Table 4 *The Participants' assessment of textual warnings on cigarette packs by gender*

	TEXTUAL WARNİNGS		1. Smoking is highly dependent.			2. Ask the doctor and your nearest health center to quit smoking.			3.Health organizations can help you quit smoking.			4.Protect your children: do not have them breathe smoke.			5. Stopping smoking reduces the risk of fatal heart and lung diseases.			6. Smoking cessation can cause a slow and painful death.			7.Smokers die at a young age.		
			V.E.	L.E.	N.E.	V.E.	L.E.	N.E.	V.E.	L.E.	N.E.	V.E.	L.E.	N.E.	V.E.	L.E.	N.E.	V.E	L.E.	N.E.	V.E.	L.E.	N.E.
GENDER	M	%	46.9	21.7	31.4	40.6	24.6	34.9	41.7	25.7	32.6	62.9	16.6	20.6	62.3	17.1	20.6	59.4	18.9	21.7	58.9	18.3	22.9
		N	82	38	55	71	43	61	73	45	57	110	29	36	109	30	36	104	33	38	103	32	40
	F	%	43.4	18.6	37.9	39.3	26.2	34.5	41.4	24.1	34.5	64.1	21.4	14.5	54.5	28.3	17.2	56.6	25.5	17.9	52.4	24.8	22.8
		N	63	27	55	57	38	50	60	35	50	93	31	21	79	41	25	82	37	26	76	36	33
	X^2		1.552			0.119			0.168			2.648			5.713			2.288			2.186		
	P		0.460			0.942			0.920			0.266			0.057			0.318			0.335		
	TEXTUAL WARNİNGS		8. Smoking reduces fertility by damaging sperm.			9.Smoking slows blood flow and causes sexual impotence.			10. Smoking causes fatal lung cancer.			11. Smoking during pregnant is harmful to your baby.			12. Smoking occludes the veins and causes heart attacks and strokes.			13.Smoking causes premature skin aging.			14.Cigarette smoke contains carcinogenic substances such as benzene, nitrosamine, formaldehyde, and hydrogencyanide.		
			V.E.	L.E.	N.E.	V.E.	L.E.	N.E.	V.E.	L.E.	N.E.	V.E.	L.E.	N.E.	V.E.	L.E.	N.E.	V.E.	L.E.	N.E.	V.E.	L.E.	N.E.
GENDER	M	%	59.4	21.7	18.9	56.0	23.4	20.6	64.6	13.1	22.3	66.9	15.9	17.2	65.7	12.0	22.3	61.7	12.0	26.3	45.7	17.7	36.6
		N	104	38	33	98	41	36	113	23	39	97	23	25	115	21	39	108	21	26	80	31	64
	F	%	41.4	28.3	30.3	44.1	31.0	24.8	59.3	20.7	20.0	69.1	7.4	23.4	60.7	15.2	24.1	60.7	19.3	20.0	37.2	22.8	40.0
		N	60	41	44	64	45	36	86	30	29	121	13	41	88	22	35	88	28	29	54	33	58
	X^2		10.772			4.549			3.275			6.544			1.027			4.118			2.613		
	P		0.005			0.103			0.194			0.038			0.598			0.128			0.271		

V.E: Very effective, L.E: Less effective, N.E: Not effective, M: Male n = 175, F: Female n = 145

Table 5 *The Participants' assessment of pictorial warnings on cigarette packs by gender*

	PICTORIAL WARNINGS																						
			V.E.	L.E.	N.E.	V.E.	L.E.	N.E.	V.E.	L.E.	N.E.	V.E.	L.E.	N.E.	V.E.	L.E.	N.E.	V.E	L.E.	N.E.	V.E.	L.E.	N.E.
GENDER	M	%	31.4	25.1	43.4	30.3	28.6	41.1	37.7	24.0	38.3	65.1	13.7	21.1	53.1	19.4	27.4	60.6	13.7	25.7	56.6	15.4	28.0
		N	55	44	76	53	50	72	66	42	67	114	24	37	93	34	48	106	24	45	99	27	49
	F	%	36.6	26.2	37.2	35.2	26.9	37.9	43.4	25.5	31.0	66.2	18.6	15.2	48.3	26.9	24.8	60.0	17.9	22.1	68.3	11.0	20.7
		N	53	38	54	51	39	55	63	37	45	96	27	22	70	39	36	87	26	32	99	16	30
	X^2		1.399			0.869			1.912			2.745			2.512			1.345			4.612		
	P		0.497			0.648			0.384			0.254			0.285			0.511			0.100		
	PICTORIAL WARNINGS																						
			V.E.	L.E.	N.E.	V.E.	L.E.	N.E.	V.E.	L.E.	N.E.	V.E.	L.E.	N.E.	V.E.	L.E.	N.E.	V.E.	L.E.	N.E.	V.E.	L.E.	N.E.
GENDER	M	%	34.3	22.3	43.4	65.7	17.7	16.6	60.6	12.6	26.9	67.4	8.6	24.0	60.6	9.1	30.3	37.7	21.7	40.6	58.9	13.1	28.0
		N	60	39	76	115	31	29	106	22	47	118	15	42	106	16	53	66	38	71	103	23	49
	F	%	42.8	23.4	33.8	47.6	23.4	29.0	58.6	14.5	26.9	73.8	6.2	20.0	58.6	15.9	25.5	42.1	22.8	35.2	60.0	15.9	24.1
		N	62	34	49	69	34	42	85	21	39	107	9	29	85	23	37	61	33	51	87	23	35
	X^2		3.425			11.306			0.266			1.620			3.629			1.024			0.876		
	P		0.180			0.004			0.875			0.445			0.163			0.599			0.645		

V.E: Very effective, L.E: Less effective, N.E: Not effective, M: Male n = 175, F: Female n = 145

4.DISCUSSION

In the study, smoking frequency was 40.9% and 49.1% of men and 31% of women were smokers. The age of starting smoking was 17.71±5.13. The studies conducted in Turkey have revealed that smoking frequency varies between 25.6% and 35.6% (7, 25-27). Smoking frequency was found to be 39.1% in a study conducted in the People's Republic of China (3), 35.1% in a study conducted with healthcare professionals in Croatia (28), 60.2% in Bangladesh (29), 16% in a study conducted in Singapore (30), and 26.9% in a study conducted in the United States of America (31). The frequency found in the study (40.9%) and the literature were similar in general. In addition, when the literature information is examined, the small age of starting smoking shows how important the problem is. When the study results are evaluated with the literature information, it is obvious that serious measures should be taken against smoking in adolescence period and necessary attention should be paid for the application of these measures.

It was found that 35.4% of the participants were affected by warnings on cigarette packs. When the studies conducted on the status of drawing attention by the warnings on cigarette packs were examined, 40% of the participants stated that textual warnings were not very effective while 60% stated that they started to think quitting to smoke or reduced smoking after textual warnings (32). When studies in the literature were examined, it was found that most of the participants were affected by warnings, the expressions on the packs should be more effective about deterrence (19); high self-efficacy along with these warnings (20), also the images' causing feelings such as fear, worry and disgust among users were effective in smoking cessation (20). Based on these results, there is no clear information indicating that warnings on cigarette packs are not effective. It is believed that studies can be conducted to determine new warning messages on this subject.

In this study, one out of five smokers (19.8%) and one out of every three people aged 40 and over were highly nicotine dependent, which is an important result needing to think. In a study comparing the nicotine dependence level and age, the rate of the individuals with "very high" nicotine dependence level at the age group of "<20" years (7.9%) was found to be significantly lower than the rate of individuals with "very high" nicotine dependence level at the age groups of 41-50 and 51-60 years (25.2%-21.8%) (33). In another study, it was determined that those with "highly dependent" (45.9%) were in the age range of 20-39 (34). In an another study conducted in Egypt, those with "very highly dependent" were found to be in the age group of 25 years (15%) (35).

When the literature is examined, it can be asserted that a very high level of dependence is generally seen in the middle ages. When considering that 40 years and older individuals were highly dependent in the study, it will be understood that the study shows similar characteristics with the literature. It is a remarkable result that the highly dependent group is concentrated at the onset ages of chronic diseases.

Another noteworthy result of the study was that the rate of those with high level of dependence was higher in the group having low education level (secondary school and lower). In a study examining nicotine dependence levels of patients who applied to the smoking cessation outpatient clinic, 40.4% were found to be heavy smokers. In the same study, it was found that most of the heavy smokers had high school and higher education level (36). In a study conducted with university students, it was determined that the rate of those with low dependence level was 56.4% and those with high dependence level was 12.7% (37). In two studies, it was determined that one fourth (25%) of those with high dependence level had primary school education level (31, 34). These results are important in terms of showing that there is an inverse positive correlation between education level and nicotine dependence levels. Individuals with low education levels status should be evaluated as being in the risky group.

The combined use of textual and pictorial warnings rather than only using textual warnings on cigarette packs is important in terms of increasing the effectiveness of the desired message. The studies revealed that pictorial warnings could be more effective in generating cognitive responses than textual warnings (38, 39), they attracted the smokers more and directed them to quit smoking (40), pictorial warnings could be quite understandable even in individuals without reading habits since they are more easily and rapidly understood compared to the textual warnings (41). In a study conducted in Jordan, it was found that images on cigarette packs were reported to be more effective in smoking cessation (36.4%) and pictorial warnings were more effective than the other warnings (in cases such as motivating smoking cessation, causing fear) (42).

The most important one among remarkable results of the study is that one out of every three people (35.9%) was affected by the warnings on cigarette packs. It was important that while the expression of *"smoking damages sperms and decreases fertility"* was more effective in men, the expression of *"Smoking during pregnancy is harmful to your baby"* was more effective in women. In addition, the picture showing that a couple sitting side by side in bed was more effective in men than in women. According to a study conducted in New Zealand, increasing the area of warnings on cigarette packs from 30% to 75% was found to be more effective in increasing the smoking cessation rate (43). In a study conducted on the status of being affected by the images on cigarette packs, it was determined that the majority of the participants were not affected by these warnings, even if they were effective, their effectiveness diminished over time, the most striking image was the "lung" image (33.3%), the second one was the "baby" image (14.2%), the most striking written expressions were "*smoking can cause painful and slow death*" and "*smokers die younger*"(44). In another study conducted to examine the opinions of university students about the warning on cigarette packs, it was found that the written expressions about the damages of smoking on body were more effective and warnings among the images pointing out that smoking

causes heat attack, smoking can cause the fetal death and reduces fertility and increases the impotence risk were more effective (16). In a study conducted with 579 students in Turgut Ozal University, it was determined that female and male students evaluated the pictures on cigarette packs differently, gender was a distinctive factor in the evaluation and female students was evaluated by giving higher scores than male students. When messages found to be most effective by male and female students in picture evaluation in the same study were examined, the most effective one was found to be "*Smoking during pregnancy is harmful to your baby*", the second one was "*smoking occludes the veins and causes heart attacks and strokes*" and the third one was "*Protect children: don't let them breath your smoke*". While female students found the disease of *"smokers die younger"* effective as fourth, the picture of *"Smoking slows the blood flow and causes sexual impotence"* was more effective in male students (18). In a study conducted in Ukraine, it was determined that 70% of the participants were affected by the expression of *"smoking causes cardiovascular diseases and lung cancer"*, expressions about pregnancy affected women more; whereas, the expressions about that smoking causes impotence and kills affected men more (45). The effect rates of textual and pictorial warnings indicating that fertility and sexuality can be affected are more remarkable than others in both men and women.

5.CONCLUSION

In the study, smoking frequency was 40.6%. 49.1% of the male participants and 31% of women were smokers. It was determined that 80.2% of the participants had low and moderate of nicotine dependence and 19.8% had high level of nicotine dependence. In the middle age group, those with high school and lower education levels had higher dependence levels.

The status of finding the textual and pictorial warnings on cigarette packs effective varied based on the smoking frequency of the participants, their previous attempts to quit smoking and attraction level of pictorial warnings. The warnings *"Smoking damages sperms and reduces fertility" and "Smoking during pregnancy is harmful to your baby"* among textual warnings and; The picture of "*the couple sitting side by side in bed*" among pictorial warnings were found to be effective.

In the light of the results of the study; it can be recommended to

- Attach more importance to this age group and drawing young people's attention to other matters (sport, music, art, etc.) since the age of starting smoking is in adolescent period,
- Consider the individuals with low education level as a priority group in smoking cessation interventions,
- Emphasize these warnings more on cigarette packs since the textual and pictorial warnings found to be effective are mostly about sexuality, damage on body caused by smoking, death, and baby/child, ,
- Give gender-specific trainings (for example, more on pregnancy and infant in women, more on sexuality in men) in smoking related interventions.

Legally, written and illustrated warnings are placed on cigarette packages. But many of these warnings have been found to be of no interest to individuals. Warnings about sexuality and fertility have been found to attract more attention. It has emerged that research on this must be carried out before new warning articles and images are placed. By conducting qualitative research on this issue, pictures and articles that people are affected by can be checked into. It will be pertinent to decide on written and illustrated warnings, taking into account cultural factors at the regional or national level.

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Clinical and Experimental Health Sciences

Urine Influences Growth and Virulence Gene Expressions in Uropathogenic *E. coli:* A Comparison with Nutrient Limited Medium

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ABSTRACT

Objective: The interactions between environmental factors and microbial biological processes are well known. Urine provides host conditions probably affecting bacterial growth and gene expressions. The aim of this study was to detect the modulations of growth and gene expressions [sfa/foc, cnf1, usp and aer] of Uropathogenic *E.coli* (UPEC) strains in urine by comparing the results with serum supplemented standard American Petroleum Institute (SAPI) medium which is defined as host-like medium.

Methods: UPEC strains C7 and C149 were incubated at 37°C and growth alterations were detected by measuring the changes in the absorbance at 600 nm in four-, six – and 24 hours. Gene expression levels were analyzed by quantitative polymerase chain reaction (qPCR). Statistical analysis of fold changes in gene expression values and growths were calculated using one-way ANOVA unpaired t-test and Tukey's post hoc test, respectively.

Results: The increase of bacterial growth in urine was found to be statistically significant ($p<0.0001$). The alterations of *aer* and *sfa/foc* expression levels were statistically significant ($p<0.001$); whereas the expression levels of *cnf1* and *usp* genes were not altered ($p>0.05$).

Conclusion: According to our results, urine as an environment *in vivo* affected both the growth and gene expression in UPEC.

Keywords: Urine, Virulence, Growth, Gene Expression, UPEC

1. INTRODUCTION

It is well known that microorganisms and their hosts, including human, have co-existed for million years. The interactions between host and microorganisms during an infection were determined by microbial virulence factors, host's immune system and chemicals produced or present *in vivo* (1-4). On the other hand, the environment of microbe *in vivo* influences bacterial pathogenicity by affecting growth and virulence mechanisms. Today, behaviors of microorganisms *in vivo* dominate research and writing (5,6).

Microorganisms encounter with various host derived environmental determinants either present or produced *in vivo* such as hormones, vitamins, bile salts, sugars, antibiotics, ions, pH etc. (7-12). Urine includes such kind of various host derived determinants and, as an environment of bacteria, alters bacterial growth and gene expressions in different ways (13-22).

The purpose of the present study was to examine whether urine influences the growth and gene expressions [*sfa/foc* (encodes fimbrial adhesions SF1C), *cnf 1* (encodes cytotoxic necrotizing factor 1), *usp* (encodes a uropathogenic-specific protein) and *aer* (encodes aerobactin)] of Uropathogenic *Escherichia coli* (UPEC) which are the most common agents of urinary tract infections (UTIs). For this purpose we compared the growth and gene expression of UPEC in urine and in serum-supplemented standard American Petroleum Institute (SAPI) medium. This medium provides a nutrient limited condition and imitates *in vivo* (23-25).

2. METHODS

2.1. Strains

In the present study two different UPECs (*E. coli* C7 strain carrying *sfa/foc, cnf1* and *usp* genes and *E. coli* C149 strain carrying *aer* gene) were used which were kindly provided

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by Prof. Dr. Shingo Yamamoto (Hyogo College of Medicine, Japan). Bacteria were kept at −80 °C for all analysis.

2.2. Media

Healthy male urine and standard American Petroleum Institute (SAPI) medium supplemented with 30% (v/v) adult bovine serum (serum-SAPI) were used as growth media in this study. Healthy male urine was used after sterilized by filtration. Serum-SAPI was defined as a nutrient-limited medium which mimics *in vivo* growth conditions (23, 24). The serum-SAPI medium was prepared as previously described in studies (23,25,26). Briefly, the medium contains 6.25 mM/L ammonium nitrate, 1.84 mM/L monobasic potassium phosphate, 2.77 mM/L dextrose, 3.35 mM/L potassium chloride, and 1.01 mM/L magnesium sulphate and pH adjusted as 7.5.

2.3. Comparison of Growth in Urine and SAPI

Overnight cultures of *E. coli* C7 and C149 were prepared in SAPI medium and these were five-fold diluted and inoculated into SAPI medium and urine. Bacteria were incubated at 37 °C. Growth alterations were detected by measuring the changes in absorbance at 600 nm in four-, six – and 24-h periods. The samples were tested in duplicate and each experiment was performed twice.

2.4. Comparison of Gene Expressions in Urine and SAPI

Total RNA isolation and cDNA synthesis

Bacteria were grown in SAPI medium and human urine for 16–24 h at 37 °C. Total RNAs were extracted from 24-h-fresh cultures by using Tripure reagent (Roche, Switzerland) according to manufacturer's instructions. Horizontal electrophoresis gel analysis and spectrophotometer measurement used to analyze of isolated RNAs quantitatively and qualitatively. We detected the concentration and purity of total RNAs using a NanoDrop 2000 spectrophotometer Thermo Scientific (Waltham-USA). Total RNAs with a ratio (A260/A280) > 1.8 were used for quantitative PCR (qPCR) analysis. Total RNAs were also screened by 1% horizontal gel electrophoresis. High quality and amounts of RNAs were converted to cDNA for qPCR assays. Reverse transcription was carried out using commercial cDNA conversion kit (Takara, Japan) according to the manufacturer's instructions. The thermal cycle conditions were as follows: 20 min at 37°C, 5 min at 85°C and cooling at 4°C. After reverse transcription step, 1:5 diluted cDNAs were used in gene expression analysis.

Quantitative polymerase chain reaction (qPCR) analysis

Quantitative PCR reactions were carried out using SYBR Green I fluorophore dye (Takara, Japan) according to the instructions of the manufacturer. 16S rRNA gene was used as housekeeping gene. We detected the expression levels of *sfa/foc* (S and F1C fimbria), *usp* (uropathogenic-specific protein) and *cnf1* (cytotoxic necrotizing factor) for C7 strain and *aer* gene (aerobactin) for C149 strain in the presence of urine and SAPI medium. Quantitative PCRs were carried out in a reaction volume of 16 µL including 1X SYBR Green I, 0. 5 pmol of primers (Table 1) and 2 µL of cDNA equivalent to 50 ng total RNA. Quantitative PCR conditions were shown in Table 2 for all genes. Sensitivity and accuracy of the protocol were tested at different levels by performing melting curve analysis, using 16S rRNA as control. Ct values were obtained and calculated using Quant Studio 5.0 software (Applied Biosystem, USA). Relative quantification strategy was used in obtaining fold changes in gene expression using $2^{-\Delta\Delta CT}$ formula. The experiments were conducted in quadruple and the results were presented as fold change for each gene.

Table 1. *Primers used in the gene expression*

Gene	Nucleotide sequence (5'-3')	Band size (bp)	References
16S rRNA	F: CCA GGA TTT GAT YMT GGC R: GAA GGA GGT GWT CCA DCC	532	27,28
sfa/foc	F: CTC CGG AGA ACT GGG TGC ATC TTA C R: CGG AGG AGT AAT TAC AAA CCT GGC A	410	29,30
usp	F: CGG CTC TTA CAT CGG TGC GTT G R: GAC ATA TCC AGC CAG CGA GTT C	615	29
cnf1	F: AAG ATG GAG TTT CCT ATG CAG GAG R: CAT TCA GAG TCC TGC CCT CAT TAT T	498	29,30
aer	F: TAC CGG ATT GTC ATA TGC AGA CCG T R: AAT ATC TTC CTC CAG TCC GGA GAA G	602	29,30

Table 2. *Quantitative polymerase chain reaction (qPCR) conditions*

Step	Time	Temperature
Pre-denaturation	2 minute	95°C
Number of cycling: 45		
Denaturation	10 second	95°C
Annealing	15 second	58°C
Extension	20 second	72°C
Cooling	30 second	40°C

2.5. Statistical Analysis

Statistical analysis of fold changes in gene expression values were calculated using one way ANOVA unpaired t-test and growths were calculated using one-way ANOVA Tukey's post hoc test. All measurements were compared to control. All results were presented as mean±standard deviation (SD). The multiple comparisons were made at a level of $p<0.05$.

3. RESULTS

3.1. Comparison of Growth in Urine and SAPI

In order to detect the effects of human urine on growth of UPECs, the absorbance values were compared to SAPI (control medium). The growth of UPEC in urine was enhanced which was found to be statistically significant ($p < 0.001$) in the 4th, 6th and 24th hours (Figure 1, Figure 2 and Figure 3).

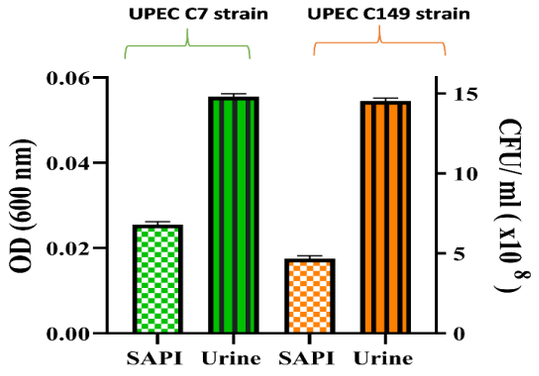

Figure 1. *Comparison of UPECs (C7 and C149 strains) growth in urine and SAPI medium in the 4th hour. The alterations were determined by comparing with control (SAPI medium). The growth alterations of bacteria in urine and SAPI were examined using one-way ANOVA followed by Tukey's post hoc test. The difference between the growth of UPECs in urine and SAPI medium were found to be statistically significant (p<0.0001).*

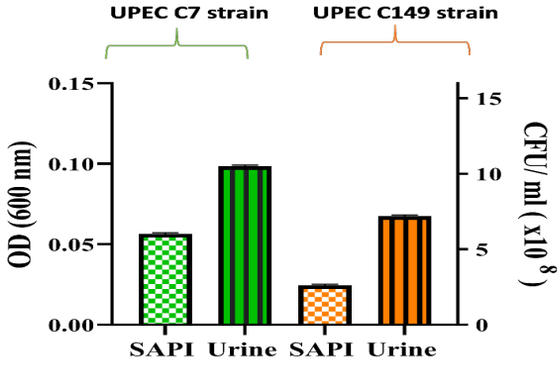

Figure 2. *Comparison of UPECs (C7 and C149 strains) growth in urine and SAPI medium in the 6th hour. The alterations were determined by comparing with control (SAPI medium). The growth alterations of bacteria in urine and SAPI were examined using one-way ANOVA followed by Tukey's post hoc test. The difference between the growth of UPECs in urine and SAPI medium were found to be statistically significant (p<0.0001).*

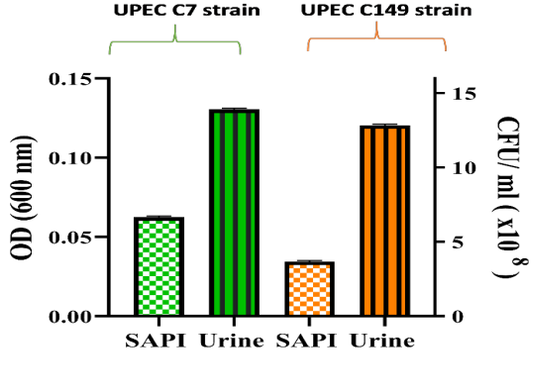

Figure 3. *Comparison of UPECs (C7 and C149 strains) growth in urine and SAPI medium in the 24th hour. The alterations were determined by comparing with control (SAPI medium). The growth alterations of bacteria in urine and SAPI were examined using one-way ANOVA followed by Tukey's post hoc test. The difference between the growth of UPECs in urine and SAPI medium were found to be statistically significant (p<0.0001).*

3.2. Comparison of Gene Expressions in Urine and SAPI

The down regulation of *aer* gene was found to be statistically significant in urine (p<0.01). The expression of *sfa/foc* gene was increased in urine (p<0.01). However, no statistically significant difference was found in the expression levels of *cnf 1* and *usp* (p>0.05) (Figure 4). Ct values in all genes ranged from 6.60 to 26.64.

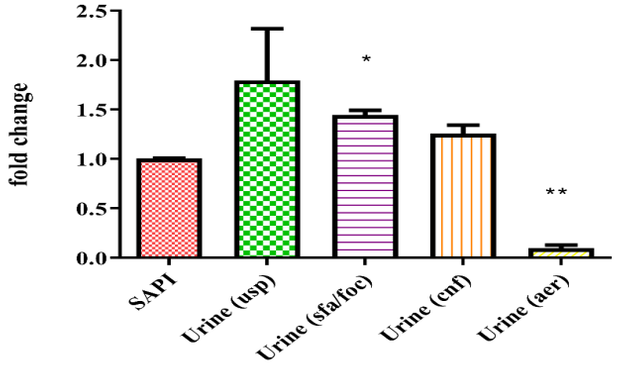

Figure 4. *Comparison of gene expressions in urine and SAPI. The alterations were determined by comparing with control (SAPI medium). Statistical analysis was calculated using one-way ANOVA unpaired t test. *, **: Significant at p<0.01 level and p < 0.001 level values, respectively.*

4. DISCUSSION

Globally a large number of people suffer from UTIs which are mostly caused by UPEC strains. UPECs have different virulence factors as compared to other *E.coli* strains. Some of these virulence factors are fimbrial adhesins encoded by *sfa/foc* genes, a siderophore for iron uptake encoded by *aer* gene, cytotoxic necrotizing factor 1 encoded by *cnf1* gene, and uropathogenic-specific protein which has endonuclease activity encoded by *usp* gene (31,32). The expression of UPEC virulence genes may be affected by environmental conditions determined by host factors. It is well known that during infectious process, bacteria sense *in vivo* environmental changes and adapt to them.

As it was stated above, not only physiological conditions such as pH, temperature, but also many host determinants either present or produced *in vivo* regulate the growth and gene expression of microorganism during infection (3 – 6,14,18,19,22,33-35). It was suggested by some authors that, urine contains high concentrations of various metabolites which induce the growth of bacteria, whereas the others define the urine as a nutrient limited medium (with regard to amounts of iron, amino acids and nucleotides) (14,16,17,20,36-38).

There are many studies aimed on the effect of human urine on bacterial growth and gene expression in different bacteria. It was shown that pH, the amount of glucose, iron, osmolality, ammonium, organic acids, creatinine and urea of urine are important factors affecting growth of bacteria (16-22, 39-41).

Our study was designed in a different way to examine the influence of human urine on growth and virulence gene expression in UPEC (urine compared to serum SAPI medium).

The bacterial growth is the first step in the infection process which is necessary for avoidance of immune response and infection. Roos et al. have shown that the *in vitro* growth ability of *E.coli* in urine was strain depended. *E. coli* 83972 strain was grown well in urine depending on the individual batch of urine used, but *E. coli* K-12 reference strain MG1655 could not grow in urine. They also reported that *E.coli* 83972 strain was grown better than the K12 strain both in Luria Bertani (LB) broth, a nutritionally rich medium and human urine. They also showed that strain 83272 was grown better than some clinical isolated *E.coli* strains (536, CFT073, NU14, and 1177) in urine which were isolated from patients with UTIs (39). Alteri and Mobley have indicated that the *in vitro* growth rates in urine of enteropathogenic and commensal *E. coli* strains was generally similar to that of UPEC's (40). In contrast to these results, Aubron et al. suggested that the *in vitro* growth of different *E. coli* strains (8 UPEC, 1 Enterohemorrhagic *E. coli*, 9 asymptomatic bacteriuria causing strains and 3 commensal strains) was significantly less than in LB medium compared to growth levels in urine. They also found that the growth ability of asymptomatic bacteriuria strains in the urine was not better than of UPEC and commensal *E.coli* strains (41).

In the present study we found that urine induced the growth of UPEC significantly ($p < 0.001$) when compared to serum-supplemented SAPI medium. Our results are consistent with previous studies; serum-SAPI medium has reduced the growth of UPEC when compared to Tryptic Soy Broth, Dulbecco's Modified Eagle's Medium etc. in the 4^{th}, 6^{th} or 24^{th} hours (27,28,42). Urine seems a good growth medium for *E. coli* due to contain several inorganic and organic compounds and the growth of UPEC was provided effectively by fresh urine for this study.

The effects of urine on microbial virulence related gene expressions were shown in many *in-vivo* and *in-vitro* studies (18, 19, 22, 33, 34, 40, 43, 44). Greene et al. concluded that when *E. coli* grown in urine, *fim* expression was found to be prevented. They also suggested that urine has inhibitory effects on FimH function (18). In a study of Hancock and Klemm the expression levels of 815 genes were examined in urine by comparing planktonic and biofilm forming strains and they reported that the expression levels of *pap* and *foc* genes were found to be not altered but *fyuA* gene (encoding siderophore receptor) expression was upregulated (19). Russo et al. found that expression level of $iroN_{E.coli}$ (encoding siderophore receptor) was increased in urine (22). King et al. found K1 capsule genes of a UPEC strain were down-regulated in urine (34). Roos et al. showed that expression levels of iron-uptake, transport system and adhesion-associated genes, *pap, sfa/foc* genes, were upregulated when *E.coli* strain grown in urine (39). Snyder et al. reported the expression levels of *E.coli* CFT073 genes both of *in vivo* and *in vitro* (urine compared to LB) conditions. They reported that many of the most highly expressed genes *in vivo* conditions were also among the most highly expressed in urine. Some of the upregulated genes were reported as related with iron acquisition systems, capsular compositions, microcin secretion genes (43). In consistent with Snyder et al., Hagan et al. suggested that *E. coli* gene expressions were generally similar in urine provided from women with UTIs and infected mouse. The most significantly differences in expression levels were reported for genes encoding adhesins (44).

In our study, expression of *aer* gene which is responsible for iron uptake in UPEC was found to be down-regulated; this result is inconsistent with other studies. The upregulation of *sfa/foc* gene related to adhesion of the pathogen to the urinary tract; this result was consistent with the previous studies (39,43). In line with all these results, we may suggest that these discrepancies related to be depend on strain, compared to medium/conditions.

5. CONCLUSION

In many studies mentioned above, the comparison of growth, expression levels of genes encoding virulence factors were investigated by using urine and standard bacteriological culture media such as Luria-Bertani, Tryptic soy broth etc. However, in our study nutrient limited SAPI medium was used which mimics *in vivo* environment. For detection of behaviors of pathogens *in vitro,* studies are needed to prepare proper alternatives for culture media to provide mimicking *in vivo* conditions.

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Clinical and Experimental Health Sciences

Turkish Adaptation of Attention Function Index: A Validity and Reliability Study

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ABSTRACT

Objective: Many cancer survivors have cognitive problems with concentration and memory after cancer treatment. The Attention Function Index (AFI) is a tool developed to evaluate cognitive processes in cancer patients. The purpose of this study was to investigate the adaptation of AFI in Turkish.

Methods: This methodological study was conducted with one hundred breast cancer survivors. Data were collected using the information form, AFI, and the European Organization for Research and Treatment of Cancer Quality of Life (EORTC QLQ-C30) scale. Internal consistency, test-retest, and item-total scores were analyzed to assess the reliability of the AFI Turkish form.

Results: The internal consistency coefficient (Cronbach's alpha) was 0.89 for the Turkish version of AFI. Confirmatory factor analysis for construct validity revealed that the original three-factor structure of AFI was not confirmed, but the two-factor structure of the AFI was confirmed by the fit indices. In the correlation analysis for criterion validity, a statistically significant and positive relationship was found between AFI total scores and EORTC QLQ-C30 total scores. There was a strong positive correlation between test and retest scores ($r = 0.524$; $p < 0.01$).

Conclusions: In this study, it was determined that the two-factor, 10-item version of the AFI, which was evaluated for validity and reliability, was well-matched with the sample in which the scale was administered. The Turkish version of AFI is a valid and reliable tool for breast cancer survivors. The scale tested in cancer survivors and can be used in clinical practice.

Keywords: Attention function, breast cancer, survivor, validity and reliability.

1. INTRODUCTION

Cognitive functions include high brain activities such as consciousness, attention, learning, memory, problem solving, decision making and calculation (1). Cognitive changes have been reported in 75% of patients receiving chemotherapy or radiation therapy. In addition, approximately one-third of cancer patients continue to experience cognitive problems even years after treatment (2,3,4,5). Cognitive functioning is affected many factors such as the psychological burden of cancer, biological factors related to the disease, side effects of cancer treatment, stress, and depression in cancer patients. The most affected cognitive domain in cancer patients have been reported as psychomotor function, learning, memory, attention and concentration (6,7).

Focus and attention capacity are essential for effective cognitive functioning. Attention is defined as the concentration of the mind on an object or thought, despite other stimuli that occur simultaneously (8). Attention, which is an organizing power for all behaviors, is effective in all cognitive areas such as getting information, maintaining and completing an activity, learning, solving problems, and interpersonal communication Selective attention is a basic cognitive capacity that provides greater sensitivity to important environmental stimuli (9,10,11). Directed attention allows the individual to concentrate on a particular object, thought or problem. İndividuals can process information efficiently and act purposefully through attention (10,11). When cognitive processes related to attention functions are disrupted, individuals have difficulty in performing plans and activities, making decisions, remembering and maintaining daily life routines in general. These cognitive deficiencies lead to significant problems in the social and occupational functioning of the patients. Therefore, in recent years, studies have focused on the evaluation of cognitive functions in cancer patients (9,10,11).

Neuropsychological tests that assess attention, memory, and processing speed are used in the assessment of cognitive disorders caused by cancer treatment (12,13). However, it is stated in the literature that clinicians need more information to diagnose cognitive problems. The best way to assess cognitive functions is to measure the patient's perception of

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his or her cognitive function. There are few tools to determine how cognitive dysfunction develops loss of activity in cancer patients.

Although research has been conducted on perception, memory and concentration problems, fewer studies have examined the impact of these perceived problems on the daily functioning of patients. This study aimed to evaluate the Turkish adaptation and validation of the Attention Function Index (AFI), which is a measurement tool to identify cognitive problems related to cancer and its treatment.

2. METHODS

2.1. Study Population

This methodological study was carried out with breast cancer survivors who applied to a Training and Research Hospital Oncology Polyclinic between April and July 2019. In calculating the sample size, the formula that the validity and reliability of the scale should be 5 to 10 times the number of items in the scale was used. For this purpose, one hundred breast cancer survivors were included in the study for the validity and reliability of AFI with 13 items. Individuals who completed breast cancer treatment at least 6 months ago, aged between 18 and 65, who accepted to participate in the study and who could read and write Turkish were included in the study. Individuals who received palliative treatment, who had pre-existing depressive or psychotic disorders, and who had used any psychoactive drug were not included in the study.

2.2. Measures

Data were collected using the information form, AFI, European Organization for Research and Treatment of Cancer Quality of Life Scale (EORTC QLQ C30). Data were collected by face-to-face interview method in the polyclinic waiting room. Data collection took an average of 10-15 minutes. For the test-retest reliability of the scale, 20 patients were re-administered AFI two weeks after initial data collection. The information form prepared by the researchers consisted of questions about demographics. EORTC QLQ-C30 scale determines the quality of life in cancer patients. The scale includes three subscales: general well-being, functional scale and symptom scale, and 30 questions. High scores on functional scales and general health status scores indicate good health status, while high scores on symptom scale indicate excess symptoms. The validity and reliability of the scale in our country were made by Demirci et al (14).

Attention Function Index is a tool developed to evaluate cognitive processes in cancer patients. AFI was developed to assess the perceived effectiveness of the individual in performing tasks and activities that require selective attention and working memory (10). Initially, AFI was developed as 16 questions and used in different populations, but then reduced to 13 items based on the results of factor analysis. The scale consists of three sub-dimensions: attentional lapses, effective action, and interpersonal effectiveness. Effective action evaluates the perceived function of the person during daily life activities that require mental effort. Attentional lapses assesses perceived difficulties during jobs that require concentration. Interpersonal effectiveness measures how people perceive their interaction in specific situations and events that need attention.

In calculating the total score, the questions 10 to 13 are reversed. Total scores are calculated as the average of each item score totals. Higher scores mean better performance and indicate less attention deficit (10).

2.3. Translation of the AFI

We received permission from the author who developed the scale by e-mail for translation and adaptation of the scale into Turkish. Content validity was confirmed by 5 experts (1 psychologist, 2 clinician nurses, 1 radiation oncologist, 1 academician nurse). The English-language version of the AFI was translated into Turkish. The AFI scale was evaluated by the experts and the intelligibility, vocabulary and cultural structure of the questions were reviewed. The expert group discussed and commented on this version of the AFI. Then AFI was translated into English by the professional translator. The scale was applied to 10 patients and the intelligibility of the questions was tested prior to the application.

The relationship between AFI scores and EQORTC QLQ C30 scale was evaluated for the criterion validity. It was predicted that there was a significant positive relationship between the Turkish version of AFI and EORTC-QLQ C30 scores. Confirmatory factor analysis (CFA) was used to assess whether the original structure of AFI was validated for the sample in this study. The internal consistency coefficient was calculated for the reliability analysis of AFI. In order to determine the in variance of AFI over time, in-class correlation analysis was performed between test and retest total scores. Item total score correlation analysis was used to determine the items to be extracted in the Turkish version of the AFI.

2.4. Ethical Statements

All procedures in the study were carried out in accordance with the Helsinki Declaration. The study has been approved by the Ankara Oncology Education and Training Hospital Clinical Research Ethical Committee (2019-03/224). Written consents were obtained to the participants after the purpose of the study was explained.

2.5. Statistical analysis

Statistical analyses were performed in IBM SPSS for Windows Version 21.0. Numerical variables are summarized as frequency, mean ± standard deviation and median [minimum-maximum]. The Turkish version of the scale was developed by translate-back translate method in the assessment of language validity. For the construct validity of the scale, confirmatory

factor analysis (CFA) was performed with Structural Equation Modeling in Amos 22.0 program. Cronbach Alpha coefficient was used for internal consistency and in-class correlation analysis was performed for test-retest analysis. Pearson correlation analysis was used for the validity of the criteria.

3. RESULTS

The average age of breast cancer survivors was 53.21 ± 12.14 years, 69% were married and 58% were primary school graduates. 43% of participants were diagnosed 1 year ago and 70% completed treatment 6 months ago. Surgical treatment was applied to 91% of the participants and the most recent treatment for 51% was chemotherapy. 64% of participants do not have any other chronic disease except cancer (Table 1).

Table 1. *Characteristics of survivors*

Characteristics		
Age (years; mean±SD)	53.21±12.14	
	n	**%**
Marital status		
Married	69	69
Single	31	31
Educational status		
Primary education	58	58
High school	26	26
University	16	16
Time of diagnosis		
0-6 months	43	43
7-12 months	37	37
Over 12 months	20	20
Time after treatment		
0-3 months	70	70
4-7 months	16	16
8-12 months	7	7
Over 12 months	7	7
Surgery		
Yes	91	91
No	9	9
The last treatment received		
Chemotherapy	51	51
Radiotherapy	28	28
Surgery	20	20
Hormone therapy	1	1
Chronic disease		
Yes	36	36
No	64	64

SD: standard deviation

3.1. Reliability Analysis

The Cronbach Alpha coefficient calculated for the 13 items in the Attention Function Index was 0.871. "Effective action" Cronbach Alpha coefficient was 0.933, "attentional lapses" Cronbach Alpha coefficient was 0.848 and the "interpersonal effectiveness" Cronbach Alpha coefficient was 0.416. Attention Function Index (AFI) total score was 6.61 ± 1.08 and the retest AFI total score was 6.66 ± 0.96. The intra-class correlation coefficient calculated between AFI total and retest total scale scores was 0.90 ($p \leq 0.001$). As a result of item-total score correlation analysis for AFI, Cronbach's alpha value increased when item 9 and item 13 were erased (0.0885 for item 9 and 0.882 for item 13) (Table 3).

Table 2. *Multi-factor model confirmatory factor analysis and fit indices of AFI*

Fit Indices	Fit indices after model was improved	Fit indices before model was improved	Best fit indices	Acceptable fit indices
CMIN/DF	3.62	1.631	$0 \leq \chi^2/df \leq 3$	$3 \leq \chi^2/df \leq 5$
GFI	0.824	0.921	≥0.90	≥0.80
CFI	0.896	0.975	0.90≤CFI≤1.00	0.80≤CFI≤0.90
RMSEA	0.151	0.080	0≤RMSEA≤0.05	0.05≤RMSA≤0.08
NFI	0.859	0.940	≥0.90	≥0.80
AGFI	0.751	0.851	0.95≤AGFI≤1.00	0.80≤AGFI≤0.95

RMSEA: the root mean square error of approximation, NFI: normed fit index, CFI: confirmatory fit index, IFI: relative fit index, GFI: the goodness of fit index, AGFI: adjusted goodness of fit index, CMIN/DF= chi-square statistics */ DF, AGFI: adjusted goodness of fit index*

Table 3. *Item total score correlation analysis results*

	Scale average when item is deleted	Scale variance when item is deleted	Corrected item total correlation	Cronbach's alpha value when item is deleted
Item 1	79.27	166.947	0.734	0.852
Item 2	79.28	162.668	0.814	0.847
Item 3	80.20	172.162	0.576	0.860
Item 4	79.32	167.917	0.717	0.853
Item 5	79.60	166.566	0.745	0.852
Item 6	79.76	169.497	0.664	0.856
Item 7	79.74	172.396	0.625	0.858
Item 8	79.54	173.342	0.557	0.861
Item 9	79.55	188.876	0.149	0.885
Item 10	79.06	169.027	0.465	0.869
Item 11	78.46	172.433	0.558	0.861
Item 12	78.60	174.525	0.467	0.867
Item 13	80.22	179.244	0.273	0.882

3.2. Validity Analysis

The KMO value is calculated as 0.817 with statistically significant Bartlett test ($\chi 2$ = 754,863; $p<0.001$). The sample size is sufficient for factor analysis. The construct validity of the AFI was assessed by confirmatory factor analysis (CFA) in two stages. As a result of the CFA analysis for the three-dimensional structure, which is the original structure of the AFI, it was seen that the goodness of fit index values was not in the required range. The factor loadings were low and the three sub-dimensional structures were not confirmed significantly. As the factor loadings of the 9th and 13th items were low

in the first stage CFA results. It was decided to perform the CFA again by removing these items. In addition, the 8th item, which has the same factor (interpersonal effectiveness sub-dimension) as 9th and 13th items, was removed from the scale and CFA was performed for the second time. While making improvements in the model, variables that reduce compliance were identified and new covariance were created for those with high covariance among the residual values. Then, it was seen that the accepted values for the fit indices were provided in the renewed fit index calculations. According to the results of the first-level analysis, when AFI of fit indexes are examined; RMSEA, 080; GFI, 921; AGFI, 851; CFI, 975; χ2 was found to be acceptable with 1.631 values (Table 2). Factor loads of each item in the AFI ranged from 0.71 to 0.94. The Cronbach's Alpha value for the 10 item AFI-TR confirmed by confirmatory factor analysis was 0.895. The Cronbach Alpha values for effective action and attentional lapses subscales were 0.933 and 0.848, respectively. Turkish modeling illustrated in supplement file defined model related 10 item Turkish form of AFI (Figure 1). There were statistically significant positive relationship between AFI total score and EORTC QLQ-C30 total score (r = 0.524, p≤ 0.001).

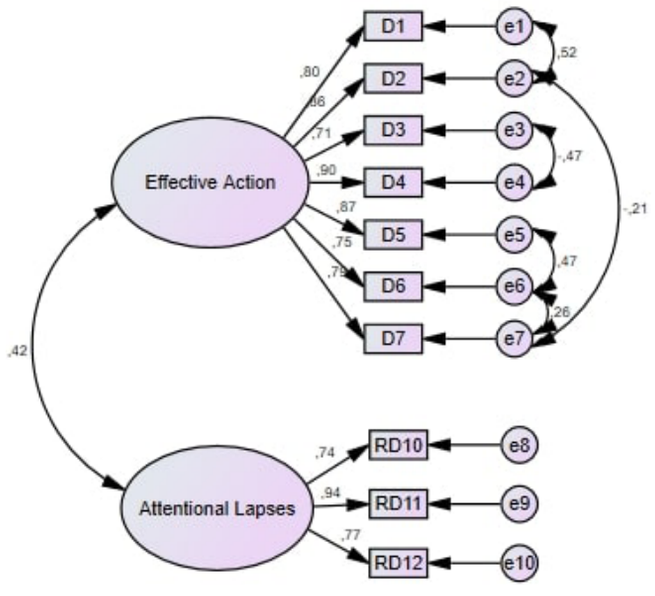

Figure 1. *Model of first level multi-factor confirmatory factor analysis of AFI*

4. DISCUSSION

Cancer patients are at risk for cognitive problems. There are few tools that provide a subjective assessment of how daily activities supported by cognitive processes affect cancer patients. Attention Function Index (AFI) was developed to measure the perceived effectiveness of patients in daily life activities supported by attention and short memory. In this study, the validity and reliability of the Turkish version of AFI with breast cancer survivors were evaluated.

One of the reliability methods is the Cronbach Alpha coefficient. It was stated that Cronbach's alpha value should not be less than 0.50. In studies using, AFI internal consistency was reported to be between 0.80 and 0.92 (10, 15, 16, 17). In the validity and reliability study of AFI in Brazil, the Cronbach's alpha coefficient was 0.86; 0.86 for effective action; attentional lapses were found to be 0.65 and interpersonal effectiveness 0.86 (18). In our study, Cronbach's alpha coefficients were 0.89 for the total scale; effective action 0.93, attentional lapses 0.84. These values indicate that the internal consistency of the Turkish version of AFI is acceptable.

According to the results of item-total score analysis for reliability analysis, it was found that the item-total score correlation coefficient value of items 9 and 13 was below 0.25. In the literature, it is stated that the item-total correlation value should be higher than 0.25 for reliability (19). According to CFA results, 9th and 13th items were determined to be removed. The lower total item correlation coefficients of these items and the increase in Cronbach's alpha value when removed from the scale revealed that these items should be subtracted from the Turkish version of AFI.

Confirmatory factor analysis is performed to evaluate the accuracy of the original structure of the scale in the new sample (20). For the construct validity of a scale, the goodness of fit values performed in the confirmatory factor analysis should be at the desired level. The most commonly used fit statistics in the literature are; χ2 / df is RMSEA, SRMR, CFI, NNFI, GFI and AGFI (21). In this study, the original loadings of the AFI were tested and the factor loadings and the fit indices of the 9th and 13th items were low. In the original form of the AFI, this sub-dimension was completely omitted, as item 8, together with item 9 and 13 in the "interpersonal effectiveness" sub-dimension, could not form a single sub-dimension. Confirmatory factor analysis was performed for the second time for two sub-dimensions (effective action and attentional lapses). According to the results of the second CFA, the fit indices for 2-dimensional and 10-item AFI were within acceptable limits. Cronbach's alpha value for the two-factor AFI Turkish form was 0.89. Depending on cultural differences in scale adaptation research, the addition, subtraction or replacement of items may occur. If one element of the scale is not suitable for the culture to which it is adapted, the substance can be changed or removed (20). In this study, the two-factor structure (effective action and attentional lapses) of the Turkish version of AFI revealed acceptable fit indices.

The test-retest reliability analysis showed that the scale showed consistent results over time. When the test-retest results are taken into consideration, it can be said that the results are close to the original study (9). Attention affects the life significantly, including perceived social and role functions of patients (22,23). In our study, the criterion validity of AFI was evaluated with the EORTC-QLQ 30 scale. In our study, a positive and significant correlation was found between AFI and

total quality of life scale scores (r = 0.52; p-value <0.0001). The correlation coefficient is interpreted as a medium between 0.50-0.69 and validity is higher than 0.7 (19). In others study evaluating the validity and reliability of AFI, it was found that there was a significant relationship between attention function and the profile of the mood state and symptom (9,16).

5. CONCLUSION

Identifying cognitive problems is important for patient-centered cancer care. Although research has been conducted on memory and concentration problems, fewer studies have examined the impact of these perceived problems on the daily functioning of patients. The results of this research show that AFI is a high reliability and validity scale for breast cancer patients and is applicable in a clinical setting. It is important to evaluate the functional outcomes specific to the loss of short memory and basic cognitive attention systems in cancer patients in order to be aware of the problems experienced by patients due to cognitive problems. It is recommended that AFI be used in different populations in future studies and that its validity and reliability are evaluated.

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Clinical and Experimental Health Sciences

Effect of Web-Based Training on Complication Control and Quality of Life of Spinal Cord Damaged İndividuals: Randomized Controlled Trial

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ABSTRACT

Objective: This study was conducted to determine the effect of web-based training on complication control and quality of life of spinal cord-injured patients.

Methods: A pre-test-post-test, experimental study including a control group. A total of 62 men participated from two different physical therapy and rehabilitation hospitals. The training, monitoring, and data collection steps were provided via a webpage (www.omurgahemsirelikegitim.com) and telephone.

Results: It was determined that there was a statistically significant difference between the experimental and control groups regarding the complications related to respiration, circulation, gastrointestinal, urinary, and musculoskeletal systems. Regarding the complications related to sexual life, comparing experimental and control groups the pre and post evaluations, detected an increase in difficulty in sexual life after the injury both experimental and control groups. There was no statistically significant difference between the two groups in terms of quality of life scale subscale scores.

Conclusion: These results show that telephone monitoring plus web-based training is effective in controlling disease complications in patients with spinal cord injury. However, to improve the quality of life, it is important to establish interventions involving individuals and families, and physical, social and mental health services.

Keywords: Education, spinal cord injuries, nursing, quality of life, home care services

1. INTRODUCTION

Spinal Cord Injury (SCI) is an important health problem that causes lifestyle changes resulting in biophysical, psychological, social, and economic dependence. After the injury, individuals might have to cope with secondary, long-term complications caused by the disease. According to a study by Van Loo and colleagues, almost half of the secondary complications, particularly in the acute phase, can be prevented after injury (urinary tract infection-UTI, constipation, etc.) (1). Therefore, it is of most importance to prevent secondary complications and to increase the quality of life of individuals. This can be done by educating and monitoring these injured individuals (2).

Although spinal cord-injured patients (SCIPs) are informed about secondary complications in the hospital setting, this information is often insufficient, or the patients cannot cope with the complications when in the home environment. To resolve these complications, spinal cord-injured patients either visit the hospital (in case of emergency) (3-5) or search the internet for information because of health problems. Because of the frequent use of the internet by SCIPs (6) and the problems their disabilities can cause when visiting health clinics. It is appropriate to use web-based training methods for these patients.

In this study, we aimed to determine the effect of a web-based training program on the quality of life and complication control in SCIPs.

2. METHODS

2.1. Study Design

This was a pre-test-post-test experimental study with a control group. Physical therapy and rehabilitation hospitals (2 large hospitals in 2 different cities in total) have been

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carried out through the webpage with individuals who were in the process of being discharged

2.2. Participants

Participation criteria included having been diagnosed with paraplegia, literacy, having computer access, having internet access, being between 18 – and 45-years-old, being open to communication and cooperation, and having been a maximum of 1 year since the diagnosis of the injury. Following a power analysis, 62 male individuals were sampled with 88% power, 31 in each group. 108 individuals were interviewed until this sample was reached (Figure 1: Research flow chart). Simple randomization and coin flip method is used.

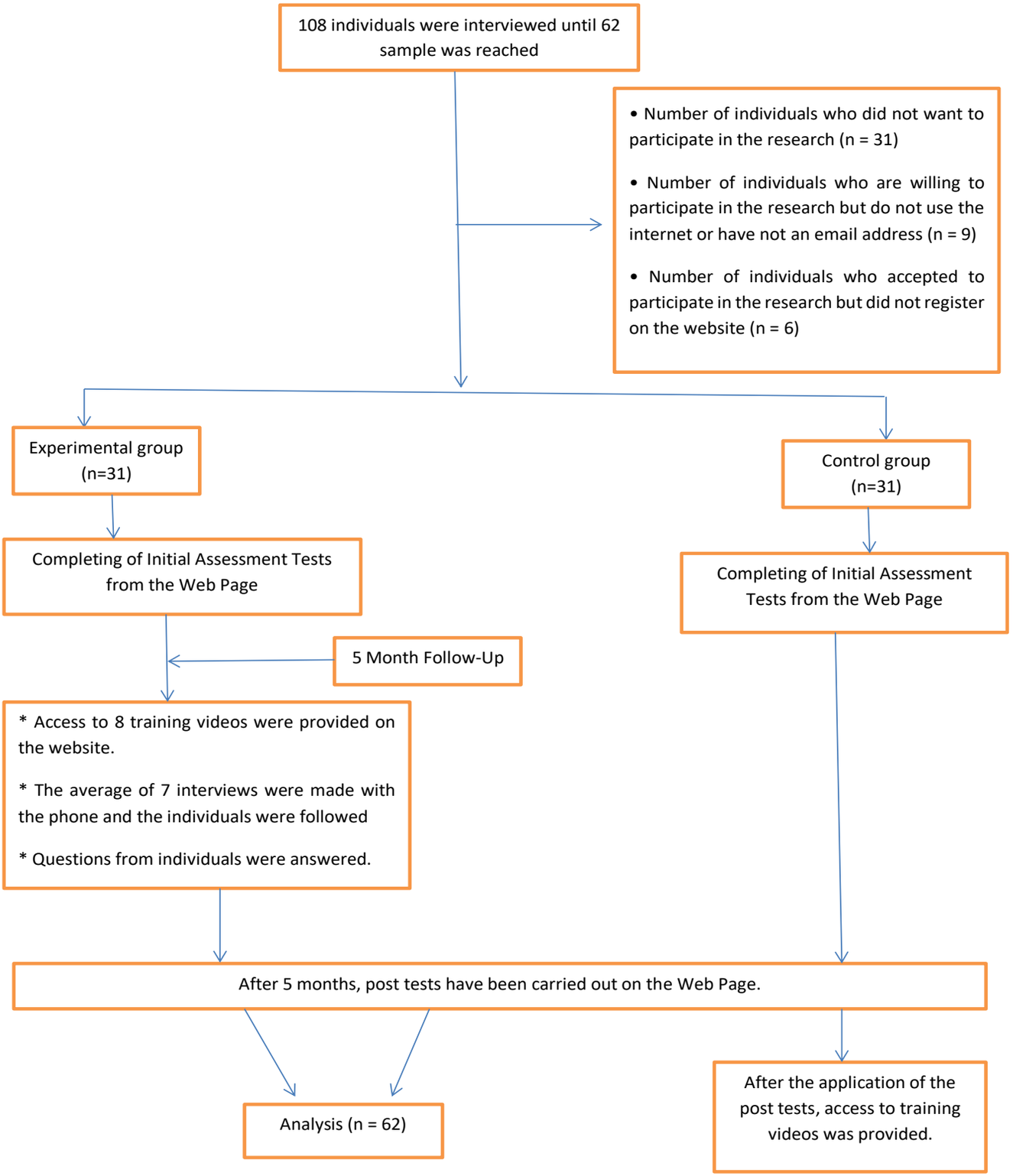

Figure 1: *Research flow chart*

2.3. Website Preparation Process

The contents of the training videos included on the webpage were prepared by interviewing researchers and three specialist faculty members, as well as performing a literature review[1,2]. The titles of the eight training videos were: General information about spinal cord injury (Training video #1, average 8 minute), Breathing, breathing exercise, assisted cough, postural drainage, (Training video #2, average 18 minute), Circulation (Training video #3, average 24 minute), Gastrointestinal, and enema application (Training video #4, average 20 minute), Urinary, clean intermittent catheterization (CIT) application, (Training video #5, average 20 minute), Musculoskeletal system problems after spinal cord injury, positioning, active and passive exercises, (Training video #6, average 18 minute), Safety tips and solutions, pressure sores (Training video #7, average 12 minute), and Sexuality (Training video #8, average 12 minute). The training videos were recorded Center for Advanced Simulation and Education Simulation Laboratory. The training videos were edited and uploaded to the webpage by a specialist.

The webpage included training videos and questionnaires. The webpage was posted to the www.omurgahemsirelikegitim.com website. Users could access the prepared training videos through their membership account, which they qualified for by completing the prepared surveys. The control group was prevented from completing the questionnaires, and the software did not allow them to access the videos without completing the post-tests or within 5 months of the registration date.

2.4. Interventions

The study data were collected by the researcher for 11 months, beginning on 1 January 2017 and continuing until reaching 62 participants and the 5-month follow-up period was achieved. Implementation steps were:

- After the preparation of the webpage, five SCIPs (these individuals were excluded from the sample) were introduced to the webpage for preliminary evaluation, and any missing aspects were eliminated.
- Preliminary interviews were conducted with those individuals who were diagnosed with paraplegia and scheduled to be discharged from the hospital, where information was given about the purpose and method of the investigation.
- For the individuals who agreed to participate in the research, they were instructed how to view the webpage on a computer or mobile phone.
- After completing the pre-tests, the experimental group gained immediate access to the training videos, whereas the control group gained access to this content 5 months after completing the pre-tests and post – tests.
- Once at 20 days an average of seven regular telephone (lasting an average of 13 minutes) interviews were conducted with the experimental group, where they were asked how much time they spent watching the training videos. Phone tracking guide content is in the form of talking about videos to watch. Some individuals made phone calls more frequently. Because when the individuals meet any problem, they call directly researcher. We talked about the solution proposal for the problem and these individuals were monitored with phone more frequently.
- There was no communication with the control group during these 5 months. Since the participants were given this information, the participants did not call the researcher.
- After 5 months, the individuals in both groups were reminded about completing the post-tests.

2.5. Ethical Considerations

Ethical approval was obtained from the GMMA (Gulhane Military Medical Academy) ethical committee (registration number: 508/Date:15.12.2015). Also, all the participants were informed about the study and written informed consent was obtained from the participants volunteering to participate in the study.

2.6. Measures from the Questionnaire Data

As part of the pre-tests, via the webpage, participants completed three questionnaires: an individual's data collection form, a form addressing the complications/problems of the participants, and a short form of the World Health Organization (WHO) quality of life scale. In the post-test; the participants repeated the complications/problems and WHO quality of life questionnaires.

2.6.1. Individual's data collection form

This form consisted of 18 questions about the participant's socio-demographic background and disease history.

2.6.2. Form addressing the complications/problems

This form included questions such as the number of complications, the complications due to SCI, what complications developed related to the system, what kind of intervention is done for the developing complication, how do you evaluate your diet, how much fluid is taken daily, how do you pass urine, how do you empty your bowels, and are you having a problem with your bedside shift. It was developed by researchers in line with the literature (1).

2.6.3. World health organization quality of life scale-short form

This scale evaluates how an individual perceives his or her quality of life. The validity and reliability studies for this form in Turkey were conducted by Eser et al. (1999). The WHO short form of the quality of life scale (WHOQOL-BREF-TR) consists of 26 questions divided into four parts: physical, mental, environmental, and social. During the Turkish validity studies, a question was added to the questionnaire, so that the total number of questions became 27. The scale has Likert type scores ranging from 1 to 5. As scores from the subscales of the scale increase, the quality of life increases. The Cronbach Alpha values calculated for examining the self-consistency of the Turkish form of the scale were found to be 0.83 in the physical field, 0.66 in the spiritual field, 0.53 in the social field, 0.73 in the environmental field. The Pearson coefficients, calculated for each question to examine the test-retest reliability, vary between 0.57 and 0.81 (7,8).

2.7. StatisticalAnalyses

All statistical analyses were performed by SPSS 22 software (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.). The normality of data was evaluated using the Shapiro Wilks test. Analyses included descriptive statistical methods (mean, standard deviation, frequency), as well as t-tests (normally distributed quantitative data) and Mann Whitney U tests (for not normally distributed quantitative data). In the evaluation of the pre and post test data showing normal distribution, t-tests were used when comparing dependent groups, and Wilcoxon Marked Rank test was used for those data that did not show a normal distribution. The Chi-Square test, Continuity (Yates) correction, and Fisher's exact Chi-square test were used in the evaluation of qualitative data, and the McNemar Bowker test was used in the evaluation of qualitative data of the pre and post tests. The confidence interval was estimated to be 95% ($p<0.05$).

2.8. Hypotheses

H1: There is no difference between the incidence of complications in individuals with and without web-based training.

H2: There is no difference between the quality of life scores of individuals with and without web-based education.

3. RESULTS

There were no statistically significant differences between the experimental and control groups in terms of age, marital status, educational status, work status, economic status, and individual characteristics of the patients ($p>0.05$). This indicates that the groups are homogeneously distributed.

3.1. Findings Related to the Use of a Training Webpage by SCIPs

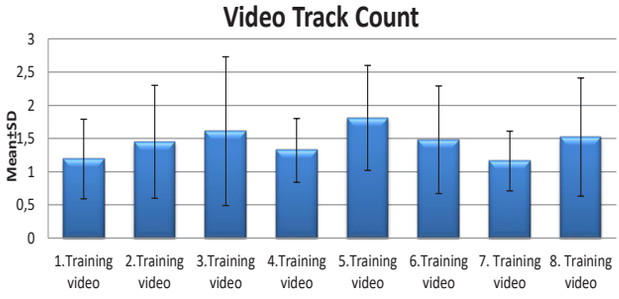

Figure 2. *Experiment Group Video Count.*

Among the videos, the video addressing urinary system problems was watched more than the others.

3.2. Findings Related to Complications/Problems of SCIPs

In the first evaluation of the experimental and control groups, the most common complications were UTI (80.6%), spasticity (69.4%), constipation (64.5%), related problems sexuality (56.5%), and orthostatic hypotension (35.5%).

3.3. Findings Related to Complications/Problems of the Systems

When comparing the two groups, we detected a difference in favor of the experimental group in case of sputum from respiratory system complications ($\chi^2 = 5.797$; $p<0.05$) (Table 1). For the complications of the circulatory system, thermoregulation impairment ($\chi^2 = 5.063$; $p<0.05$) and orthostatic hypotension ($\chi^2 = 6.229$; $p <0.05$) were less frequent in the experimental group than the control group ($p<0.05$). There were no significant differences between the groups for the gastrointestinal system complications (indigestion and heartburn) ($p>0.05$). However, at the post-test, the experimental groups had a significantly greater decrease in the rate of constipation than the control groups ($\chi^2 = 8.015$; $p<0.01$). In the pre – and post-test evaluation of the urinary system complications, there was no statistically significant difference between the two groups in terms of urinary tract infection (UTI) ($p>0.05$); however, for the experimental group, there was a significant decrease in UTIs when comparing the pre – and post-test evaluations ($p<0.05$). Among the musculoskeletal complications, only falls was statistically different between the groups ($\chi^2 = 5.365$; $p<0.05$). Regarding the complications related to sexual life, comparing the pre and post evaluations, we detected an increase in difficulty in sexual life after the injury ($p<0.05$) and problems in sexual intercourse ($p<0.01$) for both the experimental and control groups.

The H1 hypothesis was rejected.

Table 1. *Distribution of Problems Experienced by the Experimental and Control Groups in the Pre- and Post-Test Systems*

			Experimental Groups		Control Groups			
			Total number of complications	n (31) (%)	Total number of complications	n (31) (%)	χ2	p
Respiratory System Complications	Problems with respiratory system	Pre-Test	7	22.6	11	35.5	0.705	.401
		Post- Test	5	16.1	10	32.3	1.407	.236
		2p	.687		.100			
	Distress breathing	Pre-Test	3	9.7	6	19.4	0.52	.471
		Post- Test	1	3.2	3	9.7	0.267	.605
		2p	.625		.375			
	Inability to cough	Pre-Test	4	12.9	9	29	1.557	.212
		Post- Test	3	9.7	9	29	2.583	.108
		2p	1		1			
	Sputum	Pre-Test	2	6.5	5	16.1	0.644	.422
		Post- Test	0	0.0	7	22.6	5.797	.016*
		2p	-		.687			
Circulatory System Complications	Edema	Pre- Test	12	38.7	14	45.2	0.066	.797
		Post- Test	6	19.4	13	41.9		
		2p	.109		.100		2.732	.098
	Thermoregulation impairment	Pre-Test	10	32.3	15	48.4	1.072	.300
		Post- Test	2	6.5	10	32.3	5.063	.024*
		2p	.039*		.227			
	Orthostatic hypotension	Pre-Test	28	90.3	30	96.8	0.267	.605
		Post- Test	2	6.5	11	35.5	6.229	.013*
		2p	.004**		.063			
	Autonomic dysreflexia	Pre-Test	8	25.8	12	38.7	0.664	.415
		Post- Test	4	12.9	10	32.3	2.307	.129
		2p	.219		.625			
Gastrointestinal System Complications	Indigestion	Pre-Test	6	19.4	6	19.4	0.001	.100
		Post- Test	2	6.5	7	22.6	2.08	.149
		2p	.219		.100			
	Heartburn	Pre-Test	5	16.1	4	12.9	0.001	.100
		Post- Test	3	9.7	4	12.9	2.08	.149
		2p	.500		.100			
	Constipation	Pre-Test	17	54.8	23	74.2	1.761	.184
		Post- Test	7	22.6	19	61.3	8.015	.005**
		2p	.013*		.454			
Urinary System Complications	Urinary tract infection	Pre-Test	24	77.4	26	83.9	0.103	.520
		Post- Test	15	48.4	18	58.1	0.259	.611
		2p	.035*		.077			
Musculoskeletal Complications	Spasticity	Pre-Test	20	64.5	23	74.2	0.304	.582
		Post- Test	19	61.3	19	61.3	0.001	.100
		2p	1		.424			
	Heterotopic ossification	Pre-Test	7	22.6	6	19.4	0.001	.100
		Post- Test	3	9.7	3	9.7	0.001	.100
		2p	.219		.508			
	Fall	Pre-Test	17	54.8	13	41.9	0.581	.446
		Post- Test	8	25.8	18	58.1	5.365	.021*
		2p	.035*		.267			
Complications Related To Sexual Life	Having difficulty in sexual life after injury	Pre-Test	23	74.2	23	74.2	0.001	.100
		Post- Test	29	93.5	30	96.8	0.001	.100
		2p	.031*		.016*			
	Problems during sexual intercourse / activity	Pre-Test	18	58.1	18	58.1	0.001	.100
		Post- Test	26	83.9	27	87.1	0.001	.100
		2p	.008**		.012*			

*[1]Continuity (Yates) Correction and Fisher's Exact Test, [2]McNemar Bowker Test, *p< .05, **p< .01*

3.4. Findings related to the quality of life of SCIPs

Table 2. *The Pre and Post Assessment of WHOQOL-BREF-TR Scores*

WHOQOL-BREF-TR Subdomains		Experimental Groups (n=31) Mean ± SD	Control Groups (n=31) Mean ± SD	[1]t	*p*
Physical domain	Pre-Test	20.52 ± 3.91	19.45 ± 4.42	1.005	0.319
	Post-Test	21.06 ± 4.01	21.06 ± 3.92	0.000	0.100
	Difference	0.55 ± 3.39	1.61 ± 2.82	-1.342	0.185
	[2]t	-0.899	-3.179		
	p	.376	.003**		
Spiritual domain	Pre-Test	21.10 ± 4.13	19.13 ± 4.19	1.861	0.068
	Post-Test	19.77 ± 3.55	19.26 ± 3.61	0.568	0.572
	Difference	-1.32 ± 3.94	0.13 ± 2.86	-1.661	0.102
	[2]t	1.871	-0.251		
	p	.071	.803		
Social domain	Pre-Test	9.26 ± 3.13	8.13 ± 3.27	1.388	0.170
	Post-Test	9.35 ± 2.70	8.45 ± 2.58	1.346	0.183
	Difference	0.10 ± 2.23	0.32 ± 2.44	-0.381	0.705
	[2]t	-0.242	-0.736		
	p	.810	.468		
Environmental domain	Pre-Test	23.84 ± 6.94	23.42 ± 7.04	0.236	0.814
	Post-Test	25.90 ± 5.95	25.16 ± 5.69	0.502	0.618
	Difference	2.06 ± 3.90	1.74 ± 4.30	0.309	0.758
	[2]t	-2.949	-2.253		
	p	.006**	.032*		

*[1]Student t-Test [2]Paired Sample t-Test *p< .05 **p< .01*

WHOQOL-BREF-TR total scores of the experimental and control groups were similar (p>0.05) (Table 2). In the experimental group, the average score of the environmental domain subscale in the post-test was significantly higher than the average score of the pre-test ($^2t = -2.949$; p>0.01). In the control group, the difference between the mean scores of the physical domain and the environmental domain subscale was statistically significant ($^2t = -3.179$; p=0.010; $^2t = -2.253$; p>0.05).

The H2 hypothesis was rejected.

4. DISCUSSION

This study demonstrates that telephone monitoring together with web-based training is effective in controlling the complications of SCIP. SCIPs who participated in the study watched the training videos, especially the video related to UTIs, which are frequent among SCIPs (Fig. 1). We found that SCIPs prefer to contact the researcher directly by telephone rather than actively using the webpage. Because the participants in the study directly called the researcher when they had a problem. Afterwards, the individuals were directed to the training videos on the web page by the researcher. This emphasizes the importance of individual counseling, as well as standard web practice and the importance of nurse follow-up programs.

All almost of SCIPs, at least one complication arised as a result of physical changes due to the injury was serious enough to require health care services.[2] The most frequent complications among the SCIPs participating in this study were UTI, spasticity, constipation, sexually related problems, and orthostatic hypotension, which is in line with the literatüre (4,5,9-11).

The proposed contents for the training videos included increasing fluid intake, breathing exercises, postural drainage, healthy nutrition, positioning, hygiene, the points to be considered in clean intermittent catheterization application, main points in bowel training, and active and passive exercises to prevent complications. Also, suggestions were made about the applications that should be done when the complication develops. In our study, it was determined that thermoregulation impairment, orthostatic hypotension, the prevalence of sputum, UTI, and constipation rates of the SCIPs in the experimental group decreased. In these results of the study, besides the web-based training given, it is thought that interviews about complications with SCIPs on the telephone are effective. However, in the literature, the reported causes of thermoregulation defects after injury are infection status and decreased or increased ambient temperature.[12] Also, increased daily fluid (2–2.5 l) and salt intake (≥ 8 g/d), pressure socks, and avoiding sudden position changes and heat have been recommended for the treatment of orthostatic hypotension (instead of pharmacological treatments).[13] In the literature, it is indicated that non-pharmacological methods are effective in bowel management, which supports the results of our study. (4-16). It is thought that the preventive

and supportive approaches in the training videos and the close monitoring of the individuals who are followed by the telephone are thought to be the reason for the decrease in the incidence of these complications in this study.

The fall rates observed in the experimental group were also reduced. Most of the falling events were due to loss of balance when attempting to walk. In one study, 43.0% of falls of SCIPs occurred within the home, and 76.0% of individuals were walking during the fall (17). The falls of SCIPs are caused by loss of balance, lower extremity muscle weakness, and environmental hazards.

Sexuality is not a topic that is easily spoken about with SCIPs (18). Sexuality is not integrated into the rehabilitation process, and can even be ignored. However, SCIPs are known to need training and counseling on sexuality (19). Similarly, in this study, the individuals who were followed-up, especially those that were single, asked questions about sexuality, and they expressed their need for information on this subject. The most common sexuality topics the participants wanted to talk about were problems related to erection/ejaculation, sexual intercourse, and reproduction. In one study, the subjects discussed sexuality, including relationships, sexual preferences, their partner, gender, the adaptation process, culture, and religion (19). In general, the sexual issues discussed vary according to the culture. It is thoughtthat the increased incidence of problems in sexual life is because the individuals who participate in this study are composed of a young population; for them, sexuality is associated with sexual intercourse and erection/ejaculation, which some do not want to discuss.

In the literature, the quality of life of SCIPs is reported to be lower than that of healthy individuals (20). There was no statistically significant difference in the quality of life total scale scores between the two groups in our study. However the environmental subscale scores of both groups and the physical subscale of the control group were statistically significant. The study participants had an average time since injury of 6 months. Mostly, SCIPs are in the process of adapting to a new life, new bodies, and new environmental conditions. In this period, individuals face physical difficulties. Moreover, based on the literature, the factors affecting the quality of life of SCIPs vary.

The quality of life of SCIPs can be influenced by physical difficulties, psychological and socioeconomic problems, and difficulties in returning to work or education (21). In some studies, the quality of life of the individuals was independently associated with secondary complications (e.g.m musculoskeletal pain, pressure scar, problematic spasticity, constipation) (22). Also, many factors influence the quality of life, such as perceived health status, subjective health, the perception of health, satisfaction, mindset, psychiatric status, and well-being (23). Recent research has found that the effect of psychosocial issues is important for quality of life, including social integration, social relations, self-efficacy, self-esteem, view of life, leisure time, and consistent emotional state (24).

Apart from disease complications and individual psychosocial states, environmental and physical obstacles also affect quality of life. Almost half (48.3%) of SCIPs reported physical obstacles related to the home environment, such as lack of lifts and ramps and inadequate space for a wheelchair to move (25). Most (79.8%) SCIPs have between 3 and 7 rooms, 12.6% have between 8–10, and there are no private rooms for the individual (25). Most (75.6%) SCIPs experience transport problems, including irregular sidewalks, special public transport for disabled people, special ramps for wheelchair users, and an absence of private parking spaces for disabled people (25).

In brief the quality of life, in general, can be affected by limitations in physical functions, as well as social life participation, environmental barriers, individual personality characteristics, individual demographic characteristics, and health perceptions. That is, the quality of life can vary depending on the person. According to the results of the study, the frequency of complications has decreased, but longer-term interventions are required to increase the quality of life of individuals.

5. CONCLUSION

It has been determined that telephone monitoring together with web-based training is effective in controlling complications in SCIPs. Among the training videos, the video addressing the urinary system was watched the most. In complications of SCI, such as constipation, orthostatic hypotension, and thermoregulation disorders, a decrease in favor of the experimental group was observed. There was no significant difference between the two groups in terms of the quality of life and sexual problems.

We propose that future studies should: monitor SCIPs by telephone and home visits (although web-based training can also be effective in the management of complications); research sexual counseling, and use broader samples of SCIPs when monitoring quality of life.

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Clinical and Experimental Health Sciences

Relationship Between Psychiatric Nurses' Resilience and Empathic Tendencies

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ABSTRACT

Objective: Resilience associated with empathy and increases nurses' job satisfaction and reduces burnout. This study aimed to determine the relationship between resilience and empathic tendencies of nurses working in the psychiatry service.

Methods: This study is descriptive and correlational. The study was conducted with 101 nurses working in a psychiatric state hospital between May 2017 and June 2017. Study data were collected using an information form, Resilience Scale for Adults, and Empathic Tendency Scale. Statistical analysis was conducted using frequency, mean, Pearson's and Spearmen's correlation analyses, and linear regression analysis.

Results: Nurses' resilience and empathic tendencies were above the median (126.84±16.09) and 70.03±7.89), respectively. A positive, weak-moderate level, linear relationship was found between the scores of resilience and empathic tendency scales. A linear relationship was found between empathic tendency and perception of future, social competence, and social resources. No linear relationship was found between structured style, perception of self, or family cohesion. Multiple linear regression analysis found that the social competence subscale was the variable that predicted the Empathic Tendency Scale score.

Conclusion: The study detected that psychiatric nurses social competence, a subscale of resilience, was effective in the nurses' empathic tendencies. It is recommended to improve nurses' social competences through practices that will improve the quality of the interaction between the patient and nurse, and nurses' empathy and resilience, which have significant effects on the patients' recovery time.

Keywords: Job Satisfaction, Empathy, Psychiatric Nursing, Regression Analysis

1. INTRODUCTION

Nursing is a health discipline that experiences intense human to human relationships. It requires providing compassionate care in a therapeutic relationship with the patient and teamwork (1). However, nurses may become vulnerable to several traumatic and stressful events directly or indirectly while providing care. In addition, there are various stressful events particular to the field of psychiatry. Psychotic symptoms include patient behaviors that could cause conflict, domestic violence, suicide attempts, verbal/physical violence committed to self or others and having potential to harm self and others and coercive restraint practices applied to these behaviors (2-4). These stressful situations originating from the profession cause nurses to feel guilt, burnout, affective disharmony, post-traumatic stress, low levels of job and life satisfaction, and depression and cause them to leave their job (1,3,5,6). Psychiatric nurses who provide care to traumatized patients are indirectly traumatized and are at risk of secondary traumatic stress (7).

Adverse events experienced in psychiatry may negatively affect the caregiver role of psychiatric nurses. Psychiatric nurses should maintain their caregiver role in spite of risky situations. Thus, recently, traditional understanding of care has been extended and the concept of resilience has been included (3,8). Nurses' resilience and ability to turn bad experiences into good experiences during the therapeutic relationship process sets a positive example for patients (3).

Resilience is a significant characteristic that causes one to pull themselves together against stressful life events. Resilience, which is a personal characteristic and a dynamic process, includes control and management of positive and negative emotions (9). Descriptions regarding resilience include different features of this concept. Earvolino Ramirez (10) defines resilience as individuals' pulling themselves together against bad situations, which means changing back to their former state after depression or injuries.

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Psychiatric nurses are considered a "resilient group" because they professionally undergo several changes and developmental processes to cope with adverse situations. Resilience is defined as "the capacity of resisting difficulties and continuing to positively develop against change" (11). Resilience has several effects on psychiatric nurses' working lives. It is a significant factor regarding job and life satisfaction, self-reliance, burnout, and depression (1,3,9,12,13). Resilience decreases the act of leaving a job, is effective in managing a high level of stress, and increases job and life satisfaction (9,12,13). Mealer et al. (13) found that a high level of resilience in nurses prevents them from having post-traumatic stress disorder, anxiety, depression, and burnout.

The literature presents different opinions and outcomes regarding the relationship between empathy and resilience (9,17-20). Resilience is associated with difficulties, stressful situations, and post-traumatic growth. The growth resulting from stressful, traumatic situations develops with increasing helping behavior, compassion, self-sacrifice, commitment, and empathy in the individual. Some studies indicate that concepts of resilience and empathy mutually affect each other (9,14-17). Empathy is among the factors affecting resilience. Resilient individuals fulfill their duties in spite of the difficulties in their job, and they empathically and willingly continue to provide care (3). In spite of their challenging working conditions, psychiatric nurses should be resilient so they can use their professional patient care skills, cope with challenging situations, and work empathically and willingly (1).

Psychiatric nurses are expected to provide optimum care in spite of the traumatic situations they experience in their troubled and stressful working lives. Thus, resilience levels of psychiatric nurses, risks, and preventive factors affecting their resiliency should be known.

The literature includes studies regarding nurses' resilience (1,3,8,11-13,21,22, 24-26). However, no study examining the relationship between resilience and empathic tendency, which is considered a preventive factor of resilience, was found. This study aimed to determine the relationship between resilience and empathic tendencies of the nurses working in a psychiatry service, and answers were sought for the following questions:

1. What are the resilience levels of psychiatric nurses?
2. What are the empathic tendency levels of psychiatric nurses?
3. Is there a linear relationship between resilience and empathic tendencies of psychiatric nurses?

2. METHODS

2.1. Study Design and Sample

This study was descriptive and correlational. The study used the random sampling method of the improbable sampling methods and aimed to reach the entire population. Study data were collected between May 2017 and June 2017. Of the 200 nurses working in the psychiatry clinics in a Psychiatry Hospital in İstanbul, the study was conducted with 117 nurses who volunteered to participate in the study. All complete and whole questionnaires – 101 questionnaires – were evaluated (response rate of 58.5%). Study Inclusion Criteria included working in the psychiatry clinic of the relevant hospital and volunteering to participate in the study.

2.2. Data Collection Tools

Study data were collected using a Personal Information Form (8 items), Empathic Tendency Scale (20 items), and Resilience Scale for Adults (33 items).

2.2.1. *Personal Information Form*: It included eight questions regarding variables such as nurses' age, gender, marital status, education, position (nurse supervisor, service nurse), general shifts, working place, and years of experience. The questions on the form were multiple-choice.

2.2.2. *Empathic Tendency Scale (ETS):* The ETS developed by Dökmen in 1988 aims to measure the individuals' potential to develop empathy in daily life (27). This 5-Likert-type scale (1=totally agree, 2=quite agree, 3=neutral, 4=quite disagree, 5=totally disagree) includes 20 items. The range of the scale is between 20 and 100. A higher total score indicates a higher empathic tendency. Dökmen (27) found the total Cronbach's Alpha value of the scale 0.82, whereas this study found it was 0.72.

2.2.3. *Resilience Scale for Adults (RSA):* Basım and Çetin (28) conducted the Turkish validity and reliability study of the RSA developed by Friborg et al. (29) in 2003. This scale includes six subscales, which are 'perception of self" (1,7,13,19,28,31), 'perception of future' (2,8,14,20), 'structured style' (3,9,15,21), 'social competence' (4,10,16,22,25,29), 'family cohesion' (5,11,17,23,26,32), and 'social resources' (6,12,18,24,27,30,33) (28,29). This is a 5-Likert type scale. If increasing resilience is associated with increasing scores, response boxes should be evaluated left-to-right as 12345. Considering this, questions numbered 1–3–4–8–11–12–13–14–15–16–23–24–25–27–31–33 would be reverse questions. However, if increasing resilience is associated with the decreasing scale scores, response boxes should be evaluated as 54321 and the reverse questions would be 2–5–6–7–9–10–17–18–19–20–21–22–26–28–29–30–32. Response boxes in this study were evaluated left-to-right. Both the original scale (25) and this study found the total Cronbach's Alpha coefficient to be 0.86.

2.3. Procedure

The potential participants were provided with verbal and written details regarding the study, including the choice to remove themselves from the study at any time (conformity with the Helsinki Declaration Principles). While the researchers explained the study to potential participants, they received support from a colleague (MAD) at the institution where the study was conducted. Written, informed consent was obtained from the final participants.

Data was collected through one on one face to face interviews that took approximately 20-30 minutes. The researchers conducted the interviews in a suitable physical environment that ensured a comfortable and effective interview. The study was conducted in a separate closed room so that the interview could not be interrupted (in the policlinic room where the patient examination is not performed or in the ward manager's room).

2.4. Ethical Considerations

Ethical permission was granted from the ethics committee of the hospital where the study was conducted (Dr. Mazhar Osman Mental Health and Neurology Training and Research Hospital, Date/Issue/Decree no:02.02.2017-4255-624). Written and verbal informed consent was obtained from the participants. This study was conducted in accordance with the principles of the Declaration of Helsinki.

2.5. Data Analysis

Study data were analyzed using IBM SPSS version 21.0 (IBM Corp. Released Armonk, NY, USA) package program. Descriptive statistics were presented as mean, standard deviation (SD), median, interquartile range (IQR), minimum (min), maximum (max), frequency, and percentage. Continuous variables' suitability to normal distribution was examined using the Shapiro-Wilk Test. Intergroup comparisons of continuous variables were conducted with independent samples t-test. The linear relationship between variables was evaluated with Pearson's and Spearman's correlation tests. Based on correlations simple linear regression analysis was used to determine the relationship size regarding the subscales of "Resilience" that were thought to affect the ETS score. ETS was introduced as the dependent variable and subscales of "Resilience" as independent variables. Simple linear regression analysis was used to determine the subscale scores of the RSA that significantly predicted the ETS score. Variables with a p-value of <0.25 in simple linear regression analysis were included in the multi-model as candidate variables. Enter method was used in multiple linear regression analysis. The significance level was set at $p<0.05$.

3. RESULTS

3.1. Individual Characteristics

The study included 101 nurses and of these nurses, 64.4% (n=65) were female, 35.6% (n=36) were male. The median age was 35 (IQR=10.5) (min=22; max=60) years and 14.9% (n=15) were high school graduates, 71.2% (n=72) had a bachelors' degree, and 13.9% (n=14) had a post-graduate degree. The median years the nurses' worked in psychiatry clinics was 6 (IQR=8) (min=1; max=36). Of the nurses, 89.1% (n=90) were service nurses and 87.1% were working in acute services.

3.2. Characteristics Regarding Resilience and Empathic Tendency

Nurses' mean empathic tendency score was 70.03 (SD=7.89) (58% of them above average). Their mean resilience score was 126.84 (SD=16.09) (64% of them above average) (Table I).

Table 1. *Mean Empathic Tendency Scale (ETS) and Resilience Scale for Adults (RSA) Scores (N=101)*

Scale and Subscales	Mean ± Standard Deviation
ETS Total	70.03±7.89
RSA Total	126.84±16.09
Structured Style	14.08±3.32
Perception of Future	15.16 ± 3.61
Family Cohesion	22.23±5.04
Perception of Self	21.87±3.95
Social Competence	19.58±3.49
Social Resources	28.86±4.52

No linear relationship was found between nurses' resilience scores and age (r_s=0.130, p=0.195) or their working years (r_s=0.071, p=0.481). The nurses obtained the highest score from the "social resources" subscale among the resilience subscales (mean=28.86, SD=4.52) (Table I).

As nurses' working years increased, empathic tendency scores significantly increased on a weak level (r_s=0.247, p=0.013). However, no significant linear relationship was found between nurses' empathic tendency scores and their age (r_s=0.120, p=0.230).

No statistically significant intergroup difference was found between nurses' resilience and ETS scores based on their gender, education level, status, or shifts (night, day) (Table II).

Nurses' scores for resilience and structured style, family cohesion, and perception of self were significantly different based on their marital status. Married nurses' scores for resilience, structured style, family cohesion, and perception of self were significantly higher than single nurses were (Table II).

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Table 2. *Comparison of resilience and empathic tendency scores based on sociodemographic characteristics (N=101)*

Demographic Variables		Empathic Tendency Scale (ETS)	Resilience Scale for Adults (RSA)						
		ETS Total	RSA Total	Structured Style	Perception of Future	Family Cohesion	Perception of Self	Social Competence	Social Resources
		Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD
Gender	Female	69.56±7.62	127.75±15.16	14.20±3.51	15.23±3.67	21.92±5.29	21.60±3.52	19.98±3.20	29.36±3.75
	Male	70.89±8.40	125.19±17.73	13.86±2.98	15.05±3.52	22.80±4.56	22.36±4.64	18.86±3.89	27.94±5.58
	Statistical Analysis* Possibility	t: – 0.80, p: 0.424	t: 0.76, p: 0.447	t: 0.48, p: 0.626	t: 0.23, p: 0.816	t: – 0.84, p:0.402	t: – 0.92, p:0.357	t: 1.56, p: 0.122	t: 1.52, p: 0.130
Marital Status	Married	71.30±7.34	129.76±16.68	14.88±3.23	15.50±3.44	23.13±4.98	22.84±3.54	19.54±3.52	29.22±4.34
	Single	68.26±8.37	122.73±14.41	12.95±3.16	14.69±3.80	20.97±4.89	20.50±4.12	19.64±3.49	28.35±4.76
	Statistical Analysis* Possibility	t: 1.93, p: 0.056	**t: 2.20, p: 0.030**	**t: 2.98, p: 0.004**	t: 1.12, p: 0.263	**t: 2.16, p: 0.033**	**t: 3.06, p: 0.003**	t: – 0.14, p: 0.887	t: 0.94, p: 0.347
Status	Nurse Supervisor	71.70±6.61	124.30±17.56	12.70±3.62	13.50±4.11	22.50±4.06	21.80±3.04	20.40±3.09	28.60±4.69
	Nurse	69.77±8.04	126.92±15.97	14.25±3.28	15.30±3.50	22.16±5.16	21.87±4.07	19.43±3.50	28.86±4.54
	Statistical Analysis* Possibility	t: 0.72, p: 0.468	t: – 0.48, p: 0.627	t: – 1.40, p: 0.163	t: – 1.51, p: 0.133	t: 0.19, p: 0.844	t: – 0.05, p:0.954	t: 0.83, p: 0.405	t: – 0.17, p:0.861
Shift	Day	69.79±8.33	126.70±16.95	13.87±3.35	14.85±3.71	22.59±4.79	21.98±4.25	19.33±3.57	29.22±4.32
	Night	70.46±6.63	126.53±13.48	14.73±3.25	15.88±3.15	21.07±5.66	21.53±3.07	20.07±3.14	27.73±5.00
	Statistical Analysis* Possibility	t: – 0.36, p: 0.714	t: 0.04, p: 0.964	t: – 1.12, p: 0.265	t: – 1.26, p: 0.209	t: 1.32, p: 0.189	t: 0.49, p:0.623	t: – 0.93, p: 0.352	t: 1.45, p: 0.148
Education Level	High School	71.53±6.96	122.86±18.04	14.13±3.70	14.73±3.26	21.40±4.61	21.40±4.61	18.53±3.92	27.26±5.72
	University	69.77±8.05	127.53±15.73	14.06±3.28	15.24±3.67	22.38±5.12	22.38±5.12	19.76±3.40	29.13±4.25
	Statistical Analysis* Possibility	t: 0.79, p: 0.430	t: – 1.03, p: 0.302	t: 0.06, p: 0.946	t: – 0.50, p: 0.615	t: – 0.69, p: 0.488	t: 0.77, p: 0.442	t: – 1.26, p: 0.208	t: – 1.49, p: 0.139

*SD=Standard Deviation, *Indepedent Sample-t*

Resilience and Empathic Tendencies

Original Article

3.3. The Relationship Between Resilience and Empathic Tendency

A positive, weak-moderate, linear relationship was found between the scores of resilience and ETS (r_s=0.371, p<0.001) (Table III). A significant linear relationship was found between three subscales (perception of future, social competence, and social resources). However, no significant linear relationship was found for the other three subscales (structured style, perception of self, and family cohesion).

Table 3. *The linear relationship between resilience and empathic tendency scores (N=101)*

	ETS Total
	r
ETS Total	
RSA Total	0.371***
Structured Style	0.039
Perception of Future	0.238*
Family Cohesion	0.122
Perception of Self	0.192
Social Competence	0.427***
Social Resources	0.253*

*r=Pearson's correlation coefficient; *p<0.05, **p<0.01, ***p<0.001, ETS: Empathic Tendency Scale, RSA: Resilience Scale for Adults*

Simple linear regression analysis found the p-value regarding the relationship between the "Structured Style" subscale and ETS scores was >0.25. Therefore, the "Structured Style" subscale score was not included in the multiple regression analysis. Among the other 5 subscales included in the multiple linear regression analysis, only the "social competence" subscale score significantly predicted the ETS score (p<0.05). There was a significant positive and weak-moderate level of correlation between the ETS score and "social competence" subscale score. As the "social competence" subscale score increased, the ETS score also increased. Five subscale scores included in the multiple linear regression analysis explained 19.6% of the change in ETS scores. Independently of the other variables, the "social competence" subscale score explained 18.3% of the change in ETS scores (Table IV).

Table 4. *Results of multiple linear regression analysis regarding the variables predicting empathic tendency scale score*

Variable	Non-standardized Coefficients		Standardized Coefficients		
	B	Standard Error	Beta	t	p
Invariant	47.351	5.776		8.198	<0.001
Social Competence Score	0.836	0.251	0.369	3.332	**0.001**
Social Resources Score	0.062	0.203	0.036	0.306	0.760
Perception of Future Score	0.192	0.224	0.088	1.859	0.392
Family Cohesion Score	-0.040	0.163	-0.025	0.243	0.808
Perception of Self Score	0.114	0.202	0.057	0.565	

Dependent variable: Empathic Tendency Scale Score, B is the non-standardized beta (B) value. This value shows how many units the dependent variable increases with each unit increment of the predictor variable

4. DISCUSSION

Considering that much has been studied in the literature (1,3,10-13, 21,22,24-26, 30-36); nurses are expected to be empathic and resilient. Upon examining the literature, the risk and protective factors related to resilience for sustaining, maintaining and improving psychological resilience have been defined, and in many studies, the resilience level, the factors affecting resilience and the results of resilience have been investigated (1,3, 8-26). However, there were few studies which the relationship between resilience and empathy were investigated (23-25).

Empathy is an important component of nursing care and therapeutic relationship, which influences the quality of care (30). The literature indicates nurses' mean empathic tendency scores range between 65.95 and 77.43 (31-35). This study found nurses' mean empathic tendency scores were 70.03±7.89, which complies with the literature.

The literature indicates various levels of resilience for nurses (1, 12, 21, 22, 24, 25). Rocha et al. (21) conducted a study with 56 psychiatric nurses in Brazil and found that 50% of the nurses had a high level of resilience and 42.9% of the nurses had a moderate level of resilience. Guo et al. (22) found that 1061 nurses in China had a moderate level of resilience. Navarro-Abal et al. (23) found that 128 nursing assistants had a moderate level of resilience. Matos et al. (1) found the resilience level of 32 psychiatric nurses was moderate. Zheng et al. (12) found the resilience level of 726 psychiatric nurses was low. Öksüz et al. (24), who used the same scale as this study, found the resilience level of 242 nurses was low (99.80±4.43). Kutluturkan et al. (25) found the resilience level of 148 oncologic nurses was high (median: 134.0, min: 122, max: 146.0). However, this study found that 64% of the nurses had a resilience score above average (126.84 ±16.08). The study results are different from the literature, perhaps because this study used different measurement tools and/or the nurses in the sample were working in different departments. However, in their qualitative study, Marie et al. (26) found that religious and cultural resources of the nurses working in the community mental health workplaces in Palestine had a significant role in their resilience. Nurses stated that political conflicts in Palestine made them receive support from spiritual values and become more determined, patient, and resilient in coping with difficulties. Accordingly, various studies conducted in different countries indicate that resilience may differ by groups with different experiences, cultures, and spiritual values.

This study found the psychiatric nurses' resilience and empathic tendencies were above the median value. In addition, psychiatric nurses with higher resilience were more empathic. Akbaş (18) examined the relationship between resilience and empathic tendency in families with special needs children, and found a positive relationship.

Morice-Ramat, Goronflot and Guihard (2018) conduct a study to explore resilience, resilience predicting factors and resilience distribution in French medical residents. They found the resilience and empathy were positively correlated (19). These findings are similar to this study.

Mathad, Pradhan and Rajesh (2017) have found a positive correlation between nursing students' resilience and empathy, but empathy has not been a predictor of resilience (20). McFarland and Roth (2016) examined the relationship between the resilience of physician assistants working in hematology and oncology clinics and their level of stress and empathy. They found that their resilience was negatively related to their stress levels, but it was not related to their level of empathy (17). This outcome was related to the following: both resilience and empathy were structural characteristics that were hard to measure. Vinayak and Judge (37) examined the relationship between psychological well-being and resilience and empathy in adolescents. They found that both empathy and resilience were predictors of the psychological well-being of female participants. Being empathetic and trying to understand others, protects the psychological well-being of individuals (37). This indicates that empathy toughens the individual psychologically.

In this study there has been found positive correlations between ETS and 3 subscales of the psychological resilience (perception of future, social competence and social resources). According to these findings multiple linear regression analysis was carried out to find the predictors of ETS. It has been found that social competence predicts ETS of psychiatric nurses. Accordingly, nurses who were supported with their resilience and social competences (sincerity and flexibility in their social relationships, ability to make friends easily and use humor positively, etc.) tended to be empathic. In the literature review, similar results were found with our study. McAllister and McKinnon (2009) indicated that resilient individuals could sustain their friendships for a longer time, gave emotional support, had a better relationship with family and friends, and utilized social support resources when needed (38). Avcı, Aydın & Özbaşaran (36) found a positive relationship between altruism levels and empathic tendencies of 218 nursing students. In addition, altruism levels of students who did not have close friends were low. This situation was interpreted as follows: a growing social relationship network would increase helping behavior or would extend the relationship network of this behavior. Patterson (2002) (14) and Lietz (2007,2011) (15,16) also found that families' resilience levels were related to helping and empathizing with other individuals experiencing similar problems. Morice-Ramat et al. (2018) found empathy is a predictor of resilience (19). According to all these findings (9,14-17,19), it can be indicated that resilience and empathy mutually affect each other. However, this study emerged that, the social competence of psychiatric nurses, which is the component of the psychological resilience, is a predictor of empathy.

5. CONCLUSION

This study found the psychiatric nurses' resilience and empathic tendencies were above the median value. Both empathy and resilience should be improved because they are significant in preserving and improving the psychology of nurses with stressful working conditions. Psychiatric nurses' resiliences' and social competencies' is a predictor of their empathic tendencies's. Therefore, we recommend enacting regulations to improve resilience and empathic tendencies of psychiatric nurses in in-service trainings and certification programs; increasing awareness of the importance of resilience and empathy; allowing communication skills programs (role-play, psychodrama, etc.) to improve empathy and social competence, which is related to empathy; allowing for organizational activities; arranging in-house and inter-institutions meetings; structuring education programs for nursing students' to improve their social competence, empathy, and resilience; and conducting descriptive and experimental studies in larger groups to determine the preventive factors affecting the improvement of nurses' resilience.

5.1. Limitations And Strengths

The present study was conducted for two months in only one hospital because of practical difficulties, time constraints, and economic limitations. Situations that could result from the organization that might affect nurses' resilience were ignored because it was conducted at one center. Reaching the entire population was aimed. Thus, the sample was chosen using the "improbable sampling" method, which is a "random sampling" method. Thus, the generalizability of the data is limited. In addition, possibilities of nurses' evaluating expressions under the influence of social likability should not be ignored.

Conducting new studies in different provinces, hospitals, and regions using similar scales in this field will contribute to the reliability and validity of the study. Empathic tendency which is a preventive factor of resilience and a characteristic a nurse should have positively affects resilience. This study revealed the relationship between resilience and empathic tendency, thereby contributing to the limited relevant literature. In addition, this study sheds light on studies to be conducted regarding nurses' resilience and empathetic tendency.

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Clinical and Experimental Health Sciences

Knowledge Level About Insects and Mites of Health School Students

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ABSTRACT

Objective: Today, diseases transmitted by insects and mites still remain an important public health problem. Therefore, the training received by health personnel and their experiences on this topic is important. This study was conducted to determine the knowledge and experiences of students, who were health personnel candidates, on insects and mites likely to be encountered in hospitals or on patients

Methods: This study is cross-sectional. No sample selection was made and 1st – and 4th-grade students in midwifery and nursing departments constituted the universe. Independent-samples t-tests compared knowledge to identify differences by students ' experiences and education about insects and mites, $\chi 2$ tests compared frequency of correct knowledge answers according to experiences and education about insects and mites.

Results: The participants stated that, in their daily lives, they mostly encountered cockroaches (77.9%) in their environment and lice (52.5%) on their bodies. In this study, the prominent finding was that both experiences and education were important in getting information on insects and mites. Students' ratio of thinking that they had sufficient knowledge on insects and mites, the ratio of recognizing insects and mites given in images, the mean scores of correct answers given to the propositions on insects and mites, and the knowledge of struggling methods were low.

Conclusion: Today's changing environmental conditions have increased the risk of confronting epidemics related to insects and mites at any time. Therefore, it is highly important for health personnel, who are actively involved in epidemics and who consult the community, to receive effective training on insects and mites during the university period.

Keywords: Insect, Mite, Knowledge Level, Nursing Education, Public Health

1. INTRODUCTION

Many diseases are carried and transmitted by arthropods (Arthropoda), especially insects (Insecta), mites and ticks (Acari) in tropical and subtropical regions of the world. These organisms operate as biological or mechanical vectors for the spread of human-to-human and animal-to-human transmitted diseases, parasites, and their eggs on earth (1). At the same time, the developmental stages of insect populations (age composition of insect populations) constitute an epidemiological risk (2). Diptera (mosquitoes, black flies, sand flies, blowflies, flesh flies, horse flies, deer flies, stable flies, and house flies), Hemiptera (bed bugs and assassin bugs), Siphonaptera (fleas), Phthiraptera (sucking lice) and Dictyoptera (cockroaches) are most important insect groups for human health (3).

Especially, hospitals are suitable premises for harboring and spreading of many pathogens. Cockroaches (Insecta: Dictyoptera) have a very important role in the spread of nosocomial infections and drug-resistant bacteria in hospitals (4). 82 pathogenic bacteria were isolated from the flies (Insecta: Diptera) collected from hospitals in the UK and 68 strains of them were found to be resistant to antibiotics (5). Cockroaches are present in many areas that humans use in their daily lives such as houses, restaurants, hotels, malls, residences (6). The production of allergens triggering asthma and rhinitis negatively affects human health by causing the transport of enteric pathogens and psychological stress. Urban populations with low-income are the most powerful risk groups for susceptibility to cockroach allergens and the development of asthma (7,8).

Pediculosis is a parasitic disease caused by human lice (Insecta: Phthiraptera). It may originate from the head, clothes, and pubic lice depending on the etiological factor. Head pediculosis is epidemic worldwide (9). The prevalence of pediculosis is variable depending on socioeconomic status, population density, and hygiene rules (10, 11).

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Fleas (Insecta: Siphonaptera) are able to transmit agents of infectious diseases in humans and animals. Flea-borne infections are common worldwide and may have a high incidence (12). These zoonotic agents are transmitted to humans mainly through bites or exposure of feces to itchy bite lesions (13).

Bedbug (Insecta: Hemiptera) is a nocturnal, flightless ectoparasite that preferably feeds on human blood (14). The bite of a bedbug causes physical and psychological problems such as itching, rashes, allergies, insomnia, anxiety; moreover, bedbugs create serious economic concerns and quality of life problems for households (15, 16).

Scabies is a skin disease caused by Sarcoptes scabiei var. hominis (Arachnida: Acari) in humans. It is commonly seen in the world and affects humans of all races and social statuses. It is transmitted by close contact and can lead to rapid epidemics in families, dormitories, kindergartens, and nursing homes (17). Ticks are considered to be the second among the vectors of disease-causing factors in humans. It is reported that there are more than 100,000 diseases caused by tick-borne pathogens (18). Therefore, they are medically important ectoparasites. In the world and in Turkey, mite – and insect-borne diseases remains to be a major public health problem. In Turkey, currently, there are 3,649,750 Syrian refugees by 2019 (19) and the increase in infectious diseases is remarkable (20). Refugees may carry new health problems to migration areas where these problems have not been there before. Therefore, it is highly important to give primary preventive health services to immigrants (21).

After the realization of family practice system in Turkey, mostly nurses and midwives have been started to be assigned in family health centers (22). The lack of environmental health personnel in family health centers necessitates midwives and nurses to have knowledge of all aspects of health, including environmental health services. It is important for midwives and nurses to have knowledge and experience about insects and mites as health consultants. Health workers should recognize insects and mites in order to protect themselves and their environment have information on the diseases and preventive methods. Experiences and education ensure the acquisition of this knowledge.

The most common insects and mites that are scabies, louse, flea, tick, bedbug, and cockroach were involved in this study. The aim was to determine the knowledge levels of students studying in midwifery and nursing departments.

2.METHODS

2.1. Participants

The cross-sectional descriptive study design was employed. 281 1st – and 4th-grade students in midwifery and nursing departments participated in this research. No sample selection was made, and it was aimed to reach the whole universe. The rate of participation was 93.3%.

2.2. Measures

A questionnaire was prepared by the researchers by reviewing the literature and it was applied to the participants. The questionnaire consists of questions about the sociodemographic characteristics, the status of encountering insects and mites, and the sources of information on insects and mites. In addition, the questionnaire included images of insects and mites, 52 propositions to determine the knowledge levels, and questions of known struggling methods.

2.3.Data Collection

The study data were collected between October and November 2018. After the approval of the Ethics Committee, the permission of the school administration was obtained. Prior to the application of the questionnaire, the students were informed and the questionnaire was applied to the volunteers. The questionnaires were applied to the students face to face in the classroom environment. The application took approximately 20-25 minutes.

2.4. Data Analysis

Data were analyzed using SPSS Version 21.0 (IBM, Armonk, NY, USA). Data were summarized as mean ± standard deviation and percentage. Chi-square test was employed for the comparison of categorical data. To compare between the two groups, independent t test was used. The level of significance was taken as 0.05.

2.5. Ethical Considerations

For this study, permission was obtained from the Ethics Committee of Nigde Omer Halisdemir University (2018/11-06). After the students were informed about the purpose of the research and the questionnaire, the questionnaire was applied to those who gave written and oral consent.

3.RESULTS

3.1. Demographic Information

The number of female students who participated in the study was 242 (86.1%) and the number of male students was 39 (13.9%). The mean age was 20.09±1.76 years. Of the participants, 62.3% were studying in the nursing department and 37.7% were studying in the midwifery department. Of the participants, 55.5% were 1st-graders and 44.5% were 4th-graders. 77.6% of the students were living in dormitories and 15.3% were living with their families. Of the students, 55.2% stated that they lived in the province before they started university, 29.2% in the district, and 10.3% in the village (Table 1).

Table 1. *Sociodemographic characteristics of students*

Sociodemographic Characteristics	Number	%
Age		
20 years and below	160	56.9
21 years and over	121	43.1
Sex		
Female	242	86.1
Male	39	13.9
Department		
Nursing	175	62.3
Midwifery	106	37.7
Class		
1st-grade	156	55.5
4th-grade	125	45.5
Place of residence		
At home with family	43	15.3
Dormitory	218	77.6
At home with friends	15	5.3
Alone	3	1.1
Other	2	0.7
Former living place		
Province	155	55.2
District	82	29.2
Small town	14	5.0
Village	29	10.3
Other	1	0.4

3.2.Evaluation of Participants' Statuses Related to Insects and Mites According to Some of Their Characteristics

The ratio of the participants who had fed an animal once in their lifetime was 54.8%. 63% of the animal feeders had fed two or more species of animals. The participants stated that they had fed many animals such as cat, dog, bird, fish, chick, cow. The ratio of those engaged in livestock farming was 14.9%. 50% of those engaged in livestock farming stated that were engaged in bovine breeding. 52.3% of the participants answered "yes" and 47.7% answered "no/no idea" to the question "Have you received information about insects and mites during your education?".

The students stated that they mostly encountered cockroaches (77.9%), lice (56.2%) and fleas (41.3) in their daily lives. The students mostly encountered lice (52.5%) on their bodies. They stated that they would mostly recognize cockroaches (59.7%) when they saw one (Table 2).

There was a significant difference between those who lived in a province and those who lived in other settlements in terms of encountering lice and fleas. According to this, people who lived in settlements such as districts, villages, and small towns encountered lice ($\chi 2=9.132,\ p=0.03$) and fleas ($\chi 2=8.885,\ p=0.03$) more than those who lived in a province.

There was a significant difference between animal feeders and those who had never feed an animal in terms of encountering lice and ticks. According to this, animal feeders encountered lice ($\chi^2=4.128,\ p=0.04$) and ticks ($\chi 2=4.803,\ p=0.02$) more compared to those who had never feed an animal. In addition, those who were engaged in livestock farming encountered scabies ($\chi^2=5.929,\ p=0.01$) and cockroaches ($\chi^2=7.380,\ p=0.00$) more.

In terms of sex, there was a significant difference between female and male students in terms of encountering lice and bedbugs. According to this, female students encountered lice ($\chi^2=7.605,\ p=0.006$) more, while male students encountered bedbugs ($\chi^2=5.212,\ p=0.02$) more.

Of the participants, 55.2% stated that they had sufficient information about lice, 35.9% about fleas, 55.2% about ticks, 13.5% about scabies, 50.5% about cockroaches, and 11.0% about bedbugs. The source of information was close environment (54.1%), courses (34.8%) and personal experiences (40.0%) for lice; close environment (55.4%), related courses (36.6%) and personal experiences (24.7%) for fleas; close environment, related press such as TV, newspaper and courses (41.3%), internet (40.0%) and books (13.5%) for ticks; related courses (55.2%), internet, close environment (36.8%) and related press such as TV, newspaper (29.0%) for scabies; close environment (56.3%), personal experiences (46.4%) and internet (13.9%) for cockroaches; and personal experiences (46.4%), internet (25.8%) and related courses (19.3%) for bedbugs.

The ratio of recognizing insects/mites given in images was 34.8% for lice, 65.1% for cockroaches, 29.1% for fleas, 59.4% for ticks, and 16.4% for bedbugs.

3.3.Evaluation of Participants' Knowledge Levels on Insects and Mites According to Their Status of Encountering and Educational Status

The students were given propositions about the insects/mites such as their appearances, characteristics, diseases

Table 2. *The Ratio of encountering insects and mites in daily life*

Insects and Mites	Status of Encountering				I saw on my body/in my environment *		I saw on somebody else's body/in another environment*		I can recognize		I cannot recognize	
	Yes		No		N	%	N	%	N	%	N	%
	N	%	N	%								
Lice	158	56.2	123	43.8	83	52.5	93	58.9	108	38.4	173	61.6
Fleas	116	41.3	165	58.7	37	31.9	87	75.0	83	29.5	198	70.5
Ticks	92	32.7	191	67.3	16	17.3	87	94.5	97	34.5	184	65.5
Scabies	13	4.6	268	95.4	1	7.7	12	92.3	6	2.1	275	97.9
Cockroaches	219	77.9	62	22.1	93	42.5	149	64.8	168	59.7	113	40.3
Bedbugs	50	17.8	231	82.2	20	40.0	36	72.0	27	9.6	254	90.4

** Multiple options were selected.*

they carry, and struggling methods and they were asked to answer them as true/false/I do not know. The answer "true" was evaluated as "1 point" and the answers "false" and "I do not know" were evaluated as "0 points". The mean scores of "true" answers given by the students to the propositions on insects and mites were given in Table 3. Accordingly, the most correct answers given to the propositions were about lice. The second most correct answers were given about ticks. The lowest score was obtained about bedbugs.

Table 3. *Mean knowledge scores of students on insects and mites*

Insect/ Mite	Number of Students (N)	Max Score	Mean ±SD	%
Lice	281	13.0	8.03±2.54	61.8
Fleas	281	6.0	2.97±1.46	49.5
Scabies	281	8.0	3.66±2.55	45.7
Ticks	281	10.0	5.80±2.43	58.0
Bedbugs	281	7.0	2.59±2.18	37.0
Cockroaches	281	8.0	3.76±2.20	47.0

No significant difference was found between midwifery and nursing departments in terms of knowledge scores on insects and mites.

Animal feeders had a higher knowledge level on lice (χ^2=8.519, p=0.000), ticks (χ^2=6.071, p=0.04), and cockroaches (χ^2=4.006, p=0.04). Knowledge score about lice was higher in those who were engaged in livestock farming (χ^2=8.857, p=0.02).

Knowledge scores according to the status of encountering insects and mites were given in Table 4. Except for scabies, those who encountered insects and mites in their daily lives had higher scores than those who did not.

Table 4. *Mean knowledge scores of students according to their statuses of encountering insects and mites*

Insect/ Mite	Encounter	N	X	SD	t	P
Lice	Yes	158	8.49	2.35	-3.514	0.001
	No	123	7.43	2.67		
Fleas	Yes	116	3.25	1.39	-2.731	0.007
	No	165	2.77	1.48		
Scabies	Yes	13	4.69	2.32	-1.483	0.139
	No	268	3.61	2.55		
Ticks	Yes	92	6.36	2.26	-2.727	0.007
	No	189	5.53	2.47		
Bedbugs	Yes	50	4.04	1.85	-5.928	<0.001
	No	231	2.27	2.13		
Cockroaches	Yes	217	4.07	2.06	-4.336	<0.001
	No	64	2.65	2.31		

When the first-graders and fourth-graders were compared in terms of mean knowledge scores on insects and mites, fourth-graders were found to have higher knowledge scores on lice (χ^2=9.240, p=0.00), fleas (χ^2=3.216, p=0.01), scabies (χ^2=4.488, p=0.00), ticks (χ^2=6.208, p=0.01). The students who received training on insects and mites during their education had higher knowledge scores on insects and mites than those who did not receive (Table 5).

Tablo 5. *Mean knowledge scores of students according to their statuses of receiving training on insects and mites*

Insect/ Mite	Training	N	X	SD	t	P
Lice	Yes	147	8.87	2.56	-6.257	<0.001
	No	134	7.10	2.18		
Fleas	Yes	146	3.38	1.46	-5.063	<0.001
	No	135	2.93	1.33		
Scabies	Yes	146	4.33	2.61	-4.787	<0.001
	No	135	2.93	2.26		
Ticks	Yes	146	6.68	2.15	-6.763	<0.001
	No	135	4.84	2.36		
Bedbugs	Yes	146	3.30	2.16	-5.995	<0.001
	No	135	1.82	1.94		
Cockroaches	Yes	146	4.30	2.09	-4.403	<0.001
	No	135	3.17	2.16		

The ratio of known struggling methods for insects and mites was 72.2% for lice. 6.5% of the answers were common struggling methods such as gas oil, vinegar, garlic, and aspirin.

The ratio of known struggling methods for fleas was 37.4% and 2.9% of those were common methods such as diesel oil and vinegar. The ratio of known struggling methods for ticks was 40.9% and 19.3% of the respondents stated that when encountered a tick, the one should apply to a health care facility and 14.5% stated personal protective measures such as wearing long clothes in green areas. 4.8% of the respondents gave incorrect answers such as removing the tick with tweezers, burning, using bleach. The ratio of known struggling methods was 18.1% for scabies, 41.3% for cockroaches, and 23.8% for bedbugs.

4.DISCUSSION

This study aimed to determine the knowledge and experiences of students, who were health personnel candidates, on lice, fleas, scabies, ticks, bedbugs, and cockroaches that they may frequently encounter in the field. Because vector-borne diseases cause significant morbidity and mortality worldwide (13). In recent years, there has been a striking change in the geographical and host areas and diseases of many vector-borne pathogens, generally due to climate change and destruction of wild habitats (12). This means that the geographical spread of mites and insects is expanding, and their life cycle processes are changing. Thus, the incidence of vector-transmitted diseases may increase due to their large scale spread.

With the health reform that started in 2003 in Turkey, the family practice system has been realized and spread all over the country by 2010. With the family practice system, midwives and nurses take an important role in the functioning of the primary health care system together with family physicians (22). Nurses and midwives can consult all individuals, families, and community who are in need in terms of health whether they are sick or healthy at any level of age (23). Consultancy of health personnel becomes more important, especially in rural areas. In this study, those who lived in rural areas and those who were engaged in livestock

farming encountered insects and mites more. From this point, it becomes more important for health personnel to have knowledge about infections that can be encountered frequently in rural areas and that are caused by insects and mites and diagnosis, treatment and prevention methods. Otherwise, health professionals who are unaware of the presence of these infections generally postpone the diagnosis and treatment and therefore these infections are often ignored when determining the cause of a patient's disease (12). Similar to the other studies conducted in Turkey, female students in this study encountered lice more and the most encountered insect on students' bodies was lice (24). Lice are ectoparasites, can be transmitted by direct human-to-human contact, and can easily cause epidemics. Pediculosis is an important health problem for primary school-age children in Turkey and in many parts of the world, including developed countries (25). Although lice infestation is less common in Turkey, it is still confronted today (26). The studies conducted on lice in Turkey are generally the review articles and focus on prevalence (24). In order to prevent lice infestations, it is recommended to make screenings at regular intervals (27). However, there is no study found describing the knowledge level of health personnel on lice. Therefore, similar studies to be conducted with health personnel are required.

In this study, participants stated that the least encountered one was scabies. Only one female student reported that she had scabies. Similarly, there are a limited number of studies on scabies that determine its prevalence in Turkey (26). The prevalence of scabies worldwide is unknown (28).

Studies conducted on fleas in Turkey mostly include animals (29). Likewise, studies on fleas in the world have been generally conducted on animals (30; 31).

The lowest knowledge score of the participants was on bedbugs. In a similar study, it was found that 70% of people who live at homes where there was bedbug infestation were unaware of the presence of bedbug (32).There are few studies conducted in Turkey on bed bug (Cimex lectularius) (33).

The participants encountered cockroaches the most in their daily lives (77.9%) and stated that they would recognize cockroaches the most when they saw one. Likewise, in the studies conducted in the world, participants stated that they encountered cockroaches in their houses ranging from 50% to 81.5% (34,35). Studies in Turkey mostly focuses on the allergenic aspect of cockroaches (36).

The importance of ticks has increased in Turkey, especially with the detection of cases of Crimean-Congo Hemorrhagic Fever. In Turkey, especially since 2006, there been an obvious increase in the number of cases, almost 5% of the cases were fatal (37). This situation has caused the printed and visual media and the Ministry of Health to focus more on the issue. In our study, the students stated that they had the highest knowledge level on ticks as well as lice. Similarly, the sources that students learn about ticks the most are the press such as television and newspapers and the close environment.

Participants' sources of information about insects and mites were generally the experiences they gained by themselves or from their close environment and the training they received.

It is crucial for healthcare professional candidates to properly know medical methods in the struggle against insects and mites. In the struggle against pediculosis it is of particular importance to do checking regularly, obey the personal hygiene rules, change clothes and bedclothes regularly and use products such as shampoo, lotion and cream against pediculosis (38). In the struggle against pediculosis our study also gave traditional, and mis known answers like gas oil, vinegar, garlic, and aspirin use. Scabies is an easily transmitted illness, and it spreads quickly in bad hygiene conditions and crowded spaces. In the struggle against scabies, it is of prime importance to know the symptoms properly, make true diagnosis and treat the patient and his/her relatives. The patient's clothes and bedclothes should be washed properly (17). In the struggle against flea, it is of prime importance to vacuum the environment properly, have the pets checked, cleaned, and treated regularly and wash the patient's clothes (39). In the struggle against flea our study also gave traditional, and mis known answers like diesel and vinegar. In the struggle against bedbugs appropriate insecticides should be applied for beds and floorings (40). The use of chemical insecticides in the struggle against cockroaches has not been chosen in recent years because of their harm to the environment, humans and other creatures and the resistance of the insects (41). Instead, boric acid and insecticide-containing jelly feed have been used in recent years (42). Also, the use of entomopathogen isolate against cockroaches is becoming widespread (43). In the struggle against ticks the people who live in endemic areas or travel to these areas should pay a particular attention to personal protection. Ticks are usually active between October-April. People should take precautions such as keeping away from areas like grasslands, waterfronts, forests, animal shelters or wearing long-sleeve and light-colored clothes, socks, gumboots and putting the trotters into the socks (44). It is necessary to often check the body and clothes for ticks and immediately remove the tick using fine-tipped pliers or tweezers near the mouth area in an upward position without breaking off and crushing the head or apply to the nearest healthcare organization. Bug-repellents should be used against tick attacks. It is of particular importance to disinfect animal shelters with acaricides and calcimine them with lime (45). In the struggle against ticks our study gave traditional and misknown answers like burning, using bleacher and removing the tick via hands or tweezers without paying attention to its integrity. Fact that the medical personnel candidates also mentioned traditional and misknown methods regarding the methods of struggle against bugs and mites, demonstrates that experiences also play an important part in learning and unless supported with education they may lead to incorrect and/or inadequate learning. The fact that the ratio of those who thought that they had sufficient information about insects/mites and the ratio of recognizing insects/mites given in images were low supports this situation. Likewise, the mean scores of

participants for propositions about insects and mites were low. In this study, the prominent finding was that knowledge of insects and mites was obtained through experiences and training. It cannot be expected that students have experience for each insect/mite, but they can be taught through courses. In relevant courses, they should be provided real insects and mites, and students should be given the opportunity to examine insects and mites. For this purpose, laboratory practices should be provided with the courses and students should also be allowed to do an internship in rural areas. Because even if students encounter insects and mites in their daily lives, their knowledge will remain insufficient unless supported by theoretical knowledge.

Considering the rapid increase and aging of information, which is the characteristic feature of the information age, nowadays, professional midwifery/nursing education should have the characteristics in a way that it can provide continuous development and adaptation to innovations through effective learning. This necessitates the selection of effective learning methods that will enable learning through experiences in the teaching-learning environment (46).

Strengths and Limitations

The strength of this study is that it is the first comprehensive study that determines the knowledge levels of students, who will be health personnel in Turkey, on commonly encountered insects and mites. The research cannot be generalized since it included only the students of the school of health in a university.

5. CONCLUSIONS

Today's changing conditions have increased the risk of confronting epidemics related to insects and mites at any time. It is highly important for health personnel, who are actively involved in epidemics and who consult the community, to receive effective training on insects and mites. Therefore, the curriculum should be reviewed, appropriate laboratory conditions should be established, and students should be ensured to gain experience through internships. There are limited studies on this topic; therefore, further scientific studies are required.

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Clinical and Experimental Health Sciences

The Effect of Mobile Application Support for Postpartum Women on Postpartum Quality of Life

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ABSTRACT

Objective: This study aims to determine the effect of a mobile application prepared by midwives on postpartum quality of life, and to present a mobile training method for use by health care professionals.

Methods: The sample for this randomized controlled study consisted of 64 (experimental group = 32, control group = 32) postpartum women for whom inclusion criteria for participation in the study were that they presented to a private counseling center had the ability to use the internet and mobile applications. The study was conducted between March 1, 2018 and July 15, 2019. Data were collected using the Maternal Postpartum Quality of Life Questionnaire (MAPPQOL) and the Web-based Education Software Scale (WBESS) to gather descriptive characteristics of the participants and obstetric data. Applicable statistical methods, which included Mann-Whitney U test, and Spearman correlation test.

Results: The mean scores on the MAPPQOL for the control and experimental group were 21.99 ± 2.97 and 20.30 ± 4.33. There was nostatistically significant difference between the mean scores obtained by the two groups on the MAPPQOL ($p = 0.073$; $p > 0.05$). Furthermore, there was no statistically significant relationship between the mean scores on the total MAPPQOL and the mean MAPPQOL subscale scores of the experimental group and the mean scores on the WBESS and the subscale scores of this scale ($p > 0.05$). It was found that the experimental group's competence level of the mobile application (62.5 %, n = 32) was very good according to their WBESS mean score.

Conclusion: Postpartum quality of life score swere found to be higher in the postpartum patients who used the mobile application and it was observed that mobile application support increased postpartum quality of life. The scope was found to be valid this comprehensive mobile training model can be in recommended for use midwifery applications.

Keywords: Midwifery, mobile application, mobile health, postpartum, postpartum quality of life, innovation in midwifery

1. INTRODUCTION

The postpartum period is considered to be a period of critical importance for the mother, baby and family (1,2,3). In recent years, guidelines have been updated and technological developments have been used to reduce maternal / neonatal mortality and morbidity rates during this critical period (4,5).

Mobile technologies are recognized as being one of the fastest-adopted technologies in human history and they have had a strong impact on society as a whole by providing cost-effective communication (6). The use of technology is seen as a promising innovation that can revolutionize the public's access to health care, the provision of quality health care and cost-effectiveness (7).

Mobile health (mHealth) is defined as "health services provided through mobile communication devices". The WHO defines it as "complementary and innovative health practices, executed through the widespread mobile communications technology and in frastructure, with beneficial contributions that serve to improve the effectiveness and function of the current health system via its numerous capacities, such as health promotion, remote disease management, health data collection and early warning system" (8,9).

The mobile health applications prepared by midwives have been shown to increase efficiency and effectiveness of care, to provide motivation and to serve as an important information source. They support clinical decision making, alleviate administrative burdens and increase the speed of data collection to be used for evaluation (10). The applications also enable midwives to reach the mother in time and to provide them with consistent, evidence-based information (11, 12).

Every parent has unique learning needs, depending on the situation, so the training materials provided must be personalized. Moreover, early discharge after birth may not give postpartum women the opportunity to acquire

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booklets or brochures regarding the care of newborn babies (13). For this reason, the use of downloadable applications for postpartum women and their spouses that feature information on the postpartum period and newborn care, breastfeeding training, general information, videos, visuals and one-to-one consultation with midwives may help them to beter adapt to their roles as mother and father, increase their quality of life, develop their self-care skills, increase their health levels and give them confidence on account of the constant reassurance that their midwives are with them. Shorey (2018) reported that their mobile application **"at home but not alone"** gave the parents the feeling of being part of a virtual community outside the hospital, the feeling of not being alone in this process and being helped by a midwife through out the postpartum period, which simultaneously made them feel safe (7).

In summary, in the postpartum period, which is considered a stressful and critical transition period, mothers can be provided with postpartum support by midwives through mobile applications, whereby their quality of life will be improved by ensuring they undergo a positive and healthy experience during this challenging period. To date, there have been no experimental mobile application studies specific to the postpartum period that have been conducted in any country worldwide, including Turkey. Therefore, being the first of its kind, this study is important for the literature, as it aims to determine the effect of a mobile application, prepared by midwives and used in the postpartum period, on the quality of life in the postpartum period and to provide a mobile training method for health professionals.

2. METHODS

2.1. Design and Sample

The study was designed as a randomized controlled study and was carried out at a private pregnancy, childbirth and postpartum counseling clinic in the province of Istanbul in Turkey from 01.05.2019 to 15.06.2019 with 64 postpartum women. The inclusion criteria for participation in the study were that the women be postpartum, between the ages of 18 and 40 years, experiencing their first, spontaneous single delivery, have no communication difficulties, no chronic diseases, no psychiatric diseases and no obstetric risks (diabetes, pre-eclampsia, PEM etc.), and be able to read and use the internet and mobile applications. The study flow diagram is presented in Figure 1.

Ethics committee approval, numbered KU-GOKAEK 2018/121 and dated 21.03.2018, was received prior to the study. Randomizations were performed at https://www.random.org on 11.01.2019. Numbers, like 61, 15, 52, 22…. are included into the experimental group.

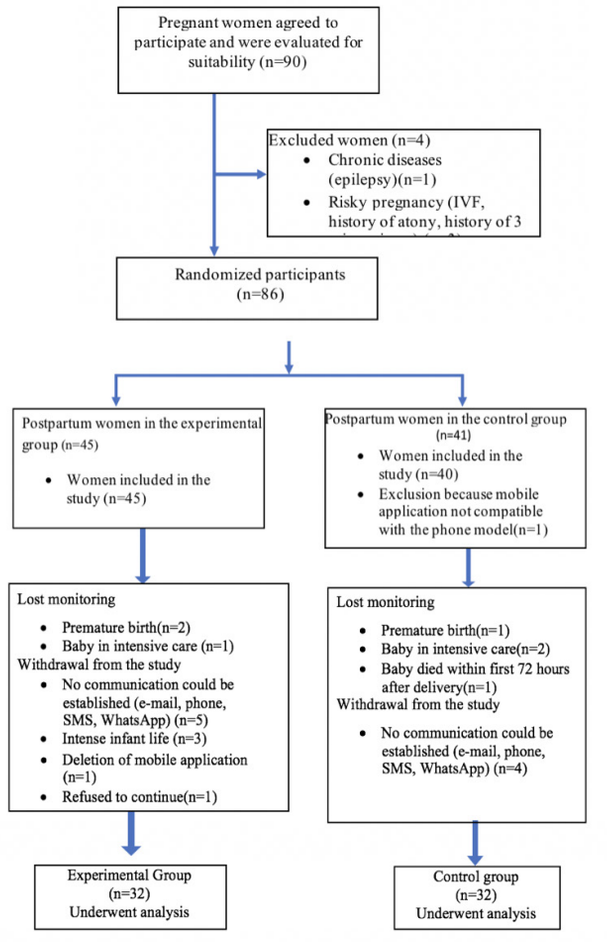

Figure 1: *The study flow diagram*

2.2. Instruments

The study data were obtained through a questionnaire consisting of 41 question sprepared by the researchers in accordance with the literature, an information booklet containing educational content to be included in the mobile application, theTraining Material Evaluation Form, a web-based education software scale and the Maternal Postpartum Quality of Life Questionnaire.

A web-based education software scale developed by Fiş Erümit in 2011, 23 items collected under four factors, and is used to evaluate Web Based Training materials. The items in the scale are structured as " strongly agree", " agree", " indecisive", " disagree" and " strongly disagree". Cronbach Alpha value of the scale was found to be 0.915 and its reliability was found to be acceptable (15).

The training material prepared by there searchers and the" Training Material Evaluation Form", prepared by Top in 2012, were sent to 12 experts and edited in line with their expert recommendations (16). The experts results were evaluated with the Kendall's coefficient of concordance test, from which a significant relationship was found (W=0.413, $\chi 2$=63.565 and SD=11, p 0.001), indicating that the experts' opinions were compatible with one another. The validity scale for the

scope of the training material, which was developed by Hill et al. (2006) and whose study on validity and reliability for use in Turkey was conducted by Altuntuğ and Ege (2012), was used in this study (17,18). The scale includes 40 items, arranged under 5 subdimensions, and is applied to determine postpartum quality of life according to the perception of the mother. The Cronbach's alpha value was determined to be 0.95(18). Prior to the study, permission to use the scale was granted by the original authors for the evaluation of the postpartum quality of life of the participating women. The educational content related to the health of the mother, baby and father was transferred to the mobile application.

In addition, to determine whether the questionnaire was comprehensible or not, 10 postpartum women under went a pre-application. The data derived from this pre-application, however, was not included in the study.

2.3. Data Collection

The mobile application was developed with the support of a software development company. The most important features of this mobile applicationarethat it is user-friendly, easy to understand, providing information content with training videos and providing one-to-one online message support to puerperant women and using it for IOS and Android operating systems. The researchers prepared the educational material, visuals and videos and questionnaires, scales and visuals were added to the mobile application, which was started after user and developer software tests were carried out (Figure 2). Users in experimental group supported with three catagories which are mother – father and newborn. For Mother: postpartum changes, mental changes, self-care of mother, breastfeeding, sexual health, reproductive health, postpartum exercise, maternal nutrician, emergency case, mother-baby attachment etc. For Father: role adaptation, participation to baby care, comminication with partner and sexual health etc. Newborn: newborn physiological characteristics, newborn care, breasfeeding, vaccine, common problems, baby development, emergency cases etc. The contents are enriched with videos that facilitate the application. For example; bath, diaper changes, breastfeeding and other problems etc. Online midwife support for questions of experimental groups.

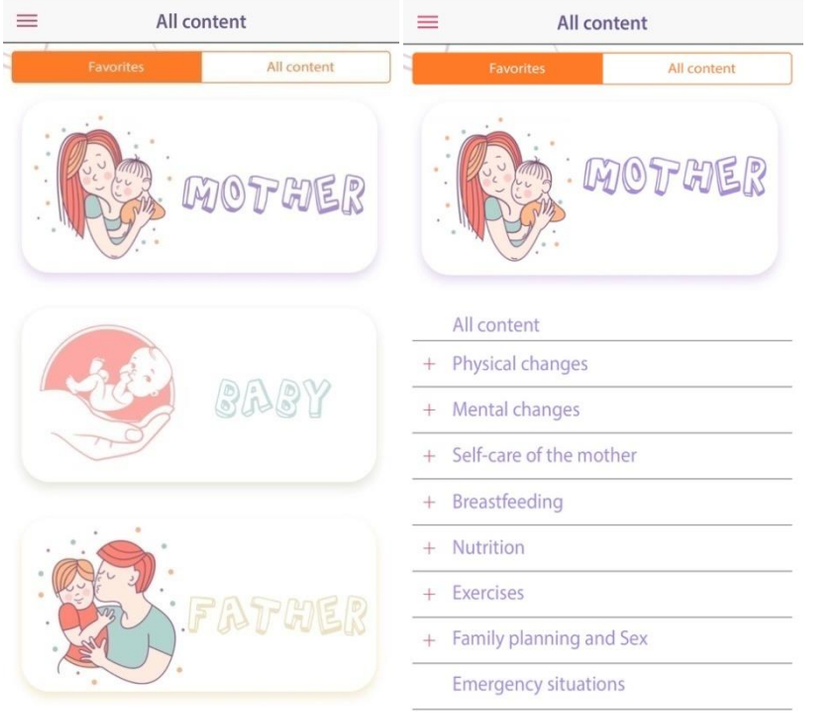

Figure 2. *Mobile application image (prepared by Pınar Mallı)*

Application steps for the experimental group:

1. Get acquainted with the pregnant women after the 30th week of pregnancy via phoneor video call; explainthecontent of the study; request information from the participating pregnant women on their mailing address, phone number and expected delivery date; and record this information,

2. Enter the contact information of the pregnant women who were selected to be part of the experimental group by randomization on to the mobile application admin panel; and send an information form and download link on how touse the mobile application,

3. Downloading of the application before delivery date,

4.Create the username and password for the pregnant women on the day of birth; distribute electronically informed consent; and login to the mobile application and choose the type of birth,

5. Submit a photo of the bracelet worn in the hospital to the study supervisor to preventf alse login; and login to the user account from the mobile application admin panel through the authentication process performed with the submitted photo,

6. Re-login of the user on to the mobile application,

7. Fill out the socio-demographic questionnaire,

8. Read and watch the educational material and contact the mobile application manager for consultation purposes via the "ask your midwife" tab, located under each subject content,

9. Fill out the Quality of Life scale six weeks after givin gbirth,

10. With the completion of the web-based education software scale, the study is concluded.

The postpartum women in the experimental group were provided with educational content via a mobile application for six weeks.

The control group was asked to login to the mobile application and fill out the questionnaire and postpartum quality of life scales. All materials that were prepared for the experimental groupwere sent to the control group via e-mail to ensure similar information.

After this process, the entries of the experimental and control groups were completed between 01.05.2019 and 24.07.2019 and later. The study was produced from a project, access to the software was granted till a month after the project ended. (Last access date: 1.09.2020)

2.4. Ethical Considerations

The study was approved by the Ethics Committee (Approval Date: KU-GOKAEK 2018/121) and conducted according to the ethics guidelines established in the Declaration of Helsinki. Written consent was obtained from patients who agreed to enroll in the study. All participants were informed about the purpose and design of the study.

2.5. Statistical Analysis

For statistical analysis, NCSS (Number Cruncher System) 2007 (Kaysville, Utah, USA) software was used. During evaluation of the data, descriptive statistical methods such as mean, standard deviation, median, frequency and percentage. Regular distribution of quantitate data was tested by Sapiro-Wilk test and analysis of the graphical outputs. Comparative analysis of the quantitative data displaying normal distribution between two groups was performed with Student t test, while quantitative data that did not display normal distribution was evaluated with Mann-Whitney U test. Comparative analysis of the quantitative data displaying normal distribution among the three or more groups was performed with OnewayAnova test and for dual comparisons Benforroni test was used. Comparative analysis of the quantitative data that did not display normal distribution among the three or more groups was performed with Kruskal Wallis test and dual comparisons Benforroni test was used. For comparison of qualitative data Chi-square test, Fisher's Exact test and Fisher-Freeman-Halton test were used. To evaluate the correlations among the qualitative variants, Pearson Correlation and Spearman's correlation analyses were used. For evaluation of the validity of education materials, Kendall correlation analysis was performed. P<0.05 was accepted to be statistically meaningful.

3. RESULTS

The meanage of the participants was 29.72±3.74, with a ranged of 20 to 38 years, and the mean duration of marriage was 3.03±1.99 years, with a range of 1 to 9 years. Other descriptive characteristics are given in Table 1.

Table 1. *Socio-demographic characteristics of the participants*

	Experimental group (n=32) n (%)	Control group (n=32) n (%)	*P Value*
Age (years)			
Min-Max (median)	**22-38 (30.5)**	**20-36 (29)**	[a]***0.289***
Mean+SD	**30.22±3.80**	**29.22±3.68**	
Marriage duration (years)			
Min-Max (median)	**1-9 (3)**	**1-9 (2)**	[b]***0.133***
Mean+SD	**3.34±2.04**	**2.72±1.92**	
Educational Status			
High School	**4 (12.5)**	**2 (6.3)**	[c]***0.672***
University	**28 (87.5)**	**30 (93.8)**	
Occupation			
Housewife	**7 (21.9)**	**4 (12.5)**	
Worker-Freelancer	**5 (15.6)**	**1 (3.1)**	[d]***0 .040****
Civil servant	**4 (12.5)**	**13 (40.6)**	
Other	**16 (50.0)**	**14 (43.8)**	
Economic Status			
Income is less/equal to expenses	**23 (71.9)**	**27 (84.4)**	[e]***0.226***
Income is more than expenses	**9 (28.1)**	**5 (15.6)**	
Family type			
Nuclear family	**32 (100)**	**30 (93.8)**	[c]***0.492***
Extended family	**0 (0)**	**2 (6.3)**	

[a]Student t Test [b]Mann Whitney U Test [c]Fisher's Exact Test
[d]Fisher Freeman Halton Test [e]Pearson Chi-Square Test
**p<0.05*

Among the participants, 90.6 % (n=58) stated that their pregnancy was planned and 95.3% (n=61) said that they wanted this pregnancy. In addition, 50 % (n=32) had a normal birth and 50 % (n=32), a cesarean section (Table 2). When examining the newborn characteristics, it was observed that their gestation weeks varied from 37 to 42 weeks, with the mean being 38.91±1.18 weeks.

***Table 2.Comparison** of obstetric characteristics of participants*

	Experimental group (n=32) n (%)	Control group (n=32) n (%)	*P Value*
Planned pregnancy			
Yes	27 (84.4)	31 (96.9)	[c]***0.196***
No	5 (15.6)	1 (3.1)	
Wanted pregnancy			
Yes	31 (96.9)	30 (93.8)	[c]***1.000***
No	1 (3.1)	2 (6.2)	
Latest type of birth			
Normal birth	16 (50.0)	16 (50.0)	[e]***1.000***
Cesarean section	16 (50.0)	16 (50.0)	
Satisfied with the type of birth			
Yes	29 (90.6)	24 (75.0)	[c]***0.098***
No	3 (9.4)	8 (25.0)	
Sufficient help from the spouse during pregnancy and birth			
Yes	29 (90.6)	24 (75.0)	[e]***0.098***
Partial/No	3 (9.4)	8 (25.0)	

[c]Fisher's Exact Test, [d] Fisher Freeman Halton Test, [e] Pearson Chi-Square Test

The participants' internet usage durations varied between 3 and 23 years and had a mean value of 12.97±4.14 years. There was no significant difference between the groups in terms of internet usage duration, time spent online, purpose of internet use and web pages found to have reliable information (p>0.05) (Table 3).

The Cronbach's alpha coefficients of the MAPPQOL subdimensions were 0.848, 0.811, 0.694, 0.843 and 0.876, respectively. The total Cronbach's alpha coefficient of the MAPPQOL scale was 0.944 and the scale was foundto be highly reliable (Table 4).

In examining the MAPPQOL sub dimensions, the "kinship-family-friend/relationship" score varied from 4.3 to 26.2, with a mean of 18.38±4.44, the "socio-economic" score varied from 12.8 to 29.4, with a mean of 23.63±3.66, "spouse/ relationship"score varied from 8.4 to 30, with a mean of 24.47±4.21, the "health/functionality" score varied from 1.5 to 28.8, with a mean of 19.57±5.18, the "psychological/baby" score varied from 6.8 to 29.7, with a mean of 21.31±5.00 and the total score varied from 6.7 to 27.9, with a mean of 21.15±3.78.

***Table 3.**Comparison of the results of regarding internet use*

	Experimentalgroup (n=32) n (%)	Control group (n=32) n (%)	*P value*
Duration of internet use (years)			
Min-Max (median)	5-20 (14)	3-23 (13)	[b]***0.924***
Mean+SD	13.06±4.06	12.88±4.28	
Time spent online			
1 hour a day	2 (6.3)	4 (12.5)	
2 hours a day	11 (34.4)	6 (18.8)	[d]***0.435***
3 hours a day	10 (31.3)	14 (43.8)	
4 hours a dayormore	9 (28.1)	8 (25)	
Purpose of internet use			
Communication	28 (87.5)	32 (100)	[c]***0.113***
Knowledge acquisition	30 (93.8)	32 (100)	[c]***0.492***
Confirming the reliability of information	17 (53.1)	21 (65.6)	[e]***0.309***
Scientific studies/ Work	19 (59.4)	20 (62.5)	[e]***0.798***
Other	8 (25.0)	9 (28.1)	[e]***0.777***
Web pages found to have reliable information			
Sites of official institutions	28 (87.5)	27 (84.4)	[c]***1.000***
Sites of experts	31 (96.9)	30 (93.8)	[c]***1.000***
Blogs	12 (37.5)	8 (25.0)	[e]***0.281***
Other	2 (6.3)	1 (3.1)	[c]***1.000***

•More than one answer was given. [b]Mann Whitney U Test [c] Fisher's Exact Test [d]Fisher Freeman Halton Test, [e] Pearson Chi-Square Test

***Table 4.** Distribution of postpartum quality of life scale scores*

	Number of questions	Score range on the scale	Min-Max (median)	Mean (SD) [a]	Cronbach's alpha
Kinship-Family-Friend /relationship	10	0-30	4.3-26.2 (19.5)	18.38(4.44)	**0.848**
Socio-economic	9	0-30	12.8-29.4 (24.1)	23.63(3.66)	**0.811**
Relationship with spouse	5	0-30	8.4-30 (25.2)	24.47(4.21)	**0.694**
Health/ functionality	8	0-30	1.5-28.8 (20.3)	19.57(5.18)	**0.843**
Psychological/ baby	8	0-30	6.8-29.7 (22.5)	21.31(5.00)	**0.876**
Total	40	0-30	6.7-27.9 (21.8)	21.15(3.78)	**0.944**

[a] 6 point Likert scale with anchors of 1 = very dissatisfied and 6= very satisfied

In Table 5, the MAPPQOL scores of the participants were compared in terms of groups. No statistical significance could be found in terms of the relationship between kinship-family-friend/relationship, socio-economic and psychological/babyscores (p>0.05). However, the spouse/relationship scores were statistically significant (p=0.044; p<0.05) and the scores obtained by the experimental group were found to be higher.

Table 5. *Distribution of web-based education software scale scores*

	Number of questions	Score range on the scale	Min-Max (median)	Mean (SD) [a]	Cronbach's alpha
Educational compliance	8	1-5	2.9-5 (4.5)	4.38(0.60)	**0.917**
Compliance with the training program	4	1-5	2.8-5 (4.5)	4.34(0.61)	**0.875**
Visual sufficiency	5	1-5	2.8-5 (4.4)	4.36(0.60)	**0.868**
Programming compatibility	6	1-5	2.5-5 (4.5)	4.33(0.68)	**0.925**
Total	23	1-5	2.9-5 (4.4)	4.35(0.58)	**0.970**

[a] 5 point Likert scale with anchors of 1 = strongly agree and 6= strongly disagree

A statistically significant difference was found between the groups in terms of health/functionality (p=0.044; p<0.05), with the scores of the experimental group being higher (Table 5). While there was no statistical difference between the two groups in terms of the MAPPQOL total score (p=0.073; p>0.05), the scores of the experimental group were nonetheless higher than those of the control group.

The Cronbach's alpha coefficients of the WBESS subdimensions were 0.917, 0.875, 0.868 and 0.925, respectively. The total WBESS Cronbach's alpha coefficient was found to be 0.970 and the scale was found to be highly reliable (Table 5). No significant relationships between the MAPPQOL total score and subdimension scores and the WBESS total score and subdimension scores were determined between the groups (p>0.05).

4. DISCUSSION

In this study, which aimed to determine the effect of a mobile application prepared by midwives on the quality of life during the postpartum period and to present a mobile training method for health workers, it was found that the participants in the experimental group had, on average, been internet users for 13.06 years, while those in the control group had been users for an average of 12.88±4.28 years (Table 3). In a study, involving pregnant and postpartum women that was carried out in Turkey in 2016, 56.7% of the women were reported to be internet users (19). Furthermore, a study carried out in America in 2015 with 100 pregnant women of different ethnicities reported that the internet usage rate was 94% (20). The Internet andTechnology PEW Research Center (2019) determined that the internet usage rate of adults in America in the year 2000, when it began to systematically monitor internet usage, was 52%. This number rose to 90 % in 2019 and it was reported that the usage rate among women alone was 91% (21). In Turkey, the internet usage rate of women was only 12.1% in 2014 but increased to 65.5% in 2018 (22). A study conducted with pregnant women in 2018 reported that 98.5% had been using the internet for between 6-10 years and 1.5% for 0-5 years (23). The internet usage rate results from the current study are similar to those reported by other studies. When examining the daily amount of time spent online it was determined that 34.4% (n=11) of those in the experimental group spent 2 hours online daily and that 43.8% (n=14) spent 3 hours online per day (Table 3).

Osma (2016) reported that 45.9% spent 0 to 2 hours daily online, 25% spent 2 to 4 hours, 10.6% spent 4 to 6 hours and 18.5% spent more than 6 hours online daily (19). The current study's results showed a higher duration spent online in the experimental group compared to that of the control group, which was an expected result. In general, internet use rates were high, a result consistent with the literature.

When examining the internet usage purposes, it was determined that most of the postpartum women in the experimental group, 93.8% (n=30), used it for knowledge acquisition, while 87.5% (n=28) used it for communication. In the control group, all participants (n=32) stated that they used it for information and communication purposes. In the study conducted by Baker and Yang in 2018 with 117 mothers, it was reported that 44% of the mothers spent time on social media sites or blogs, while the remainder of them used the internet for communication; furthermore, the same study found that 89% viewed their friends on social media networks as a kind of social support and that the women used the internet both for a source of knowledge and for social support (24). A study involving 134 pregnant women reported that 76.1% used the internet for "social networks/ shopping /knowledge acquisition", 35.1% did not think they had sufficient knowledge and 29.9 % used it to retrieve information quickly since they had difficulties in reaching health personnel.[23] The Household Information Technologies (IT) usage research report of 2017 showed that 28.6 % of women in that year and 31% of women in 2018 used the internet to acquire knowledge and information from websites of public institutions.[22]Women in the postpartum period need more information and support, which may be the reason for the high internet usage rates.

During the postpartum period, mothers face many challenges and difficulties in providing care for themselves and their babies and these situations affect the quality of

life after delivery. (25). No significant difference between the two groups was observed in their total quality of life scores (p=0.073; p>0.05), but the experimental group did have higher scores (Table 4). For the primipara in the current study's experimental group, who did not have any maternity experience, the increase of the quality of life score with the aid of midwife support via the mobile application, which helped them to adapt to the new conditions after birth and to learn the physiological changes that both the mothers and their babies would undergo, was one of the most remarkable results. While in recent years, the aim of medical care in general has been to increase quality of life, these efforts should be even more pronounced in the postpartum period. It is believed that this can be achieved with the help of mobile applications. The father category in the mobile application developed for this study, which included information for the father on how to support the spouse in terms of breastfeeding and communication suggestions, is thought to be one of the reasons behind the higher scores seen in the experimental group, as compared to those in the control group. These results show that maternal and infant health can be positively affected by spouse participation during the postpartum period.

The mobile application was assessed with the WBESS, and the mean score was determined to be 4.35±0.58. The fact that the content of the mobile application was prepared by the midwives in an unbiased manner and based on evidence is important for web-base d educational material (26,27).

The sufficiency level of the material used in the current study was evaluated as medium by 12.5% (n=4), as good by 25.0% (n=8) and as very good by 62.5% (n=32) of the participants in the experimental group. In the current study, the quality of life score of the postpartum women that used the mobile application developed by midwives was higher compared to the women that did not use it. Moreover, the very good sufficiency score that the women from the experimental group ascribed to the WBESS showed that the application positively affected the postpartum period and that the postpartum women were generally satisfied with the application.

In 2017, the mobile application "Health care beyond pregnancy", created to increase the participation rate of postpartum visits, showed that the participation rate of postpartum women who were using the application and their compliance increased (28). Again, in 2017, a systematic review titled "The Role of Mobile Health Applications", carried out to develop the field of prenatal and postnatal care in low and middle-income countries, emphasized that mobile applications, which is one form of mobile health, can improve pregnancy and postpartum care services (29-30). In a study conducted in Ghana, where midwives used a mobile application called mClinic, the midwives reported that the application was useful, easy to use and control and they definitely accepted it as an effective application (10).

A study conducted in Spain examined an application named NaïveBayes, whose aim is the early prediction and detection of postpartum depression. This application provides early intervention in postpartum depression through a simple questionnaire addressing the risk of developing postpartum depression with in the first week. The application can also be used by health professionals who want to monitor patient tests. It has been reported o be easy to use, culturally sensitive and cost-effective (30).

Throughout the world, mobile applications are usedf or different purposes for postpartum women. During the development of the mobile application tested in the current study, all these differences were taken in to consideration and technological features that others did not have were added, along with evidence-based information that was prepared by midwives. It can be said that with these features, the mobile application presented in this study proved to sufficient and successful.

Limitations

The current study did have several limitations, including primarily, a fairly small sample size of postpartum women, difficulties in data collection and planning, technical errors related to the mobile application, and limited financial opportunities. Other less striking limitations were that certain desired options within the mobile application could not be presented and that some of the postpartum women failed to continue to participate to the end of the study.

5. CONCLUSIONS

It was clearly observed that the mobile application support prepared by midwives increased the postpartum quality of life for the women who participated. The Cronbach's alpha coefficient in the current study was 0.970, which indicated that the scale is highly reliable and can be safely used by adults, in addition to students, for the assessment of material. In light of the study results, which showed that the users were very satisfied with the application, that the educational content was in agreement with expert opinions and that its scope was valid, it is believed that this application could serve as an education model for midwifery applications.

Thus, it is recommended that national and international studies conducted with the aim of supporting postpartum women and midwives focus on supporting midwives/ health professionals in creating timely and evidence-based information that pregnant and postpartum women can safely access via the internet, increasing the digital media literacy of midwives, pregnant women and postpartum women, developing studies and motivational works on this subject, spreading the use of mobile applications in this field and developing suitable equipment.

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Clinical and Experimental Health Sciences

The Effects of Continuous Labor Support by Midwife: A Randomized Controlled Trial

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ABSTRACT

Objective: The aim of this study was to evaluate the effects of continuous labor support by midwife.

Methods: This study was a randomized controlled experimental design. Seventy primipara women were randomized into two groups, the continuous labor support by midwife group (n=35) and control group (n=35). In the experiment group was given the continuous midwife support and in the control group were undergone to routine hospital care in the clinic. Visual Analog Scale was used to assess women's anxiety level and coping with labor pain. All interventions and childbirth time were recorded by the researcher.

Results: Anxiety level decreased and the level of coping with labor pain increased in the experimental group ($p<0.05$). The total childbirth time in the intervention group was shorter by 2 hours and 21 minutes. Labor induction, episiotomy, amniotomy and perineal trauma were higher in the control group ($p<0.05$).

Conclusion: Continuous labor support should be provided at each childbirth to enhance childbirth outcomes.

Keywords: Continuous labor support, randomized controlled study, midwife, childbirth, Turkey

1.INTRODUCTION

Association for the Improvement in Maternity Services (AIMS) in the United Kingdom, proposed the definition of normal childbirth the presence or absence of intervention. According to this definition, the childbirth is divided into three categories.

1. Operative or interventions childbirth (caesarean section, forceps, vacuum),
2. Obstetric childbirth (artificial rupture of membranes (ARM), prostaglandin gel, labor induction, and episiotomy)
3. Normal childbirth (1).

Normal childbirth should occur spontaneously and without intervention, and it is a process in which the mother and baby continue to live healthy (1). Thus, normal childbirth should not have a serious burden on the national economy.

According to this classification, when examining Turkey's childbirth data, unfortunately the situation does not seem very pleasant. The first group of the operative/interventions childbirth, Turkey with 52% incidence of caesarean section rate is the country with the highest caesarean section rates in the Organization for Economic Co-operation and Development (OECD). At the same time, attempts to have normal childbirths after caesarean section are limited. Thus, these high rates remain constant within the framework of a "once caesarean section, always caesarean section" philosophy. Also, it is known that elective caesarean section causes very high childbirth costs in countries (2).

Obstetric childbirth rate as a second group in the AIMS classification, is around 45 % in Turkey (2). Childbirths are performed vaginally, episiotomy applications and are often carried out using labor induction. Moreover, in Istanbul as one of Turkey's most developed and most crowded city is given the birth services by obstetricians. Although midwives

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are graduated with the skills and knowledge to manage the antenatal, innatal and postnatal processes during their four-year bachelor education, midwives in the maternity unit are often interested in documentation and organization. Whereas it is more desirable for obstetricians to participate in the management of childbirth in cases of deviation from normal and to develop themselves in this field. While obstetricians spend their effort and time by playing an active role in the normal childbirth process, but also midwives who are specially trained for this field are losing ability over time in our country. For this reason, it is not possible to give birth support to women without interruption in our country, and this care is provided by different people. Besides communication with the pregnant woman is only during examinations (dilatation, effacement, and so on.) and a very short period of communication is established with the woman. It is beyond doubt that the cost of this situation is very high.

In the last group of normal childbirth rate in Turkey it is very low. Very high-income families manage the process by receiving continuous labor support. Continuous labor support is included physical support, emotional support, information support and advocacy during labor and childbirth (3-5). Physical support is the act of directly assisting the woman in physical terms (using non-pharmacological methods of coping with pain, helping her to stand up, and so on.). Emotional support is the using expressions of emotional support, love and respect, and also contains that making them feel by their side in the whole process, making them express their feelings and establishing sentences that empower, praise and motivate the woman. Information support is providing direct information (such as duration of childbirth, effacement, dilatation, fetal head level) and positive feedback, and advocacy support refers to advocacy for women's rights on behalf of women. Also, continuous labor support includes that allowing her to stand up unless there is a risk and supporting oral intake. Besides, for the support provided to be continuous, it should cover at least 80-85% of the childbirth process and should be given by the same person (s) as much as possible (6).

This study was planned as a randomized controlled study to investigate the effects of continuous labor support. In this study, it is important because midwives have the potential to determine the effects on the labor process when they are included in the birth.

2.METHODS

2.1. Specific Objective/Hypothesis:

H1: There is a difference in the anxiety level between the experiment group and the control group.

H2: There is a difference in the level of coping with labor pain between the experiment group and the control group.

H3: There is a difference between in the interventions childbirth the experiment group and the control group.

2.2. Design:

The study was approved by the Istanbul Medeniyet University Ethics Committee of Clinical Research of Goztepe Training and Research Hospital (Date: 26.10.2017, Number:0293). Firstly, after participant's hospitalization, pregnant women were informed about the study by the researcher. Experiment or control group discrimination was provided for those who agreed to participate in the study. The trial was reported according to the CONSORT guidelines (Figure 1).

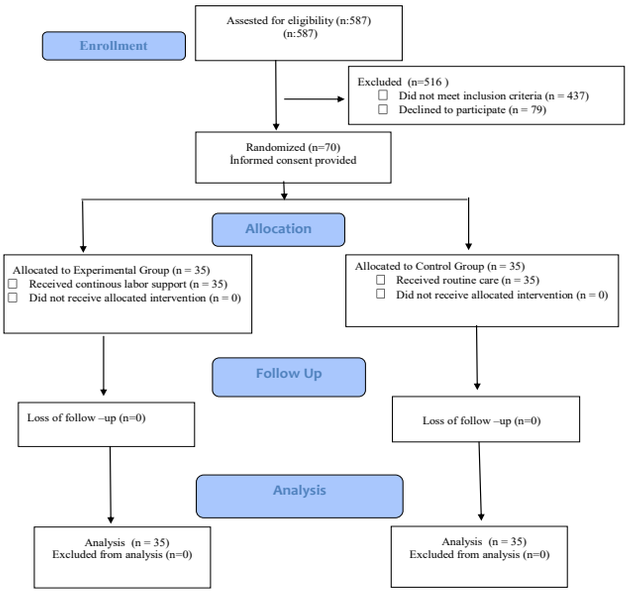

Fig. 1: *CONSORT flow diagram*

Data were collected from primipara pregnant women who were recruited from the Gynecology and Obstetrics Clinic of Goztepe Training and Research Hospital between November 2017 and May 2018, through a randomized controlled experimental study. The aim of this study is to examine the effect of continuous labor support on childbirth outcomes. With a power of 0.8 and an acceptable Type I α error size of 0.05, each group required 35 participants. The women were single-blind randomized into two groups, the experiment and control.

The primary aim of this study was to evaluate the effect of continuous labor support anxiety level and coping with labor pain level using Visual Analog Skala (VAS). The validity and reliability of VAS in all cultures has been established and is also a very easily applicable scale (7). VAS is a valid and reliable scale in all cultures and can be applied very easily. In this study, a 10 cm VAS was used and based on the woman's hand marking. Childbirth interventions and perineal trauma related to childbirth were made by marking "present" or "absent". Childbirth time recorded by researcher. The research flow is given in Figure 2.

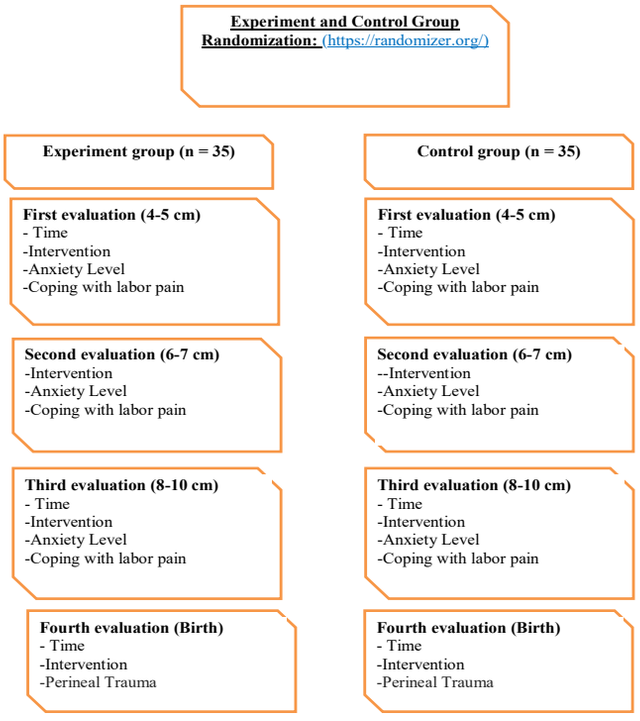

Fig. 2: *Research Flow Chart*

Care services are provided in reserved rooms for every pregnant woman in this hospital. The women in the experiment group were given individualized continuous labor support consisting of four components from the active phase to the birth moment. Furthermore, it was ensured that the majority of the women's time was spent with the midwife. Emotional support was tried to be given, in order to create a feeling of being safety atmosphere and comfort in the pregnant woman, to make the woman feel that she was being cared for and to create the feeling that she was in control of the process. For physical support the birth room was made darker and the labor created as quiet an environment as possible during the care. Therapeutic touch, hand holding, standing, moving and deep breathing exercises were performed. For information support, information was shared with the woman about the dilatation, effacement, and birth process. The advocacy component contained the protecting the pregnant woman, understanding her needs, taking care of her privacy, and respecting her, helping her make health-care choices (for example, not to let routine connecting to the NST, allowing her to freedom of movement, allowing her to drink water, etc.).

The length of the active phase at birth should not exceed 12 hours in nullipars, and the length of the transition phase should not exceed 3 hours. The second stage of labor should not exceed an hour and the third stage should not exceed half an hour (1). Pregnant women in the control group were also cared for by the same midwife from the active phase from the active phase to the childbirth accordance with hospital protocols. Hospitals in Turkey do not routinely use non-pharmacologic methods to reduce labor pain. According to this hospital protocol in routine care, information was shared after each examination and deep breathing exercises were provided during contractions. Dilatation and effacement are determined at regular intervals for women in the control group. NST and induction are frequently used. Oral intake is not allowed and there is often no freedom to change positions.

2.3. Inclusion and Exclusion Criteria:

All primipara pregnant women included in this study did not attend antenatal education classes. However, as inclusion criteria;

- Started labor process and hospitalized,
- Term and singleton pregnancy,
- A live/healthy fetus,
- Spontaneous vaginal delivery,
- Longitudinal and vertex position of the fetus,
- Active phase (dilatation = 4cm and above),
- Body Mass Index (BMI) under 30 and are estimated,
- Ultrasonographic baby weight <4 kg,
- Who had not previously been diagnosed and treated for anxiety,
- Who agreed to participate,
- Given consent were included in the study.

Exclusion Criteria;

- Maternal and fetal complications,
- Pregnant women who have a head-pelvic non-compliance,
- A fetal hypoxia (distress),
- Early Membrane Rupture (EMR),
- Risk of fetal anomaly,
- Have any language-communication problems in pregnant women,
- Discontinuation of the study at any stage of the study,
- Cesarean section

2.4. *Randomization:*

The random.org site was used to determine which women were included in the control group or in the experiment group. The number of experiment and control groups determined by random.org is as follows.

Numbers experiment: 22, 19, 51, 26, 2, 63, 39, 61, 32, 11, 56, 64, 35, 37, 25, 66, 6, 8, 31, 29, 34, 42, 59, 48, 16, 58, 24, 67, 70, 18, 38, 53, 45, 13, 28th pregnant women.

Number control: 23, 4, 49, 54, 46, 43, 36, 62, 41, 21, 65, 30, 5, 14, 68, 50, 7, 10, 20, 44, 60, 12, 57, 3, 55, 47, 27, 15, 17, 69, 9, 71, 1, 40, 33, 52nd in the pregnant women.

2.5. Blinding (masking):

First of all, pregnant women who meet the inclusion criteria of the study were directed to the researcher by a physician who did not know the aim of the study. Afterwards, necessary explanations were made to each woman by the researcher. Written and verbal consents of the women who accepted to participate in the study were obtained at this stage. After approval, the women were included in the experiment or control group according to the previously determined and above-mentioned numbers. Experiment and control groups were not given maintenance simultaneously. After each woman's childbirth, the other pregnant women were included in the study. The data obtained were entered into SPSS trial program by researcher. The analyses were performed by a statistician without specifying the experiment and control groups in order to prevent possible bias.

2.6. Statistical Analysis:

The demographic and clinical characteristics of the experiment and control groups were compared with the chi-square test. Anxiety level, coping with labor pain levels and childbirth time were evaluated with Mann-Whitney U Test and interventions and perineal trauma were evaluated with chi-square test.

2.7. Measurement and Instruments:

The data collection flow is detailed in Figure 2. Childbirths are this hospital are performed by obstetricians. In this study, obstetricians were not informed about the study to prevent possible biases. Anxiety level and coping with labor pain were determined with VAS. Childbirth time and interventions were recorded at intervals. The fee to be paid when the participants were discharged was obtained from the patient records.

3.RESULTS

Demographic characteristics of the women participating in the study are given in Table 1.

Table 1. *The characteristics of the participants (n = 70)*

Demographic Characteristics		Experiment Group (n=35)		Control Group (n=35)		Analysis	
						χ^2	p
Age		24,11±3,91	24,00	23,86±4,31	23,00	21,945	0,145
Marriage Period (months)		19,86±9,25	18,00	20,51±9,92	18,00	7,546	0,580
BMI		28,19±3,18	28,80	29,12±3,96	28,6	50,000	0,394
Family Type	Nuclear Family	30	85,7	32	91,4	0,439	0,355
	Extended Family	5	14,3	3	8,6		
Educational level	Under 8 year	15	42,8	20	57,1	0,557	0,557
	Over 9 years	20	57,2	15	42,9		
Economic level	Low income	8	22,9	5	14,3	0,332	0,332
	Average Income	8	22,9	5	14,3		
	High income	19	54,3	25	71,4		

There was a statistically significant difference between the experiment and control groups anxiety level and coping with labor pain (p <0.01) (Table 2).

Table 2: *Comparison of anxiety level and coping with labor pain of the study groups (n = 70)*

Anxiety Level	Group				Analysis	
	Experiment		Control		Z_{MWU}	p
Dilatation (4-5 cm)	5,63	1,65	4,77	1,65	-2,090	0,307
Dilatation (6-7 cm)	3,83	0,82	6,71	1,51	-6,453	<0,001
Dilatation (8-10 cm)	2,00	,84	9,12	1,23	-7,261	<0,001
Coping with Labor Pain						
Dilatation (4-5 cm)	4,82	2,20	5,14	2,30	-,560	0,575
Dilatation (6-7 cm)	6,60	1,56	4,06	1,49	-5,620	<0,001
Dilatation (8-10 cm)	8,69	,83	2,44	1,74	-6,862	<0,001

Mann-Whitney U Test; Data are represented as mean ± standard deviation.

There was a statistically significant difference between the experiment and control groups such as amniotomy and labor induction. None of the participants in the experiment group developed perineal trauma related to childbirth. A total of 15 women in the control group (42.9%) were determined perineal trauma (p <0.01) (Table 3).

Table 3. *Comparison of participant labor interventions (n = 70)*

Labor Interventions		Intervention				Analysis	
		Yes		No			
Labor induction	Experiment	-	-	35	100	66,111	<0,001[a]
	Control	34	97,1	1	2,9		
Episiotomy	Experiment	27	77,1	8	22,9	2,696	0,094[a]
	Control	32	91,4	3	8,6		
Amniotomy	Experiment	2	5,7	33	94,3	38,445	<0,001[a]
	Control	27	74,9	8	25,1		
Perineal Trauma	Experiment	-	-	35	100	19,091	<0,001[a]
	Control	15	42,9	20	57,1		

[a]*Chi-square test*

The total childbirth time in the intervention group was shorter by 2 hours and 21 minutes (p <0.01) (Table 4).

Table 4. *Comparison of participants in terms of childbirth time (n = 70)*

Childbirth Time	Group				Analysis	
	Experiment		Control			
	Mean	SD	Mean	SD	Z_{MWU}	p
Time from 4 cm to 8 cm[b]	1:55	0:35	3:17	1:34	-4,008	<0,001[a]
Time from 8 cm to 10[b]	1:08	0:23	1:47	0:47	-3,950	<0,001[a]
Childbirth	0:23	0:07	0:47	0:28	-3,955	<0,001[a]
Plasental delivery	0,39	0:15	0:35	0:12	-3,486	<0,001[a]
Total childbirth time[b]	3:25	0:55	5:46	2:27	-4,656	<0,001[a]

[a]Mann-Whitney U Test; [b]hh: mm (hour: minute)

The only limitation of this study is that it is performed with primipara women. Furthermore, the study results may change when multiparous women are included.

4. DISCUSSION

According to Tumbilin and Simpkin (8), psycho-biological reactions such as anxiety and fear in pregnant women come into play in cases of fear, embarrassment, frustration, restriction, and feeling disrespected and ignored at childbirth process. These reactions may be reversed during the intrapartum period by giving the woman continuous support. As a matter of fact, in our study, anxiety significantly reduced in women receiving continuous labor support. Similar to our study, Bohren et al. (6), Dickinson et al. (9), Hodnett (10),Sangestani et al. (11) , Sehhatie et al. (12), Sydsjö et al. (13), and determined that the continuous one-to-one support reduces anxiety in childbirth. In addition, in a study reported that birth support is the most effective factor in reducing anxiety at childbirth after epidural anesthesia (14). Moreover, in a meta-analysis study was reported that the positive effects of labor support at childbirth on anxiety and depression continued in the postpartum period (15).

When anxiety is not controlled during intrapartum period, it causes epinephrine release (16). Increased epinephrine induces peripheral and uterine vasoconstriction and so causing anoxia in the tissues and increasing the pain sensation. Therefore, continuous labor support provided to the woman in labor process may be effective in coping with labor pain by controlling anxiety. Labor pain is subjective and affected by a wide variety of factors. Therefore, it is recommended that to evaluate the levels of coping with labor pain rather than pain levels (10,16). As a matter of fact, in this study, the mean scores of coping with labor pain in the experiment group receiving continuous labor support increased statistically. This result is in parallel with the findings of many studies in the literature (16,17). Support given at this stage of childbirth, it makes a significant difference in the level of coping with labor pain in women.

In this study, the effect of labor support on interventions during childbirth process was evaluated in terms of using of labor induction (oxytocin), forceps, vacuum, episiotomy, epidural analgesia and artificial rupture of membranes. There was a statistically significant difference between the experiment and control groups in using of labor induction and artificial rupture of membranes (p <0.01). In the meta-analysis of randomized controlled studies by Hodnett et al. (10) was found that continuous labor support reduced interventions in labor process, similar to our study. However, Sandall et al. (18) and Man Wang et al. (19), unlike these results, they did not detect any change in the intervention rates in the group they gave birth support.

In Turkey, the use of labor induction is almost routine, and it is an extremely costly workload that directly increases the cost of normal childbirth. It is a remarkable fact that the continuous labor support determined in this study reduces the need for oxytocin. In fact, although labor induction was applied to all women (97%) in the control group, total childbirth time was longer than the intervention group. These results is compatible with the results of Sehhatie's study results (12). Continuous and appropriate midwifery care plays the role of oxytocin. Demirel and Celik (20) stated that the nature childbirth was intervened by drawing attention to the complications of the labor induction. It is reported that the only cost of labor induction is met in cases when labor is completed vaginally, and when the Bishop Score has 6 points and above, however except this situation induction is only cost increasing (21). For this reason, it has been suggested to take into consideration patient/physician preferences as well as the cost of induction of labor (22). However, in another recent study by Alfirevic et al. stated that the using of the low-dose oral misoprostol instead of oxytocin has been reported to be more cost-effective in induction of labor (23). In a study that supported this view, was found that the using of the misoprostol was found to be much more cost-effective than using oxytocin-containing fluids (24). For this reason, in addition to patient/physician preferences, current and evidence-based cost-effective interventions should not be ignored.

Episiotomy is a routine intervention performed today, to facilitate the childbirth of the fetus especially in the first pregnancy and to prevent postpartum perineal trauma in women (25, 26). Sandall et al. (18) in the meta-analysis similar to our study, found that continuous birth support provided a reduction in the rate of episiotomy. As determined in our study, routine episiotomy, especially in the primipara pregnant women is performed in our country. Therefore, continuous birth support did not change the rates of routine episiotomy. Failure to achieve this change can be explained not by the ineffectiveness of continuous midwifery support provided, but also by the fact that using of the routine habits and gynecologists are more likely to be more effective in the management of the childbirth process.

In this study, none of the participants in the experiment group occurred perineal trauma. Insisting on the limitation of the duration of the second stage of labor, also obliges the person assisting the delivery to intervene the process and promptly obliges to try to terminate the delivery immediately

if the desired time limit is exceeded. Limiting the duration of the second stage in birth process increases the pH of the newborn**,** but this may lead to more interventions in childbirth. Therefore, every intervention causes perineal area integrity to deteriorate (25,26). The results of the meta-analyses in the current literature, similar to our results, were determined that continuous labor support was effective in maintaining the integrity of the perineal area (18). In addition, various degrees of perineal damage (due to prevention of vertical positions, limitation of mobility, the induction of labour, and so on.) repair of these perineal injuries and the use of antibiotics increased the direct cost of childbirth in the control group. In the short term, increasing the workload of health personnel directly, delaying the discharge of the woman from the hospital, interrupting the mother-infant connection and increasing future breastfeeding problems may affect the cost of birth. In the long term, perineal trauma associated with labor may lead to chronic incontinence and dyspareunia, which may adversely affect the quality of life and self-confidence, leading to additional costs (27). However, a study by Sundquist (28) determined that 45% of perineal traumas caused additional various complaints (incontinence, hemorrhage, infection, and so on.), leading to additional costs to the system over a period of 4-8 years. Therefore, in the cost calculations of perineal traumas, the pricing approach only for the period from the hospital to discharge may lead to the ignorance of the magnitude of the cost (29, 30). In addition, from social aspects, social stigmatization, prolonged separation from the spouse and also the presence of negative emotional feelings may lead to health seeking behaviors and therefore that this situation returns to the health system as a cost (31). WHO reports that perineal trauma related to childbirth affects millions of women whose number is not clearly known each year (32). For this reason, WHO is evaluating episiotomy and obstetric anal sphincter injuries or perineal injuries as health system and health care quality indicators (32-34). World Health Organization has published a report on the prevention of perineal trauma techniques at childbirth is stated that this undesirable outcome can be prevented by giving perineal massage training to in-service trainings to health personnel and this massage style is a low cost intervention. Moreover, it has been reported that perineal trauma would be prevented by this procedure and therefore would be less costly than normal care due to the decrease in the use of suture material and local anesthetic (32).

Although Friedman's labor curve continues to be discussed, it is reported that prolongation of childbirth increases cesarean section rates and interventions at childbirth (35,36). In this research, the total childbirth time in the intervention group shortened by 2 hours and 21 minutes and this situation was parallel to previous studies on continuous birth support (6, 10). As a matter of fact, the shortening of childbirth time in the intervention group reduced the number of interventions and direct costs (EFM, labor induction, enema, amniotomy etc). In addition, the shortening of the childbirth time accelerates the return of the mothers and their babies who cannot be calculated financially to their comfortable home-life, reduces the workload of the midwife/nurse, reduces the risk of exposure to hospital infections and provides more effective use of patient beds (32).

As a result, with continues midwife support, womens' levels of anxiety decreased and levels of coping with pain increased. There has also been a significant reduction in birth interventions. Birth is an unrepeatable and unique experience. For this reason, we can ensure that every woman has a positive birth experience by providing midwife support.

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Clinical and Experimental Health Sciences

The effect of various canal contents on the accuracy of two electronic apex locators in detecting different size of root perforations

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ABSTRACT

Objective: This study was to investigate the effect of different canal contents on the accuracy of Gold Reciproc Motor (GRM; VDW, Munich, Germany) and DentaPort ZX (Morita Co, Kyoto, Japan) in the determination of artificial root perforations.

Methods: Forty mandibular premolar teeth were included in this study. The crowns of the teeth were removed and the root lengths were standardized to be 14±1 mm. Roots were divided into 2 groups (n=20). Artificial root perforations were created 0.5±0.1mm and 1±0.1 mm in size respectively. The actual lengths (AL) up to the perforation areas were measured under the stereomicroscope. Electronic measurements (EL) were obtained by GRM and DentaPort ZX in dry conditions and the presence of NaOCl (5.25%), EDTA (17%) and blood. The difference was calculated by subtracting the ALs from the ELs. This difference was positive when the measurement was longer than the AL and negative when the measurement was shorter. The Friedman and Wilcoxon signed-rank tests were used to analyze the data ($p<0.05$).

Results: There were no significant differences amongst the different intracanal conditions for both apex locators in teeth with perforation of 1 mm. In the teeth with a perforation of 0.5 mm DentaPort ZX measurements were not affected by intracanal conditions and the most accurate measurement was obtained when the canal was dry with GRM.

Conclusion: Within the limitation of this study, intracanal conditions did not affect the measurements of DentaPort ZX in both perforation sizes, whereas in 0.5 mm perforation size, GRM measurements were affected by intracanal conditions..

Keywords: Blood, DentaPort ZX, Gold Reciproc motor, irrigation solutions, root perforation.

1. INTRODUCTION

Apical root perforation is defined as an artificial opening that constitutes a nonanatomical pathway between the root canal system and periodontal tissues. Root perforation may occur due to excessive use of a rigid file having cut tip, over the instrumentation of a curved root canal, inappropriate preparation of the post cavity and pathological conditions such as external or internal root resorption (1, 2). It has been reported that apical root perforation is an important complication occurring in the root canal treatment with a frequency of 3-10% (3). After perforation, the bacterial infection that spreads from the root canal to the periodontal tissues, from the periodontal tissues to the root canal or from both, affects the healing by causing pain, swelling, suppuration and resorption of the bone. In addition, a rapid periodontal loss may occur with the expansion of the gingival epithelium into the perforation zone (4). But early diagnosis and treatment can improve prognosis (5, 6).

It is important to know the localization of the perforation so that the root canal preparation, intracanal medicament application and repair of the perforation area can be made appropriately. Localization of the perforation can be determined by the use of paper points for indirect detection of the bleeding point, direct observation of bleeding and the use of devices such as conventional periapical radiography, cone beam computed tomography (CBCT) and electronic apex locator (EAL) (1, 7). Small-sized perforations on the buccal or lingual surface of the tooth may not be detected in traditional radiographs because it displays anatomical structures in only two dimensions. (5). EALs are frequently preferred by dentists because of the advantages such as greatly reducing the number of radiography taken and increasing patient comfort (8). EALs can identify cases where there is a connection between the root canal and the periodontium, such as root fractures, cracks and internal or external resorption (1).

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The use of these devices to determine the working length was first proposed by Custer and the electrical resistance characteristics of the oral tissues were improved after examination by Suzuki (9, 10). DentaPort ZX (Morita Co, Kyoto, Japan) a third-generation EAL, calculates and reports the ratio of two different frequencies simultaneously (11). Also, it was reported that the accuracy of measurement by DentaPort ZX was not affected by vital pulp tissue and exudate (12, 13). The Gold Reciproc Motor (GRM) (VDW GmbH, Munich, Germany) is an endodontic engine with an integrated electronic apex locator. The integrated EAL can be used both during preparation and separately (14). This study aimed to evaluate the reproducibility and accuracy of two EALs in the presence of various canal contents (NaOCl, EDTA, saline and human blood) and simulated two different size root perforations. The null hypothesis of the study; in the case of root perforations of two different sizes, one with a diameter of 0.5 mm and one 1 mm, there is no difference between the accuracy of the two EALs in the presence of different irrigations in the root canal.

2. METHODS

The study design was approved by Abant Izzet Baysal University Clinical Researches Ethics Committee (2019/207). After power calculation based on a similar methodological study, 20 mandibular premolar teeth were included for each perforation size in this study. The same samples were used for each irrigation solution and each EAL in both groups in order to ensure standardization in applications (1).

Forty mandibular premolar teeth with a single root and single canal extracted for orthodontic and periodontal reasons were included in the study. Periapical radiographs were taken for buccolingual and mesiodistal directions for each tooth, and it was confirmed that the root canal development of the teeth was complete, there was no calcification, fracture and no root canal treatment. The calculus on the tooth surfaces was cleaned with a periodontal curette. Following sample selection, the teeth were disinfected for 48 hours at 4 °C in solution of 2.5% NaOCl (Endosolv Hp; Imıcryl, Konya, Turkey). Teeth were stored in 0.1% NaOCl until used in the study.

The endodontic access cavity was prepared and then the apical patency was checked using the # 10 K type file (Dentsply Maillefer, OK, USA). To obtain a fixed reference point and standardization during the measurements, the crowns of the teeth were removed by the diamond drill (Diatech, Charleston, USA) under water cooling. The roots were standardized to 14 ± 0.1 mm. The working length was determined to be 1 mm shorter than the apical foramen using the # 10 K type file. Canals were prepared up to the 25 size using K type file. After preparation, the canals were irrigated with 2 ml of 5.25% NaOCl followed by 2 ml of distilled water and dried with paper points (DiaDent Group, Chongju, Korea). 40 teeth were randomly numbered and divided into two groups, each consisting of 20 teeth;

Group 1: Drill was placed at the proximal surface of the roots at a distance of 4 ± 0.1 mm from the apical and at a 90-degree angle and artificial perforation areas were created with a diameter 0.5 ± 0.1 mm.

Group 2: Drill was placed at the proximal surface of the roots at a distance of 4 ± 0.1 mm from the apical and at a 90-degree angle and artificial perforation areas were created with a diameter 1 ± 0.1 mm. The diameter of the perforation areas was verified by electronic caliper (Mitutoya, Kawasaki, Japan).

Before the electronic measurement (EL) stage, the actual lengths (AL) of the canals up to the perforation area were measured by using the # 25 K type file at 20X magnification under the stereomicroscope (Stemi DV4; Carl Zeiss, Gottingen, Germany). To mimic the periodontal ligament during EL, the teeth were embedded in alginate (Blueprint, Dentsply, England) and the lip clip was contacted with alginate during measurement. When canals were dry and the presence of the NaOCl, EDTA (IMICRYL, Konya, Turkey) and human blood in canals, EL measurements were made using DentaPort ZX and GRM.

For the EL, the # 25 K type file was placed inside the canal and when the last green line signal was seen in both EALs, the stopper of the file was brought to the reference point and this length measurement using endodontic ruler (Mini-Endo-Bloc; Dentsply Maillefer) and recorded as EL. All measurements for solutions were made after irrigating the canals with 2.5 ml of fresh solution. Canals were irrigated with 5 ml of distilled water and dried with paper points to completely remove the previous remaining solution between the different solution groups. All irrigation procedures were performed with a lateral perforated needle (31 gauge NaviTip Sideport; Ultradent Products Inc., South Jordan, UT, USA). Finally, measurements were made in the presence of human blood (within 4 hours) in the canal. Blood was drawn from the healthy volunteer (20 ml) and was stored in EDTA anticoagulant-containing tubes (K2EDTA blood tube, BD Vacutainer®, Plymouth, UK), preventing coagulation, both before and during the procedure. Each measurement was repeated 3 times and the mean of these 3 values were determined as EL. All measurements were made by the same operator experienced in the use of EAL.

Statistical Analysis

All statistical analyses were performed using SPSS for Windows (ver. 16.0, SPSS Inc., Chicago, IL, USA). The Friedman and Wilcoxon signed-rank tests were used to analyze the data. The significance was determined at $p<0.05$.

3. RESULTS

There were no significant differences among the different intracanal conditions for both apex locators in teeth with perforation of 1 mm (for GRM group: p=0.49; for DentaPort ZX group: p=0.65) (Table 1). In the teeth with a perforation

of 0.5 mm DentaPort ZX measurements were not affected by intracanal conditions (p=0.07) and the most accurate measurement was obtained when the canal was dry with GRM (p<0.001) (Table 2). Also, there was no significant difference between the two apex locators in the presence of all intracanal irrigants in teeth with perforation of 1 mm and 0.5 mm (p>0.05).

Table 1. *Mean values of the difference between the electronic lengths and the actual lengths of the group with 1 mm perforation*

	NaOCl Mean±SD	EDTA Mean±SD	Blood Mean±SD	Dry Mean±SD
Dentaport ZX	0.27± 0.58^{ax}	0.35±0.52^{ax}	0.28±0.64^{ax}	0.27±0.55^{ax}
GRM	0.20±0.50^{ax}	0.33±0.56^{ax}	0.49±0.82^{ax}	0.30±0.52^{ax}

SD: standard deviation; Significant differences between columns (a,b) and lines (x,y) are indicated by superscripts.

Table 2. *Mean values of the difference between the electronic lengths and the actual lengths of the group with 0.5 mm perforation*

	NaOCl Mean±SD	EDTA Mean±SD	Blood Mean±SD	Dry Mean±SD
Dentaport ZX	0.65±0.74^{ax}	0.84±0.67^{ax}	0.54±0.87^{ax}	0.73±0.93^{ax}
GRM	1.07±2.10^{ax}	0.87±1.134^{ax}	1.05±1.01^{bx}	0.009±0.62^{by}

SD: standard deviation; Significant differences between columns (a,b) and lines (x,y) are indicated by superscripts.

4. DISCUSSION

During the root canal treatment, root perforations may occur due to various procedures. It is important to localize root perforations for the success of endodontic treatment (15). In the detection of root perforations, radiographs are frequently used in endodontics. However, Shemesh et al. (16) demonstrated that periapical radiographs were very limited in their ability to detect root perforations and that even CBCT could not detect certain perforations. Considering this situation, the use of EALs which do not expose the patient to ionizing radiation in the detection of root perforations is advantageous. In this study, in the presence of four different canal contents, the accuracy of two different EALs was investigated in the determination of localization of artificial root perforations having two different sizes.

In vitro studies on EALs have suggested the use of different embedding environments that simulate the electrical resistance of human tissues. Therefore, it has been suggested to use % 2 agars, gelatin, saline solution and alginate to mimic the clinical situation in in-vitro studies (17-22). Baldi et al. (23) reported that different dental embedding environments (alginate, gelatin, saline solution, sponge, agar) did not affect the accuracy of EAL. In contrast, Chen et al. (24) found that alginate was more successful in the accuracy of EALs than sugar-free gelatin and 9% sodium chloride. In the current study, similar to that of Altunbaş et al. (5, 11), Chen et al. (24) and Tinaz et al. (25), the teeth were embedded in alginate, an electroconductive material that is easy to prepare and cost-effective.

There are differences in the results of studies investigating the accuracy of EAL in different canal conditions in the literature. Marigo et al. (26) reported that DentaPort ZX and Raypex 6 did highly accurate measurements without being affected by the presence or absence of NaOCl on human cadavers. Ebrahim et al. (27) reported that the accuracy of DentaPort ZX was not affected by the canal content in determining the working length. Similarly, Duran-Sindreu et al. (9) reported that NaOCl and CHX did not affect the accuracy of IPEX and Root ZX in determining the working length. Li et al. (28) also reported that EALs were not affected by the canal contents in the determination of the localization of the artificial perforation areas. In accordance with the results of these studies, DentaPort ZX in two perforation sizes and GRM in 1 mm perforation size were not affected by the presence of different canal contents. In contrast to these findings, Altunbaş et al. (5) reported that Dentaport ZX was more accurate in the presence of EDTA compared to NaOCl in detecting the localization of 1.5 mm diameter perforation. The differences between the results may be due to factors such as the diameter and location of the perforation and EAL selection. However, GRM gave the best result in dry conditions in localization of 0.5 mm perforation. Considering this situation, it is thought that GRM can give misleading results in the presence of irrigant or bleeding in the canals with small perforated teeth.

In the present study, there was no difference between DentaPort ZX and GRM in determining the localization of 1 mm perforation. However, in determining the localization of 0.5 mm perforation, DentaPort ZX in the presence of blood and GRM in dry conditions was more accurate. To the best of our knowledge, there is no study comparing the accuracy of DentaPort ZX and GRM in the literature. Therefore, the results of our study could not be directly compared with other studies. The reason why two devices give different results in dry conditions and the presence of blood can be explained by the different working principles of EALs. Similar to Tinaz et al. (25) and Gomes et al. (29), in this study, some standard deviation (SD) values were found to be high (in presence of NaOCl solution in the canal to localize the 1mm perforation with GRM). This situation can be related to the claim that the accuracy of EALs mentioned earlier in the literature is affected by root canal anatomy (30). The literature reported that low SD shows the consistency of EALs. (6, 9) In this study, both DentaPort ZX and GRM had a lower SD in all canal conditions compared to 0.5 mm perforations in localization of 1mm perforation. This situation showed that both EALs were more reliable in detecting 1 mm perforation. In some studies (1, 8), investigating the accuracy of EALs, ± 0.5 mm was accepted as an acceptable error range, while in some studies (31) the tolerance ranges of ± 1mm were accepted. In this study, DentaPort ZX had an acceptable error range in all groups. In contrast, GRM had a larger SD than the error range accepted in the literature in the presence of NaOCl, EDTA, and blood at 0.5 mm perforation.

5. CONCLUSION

Within the limitations of this study, there was no difference between DentaPort ZX and GRM in determining the localization of 1mm perforation. In the presence of NaOCl, EDTA and blood in the canal, the DentaPort ZX showed more reliable results in determining the localization of 0.5 mm perforation. In light of this information, we think that the use of DentaPort ZX may give the clinician more accurate diagnosis and treatment planning in small perforated teeth. The use of GRM may be disadvantageous in cases where bleeding with perforated teeth cannot be stopped for localization of perforation.

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Clinical and Experimental Health Sciences

Association of Physical Fitness Indicators with Health Profile and Lifestyle of Children

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ABSTRACT

Objective: High physical fitness (PF) level is a significant health determinant in children and adolescents so that it is important to identify the factors affecting PF in this population. Despite available studies highlighting the relationship between PF and characteristics of children, there is still a need to uncover how the health status and lifestyle of children impact different PF indicators. Thus, the purpose of this study is to investigate the relationship between physical fitness, and the health profile and lifestyle of children.

Methods: This study was conducted with 110 (58 girls; age 11.85±0.35) adolescents between February and March 2020. The preditors of PF which were gender, body mass index, physical activity level (PAL) measured via Physical Activity Questionnaire (PAQ), motivation measured via Participation Motivation Questionnaire (PMQ), sleep time, and tablet usage time regressed against PF related outcome measured using 6 Minutes Walk test (6MWT), T-Test, vertical jump test and broad jump test (BJT).

Results: There were significant associations between T-test performance, and gender, BMI (being obese), and PAL. PAL and gender were also significant predictors for 6MWT and BJT respectively. PF was not significantly associated with motivation, sleep, and table usage time. A high level of physical activity, being male, and low BMI score resulted in better PF performance.

Conclusion: The health profile and lifestyle of adolescents may estimate the significant proportion of variabilities observed in physical fitness levels in adolescents.

Keywords: Physical Fitness, Adolescent, Physical Activity, Healthy Lifestyle

1. INTRODUCTION

Physical Fitness (PF) is defined as a state of health associated with aerobic capacity, flexibility, muscular endurance, and muscular strength, which is linked to the ability to perform aspects of sports and outdoor recreational activities (1).

Improving physical fitness during adolescence is crucial to avoid the development of chronic disease in adulthood (2, 3) and to improve health-related quality of life (4). It is an important factor leading to success in youth sports and athletic events (5, 6). Further, youth`s academic achievement (7, 8), and participation in physical (9) and social activities (10) have also been linked to physical fitness.

Studies in the adult population emphasized the impact of biological and lifestyle factors on physical fitness (11). Sex, for example, is reported as an important determinant for physical activity level and participation in sports in adults; yet, the difference between sex was not conclusive in youth (12). Also, the relationship between body mass index (BMI) and fitness level has been largely documented in both adult (13) and adolescent populations [14] relating to the prevalence of obesity (15). Although several studies illustrated an inverse relationship between the BMI and physical fitness level (16), the trend was opposite in others (17).

One of the worrying findings is that sedentary lifestyle and inadequate physical activity are becoming more common in adolescents (18) which is carried into adulthood (19). Recent studies highlighted the use of electronic devices as the most important factor in this behavior (20,21). It was shown that the use of electronic devices has significantly deteriorated the level of physical activity in adolescents (22, 23). Studies were done in Turkish adolescents also contributed evidence to this phenomenon; where they showed a significant association between the use of the mobile device and the reduced time invested for physical activity (24). A longitudinal study in England adolescents also showed that physical activity was affected inversely by the increase in screen time (25). Despite the recommendations from health agencies like World Health

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Organization (WHO) to reduce the time spent on the screen (26), the use of mobile devices is becoming more common in adolescents which in turn influences their physical fitness levels (25). Understanding the relationship between lifestyle factors, health profiles, and level of physical fitness is still a research area of interest to better design interventions for adolescents and prevent them from moving into unhealthy adulthood.

The purpose of this study is to estimate the extent to which physical fitness levels are associated with sex, BMI, physical activity, sedentary, tablet using, sleep time in healthy adolescents.

2. METHODS

2.1. Participants

Healthy adolescents aged between 9 to 14 years who are secondary grade schools in Istanbul participated in this study. The data was collected between February-March 2020 in two secondary grade schools in Istanbul. Those two schools were selected across Istanbul using a random sampling method.

A total of 110 adolescents (average age 11.85±0.35; 47% male) with no diagnosis of neurological, cardiovascular, metabolic, rheumatic, or vestibular diseases, no injuries or previous surgery participated in the population-based cross-sectional study.

Written informed consent from parents and assents from the adolescents were obtained before participating in this study. Assessments were conducted within the school hours as permitted by the school administration.

The study's ethical approval was obtained from Marmara Research Ethics Committee (No:178 Date: 05.12.2019).

2.2. Measurements

2.2.1. Personal factors

Age, sex, height, and weight were obtained using a standardized data collection form created by the researchers. Additionally, information on sleep times and tablet usage times were obtained.

2.2.2. Physical fitness assessment

The outcome of this study is Cardiorespiratory Fitness (CRF) which was measured using the 6 Minute Walk Test (6MWT) according to American Thoracic Society Guidelines (27). The distance walked within 6 minutes was measured.

2.2.3. Physical Activity Level

The activity level was obtained from the Physical Activity Questionnaire (PAQ). The PAQ includes 10 items that capture activities in and out of school during the last seven days. Except for the last question, each item scores on a 5 Likert scale and produces an activity score between 1-5. Score 1 implies low physical activity whereas a score of 5 implies high physical activity. The points given to the 9 questions are collected and the total score was obtained by dividing the number of questions. Psychometrics of PAQ for the Turkish version was conducted by Erdim at all (28).

2.2.4 Motivation in Participating in Sports

Participation Motivation Questionnaire (PMQ) consists of 30 items including the reasons for participation in sports. The PMQ has 8 dimensions which are skill development, team membership / spirit, entertainment, friend, achievement / status, physical fitness /energy spending, movement / being active, and contest. It is scored on a 3 Likert scale. (1 very important, 2 less important, 3 not important). Psychometrics of PAQ for the Turkish version was conducted in 9-17 aged group students by Oyar at all (29).

2.2.5 Agility

Agility is measured using the T-test. The completion time of the 4-cones course at a certain distance is recorded. T-Test was applied according to Semenick's Test Protocols (30). The assessment was repeated only one time.

2.2.6 Vertical Jump and Broad Jump Test

Vertical and Broad Jump tests were used to measure the lower limb muscle strength (31). The Eurofit test battery was applied for the test procedure. In the Vertical jump test, the person jumps vertically with support from the knees. The distance between the endpoint the person reaches and the starting point is measured. Standing Broad Jump Test is measured on a non-slip floor, double foot jumping as far as possible. The distance between the starting point and the heel after landing is measured. Two attempts were allowed in both tests. The vertical jump test is a variation of the Broad Jump Test (32).

2.3. Analysis

Descriptive statistics were used to summarize the demographic information of the participants and all performance scores. The distributions of the data were visually evaluated by histograms, and Quantile–Quantile plots; and tested using the Shapiro–Wilk test. Before the main analysis, the collinearity among independent variables was examined using Variance Inflation Factor (VIF) and regression correlation matrix for Klein Goldberger model. The outcomes of interest, 6MWT, T-test, vertical jump test, and broad jump test, were regressed against six independent variables: sex, BMI percentile, sleep time, tablet usage time, PMQ, and PAQ. The categorical variables (sex and BMI percentile) were included in the regression models. Reference categories for was normal level for BMI (>5 and <85th percentile) and

female for sex. The model was visually evaluated for linearity, heteroscedasticity, and normality of the residuals. The alpha level was set .05. All analyses were done is R statistical software using the packages of 'olsrr'and 'lubridate' (Version 3.6.0, St .Louis, Missouri, USA) (33).

3. RESULTS

Table 1 summarizes the demographic and characteristics of participants including age, gender, BMIz, sleeping time, tablet usage time, participation motivation questionnaire, physical activity questionnaire, 6MWT, T-test score, vertical jump test, and broad jump test.

Table 1. *Baseline characteristics and predictors*

Variables (n)	Mean (SD)	N (%)
Age	11.85 (0.35)	
Gender		
Female	-	58 (53)
Male	-	52 (47)
BMI WHO classification		
BMI percentile <5:Underweight		4 (4)
BMI percentile ≥5 and <85:Healthy Weight		65 (59)
BMI percentile ≥85 and <95:Overweight		26 (24)
BMI percentile ≥95:Obese		14 (13)
BMIz score	0.19 (0.03)	134 (100)
Life-style and activity		
Sleeping time (m)	528.12 (77.32)	90 (100)
Table usage time	128.79 (102.69)	90 (100)
PMQ	40.87 (6.70)	90 (100)
PAQ	2.83 (0.68)	134 (100)
Physical fitness		134 (100)
6MWT (m)	541.59 (58.42)	134 (100)
T-test (s)	16.42 (2.58)	
Broad jump (cm)	124.63 (25.68)	134 (100)
Vertical jump(cm)	25.64 (4.43)	134 (100)

BMI: Body Mass Index, PMQ: Participation Motivation Questionnaire, PAQ: Physical Activity Questionnaire, 6MWT: 6 Minutes Walk Test. SD: Standard deviation

Multiple regression analysis

The result of multiple regression analyses is presented in Table 2. The correlation coefficients between predictors were tolerable (r < 0.5) (34). The predictors included in the analysis explained 16-41 % of the variation in physical fitness indicators (Table 2). The analyses showed that only three of the predictors-gender and BMI and PA – had significant relationships with physical fitness indicators (Table 2). Being female was associated with increased time in the T-test and shorter distance in BJT (Table 2). Being obese was also significantly related to a longer time in the T-test. On the other hand, having a higher PAQ score was significantly associated with a shorter time in the T-test and higher distance in 6MWT. There were no significant relationships between physical fitness indicators and three predictors (motivation, sleep, and table usage time) (Table 2).

Table 2. *Multiple regression analysis: relationship between each predictor and physical fitness indicators*

OUTCOMES (PHYSICAL FITNESS INDICATORS)								
	6 MWT score		**T test score**		**VJT score**		**BJT score**	
PREDICTORS (range)	*β*	*p*	*β*	*p*	*β*	*p*	*β*	*p*
Gender (female)	4.438	0.715	1.24	**0.007**	-1.029	0.292	-12.44	**0.018**
BMIz								
Underweight <5th percentile	-8.125	0.786	0.946	0.367	-1.171	0.626	6.457	0.613
Overweight >85 and <95th	-26.15	0.401	1.432	0.217	-2.593	0.299	-4.509	0.733
Obesity	-59.48	0.090	4.423	**0.001**	-4.41	0.115	0.285	0.285
Sleep time (360,840)	-23.09	0.552	0.701	0.625	-0.755	0.806	-3.98	0.808
Table usage time (0,600)	13.78	0.06	-0.304	0.264	-0.381	0.515	-4.504	0.149
PMQ (30,57)	-46.60	0.22	2.681	0.064	-5.016	0.107	-26.62	0.107
PAQ (1.31,4.41)	98.52	**0.002**	-4.647	**0.001**	4.24	0.109	25.79	0.066
R^2	**0.20**		**0.41**		**0.16**		**0.28**	

BMI: Body Mass Index, PMQ: Participation Motivation Questionnaire, PAQ: Physical Activity Questionnaire.

4. DISCUSSION

This study aimed to show the relationship between physical fitness indicators and characteristics and lifestyle of adolescents aged 11-12 years. Based on the results, the health profile and lifestyle of adolescents may estimate the significant proportion of variabilities observed in physical fitness level in adolescents that was ranged from 16 to 41 %. Being female and being obese were significantly associated with a low fitness level while a high level of participation in physical activity was a significant indicator of better fitness. On the other hand, the motivation and time spending on sleep and table usage were not significantly related to the physical fitness level of the participants.

Physical fitness is a significant health marker of adolescents that predict their aerobic and anaerobic capacities allowing us to estimate the risk of cardiac and health problems in adulthood, participation in social and physical activities, academic performance, and psychosocial problems. This study adopted 6MWT to measure the aerobic capacity and endurance rather than direct measures of VO2 max expenditure to reflect adolescents` ability to perform daily activities. Where VO2 max was measured, boys were consistently reported to have a higher level of VO2 max capacities than girls (35). Though, the gender differences in 6MWT were not as conclusive in the literature (36,37). The current study reported no differences in distance covered within six minutes between gender which was inconsistent with the previous study done in a similar population, Turkish children and adolescents, where Kanburoglu et al presented outstanding performance of boys compared to girls (38). Comparable performance between gender in the current

study may be a result of unmatched characteristics between girls and boys in the lifestyle or physical activity level of the participants. Kanburoglu et al compared the performance of girls and boys after separating the participants with respect to physical activity (PA) level as sedentary, active, and very active (38). The group differences were evidence in each PA level where boys covered a greater distance than girls. On the other hand, compatible with the current study, they found no differences among the adolescents with different levels of BMI in 6MWT. Indeed, 6MWT is presented as a valid test that can distinguish obese adolescents from those with normal weight (39) which was not the case in Turkish adolescents (38). In regard to oxygen uptake, obese adolescents typically presented with higher or relatively comparable oxygen consumption level with those with normal weight (40) which may be a factor leading to a comparable performance in 6MWT considering the nature of the test measuring aerobic capacity and endurance.

This study also showed that the fitness levels of Turkish adolescents highly vary dependent on the amount of time they invest in physical activity. A negative relationship between a sedentary lifestyle and physical fitness has been consistently shown in adolescents with varying age groups. Carson et al, for example, showed poorer cardiorespiratory capacity and endurance in adolescents who spent time on screen more than their peers (21). Nevertheless, the results of our study did not provide supportive evidence; on the contrary, the table usage time and sleep time were not significantly associated with physical fitness level through physical activity time was.

Increased screen time has also negatively affected the locomotor skills and muscular strength of adolescents in some studies (25,41). Despite these strong evidences, a recent meta-analysis reported no significant relationship between sedentary time and physical fitness level in either boys or girls (42). Studies suggest lifestyle with sports participants contributor for PA levels (42). Higher PA habitual benefit for cardiorespiratory and agility strength as an important healthy biomarker (43). Participants who have higher PA levels show greater performance in the T-test as agility test and 6MWT as cardiorespiratory capacity. These results were similar to current studies which provide an association between PA, sedentary behaviors, and physical fitness (4). The evidence indicates meeting the recommended PA level contributes to spending less time (44,45).

Although evidence emphasized that PA and sedentary time different dimensions of lifestyle (46,47). There are inconsistent results in the studies. Studies found that children who spent time on the screen, they less active. On the other hand, these studies found that active adolescents spend a lot of time on screen (48).

Telama at all. suggested that PA habitual tends to PA in adulthood in their 21 tracking study (49). PA represents any physical movement produced by skeletal muscles, it improves physical fitness status (50).

There was no available evidence for Turkish adolescents to show the relationship between physical fitness and lifestyle. This study provides to determine the effect of gender, BMI, physical activity, sedentary, tablet using, sleep time on the physical fitness levels in Turkish adolescents. The predictors included that three of the predictors-gender and BMI and PA – had significant relationships with physical fitness indicators. Obesity was also significantly related to a longer time in the T-test. On the other hand, PA was significantly associated with a shorter time in the T-test and higher distance in 6MWT.

Future studies may also investigate the effect of lifestyle intervention on physical fitness levels in adolescents.

5. CONCLUSION

The results of the current study present that the health profile and lifestyle parameters may contribute to physical fitness such as cardiorespiratory fitness and agility in Turkish adolescents. In conclusion, lifestyle management and obesity should be a major focus in public health.

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Clinical and Experimental Health Sciences

The Impact of Body Mass Index Values on the Quality of Cardiopulmonary Resuscitation: A Manikin Study

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ABSTRACT

Objective: The purpose of this study is to assess the impact of body mass index (BMI) on the quality of cardiopulmonary resuscitation (CPR) by using a manikin.

Methods: 50 people composed of research assistants, intern doctors, emergency medical technicians and nurses who had previous cardiopulmonary resuscitation experience performed CPR on Laerdal Skillmeter Resusci-Anne® with SimPad manikin during the study. BMI data of participants were recorded and then the participanst were categorised as BMI <21 and BMI >21. Compression data obtained from the summary section of SimPAD QCPR were compared with the participants BMI values.

Results: 18 (36%) out of 50 participants were male, while 32 (64%) were female. 16 (32%) out of 50 participants were in the slim group, while 34 (68%) were in the normal group. Mean age of participants was calculated as 26.8±4.2, and mean BMI as 22.56±3.32. Mean compression depth in the slim group was significantly lower in comparison to the normal group (slim51.94±4.64, normal 55.79±4.35, p=0.006). Compression ratiowith sufficient depth in the slim group was statistically lower than the normal group (slim 66.19±25.79, normal 87.29±19.36, p=0.002). A statistically significant positive correlation was found in the lineer regression analysis conducted between mean compression depth and BMI (r2:0.179, p=0.002). Moreover, a significant positive correlation was observed in the pearson correlation analysis of mean compression depth and BMI (r: 0.423, p= 0.002).

Conclusion: As a result, it was found out that low BMI values are associated with low mean compression depth.

Keywords: Body Mass Index, cardiopulmonary resuscitation, basic cardiac life support.

1. INTRODUCTION

The prognosis of out-of hospital cardiac arrest (OHCA) is bad (1). Annually, itresults in300,000 people's death (2). The most important method to reduce this mortality is to increase the quality of cardiopulmonary resuscitation (CPR). It is know that simple changes such assufficient compression rate, sufficient compression depth, compression allowing for chest recoil, minimising compression interruptions and avoiding exteme ventilation increase survival rates by increasing CPR quality (3-5).

It has been stressed out that anthropometric variables have an impact on CPR quality (6). There are studies on the fact that anthropometric parameters affecting CPR include body weight, height, physical fitness and muscle power (7-9).

Our purpose is to compare data that could have an impact on CPR quality based on Body Mass Index (BMI) parameter by using a manikin.

2. METHODS

On June 5, 2020 this prospective simulation manikin study had an ethics committee approval by Necmettin Erbakan University Meram Medical Faculty Pharmaceutical and Non-Medical Device Studies Ethical Committee by the decision number of 2020/2570.

Necmettin Erbakan University Meram Medical Faculty Pharmaceutical and Non-Medical Device Studies Ethical Committee by the decision number of 2020/2570

50 people composed of different professional groups working at our clinic (research assistants, intern doctors, emergency medical technicians and nurses) that have previous cardiopulmonary resuscitation experience, are knowledgeable about advanced cardiac life support and basic life support were randomly selected for the study on

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a voluntary basis. The participants signed a letter of consent for the study.

Laerdal Skillmeter Resusci-Anne® with SimPad manikin was used in the study. The participants were asked to perform non-stop compressionfor 2 minutes on the manikin. The manikin was introduced to the participants prior to compression. It was ensured that they had the sufficient time to perform CPR on the manikin. The manikin was planned to lie flat on its back on the ground during compression (supine position).

A metronom was used during compression to minimise the impact of compression rates on chest recoil (10). The metronom was arranged in a way to provide voice prompts 110 times per minute to achieve a rate of 100–120 compressions per minute as stated by the American Heart Association (AHA) and the European Resuscitation Council (ERC) guidelines (11,12).

The data of CPR (after 2 minutes of compression) on the manikin were automatically generated by the summary section of SimPAD QCPR. Mean compression depth (mm), mean compression rate (compression/minute), compression ratio with a complete chest recoil (%), compression ratio with sufficient depth (%), compression ratio with sufficient rate(%) values were obtained from the summary section of SimPAD QCPR. The manufacturing company defined that the sufficient depth was between 50 and 60 (mm) in reference to AHA and ERC guidelines. The manufacturing company defined sufficient rate was between 100 and 120 (compression/minute) in reference to AHA and ERC guidelines. In addition, age, gender, profession, body mass index information of the participants were also recorded.

Though those below 20 are considered slim in BMI calculations (13), our study categorised BMI values as below and above 21. The group with BMI<21 was categorized as slim, while the group with BMI≥21 was categorized as normal. The reason we categorized it in this way was to reach a sufficient number of group populations to make statistical comparison. In addition, the participants were divided into 3 groups according to the cut-off BMI values of 21 and 23 (BMI<21, 21≤BMI<23 and BMI≥23).

The compression values on the manikin were compared between the groups. SPSS 20.0 (SPSS Inc., Chicago, IL) package was used to perform such a comparison and analyse the data statistically. Analyses of normality of the data were made by using histograms and Kolmogorov–Smirnov test.Non-normally distributed quantitative data were stated as median (25%-75% quarters), while normally distributed quantitative variables were stated as mean±standard deviation (SD), and categorical variables were stated as frequency (percentage) [n (%)]. The differences between two groups were investigated using the Mann–Whitney U test in non-normally distributed quantitative variables, while Student's t-test was used for normally distributed quantitative variables. The differences between more than two groups were investigated using the Kruskal-Wallis test in non-normally distributed quantitative variables, while one-way Anova test was used for normally distributed quantitative variables. Dunnett's T3 test was used as a post hoc analysis test for non-normally distributed quantitative variables while Bonferroni test was used as a post hoc analysis test for normally distributed quantitative variables. We used the Bonferroni correction for multiple comparisons. Pearson correlation analysis and linear regression analysis were performed to assess the relationship between mean depth and BMI. p <0.05 value was accepted as statistically significant.

3. RESULTS

18 (36%) out of 50 participants were male, while 32 (64%) were female. 18 (36%) of the participants were assisstant doctors, 21 (42%) were intern doctors, 10 (20%) were nurses and 1 (2%) was emergency medical technician (EMT). Mean±SD age of the participants was 26.8±4.2, while mean±SD BMI was found to be 22.56±3.32.

Sixteen (16 (32%)) of the participants were in the slim group and 34 (68%) were in the normal group. Mean compression depth values in the slim group were significantly lower than the normal group (slim 51.94±4.64, normal 55.79±4.35, p=0.006). Compression ratio with sufficient depth in the slim group was statistically significantly lower in comparison to the normal group (slim 66.19±25.79, normal 87.29±19.36, p=0.002). Detailed information about compression data and comparison in between the groups (the cut-off BMI value of 21) are available in Table 1.

Table 1. *Results of compression data between the groups*

	Slim (mean±SD)	Normal (mean±SD)	p value
Mean Compression Depth(mm)	51.94±4.64	55.79±4.35	0.006
Mean Compression Rate (compression/minutes)	111.63±1.66	112±3.03	0.647
Compression Ratio with Complete Chest Recoil (%)	85±14.63	80.74±17.68	0.406
Compression Ratio with Sufficient Depth (%)	66.19±25.79	87.29±19.36	0.002
Compression Ratio with Sufficient Rate (%)	94.75±6.12	92.74±10.41	0.478

SD: Standard deviation

The number of participants with BMI<21 was 16 (32%), the number of participants with 21≤BMI<23 was 17 (34%) and the number of participants with BKI≥23 was 17 (34%). Mean compression depth of the BMI≥23 was statistically higher than that of the BMI<21 (BMI≥23: 57.94±2.74, BMI<21: 51.94±4.64, p<0.001). Mean compression depth of the BMI≥23 was statistically higher than the 21≤BMI<23 (BMI≥23: 57.94±2.74, 21≤BMI<23: 53.65±4.66, p=0.011). Compression ratio with sufficient depth of the BMI≥23 was statistically higher than that of the BMI<21 (BMI≥23: 96.41±6.73, BMI<21: 66.19±25.79, p<0.001). Detailed information about

compression data and comparison in between the groups (the cut-off BMI values of 21 and 23) are available in Table 2.

Linear regression analysis of mean compression depth (dependant) and BMI (independent) showed a statistically significant (r^2=0.179) positive relationship (p=0.002). 'Expected mean compression depth=40.893+0.606*BMI' in line with the calculated regression formula. Moreover, a significant positive correlation was observed between mean compression depth and BMI in the Pearson's correlation analysis (r=0.423, p=0.002).

Table 2. *Results of compression data between the groups (the cut-off BMI values of 21 and 23)*

	BMI<21 (mean±SD)	21≤BMI<23 (mean±SD)	BMI≥23 (mean±SD)	p value	p (I-II)*	p (I-III)**	p (II-III)***
Mean Compression Depth(mm)	51.94±4.64	53.65±4.66	57.94±2.74	<0.001	0.713	<0.001	0.011
Mean Compression Rate(compression/ minutes)	111.63±1.66	112.06±3.5	111.94±2.58	0.894	0.999	0.999	0.999
Compression Ratio with Complete Chest Recoil (%)	85±14.63	81.29±18.17	80.18±17.71	0.698	0.999	0.999	0.999
Compression Ratio with Sufficient Depth (%)	66.19±25.79	78.18±23.48	96.41±6.73	<0.001	0.294	<0.001	0.037
Compression Ratio with Sufficient Rate (%)	94.75±6.12	92.24±11.39	93.24±9.66	0.743	0.999	0.999	0.999

*SD: standard deviation; *: p values are obtained from the paired comparisons of parameters of BMI<21 and 21≤BMI<23 groups; **: p values are obtained from the paired comparisons of parameters of BMI<21 and BMI≥23 groups; ***: p values are obtained from the paired comparisons of parameters of 21≤BMI<23 and BMI≥23 groups*

4. DISCUSSION

We have to take the necessary measures to perform quality cardiopulmonary resuscitation. Anthropometric variables are among one of the factors that will have an impact on CPR's quality. We compared compression data that will affect CPR quality with BMI values in our study.

Mean depth and compression with sufficient depth ratios were significantly lower in the slim group with BMI values below 21 in comparison to the other group. In their manikin study involving 102 nursing students, Roh et al. pointed out that mean depth measurements of the group with BMI values below 18.5 were significantly lower than the other groups (14). The data of the study are compatible with the literature.

Linear regression analysis indicated a significant positive correlation between BMI and mean compression depth data. At the CPR study conducted by Oh et al. with 107 medical students on a manikin, a positive correlation was found between body weight and mean compression depth (15). Regression equation in the same study revealed that rescuers should weigh minimum 70.5 kg to achieve a chest compression depth of 50 mm. The data of the study are compatible with the literature.

A significant positive correlation was observed between BMI and mean depth in our study. The highest positive correlation was found between mean depth and body weight in the correlation analysis of anthropometric variables and CPR data in the CPR study by Oh et al. conducted with 107 medical students on a manikin (15). The same study showed a significant positive correlation between BMI and mean depth. Similarly, the study of Méndez-Martínez et al. including 112 nursing and physiotherapy students found out a significant positive relationship between BMI and weight (16). The data of the study are compatible with the literature.

The study by Contri et al. where 333 participants performed CPR on a manikin indicated that people who are heavier, who have a greater BMI achieve less chest recoil (6). In our study, chest recoil ratio was found out to be higher in the slim BMI group but the difference in between was not statistically significant. The importance of achieving higher chest recoil decreases due to lack of sufficient depth.

5. CONCLUSION

As a conclusion, it was found out that low BMI values are associated with low mean compression depth. Effective trainings to achieve sufficient mean depth should be provided as out-of-hospital arrest patients for whom a low mean depth CPR is performed, have a higher mortality (17,18). However, it is observed that low weighing individuals could not achieve the sufficient chest compression depth though they have participated in effective CPR trainings (19). Therefore, we should be more careful and sensitive when we provide CPR trainings to low weighing professionals (14,19). We are in the opinion that we should be more sensitive in terms of CPR training of professionals with low BMI values and besides, professionals with higher BMI values should be responsible for compression during CPR as long as there is a sufficient number of professionals to do so.

The limitation of the study could be considered as the low number of participants. The low number of participants especially in the slim group constitutes another limitation as it reduces the power of statistical comparison. The factors such as being a manikin study, failure to evaluate the survival rates can be considered as another limitations of our study. A separate limitation is that compression data cannot be compared according to gender. Because male gender with low BMI values may be different from female.

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Clinical and Experimental Health Sciences

The Potent Cytotoxic and Oxidative Effects of β-2 Selective ICI-118,551 on Breast Adenocarcinoma Cell Lines with Different Aggressiveness

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ABSTRACT

Objective: Beta-blockers are a group of drugs used in the treatment of cardiovascular diseases. On the other hand, the potential anticancer effects of these drugs have become increasingly important in recent two decades. In this paper, the effects of beta-1 selective esmolol, beta-2 selective ICI-118,551 and non-selective nadolol on breast cancer cell lines with different aggressiveness were investigated for the first time.

Methods: A standard spectrophotometricMTT assay was used to determine cell viability. Catalase activities and malondialdehyde levels were measured spectrophotometrically based on the reduction of absorbance resulted from hydrogen peroxide decomposition and the formation of thiobarbituric acid – malondialdehyde product, respectively.

Results: It was found that beta-2 selective ICI-118,551 was the most effective one among investigated blockers against MCF-7 and MDA-MB-231 cell lines. Additionally, it was seen that 50-150 µM ICI-118,551 treatment for 48 hours significantly changed catalase activities and malondialdehyde levels in both breast cancer cell lines in favour of radical production.

Conclusion: The obtained results showed that beta-2 adrenergic receptor specific antagonism plays a significant role in beta-blocker induced breast cancer cell death. The outstanding suppression in catalase activities and concomitant increase in radical levels appear to contribute to potent cytotoxic effect of ICI-118,551 on breast adenocarcinoma. Consequently, it can be clearly interpreted that ICI-118,551 may be a valuable option in the treatment of breast cancer.

Keywords: Esmolol, ICI-118,551, nadolol, breast adenocarcinoma.

1. INTRODUCTION

Adrenergic receptors, also called as adrenoceptors, are the cell surface components that play a central role in the sympathetic nervous system and form a class of G protein-bound receptors.They are classified as alpha (α-1 and α-2) and beta (β-1 and β-2) based on the interactions with their agonists and antagonists.Adrenergic receptors are the targets of medications such as α – and β-blockers as well as catecholamines including norepinephrine and epinephrine. The classification of these α – and β-blockers is done based on the type of receptor affected and these drugs are used in the treatment of conditions such as high blood pressure, migraine, irregular heart rhythm, heart failure, heart attack and chest pain (1).In addition to the routine use of adrenergic receptor blockers in the treatment of the specified ailments, their effects on proliferations of various healthy and cancerous cell/tissue types have been also investigated, especially in studies conducted over the last 20 years. It should be noted that these researches are very valuable in terms of focusing both the side effects and possible off-label usages of the so-called medications with known pharmacology.For instance, it was found that while non-selective β-blockers carvedilol and propranolol, and β-1 selective atenolol suppressed endoplasmic reticulum stress, oxidative stress and cell death in human coronary artery endothelial and liver cancer cells (2), another β-1 selective blocker nebivolol inhibited cell proliferation and induced death in human coronary smooth muscle and endothelial cells (3).On the contrary, Uzar and his friends stated that the same blocker protected rat brain from ischemia-induced damage by preventing oxidative stress and cell death(4). The suppression in myocardial cell death was shown for β-1 selective blocker metoprolol (5-7).In a study conducted by Smith and Smith, propranolol and β-2 specific blocker ICI-118,551 were shown to induce death in peripheral lung capillary endothelial cells (8). It was found that longevity of patients with ovarian cancer who take atenolol, propranolol, metoprolol, non-selectivelabetolol and carvedilolblockers

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significantly increased compared to patients who did not use (9).In a similar study conducted by Powe et al., it was found that metastasis formation decreased in patients who started β-blocker treatment before breast cancer diagnosis (10). It was stated in another observationally-based study that while atenolol had no effect, propranolol significantly decreased the mortality rates of breast cancer patients (11).It was also shown for propranolol that this beta-blocker inhibited proliferation and induced significant death in endothelial cells from hemangioma (12-17). Besides hemangioma endothelial cells, propranolol was found to induce cell death in several cancer types including pancreatic and stomach carcinomas, neuroblastoma, and melanoma (18-21). From thisliterature view, it is clearly seen that adrenergic receptor blockers have reverse effects on cell viability depend on the type of affected cell/tissue. In this study, the effects ofβ-1 selective esmolol, β-2 selective ICI-118,551 and non-selective nadolol on breast cancer cell proliferation were examined for the first time. For this aim, two breast cancer cell lines having different aggressiveness were used. Our results showed that all three drugs, but especially β-2 selective ICI-118,551, have promising activities on breast adenocarcinoma. In addition, it was found that the most effective beta-blocker ICI-118,551 suppressed antioxidant system and caused the formation of oxidative stress, which were determined by catalase activities and malondialdehyde (MDA) levels, respectively.

2. METHODS

2.1. Materials

All chemicals used were of analytical grade or higher where appropriate and obtained from Sigma-Aldrich, Inc. (St. Louis, MO, USA) unless otherwise stated.

2.2. Cell Culture

The human breast adenocarcinoma cell lines, MCF-7 and MDA-MB-231, were obtained from American Type Culture Collection (ATCC, USA). Both cell lines were cultured with high-glucose Dulbecco's modified Eagle's medium (DMEM) supplemented with 100 IU/mL penicillin, 100µg/mLstreptomycin and 20% fetal bovine serum (FBS) in a humidified atmosphere of 95% air with 5% CO_2 at 37°C.

2.3. Determination of Cell Viability

The effects of esmolol, ICI-118,551 and nadolol on the viability of MCF-7 and MDA-MB-231 cell lines were investigated through MTT assay which based on the reduction of the tetrazolium salt (3-(4,5-Dimethyl-2-thiazolyl)-2,5-diphenyl-2H-tetrazolium bromide) to its insoluble formazan as a result of metabolic activity (22). In the assay, briefly, breast cancer cell lines were seeded into 96-well plates at a density of $1x10^4$ per 100 µLwell and allowed to attach for 24 h before drug treatment. Then, the cells were exposed to various concentrations of β-blockers (5–250 µM) for 24 and 48 h. After treatment period, 25 µL MTT solution (5 mg/mLphosphate-buffered saline, PBS) was added and the plates were located in an incubator with 5% CO_2 at 37 ^{0}C. After 4 h incubation time, insoluble formazan crystals were dissolved in dimethyl sulfoxide (DMSO) and then cell growth was assessed by measuring the absorbance at 570 nm. Cell viability was expressed as percentage survival, with 100% survival taken as that observed in related control cells. Because DMSO was used as the drug solvent, control cells were treated with maximum 0.1% or lower concentrations of DMSO. The solvent in the used concentration range was non-toxic and did not influence the viabilities of both cell lines.

2.4. Crude Extracts Preparation For Biochemical Analysis

Commercial RIPA Buffer (Sigma, R0278, USA) was used for the cell lysis procedure. Briefly, growth medium was removed by aspiration and cells were washed two times with Dulbecco's phosphate-buffered saline (DPBS) to remove residual medium. After final washing step, an appropriate volume of RIPA Buffer (1 mL for $0.5\text{-}5x10^7$ cells) was added and cells were incubated on ice for five min. Then, the plates were scraped and the lysates were clarified by centrifugation at 12,000 rpm for 10 min at 4 ^{0}C. Supernatants were carefully transferred into clean tubes and stored at –70^{0}C for future use.

2.5. Biochemical Analysis

2.5.1. Catalase activity

Catalase activity was determined according to the Aebi method (23). The method is based on the reduction of absorbance at 240 nm resulted from hydrogen peroxide (H_2O_2) decomposition by catalase at 25 ^{0}C. 10.5 mM H_2O_2 prepared in 50 mM phosphate buffer (pH 7.0) was used in the assay. 1 U enzyme activity is defined as the amount of enzyme required to decompose 1 µmol H_2O_2 under standard conditions. Enzyme activity was calculated using the molar extinction coefficient of H_2O_2 (39.4 L $mmol^{-1}cm^{-1}$).

2.5.2. Membrane lipid peroxidation levels

MDAis a stable by-product of membrane lipid peroxidation. To assess the membrane lipid peroxidation levels, the formation of MDA was measured by using the thiobarbituric acid (TBA) reaction (24). Briefly, 500 µL cell lysate was incubated with 500 µL10% trichloroacetic acid (TCA) for 15 min at 90 ^{0}C. After 10 min centrifugation, 500 µL supernatant was mixed with 500 µLTBA and again incubated for 15 min at 90 ^{0}C. The absorbance of MDA-TBA product in 532 nm was recorded against blank. Lipid peroxidation levels were calculated using the molar extinction coefficient of MDA ($1.56x10^5$ mol L^{-1} cm^{-1}).

2.5.3. Total protein levels

Bradford method was used for the measurement of the total protein concentration in the cell lysates (25). Briefly, 100 µL sample was mixed with 900 µL Bradford reagent prepared by using Coomassie Brilliant Blue G-250 dye and after 2 min incubation, the absorbance in 595 nm was recorded against blank.Bovine serum albumin (BSA) was used asa standard.

2.6. Statistical Analysis

The data are presented as the mean ± S.E.M. The differences in variance were analyzed statistically using a one-way analysis of variance (ANOVA) test by Graphpad prism 5.0 statistics software (GraphPad, La Jolla, CA, USA). Tukey's test was used as a post hoc.

3. RESULTS

3.1. The Effects of Beta-Blockers on Breast Adenocarcinoma Cell Viability

The antiproliferative effects of 5-250 µM β-1 selective esmolol, β-2 selective ICI-118,551 and non-selective nadolol on breast cancer cell lines were investigated for 24 and 48 h. For this aim, two different cell lines with different aggressiveness, MCF-7 and MDA-MB-231, were used. MCF-7 cell line which has a normal expression of human epidermal growth factor receptor 2 (HER2) is estrogen – and progesterone-receptors positive. On the other hand, MDA-MB-231 cells are triple negative and therefore more aggressiveand less chemosensitive to conventional cytotoxic agentsthan the first one (26).We observed that there was no any significant difference between control and5-10µM esmolol treated groups after 24 h treatment in MCF-7 cell line.Although 25-250 µM esmolol could significantly inhibit cell viability compared to the control, the cytotoxicitydid not gradually increase with the increasing concentrations of the drug (Figure 1A).This cell line became sensitive to the lowest concentrations of esmolol after an additional 24 h of treatment. The same pattern for higher concentrations of the drug wasalso recorded but cell viability could not be reduced below 56% (Figure 1B). It was observed that MDA-MB-231 cell line was more resistant to esmolol (Figure 2). Whilecell viability could not be significantly reduced compared to the control group up to 150 and 250 µM of esmolol for 24 and 48 h, respectively, it was even insignificantly induced at lower concentrations of the drug. The viability percentage of MDA-MB-231cells treated with the highest concentration of esmolol was determined as 68.40±11.72. Unlike esmolol, ICI-118,551 was observed to be highly effective against breast cancer cell proliferation (Figures 3 and 4). As can be seen from Figure 3A, 25-250 µM ICI-118,551 treatment for 24 h caused significant inhibition of MCF-7 cell proliferation compared with the control group and this inhibition was generally correlated with the increasing concentration of the drug. This potent cytotoxic effect of ICI-118,551 was further enhanced by 48 h treatment and viability decreased up to 5.33±1.13 (Figure 3B). More aggressive breast cancer cell line MDA-MB-231 was again found more resistant to this blocker,but especially for highest concentrations and longer treatment period. Nevertheless, it was observed that cell viability significantly reduced below 50% from 100 µM onwards in both 24 and 48 h treatments. Despite it was observed that nadolol was slightly more effective than esmolol, viability values below 50% could not be obtained for both cell lines (Figures 5 and 6). As is the case with β-1 selective esmolol and β-2 selective ICI-118,551, triple negative MDA-MB-231 cell line showed more resistance to non-selective nadolol than MCF-7. Given all these results, it is obvious that β-2 selective ICI-118,551 is much more effective on breast cancer than other investigated blockers.

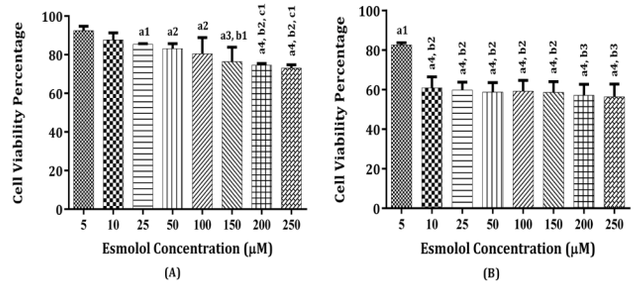

Figure 1. *The effects of different concentrations of esmolol on viability percentage of MCF-7 cells for 24 h (A) and 48 h (B). Data with error bars show the mean ± S.E.M of three experiments. adenotes significant differences between other studied groups and control group ([a1]p<0.05; [a2]p<0.01; [a3]p<0.001; [a4]p<0.0001), b denotes significant differences between other studied groups and 5 µM esmolol treated group ([b1]p<0.05; [b2]p<0.01; [b3]p<0.001), c denotes significant differences between other studied groups and 10 µM esmolol treated group ([c1]p<0.05) by Tukey's multiple range tests.*

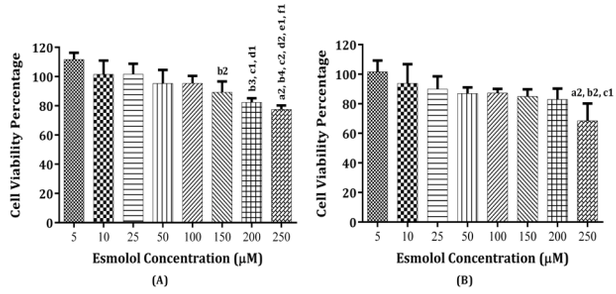

Figure 2. *The effects of different concentrations of esmolol on viability percentage of MDA-MB-231 cells for 24 h (A) and 48 h (B). Data with error bars show the mean ± S.E.M of three experiments. adenotes significant differences between other studied groups and control group ([a2]p<0.01), b denotes significant differences between other studied groups and 5 µM esmolol treated group ([b2]p<0.01; [b3]p<0.001; [b4]p<0.0001), c denotes significant differences between other studied groups and 10 µM esmolol treated group ([c1]p<0.05; [c2]p<0.01), d denotes significant differences between other studied groups and 25 µM esmolol treated group ([d1]p<0.05; [d2]p<0.01), e denotes significant differences between other studied groups and 50 µM esmolol treated group ([e1]p<0.05), f denotes significant differences between other studied groups and 100 µM esmolol treated group ([f1]p<0.05) by Tukey's multiple range tests.*

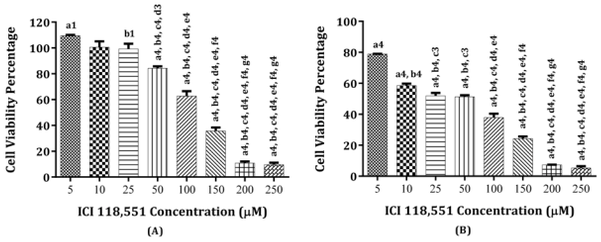

Figure 3. *The effects of different concentrations of ICI-118,551 on viability percentage of MCF-7 cells for 24 h (A) and 48 h (B). Data with error bars show the mean ± S.E.M of three experiments. adenotes significant differences between other studied groups and control group (^{a1}p<0.05; ^{a4}p<0.0001), b denotes significant differences between other studied groups and 5 μM ICI-118,551 treated group (^{b1}p<0.05; ^{b4}p<0.0001), c denotes significant differences between other studied groups and 10 μM ICI-118,551 treated group (^{c3}p<0.001; ^{c4}p<0.0001), d denotes significant differences between other studied groups and 25 μM ICI-118,551 treated group (^{d3}p<0.001; ^{d4}p<0.0001), e denotes significant differences between other studied groups and 50 μM ICI-118,551 treated group (^{e4}p<0.0001), f denotes significant differences between other studied groups and 100 μM ICI-118,551 treated group (^{f4}p<0.0001), g denotes significant differences between other studied groups and 150 μM ICI-118,551 treated group (^{g4}p<0.0001) by Tukey's multiple range tests.*

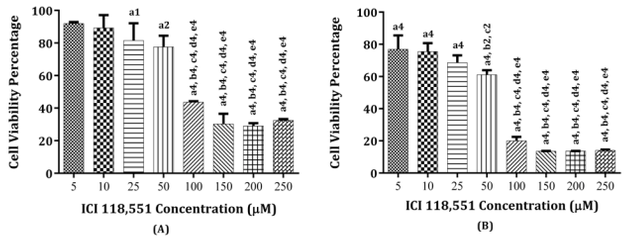

Figure 4. *The effects of different concentrations of ICI-118,551 on viability percentage of MDA-MB-231 cells for 24 h (A) and 48 h (B). Data with error bars show the mean ± S.E.M of three experiments. adenotes significant differences between other studied groups and control group (^{a1}p<0.05; ^{a2}p<0.01; ^{a4}p<0.0001), b denotes significant differences between other studied groups and 5 μM ICI-118,551 treated group (^{b2}p<0.01; ^{b4}p<0.0001), c denotes significant differences between other studied groups and 10 μM ICI-118,551 treated group (^{c2}p<0.01; ^{c4}p<0.0001), d denotes significant differences between other studied groups and 25 μM ICI-118,551 treated group (^{d4}p<0.0001), e denotes significant differences between other studied groups and 50 μM ICI-118,551 treated group (^{e4}p<0.0001) by Tukey's multiple range tests.*

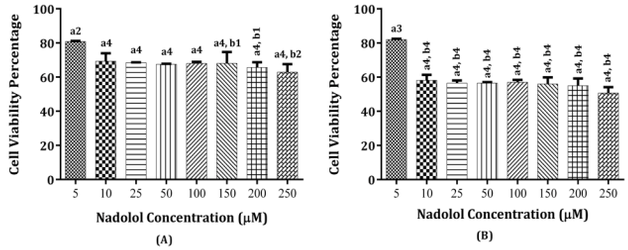

Figure 5. *The effects of different concentrations of nadolol on viability percentage of MCF-7 cells for 24 h (A) and 48 h (B). Data with error bars show the mean ± S.E.M of three experiments. adenotes significant differences between other studied groups and control group (^{a2}p<0.01; ^{a3}p<0.001; ^{a4}p<0.0001), b denotes significant differences between other studied groups and 5 μM nadolol treated group (^{b1}p<0.05; ^{b2}p<0.01; ^{b4}p<0.0001) by Tukey's multiple range tests.*

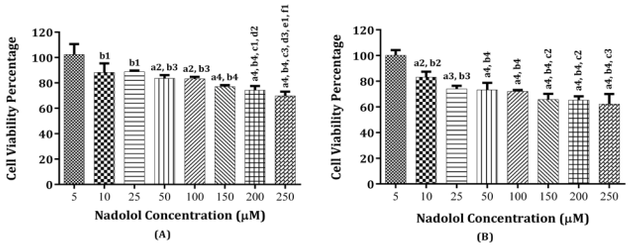

Figure 6. *The effects of different concentrations of nadolol on viability percentage of MDA-MB-231 cells for 24 h (A) and 48 h (B). Data with error bars show the mean ± S.E.M of three experiments. adenotes significant differences between other studied groups and control group (^{a2}p<0.01; ^{a3}p<0.001; ^{a4}p<0.0001), b denotes significant differences between other studied groups and 5 μM nadolol treated group (^{b1}p<0.05; ^{b2}p<0.01; ^{b3}p<0.001; ^{b4}p<0.0001), c denotes significant differences between other studied groups and 10 μM nadolol treated group (^{c1}p<0.05; ^{c2}p<0.01; ^{c3}p<0.001), d denotes significant differences between other studied groups and 25 μM nadolol treated group (^{d2}p<0.01; ^{d3}p<0.001), e denotes significant differences between other studied groups and 50 μM nadolol treated group (^{e1}p<0.05), f denotes significant differences between other studied groups and 100 μM nadolol treated group (^{f1}p<0.05) by Tukey's multiple range tests.*

3.2. The Effects of ICI-118,551 on Catalase Activities of Breast Adenocarcinoma

Catalase is one of the main antioxidant enzymes that catalyzes the dismutation of H_2O_2 to molecular oxygen and water. In this study, catalase activities of MCF-7 and MDA-MB-231 cells treated with 50-150 μM ICI-118,551 for 48 h were determined. It was found for all treatments that catalase activities were significantly decreased compared to related controls (p<0.0001) (Figure 7A-B). These decreases were reached to about 14.7 – and 11.6-folds at 150 μM in MCF-7 and MDA-MB-231 cell lines, respectively.

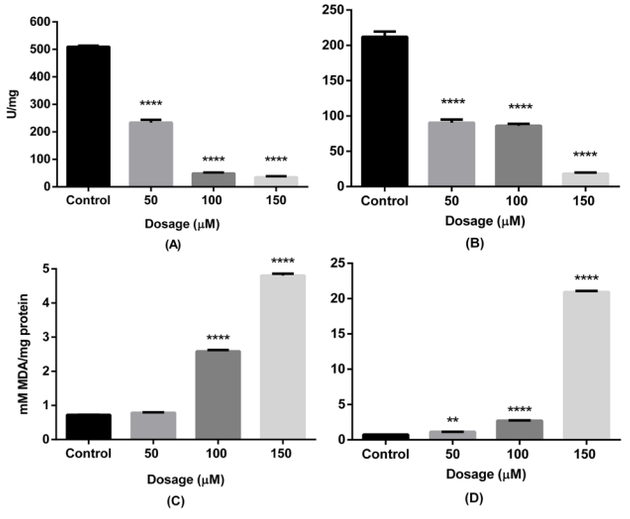

Figure 7. *The effects of different concentrations of ICI-118,551 on catalase activities of MCF-7 (A) andMDA-MB-231 (B) and MDA levels of MCF-7 (C) andMDA-MB-231 (D) cells for 48 h. Data with error bars show the mean ± S.E.M of three experiments. **=p<0.01; ****=p<0.0001 denotes significant differences between control and other studied groups by Tukey's multiple range tests.*

3.3. The Effects of ICI-118,551 on MDALevels of Breast Adenocarcinoma

In this paper, we also dealt with MDA levels of the samples treated with 50-150 µM ICI-118,551 for 48 h. As very well known, MDA level is a reliable indicator of lipid peroxidation resulting from oxidative stress. As can be seen from Figure 7C-D, all treatments caused the significant increases in MDA levels, except 50 µM ICI-118,551 treated MCF-7 cells. MDA levels of MCF-7 and MDA-MB-231 cells gradually increased with the increasing concentrations of the blocker and reached to 4.81±0.06 and 20.93±0.18 by increasing about 6.68 – and 28.67-folds compared to related controls, respectively. There were moderate negative correlations (r_{MCF-7}=-0.778; $r_{MDA-MB-231}$=-0.731) between catalase activities and MDA levels of both cell lines. These findings clearly showed for the first time that the significant suppressions in catalase activitiesand concomitant increases in radical levelscontributed to potent cytotoxic effect of ICI-118,551.

4. DISCUSSION

In this paper, the effects of β-1 selective esmolol, β-2 selective ICI-118,551 and non-selective nadolol blockers were examined on MCF-7 and MDA-MB-231 cell lines. According to the obtained findings, it was seen that ICI-118,551 rather than esmolol and nadolol has very potent cytotoxic effects on both breast adenocarcinoma lines. As mentioned previously, β-blockers exert their intracellular effects via interaction with theassociated adrenergic receptors. Hence, the apparent cytotoxicity of β-2 selective ICI-118,551 on the stated cell lines indicate in a sense that β-2 adrenergic receptor-specific antagonism plays an important role in β-blocker induced breast cancer cell death. As a matter of fact, similar results have been reported in some other studies. For instance, Wolter et al. compared the effects of β-1 and β-2 specific blockers on neuroblastoma cell line with non-selective blocker propranolol and showed that this non-selective blocker mainly induced death with β-2specific antagonism (20). It was stated in other recent studies that non-selective propranolol and β-2 selective ICI-118,551 but not β-1 selective metoprolol and atenolol were found to be quite effective against human breast and colorectal cancers (27,28). However, there are some data that contradict these results (29). The variations in the expression levels of differentβ-adrenergic receptor subtypesin different cell types can be demonstrated as the responsible for this situation. On the other hand, off-target effects of ICI-118,551 on human breast cancer cells should be considered and further investigated due to the inability to reach similar results with non-selective nadolol.

It is known from other studies that β-blockers have some anti-oxidative effects on healthy/non-cancerous cells and tissues (30,31). On the other hand, according to our literature view, there is no any other research dealing with the effects of β-blockers on antioxidant system of cancerous cells. Our results indicated that oxidative stress, which wascharacterized by MDA levels, increased as a result of β-2 selective ICI-118,551 treatment in both cancer cell lines. As it is known, increase in intracellular radical levels, occurrence of oxidative stress and resultant damage in biomolecules is a cascade-like process leading the cell to death. Hence, it is clear that increased oxidative stress status as one of the results of significant decreases in catalase activities contributed to ICI-118,551 induced toxicity.

5. CONCLUSION

As a conclusion, all these results reveal the potential cytotoxic and oxidative effects of ICI-118,551 on human breast cancer cell lines. The findings obtained on the aggressive MDA-MB-231 model which is resistant to chemotherapy are particularly important. Although high concentrations seem to be required to reach the effective doses in *in vitro* studies, it is well known that there are significant differences in these doses when compared to *in vivo* models which require much lower doses of β-blockers. Therefore, β-2 selective ICI-118,551 may be seen as a potential candidate in the treatment of human breast cancer. Considering the difficulties of the new drug development stages, it is extremely important to find the usability of β-blockers having no side effects and with known pharmacology in cancer treatment. Finally, we must state that these results should be supported by further *in vivo* studies.

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Clinical and Experimental Health Sciences

Assessment of Awareness and Knowledge of Oral Cancer Among Tobacco-Using Dental Patients

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ABSTRACT

Objective: The aim of this study is assesment of awareness and knowledge of oral cancer in a group of tobacco users.

Methods: The study group consisted of 100 adult patients aged 18 years and over who applied to Marmara University Faculty of Dentistry Oral and Maxillofacial Radiology Clinic for routine examination. The patients were asked to complete a 16-point questionnaire evaluating the effects of smoking on oral cancer.

Results: The participants in our study identified oral cancer symptoms as swelling / mass formation (60%), wound in mouth (58%), loss of sensation (39%) and pain (38%). There was statistically significant difference between the responses given to "What are the causes of oral cancer?", "what are the symptoms of oral cancer?" and "What are the diagnostic methods for oral cancer?" between women and men ($p < 0.05$). The rate of responding to the question "What do you think are the causes of oral cancer?" as "alcohol use" in women (63.3%) was significantly higher than men (39.2%) ($p= 0.027$; $p <0.05$). There was no statistically significant difference between genders regarding "smoking" and "chewing tobacco" as oral cancer factor ($p > 0.05$).

Conclusion: It is concluded that women smoker individiuals have more awareness, knowledge level and positive attitudes about oral cancer compared to men. Increasing level of knowledge of individuals about oral cancer, routine examination of individuals at high risk group and development of national policies with this purpose can make a contribution to improve the level of consciousness.

Keywords: Oral Cancer, Smoking, Public Awareness

1. INTRODUCTION

Oral cavity cancers were the seventh most commonly occurring cancer and, in terms of mortality, the ninth deadliest by cancer site in the world as stated by World Cancer Report 2014 (1–6). Besides skin and thyroid cancers, after larynx carcinoma, oral cavity cancers are supposed to be the second most common head and neck malignancy in Turkey (7). Oral squamous cell carcinoma represents one of the most common but scarcely known malignancies worldwide. The etiology of oral squamous cell carcinoma is strongly related to lifestyle habits and behavior, especially tobacco smoking and alcohol abuse.

Tobacco and alcohol use is the primary risk factors for oral cancer in patients over the age of 45 years (8,9). Low consumption of fruits and vegetables, immunodeficiency exposure to the sun, socio-economic status, and infection with human papilloma virus (HPV) are some of the other risk factors for oral cancers (10-12). Previous studies in literature revealed that the incidence of oral cancer increases with smoking tobacco, older age, and alcohol consumption (1,5 13,14).

Epidemiological studies have shown that the risk of developing cancer in smokers is 5-9 times higher than in non-smokers. This rate may increase to 17 times in individuals consuming more than 80 cigarettes per day. The risk of having a second malignant upper respiratory disease increases by 2 to 6 times in patients who have been treated and continue smoking (15).

In a study conducted by Formosa et al. (16), a self-administered questionnaire was designed and consisted of the questions to ascertain socio-demographic information, awareness and knowledge of oral and pharyngeal cancer. The study revealed that 52.3% of the respondents were aware of the existence of oral cancer. Of those who were aware of oral cancer, 92% agreed or strongly agreed that smoking is a strong risk factor for oral cancers.

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Peker et al. (17) evaluated levels of public awareness and knowledge about early signs and risk factors of oral cancer among a group of dental patients in Turkey. The results of the study reveals that 79.2% of the participants were unaware of the early signs related to oral cancer and 29.9% of them were unaware of risk factors of the disease. There were no statistically significant differences between age, gender, and education levels for awareness of risk factors. Therefore, the primary aim of this study was to assess the awareness and knowledge of oral cancers and smoking as a risk factor among group of smokers.

2. METHODS

The study protocol of this thesis study was approved by Marmara University School of Medicine Non-Interventional Clinical Research Ethics Committee on 14.06.2019 with protocol number 09.2019.553. This research was carried out in Marmara University Faculty of Dentistry, İstanbul, Turkey. In this study, the study group consisted of 100 patients aged 18 years and over who applied to the Department of Oral and Maxillofacial Radiology for routine examination. A questionnaire consisting of 16 questions evaluating oral cancer information and smoking, including questions about sociodemographic examination, was administered to the study group.

Statistical Analysis

IBM SPSS Statistics 22.0 (IBM SPSS, Turkey) program is used for statistical analysis. Descriptive statistical methods (frequency) as well as qualitative data were compared using the Chi-Square test, Fisher's Exact Chi-Square test, Continuity (Yates) Correction, and Fisher's Freeman Halton test. Significance was assessed at $p < 0.05$ level.

3. RESULTS

The study was performed on 100 patients, over 18 years old, and 49 (49.0%) female and 51 (51.0%) male were included (Table 1).

In the study, 75% of the participants considered the age group most affected by oral cancer as 40 years and older, while 19% considered young adults and 6% considered childhood (Table 2). The rates of participation in the statement "causes of oral cancers" are 78% smoking, 55% chewing tobacco, 51% drinking alcohol, 43% genetic predisposition, 41% unhealthy nutrition, 41% chemicals, 39% irregular life and stress, 33% decayed teeth, 27% inappropriate dentures, 10% other answers and 10% of the participants have no idea (Figure 1). In addition, it is reported that 47% of smoker patients in our study get information about oral cancer from their dentists. The participants stated that they would quit smoking (70%), eat well (52%), take medication (20%) for prevention of oral cancer. There was no statistically significant difference between the amount of daily cigarette smoking by gender ($p>0$ .05) (Table 3) (Figure 2).

Table 1: *Distribution of demographic characteristics*

		n	%
Gender	Woman	49	49.0
	Male	51	51.0
Age	18-20 years	4	4.0
	20-30 years	56	56.0
	30-40 years	24	24.0
	40-50 years	12	12.0
	Over 50 years	4	4.0
Marital status	Married	37	37.0
	Single	63	63.0
Education	Primary education or lower	10	10.0
	Secondary education	9	9.0
	High school	19	19.0
	College	62	62.0
Occupation	Retired	4	4.0
	Self-employed	30	30.0
	Artisan	7	7.0
	Merchant	2	2.0
	Mid-level executive	8	8.0
	Officer	14	14.0
	Employee	14	14.0
	Housewife	21	21.0
Medical condition	Healthy	82	82.0
	Has a medical issue	18	18.0
Diseases	Other	11	61.0
	Diabetes	2	11.1
	Diabetes + Other	1	5.6
	Diabetes + Hypertension	1	5.6
	Hypertension	2	11.1
	Cardiovascular system diseases	1	5.6
Smoking duration	< 5 years	40	40.0
	6-10 years	20	20.0
	More than 10 years	40	40.0
Daily cigarette use	<1 package per day	62	62.0
	1 package per day	32	32.0
	More than 1 package per day	6	6.0
Diseases caused by smoking	Does not cause any disease	4	4
	COPD	80	80
	Lung cancer	86	86
	Coronary heart diseases	65	65
	Pancreatic cancer	28	28
	Oral cancer	71	71
	Other	21	21

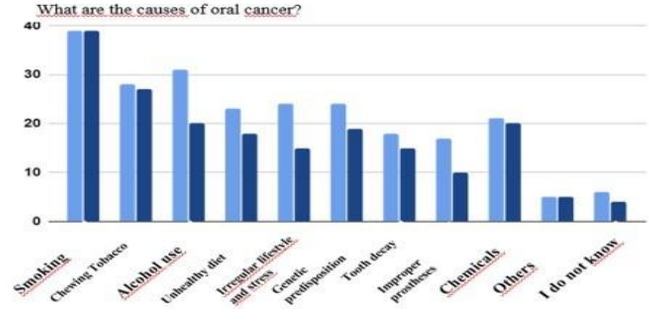

Figure 1.Distribuiton *of participants answers for causes of oral cancer.*

Table 2: *Evaluation of information on oral cancer*

		n	%
Age group most affected by oral cancer	Children	6	6
	Young Adults	19	19
	40 years and older	75	75
Causes of oral cancer	Smoking	78	78
	Chewing Tobacco	55	55
	Alcohol use	51	51
	Unhealthy diet	41	41
	Irregular lifestyle and stress	39	39
	Genetic predisposition	43	43
	Tooth decay	33	33
	Improper prostheses	27	27
	Chemicals	41	41
	Other	10	10
	I do not know	10	10
Symptoms of oral cancer	Wound in mouth	58	58
	Swelling / mass formation	60	60
	Pain	38	38
	Bleeding of the gums	27	27
	Loss of sensation	39	39
	Other	11	11
	I do not know	27	27
Oral cancer diagnosis methods	Regular inspection and control	68	68
	Non-neglect of wounds	48	48
	Consult a doctor if there is a problem	61	61
	Other	5	5
	I do not know	16	16
Oral cancer prevention methods	To use medicine	20	20
	Stop smoking	70	70
	Healthy eating	52	52
	Other	10	10
	I do not know	23	23
The consequences of oral cancer	Tooth loss	47	47
	Jaw-related damage / tissue loss	62	62
	Spread / affection of lymph nodes	45	45
	Inability to heal	38	38
	Death / life hazard	51	51
	Other	7	7
	I do not know	24	24
Sources of information on oral cancer	Family	9	9
	Dentist	47	47
	Press (television, internet etc.)	32	32
	Other (friends, patient)	24	24
	I do not have any information sources	36	36

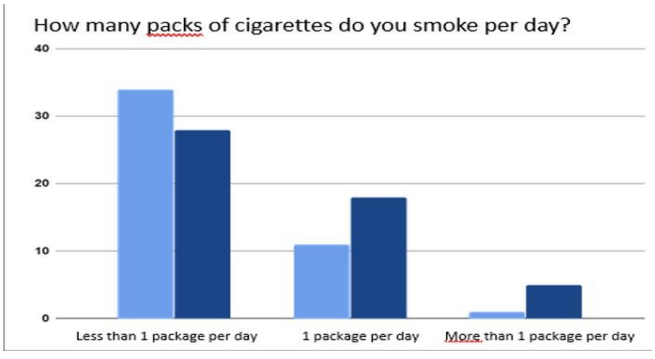

Figure 2. *Assessment of daily smoking by gender*

Table 3: *Assessment of daily smoking by gender*

Daily cigarette use	Woman	Male	p
	n (%)	n (%)	
Less than 1 package per day	34 (69.4%)	28 (54.9%)	0.182
1 package per day	14 (28.6%)	18 (35.3%)	
More than 1 package per day	1 (%2)	5 (9.8%)	

Fisher Freeman Halton Test

Woman participants (63.3%) who answered "alcohol use" to the question "What do you think causes oral cancer?" is highly statistically significant than that of man patients (39.2 %) (p=0.027, p<0.05). To the question "What do you think are the symptoms of oral cancer?", woman patients rate of answering "wound in mouth" (69.4 %) is stastistically higher than man participants (47,1%) (p=0 ,040, p<0 ,05). There was no statistically significant difference between genders in terms of the answers **"**swelling / mass formation" , "pain" , "gingival bleeding" and "loss of sensation" as a sign of oral cancer (p>0,05). The rate of woman patients "referring to a doctor when there is a symptom" as a method of diagnosis of oral cancer (73, 5%) was statistically higher than that of men (49%) (p=0,021; p<0,05). There was no statistically significant difference between the genders in terms of answers to the questions **"**What do you think are the methods of prevention from oral cancers?", "What do you think are the consequences of oral cancer?, "What are your sources of information about oral cancers?" (p>0,05) (Table 4).

Table 4: *Evaluation of information on oral cancer by gender*

		Woman	Male	p
		n (%)	n (%)	
Age group most affected by oral cancer	Childhood	4 (8.2%)	2 (3.9%)	[1]0.446
	Young Adult	11 (22.4%)	8 (15.7%)	
	40 years and older	34 (69.4%)	41 (80.4%)	
Causes of oral cancer	Smoking	39 (79.6%)	39 (76.5%)	[2]0.892
	Chewing Tobacco	28 (57.1%)	27 (52.9%)	[3]0.673
	Alcohol use	31 (63.3%)	20 (39.2%)	[2]0.027 *
	Unhealthy eating	23 (46.9%)	18 (35.3%)	[2]0.327
	Irregular life and stress	24 (49%)	15 (29.4%)	[2]0.072
	Genetic predisposition	24 (49%)	19 (37.3%)	[2]0.326
	Tooth decay	18 (36.7%)	15 (29.4%)	[2]0.572
	Improper prostheses	17 (34.7%)	10 (19.6%)	[2]0.141
	Chemicals	21 (42.9%)	20 (39.2%)	[3]0.711
	Other	5 (10.2%)	5 (9.8%)	[4]1.000
	I do not know	6 (12.2%)	4 (7.8%)	[4]0.521
Symptoms of oral cancer	Wound in mouth	34 (69.4%)	24 (47.1%)	[2]0.040 *
	Swelling / mass formation	33(67.3%)	27 (52.9%)	[2]0.206
	Pain	21 (42.9%)	17 (33.3%)	[2]0.438
	Bleeding of the gums	17 (34.7%)	10 (19.6%)	[2]0.141
	Loss of sensation	23 (46.9%)	16 (31.4%)	[2]0.164
	Other	7 (14.3%)	4 (7.8%)	[2]0,478
	I do not know	9 (18.4%)	18 (35.3%)	[2]0.093

Table 4: *(Continued)*

Oral cancer diagnosis methods	Regular inspection and control	36 (73.5%)	32 (62.7%)	[2]0,350
	Non-neglect of wounds	32 (65.3%)	16 (31.4%)	[2]0.001 *
	Consult a doctor if there is a problem	36 (73.5%)	25 (49%)	[2]0.021 *
	Other	4 (8.2%)	12)	[4]0,200
	I do not know	5 (10.2%)	11 (21.6%)	[2]0.202
Oral cancer prevention methods	To use medicine	9 (18.4%)	11 (21.6%)	[2]0.881
	Stop Smoking	38 (77.6%)	32 (62.7%)	[2]0.162
	Eat well	28 (57.1%)	24 (47.1%)	[3]0.313
	Other	5 (10.2%)	5 (9.8%)	[4]1.000
	I do not know	9 (18.4%)	14 (27.5%)	[2]0.400
Oral cancer results	Tooth loss	25 (51%)	22 (43.1%)	[3]0.430
	Jaw-related damage / tissue loss	31 (63.3%)	31 (60.8%)	[2]0.961
	Spread / affect the lymph system	24 (49%)	21 (41.2%)	[3]0.433
	Inability to heal	22 (44.9%)	16 (31.4%)	[3]0.164
	Death / life hazard	24 (49%)	27 (52.9%)	[3]0.692
	Other	4 (8.2%)	3 (5.9%)	[4]0.712
	I do not know	12 (24.5%)	12 (23.5%)	[2]1.000
Sources of information on oral cancer	Family	4 (8.2%)	5 (9.8%)	[4]1.000
	Dentist	23 (46.9%)	24 (47.1%)	[3]0.990
	Press (television, internet etc.)	15 (30.6%)	17 (33.3%)	[2]0.938
	Other (friends, patient)	12 (24.5%)	12 (23.5%)	[2]1.000
	I do not have any information sources	18 (36.7%)	18 (35.3%)	[2]1.000

[1] *Fisher Freeman Halton Test* [2] *Continuity (yates) correction* [3] *Chi-square Test* [4] *Fisher's Exact Test*
** p <0.05*

4. DISCUSSION

Oral cancer is defined as cancers arising on the lip, oral cavity, and oropharynx and it has been estimated that changes in the world's demography would result in an increase of incidence rates of oral cancer by 62% in 2035 (18,19). Consumption of cigarettes with high concentrations of alcohol increases the risk of oral cancer 6-15 times in people over 50 years of age (20). Public awareness on oral and cancer and potentially malignant disorders and their risk factors is crucial for prevention and early detection of oral cancer.

Wimardhani et. al. (18), investigated the awareness of oral cancer among adults in Jakarta and a previously-tested questionnaire on 1000 adults in Jakarta was used in their study. They reported that only 53.2% of participants were aware of oral cancer and all of the smoker adults knew that tobacco increased the risk for oral cancer. Moreover, health warnings were the main source of information about oral cancer. In our study, 78% of participants considered smoking as a cause of oral cancer and 47% of the patients stated that dentists are the sources of information for their oral cancer awareness.

In another study, Varela-Centelles et al. (21), portrayed the level of oral cancer knowledge and awareness in a Spanish general population. An anonymous questionnaire applied to 1,041 individuals and it is reported that 72% of the participants were familiar with oral cancer. Participants were also asked about the main signs or symptoms of oral cancer, and the most frequently (22%) mentioned as the first warning sign was a non-healing ulcer. Tobacco smoking generally was recognised as the most important (57%) risk factor for oral cancer.

Formosa et al. (22), investigated public awareness/knowledge on oral cancer in Australia and over half (52.3%) of the respondents were aware that cancer could occur in the mouth and the gender did not influence the awareness (X2=1.466, p=0.226). In our study, 75% of the participants considered the age group most affected by oral cancer as 40 years and older, while 19% considered young adults and 6% considered childhood. Formosa et al. reported that of those who were aware of oral cancer, 92% agreed that smoking is a strong risk factor for oral cancer. They have also stated that the greatest awareness was found among the youngest age group 20-39 (61.4%) while the lowest (39.8%) was found among the respondents over the age of 60 years. In terms of the source of information for being aware of oral cancer the study found that mass media (newspapers, television, and radio) play a sizeable role being the leading source of information. It was also evident that dentist has been the second highest source of information. Similarly, 47% of smoker patients in our study gets information about oral cancer from their dentists. The present study revealed that the knowledge on the signs of oral cancer was poor in that only below 50% were aware of different presentations of cancer in the mouth. Similarly, in our study, 58% of the partidcipants stated wounds in mouth, and 60% of them stated mass formation as main symptoms of oral cancer. Park et al. (23), in their study in Western Australia also found compatible results in that 49% of the participants did not know any signs or symptoms of oral cancer.

In a study conducted by Aydın (24), dental patients' oral cancer awareness and attitudes were assesed. In their study 44% of the study participants had never heard of oral cancer, yet smoking was the most frequently identified cause and sore in the mouth was the most frequently identified symptom. In our study, smoking took the first place with 78% and followed by 55% tobacco chewing (55%). Their study also reported that 4% of the participants would consult a doctor when a symptom is present, similiar with our study (5%). In addition, the rate of woman patients "referring to a doctor when there is a symptom" as a method of diagnosis of oral cancer (73.5%) was statistically higher than that of men (49%) (p=0 ,021; p<0.05) in our present study.

Peker and Alkurt (17) also reported the levels of public awareness and knowledge about early signs and risk factors of oral cancer among a group of 1022 dental patients in

Turkey and found that in total 60.7% of participants had never heard of oral cancer. While 79.2% of the participants were unaware of the early signs related to oral cancer, 29.9% of them were unaware of risk factors of the disease. The risk factors associated with oral cancer that were most often correctly identified by the participants were smoking (57.6%, n=589); regular consumption of alcohol (27.9%, n=285); excessive exposure to sunlight (15%, n=153); eating hot, spicy foods (9.9%, n=101); and biting the cheek or lip (6.8%, n=69) respectively. There were no statistically significant differences between age, gender, and education levels for awareness of risk factors. In our study the rates of participation in the statement "causes of oral cancers" are 78% smoking, 55% chewing tobacco, 51% drinking alcohol, 43% genetic predisposition, 41% unhealthy nutrition, 41% chemicals, 39% irregular life and stress, 33% decayed teeth, 27% inappropriate dentures, 10% other answers and 10% of the participants have no idea. Moreover, woman participants (63.3%) who answered "alcohol use" to the question "What do you think causes oral cancer?" is highly statistically significant than that of man patients (39.2 %) ($p=0.027$, $p<0.05$). To the question "What do you think are the symptoms of oral cancer?", woman patients rate of answering "wound in mouth" (69.4 %) is stastistically higher than man participants (47.1%) ($p=0.040$, $p<0.05$).

This study's reliance on self-reported data may be seen as a limitation. Respondents may exaggerate, or they may under-report the severity or frequency of conditions. Patients might also simply be mistaken or misremember the material covered by the survey.

5. CONCLUSION

It is concluded that in comparison to men, women smokers have higher levels of understanding, education, and optimistic attitudes toward oral cancer. However, the issue of delayed diagnosis can be addressed by patient self-examination of early symptoms of illness and the development of effective interventions to improve clinician awareness and preventive attitudes. Moreover, a comprehensive knowledge on oral cancer to undergraduates and dental graduates should be given through a review of dental curriculum and formal continued education.

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Clinical and Experimental Health Sciences

Are Kinesiophobia and Functional Performance Related to Ability to Forget the Artificial Joint in Patients with Total Hip Arthroplasty?

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ABSTRACT

Objective: The aim of this study was to investigate the relationship between kinesiophobia and functional performance with the ability to forgetthe artificial joint in patients with total hip arthroplasty (THA).

Methods: Fifty-seven volunteer patients aged between 40-65 years who have undergone THA surgery in the last 1-3 years were included in this study. The Forgotten Joint Score (FJS-12) for evaluating the ability to forgetting the artificial joint, the 6-Minute Walk Test for determining the functional performance, and the Tampa Scale for Kinesiophobia (TSK) for evaluating kinesiophobia were used.

Results: There was a moderate correlation between the FJS-12 and TSK ($r = -0.571$; $p<0.001$) scores; and moderate correlation between the FJS-12 and the 6-Minute Walk distances (6-MWD) ($r = 0.408$; $p<0.001$). The ability to forget the artificial joint in patients with THA was found to be related to kinesiophobia and functional performance.

Conclusion: The results of this study demonstrated that the awareness of artificial joint should be taken into consideration when performing physiotherapy and rehabilitation practices to decrease kinesiophobia and increase functional performance. Additionally, complementary approaches aiming to reduce the awareness of artificial joint should be added to the rehabilitation program of the patients with total hip arthroplasty.

Keywords: Arthroplasty, awareness, functional performance, hip.

1. INTRODUCTION

Total Hip Arthroplasty (THA) is one of the most commonly used procedure in the late treatment of hip osteoarthritis (1). Arthroplasty surgery, which aims to reduce pain and improve physical function, enables the patient to participate in daily living activities and return to an active lifestyle (2, 3). Patients undergoing THA surgery complain of pain and loss of motion before surgery. Therefore, THA surgery outcome measures are more related to decreased pain complaints and increased mobility. Although the functional status is good after surgery, patients with THA have less participation in daily living activities. One of the reasons for this is maybe that the patients develop artificial joint awareness and cannot forget the new joint (4, 5).

Conventional classification systems that evaluate outcomes after TKA often focuses on objective parameters such as range of motion and strength, or clinician ratings and degrees of pain. However, expectations of patients after TKA may different importantly from the expectations of clinicians and may not be sufficient to reflect the needs and views of patients (6-8). It is thought that the expectations of approximately 20-30% of patients after joint arthroplasty surgery are not fully satisfied expectations (7). Therefore, patient-reported outcome measures, including patient-specific or joint-specific parameters such as pain, the function of daily living activities and joint awareness, are increasingly recognized as an important part of postoperative outcome assessment (6, 9). Patient-reported outcomes (PRO) measures which providing a patient-centered view of treatment evaluation are a key parameter for evaluating outcomes after THA surgery (10-12).

Kinesiophobia is a poor adaptation strategy that causes patients to avoid physical activity due to fears related to pain (13). It has been reported that the incidence of kinesiophobia in orthopedic trauma patients may be as high as 52.8% (14). Doury-Panchout et al. (15), in a study investigating the effect of kinesiophobia on healing after surgery, was shown that

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the presence of kinesiophobia in total knee arthroplasty (TKA) had a negative effect on healing.

THA surgery is a surgical procedure that usually results in a significant decrease in pain and improvements in patients' functional capacity. However, despite the decrease in pain on the operated side, it has been reported that in many cases, motor skills do not reach normal levels (16-18). The ability to walk, which is related to leading an active and independent life, is an important component of lower extremity function. Evaluation of functional performance after THA provides important information about the healing process. Some studies have shown that patients feel less pain and walk better than preoperative 3 months after THA (19, 20). However, further studies have shown that the walking distance of patients months and years after THA is less than that of healthy individuals of the same age, hip flexibility and muscle strength are worse than unaffected hips (17, 21).

In the literature, there are studies comparing and evaluating the functional capacity of patients before and after THA (22-24). However, in the literature, there is no study to investigate the relationship between kinesiophobia and functional performance with the ability to forget the artificial joint in patients with THA. It is not known whether the patient's fear of movement and functional performance are relateds to the artificial joint awareness. Therefore, the aim of this study was to investigate the relationship between kinesiophobia and functional performance with the ability to forget the artificial joint in patients with THA. The authors hypothesized that the ability to forget the artificial joint would be associated with kinesiophobia and functional performance in patients with THA.

2. METHODS

In this study, 57 patients who had undergone THA surgery between the ages of 40-65 yearsat least 1 and at most 3 years were included. The study was approved by the Hacettepe University Ethics Committee for Non-Interventional Clinical Investigations (GO17 / 878-31). Before starting the study, volunteered patients were informed verbally about the purpose of the study, the duration of the assessment. Patients signed an informed consent form that they were willing to participate in the study. Patients who have undergone lower extremity surgery other than THA, signs of infection and have a history of THA revision or dislocation were excluded from the study.

2.1. Assessment of the Ability to Forget the Artificial Joint

The FJS-12 was used to evaluate the ability to forget artificial joint of patients with THA. The FJS-12 is a scale that questions the artificial joint awareness during various daily living activities in order to determine the ability of patients to forget the artificial hip joint(25). A validated Turkish version of the FJS-12 was used in this study (26). A 5-point Likert system is used in the scoring (None: 0, Almost none: 1, Rarely: 2, Sometimes: 3, Always: 4). All answers to the questionnaire (0; 1; 2; 3; 4) are summed and divided by the number of completed questions. The calculated average value is multiplied by 25 so that the total score is in the range 0-100. The number found is subtracted from 100. High scores indicate how much (%) the patient can forget their side of the surgery and adapt to their life. In other words, a high score indicates a high degree of "forgetting" the artificial joint – i.e. a low degree of awareness(26).

2.2. Assessment of Kinesiophobia

The Tampa Scale for Kinesiophobia (TSK) was used to evaluate the presence of kinesiophobia . The TSK is a 17-item scale developed to measure kinesiophobia / re-injury. The kinesiophobia of the patients included in this study was measured with the Turkish TSK (27). The scale uses a 4-point Likert rating (Strongly disagree: 1, Disagree: 2, Agree: 3, Completely agree: 4). A total score is calculated by reversing questions 4, 8, 12 and 16. Patients have a total score of from 17 to 68. The high score of the person on the scale shows that kinesiophobia is also high (28).

2.3. Assessment of Functional Performance

In order to determine the functional performance of the patients, 6-MWD was performed. This test which is one of the tests used to evaluate functional performance in patients with THA is a simple, sensitive and valid method used in the clinic (29). The distance to walk according to age, sex, height and body weight is calculated (30). For each patient, the distance walking is calculated in meters and as a percentage of the theoretical distance. Patients were asked to walk on a flat surface for 6 minutes. During the test, standard expressions were used to the patients during their gait. For each patient, the distance walking was calculated and recorded in "meters" and as a percentage of the theoretical distance (expected walking distance) (Figure 1).

Figure 1. *Six minute walking distance*

2.4. Statistical Analysis

The data obtained were evaluated with SPSS 23.0 software program (IBM SPSS Statistics version 23.0, IBM Corp. Armonk, New York, ABD). The normal distribution of the variables was determined by visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov / Shapiro-Wilk tests). Descriptive analyzes mean and standard deviation for numerical variables; frequency tables for ordinal variables (n) and proportions (%) are shown.

Mann-Whitney U test was used to determine whether FJS, TSK scores, and 6MWD values differ by gender. Kruskal Wallis analysis was used to compare the joint awareness, kinesiophobia, and functional performance according to the preoperative diagnosis. In addition, Spearman Correlation Analysis was used for the variables that do not show normal distribution to the determine relationship between the ability to forget the artificial joint, kinesiophobia, functional performance.

3. RESULTS

A total of 57 patients (12 males; 45 females) were evaluated in this study. Demographic characteristics of patients such as educational status, preoperative diagnosis, job and mean BMI values are summarized in Table 1.

Table 1. *Sociodemographic characteristics of the patients.*

	Mean (SD, Minimum-Maximum)
Gender, n (%)	
Female	45 (78.9 %)
Male	12 (21.1 %)
Age	55.39 (7.8, 40-65)
Height (cm)	163.19 (9.5, 145-182)
Weight (kg)	75.63 (14.3, 50-120)
Body mass index (kg/m²)	28.25 (4.6, 20.3-44.19)
Duration after surgery (months)	24.78 (4.6, 12-36)
Diagnosis, n (%)	
Primary osteoarthritis	30 (52.6 %)
Avascular necrosis	12 (21.1 %)
Developmental dysplasia of the hip	11 (19.3 %)
Fracture of femur	4 (7 %)
Education status n (%)	
Primary school	28 (49.1 %)
Middle school	5 (8.8 %)
High school	11 (19.3 %)
Bachelor	13 (22.8 %)
Occupational status n (%)	
Housewife	24 (42.1%)
Working	17 (29.8 %)
Retired	16 (28.1%)
Patient reported outcomes	
Forgetten Joint Score-12	31.25* (35.45†, 0-100)
Tampa Scale Kinesiophobia	46.0* (10†, 27-64)

*SD: Standard Deviation, THA: Total Hip Arthroplasty, *: Median, †: Interquartile Range (IQR)*

The minimum, maximum, median and Interquartile range (IQR) values of the FJS-12, TSK scores are shown in Table 1.

No statistically significant difference was observed in the distribution of the FJS-12, TSK scores, and 6-MWD of the patients according to gender (respectively p=0.638, p=0.462, p=0.610).

The comparison of joint awareness, kinesiophobia, and functional performance results according to the preoperative diagnosis is summarized in Table 2. Kruskal Wallis analysis showed that the results were similar according to the preoperative diagnosis.

Table 2. *Comparison of FJS, TSK, and 6-MWD according to preoperative diagnosis*

	Preoperative diagnosis	n	χ^2	p
FJS-12	Primary osteoarthritis	30	2.04	0.563
	Avascular necrosis	11		
	Developmental dysplasia of the hip	4		
	Fracture of femur	12		
TSK	Primary osteoarthritis	30	0.13	0.988
	Avascular necrosis	11		
	Developmental dysplasia of the hip	4		
	Fracture of femur	12		
6-MWD	Primary osteoarthritis	30	3.99	0.262
	Avascular necrosis	11		
	Developmental dysplasia of the hip	4		
	Fracture of femur	12		

FJS-12: Forgotten Joint Score, TSK: Tampa Scale for Kinesiophobia, 6-MWD: 6-Minute Walk Distance, χ^2: Chi-Square,

The mean and minimum-maximum values of 6-MWD, which are theoretically calculated for patients (expected walking distance) and are walking distance during the test, are shown in Table 3. All of the patients included in the study were able to walk less than the expected walking distance. In addition, it was found that 68.08% of the theoretical distance calculated in 6-MWD was able to walk.

Table 3. *Walking distance and expected distance in 6-MWD.*

n=57	Walking Distance (m)		Expected Distance (m)	
	Mean (SD)	Minimum-Maximum	Mean (SD)	Minimum-Maximum
6-MWD	357.49±55	231-483	529.48±61	370.32-745.20

6-MWD: 6-Minute Walk Distance, 6-MWT: 6 Minute Walking Test, SD: Standard Deviation

The Spearman correlation analysis showed that there was a moderate negative correlation between the FJS-12 and TSK (r= – 0.571; p<0.001); and moderate correlation between the FJS-12 and 6-MWD (r= 0.408; p<0.001) (Table 4).

Table 4. *Correlation analysis between FJS-12, TSK and 6-MWD*

n=57		r	p
FJS-12	TSK	-0.571	<0.001
	6-MWD	0.408	<0.001

r: Spearman Correlation Coefficient, FJS-12: Forgotten Joint Score, TSK: Tampa Scale for Kinesiophobia, 6-MWD: 6-Minute Walk Distance

4. DISCUSSION

This study is an important study in terms of investigating the relationship between the ability to forget the artificial joint and kinesophobia and functional performance in patients with THA. The main results of this study showed that the ability to forget the artificial joint in patients with THA is correlated with kinesiophobia and functional performance. The second important result of this study is that kinesiophobia is still high in patients even in the postoperative second year after surgery, functional performance is not at the expected level, and the ability to forget the artificial joint, ie adaptation to ADL, is insufficient.

Patient-reported outcome measures (PRO) are a key parameter to evaluate outcomes after THA surgery (12). The FJS-12 is a patient-reported outcome scale developed to evaluate joint awareness in the hip and knee joints during various activities in daily life that gives information about how much patients can forget their artificial joints and adapt to daily life (4). Unlike other outcome measures reported by the patient, which measures parameters such as pain, stiffness, difficulties in daily living activities, the FJS-12 emphasizes "awareness''. In this study, the FJS-12 scale was used to evaluate the ability to forget the artificial joint.

Hamilton et al. (4) were reported the FJS-12 scores as 56.8 and 62.1 points 6 and 12 months after THA surgery. In another study, Thienpont et al. (31) stated that the FJS-12 score was 70 points for patients with THA in the 12th postoperative month of 75 patients (mean age 67) whom they evaluated before and after THA and TKA surgery. Similarly, Matsumoto et al. (32) were stated the FJS-12 scores as 61.1 in healthy individuals, 55.2 in OA patients and 45.8 in patients with THA in the first year after surgery.

The mean FJS-12 scores in this study was 36.58. Unlike the studies in the literature (4, 31, 32), the FJS-12 scores of the patients in the current study were low. In other words, low degree of forgetting their artificial joint was found in our patients after average 24 months following THA surgery. These results showed that our patients had still difficulty in adapting their new artificial joints during daily life. One possible explanation of this low score migth be high kinesiophobia. In addition, during the assessment patients verbally stated that they experienced fear of falling and this fear brought the prosthesis into their minds during their daily life activities. Therefore one of the reasons for high FJS-12 scores may be fear of falling in patients. Fear of dislocation may also be the reason to focus their attention on their artificial prosthesis during daily living activities. Another reason of high FJS-12 scores might be the lower rate of returning to work after surgery. Since the majority of the patients in the current study were housewives (42.1%) or retired (28.1%). Therefore, the limited daily living activities and low educational status (80% under bachelor degree) might canalize their attention on their artificial prostheses.

Kinesiophobia is described as the irrational and debilitating fear of physical movement and activity resulting from a sense of fragility caused by painful injury or re-injury (33). In the literature, studies evaluating the kinesiophobia of patients after THA surgery are limited. Sengül et al. (34), in their study that evaluated the fear of pain-related movement in patients with 58 patients who underwent prosthesis surgery (at least 2 years after surgery) for hip fracture or OA, found that the scores of the TSK were higher in both groups and that there was a high-strength relationship between the TSK and the Harris Hip Score.

In the postoperative period, kinesiophobia develops and patients are reluctant to move. As a result of their studies, it has been shown that even if they have high physical activity levels, the fear of moving in the postoperative period continues. As a matter of fact, according to one of the results of the current study, there was a statistically significant correlation between the FJS-12 and TSK scores of patients after THA surgery (at average 24 months). The fact that patients have been aware of the presence of artificial joints even long after their surgery showed that they had still high kinesiophobia.

Padovan et al (35) examined the effects of a new holistic approach on pain, fear of motion and quality of life in patients who underwent total hip arthroplasty, have evaluated the kinesiophobia with the Tampa Scale for Kinesiophobia and have found the experimental group's baseline TSK score as 30.6 and the control group as 36.53. Temporiti et al (36) examined the gait analysis after bilateral and unilateral total hip arthroplasty, and found that the TSK score of patients with unilateral arthroplasty was 36.4, and that of patients with bilateral arthroplasty was 34.1. In contrast to this study, the TSK scores of the patients with TKA in our study were higher. This indicates that the kinesiophobia is still higher in our sample. The high kinesophobia scores may be due to the high artificial joint awareness. Correlation between artificial joint awareness and kinesiophobia scores supports this situation. In addition, the fear of dislocation may have contributed to the high rate of kinesophobia.

One of the outcome measures of THA surgery is the improvement of function. Additionally, one of the goals after THA surgery is to provide normal speed and adequate gait since gait is an important function of the lower extremity. Improvement of the physical function is evaluated by objective performance tests such as 6-MWD (37, 38). Evaluation of gait after THA surgery indicates functional performance in THA patients.

De Groot et al. (22) evaluated the walking capacities of patients by using 6-MWD at different periods after TKA and THA surgery, and found that the walking distance of the patients was 370 m at 3rd months, and 399 m at 6th months after surgery. Similarly, Heiberg et al. (39), the physical function by using 6MWD during the first year after THA surgery, and found that the walking distance of the patients was 401 m before surgery, 437 m at the 3rd month and 512 m at the 12th postoperative month.

Laupacis et al. (24), in their studies examining health-related quality of life after THA surgery, evaluated patients before and after surgery and stated that there was a considerable recovery in all health-related quality of life measurements and 6-MWDafter surgery. In two years, the average 6-MWD increased from 247 m to 408 m. In the present study, the average 6-MWD of the patients was 357.49 meters. All the patients whose walking distance were calculated according to variables such as age, height and weight remained below the expected walking distance. The patients with THA walked only 68.08% of the calculated expected walking distance, theoretically. This study examined the long-term results of THA surgery and showed that patients' functional performance was still low. Parameters such as kinesiophobia, avoidance movement to protect prosthesis and high artificial joint awareness might have contributed to low functional performance results in 6-MWD.In addition, there was a moderate relationship between the ability to forget the artificial joint and functional performance in patients with THA. These results showed that the patients' functional performance would be higher as they could forget their artificial joints to adapt to daily life.

In this study, preoperative diagnosis status did not affect the results. The joint awareness and kinesiophobia level and functional performance of the patients with THA were similar between preoperative diagnosis. Not showing a homogeneous distribution of preoperative diagnosis may have caused these results.

The current study has some limitations. The most important limitation of our study is the absence of preoperative 6-MWD data of individuals with THA. Additionally, small sample size and cross-sectional design of the present study might be insufficient to generalize the results. Thus, pre-post follow-up studies involving larger sample sizes are needed. Future studies should also focus on parameters such as balance, fear of falling, quality of life, anxiety, and depression that might be associated with artificial joint awareness.

5. CONCLUSION

The ability to forget the artificial joint is associated with kinesiophobia and functional performance in patients with THA. This study shows that artificial joint awareness and high kinesiophobia develops in patients with THA and patients have a tendency to protect their artificial joints in long-term after surgery. Kinesiophobia and low adapting to artificial joint may cause impairment in functional performance accompanying with the limiting participation in daily living activities in the long term. Therefore, the artificial joint awareness should be taken into consideration while performing physiotherapy and rehabilitation to increase functional performance and to reduce kinesiophobia. We suggest a holistic approach aims to reduce the awareness of artificial joint should be added to the rehabilitation program of the patients with total hip arthroplasty.

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Clinical and Experimental Health Sciences

The Relationship Between Fat Tissue & Lean Body Mass and Sit to Stand Task in Obese Individuals

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ABSTRACT

Objective: Obesity, currently one of the important health issues, can be defined through Fat Tissue Mass (FTM) and Lean Body Mass (LBM). The study aimed to investigate to what extent do FTM and LBM are associated with movement strategies of Sit-to-Stand (STS) task in individuals with obesity.

Methods: Forty-nine obese individuals (52,83 ± 7,39) with no diagnosis of any health condition included in the study. The Balance Master System was used to evaluate the STS movement. STS task was analyzed by means of Weight Transfer Time (WTT) (second), Rising Index (RI) (force exerted by legs-%Body Weight), the Center of Gravity (COG) sway velocity (degrees per second). The FTM and LBM were regressed against each STS parameter including age as a covariate.

Results: The regression models could explain 10-21% of the variabilities in STS parameters: RI (21%), COG sway velocity (11%), WTT (10%). FTM significantly related to RI (β: – 0.287, p=0.040), but not with COG sway velocity (β: 0.270, p=0.073) and WTT (β: – 0.038, p=0.802). LBM was significantly associated with RI (β: 0.435, p=0.003); yet, not with COG sway velocity (β: – 0.100, p=0.066), WTT (β: – 0.092, p=0.549).

Conclusion: This study revealed that FTM and LBM can explain the significant percent of the variation in RI during STS task, meaning a decrease in FTM and an increase in LBM provided support to rise during STS task. Moreover, an increase in FTM deteriorated postural stability. Improving LBM and decreasing FTM would be an effective strategy to improve STS in the obese population to increase their agility and could encourage physical activity participation.

Keywords: Obesity, Fat Tissue Mass, Lean Body Mass, Sit to Stand Task

1. INTRODUCTION

Obesity is currently becoming one of the most important public health issues. World Health Organization has stated that obesity had reached epidemic proportions globally (1). Furthermore, Finkelstein et al. reported an estimated obesity prevalence for the year 2030 through regression modeling and suggested that there will be an increase by 33% in obesity prevalence and 130% in severe obesity prevalence (2).

Parallel to the global increase in this health hazard, researches relating to various aspects of obesity has receiving a great deal of interest. However, functional limitations imposed by obesity and biomechanical alterations in daily functions have not been largely studied (3).

Existing literature proved that individuals with higher body weight have poor functional capacities. They also use altered strategies through functional tasks due to excessive and poorly disturbed fat tissue mass (4-6). The effect of higher Body Mass Index (BMI) including Lean Body Mass (LBM) and Fat Tissue Mass (FTM) on a higher level of functional limitations were first mentioned by Zioco et al. They indicated that lower LBM and higher FTM ratios increase the odds of functional limitations (7). The limited published studies in this field have mainly focused on the effect of obesity on plantar pressure distributions, postural balance and postural control during walking (3).

Changing a seated position to a standing, STS, is a fundamental movement for participation in many activities of daily living (8). A healthy individual performs STS movement approximately 60 times in a day (9). The ability to perform proper STS movement is considered to be an important determinant of functional fitness and independence. This task requires sufficient muscle strength to vertically accelerate body mass against the gravity and postural control ability from beginning to the end of the movement (10,5,6). The increase in BMI considerably reduces trunk and lower extremity strengths, body power and ability to control postural stability (11). These functional disturbances may

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result in significant impairments in individuals` functional ability on sit-to-stand activity (STS).

If individuals are less capable of a rising body from a sitting to a standing position they might avoid performing STS movement as often (12). This behavior limits the participation of physically active tasks and encourages the sitting for long periods which would cause vigorous obesity and inactivity cycle.

Despite its importance in activities of daily living little research exist regarding the STS movement and its determinants in the obese population (13,14). Furthermore, better knowledge of the implication of BMI by means of FTM and LBM on the STS movement of obese individuals would help us to develop proper interventions to improve their functional performance. It would also help to manage limited participation in physical activity indirectly by managing FTM and LBM. Therefore, the purpose of the current study was to investigate to what extent do FTM and LBM are associated with movement strategies of STS task in obese individuals.

2. METHODS

2.1. Participants

49 obese individuals (age: 52,83 ± 7,39, BMI: 35,56 ± 5,71) participated into the study. Inclusion criteria were (1) being at the age between 18-65; (2) BMI>30 kg/m^2; (3) able to stand without support from a chair. Exclusion criteria were (1) cardiovascular weakness; (2) having neurological, metabolic, rheumatic or vestibular diseases; (3) injuries or previous surgery on the legs and no clinical knee and ankle instability; (3) having cognitive and behavioral problems. The participants were recruited from the Marmara University Department of Physiotherapy and Rehabilitation.

The study design was approved by the local ethical committee Marmara University Clinical Research Ethics Committee, Istanbul, Turkey (06.10.2017 – Protocol ID: 09.2017.604). All subjects were taken demographic features; age, height, weight and signed informed consent before participating in this study.

2.2. Measurements

Body composition

Body composition components which are BMI, LBM and FTM were measured without shoes and in light clothes by using a bioelectrical impedance analysis (BIA) based on a body composition analyzer (TANITA BC-418MA) (25).

Sit to Stand Assessment

The STS movement was evaluated by the Balance Master System (NeuroCom version 8.1, International, Inc., USA). The evaluation procedure for STS movement was completed according to the manufacturer's instructions (15).

All STS movements were performed on a long force platform comprising two force plates on barefoot. Force sensors located under the force platform measure the vertical forces exerted by the feet.

The measurements started from a seated position on an armless and backless chair, with arms resting by the sides. The participants were instructed to face the monitor while sitting, to keep both legs at shoulder width and to place their feet symmetrically and parallel to each other on the force platform. Participants were allowed to practice as much as trial they need to become familiar with the test procedure prior to data collection. They asked to follow the signs and react to them as quickly as possible. The test starts when the green "Go" sign appears on the monitor and participants were instructed to stand up as fast as possible without arm support. After a while, the monitor shows the "Hold Steady" sign. At this point, participants were asked to maintain their upright position. Steady standing lasts for 5 seconds to complete one STS trial. The system requires three STS trial and give a mean score obtained from these three trials for each parameter of STS.

STS task was investigated through some essential parameters such as weight transfer time, rising index, sway velocity and weight-bearing symmetry by the software of the system:

Weight transfer time (WTT), which is expressed in seconds (s), is defined as the amount of time between the onset of the "Go" sign to move and the arrival of the center of gravity (COG) over the feet. Low scores are defined as good and high scores are bad. Rising index (RI) (expressed as a percent of body weight, %) is the amount of force exerted by the legs during the rising phase of the STS movement. Insufficient lower extremity force will result in a failure to rise to a fully upright position. Low scores obtained from the rising index are considered as worse and high scores are good. Sway velocity, degrees per second, is the average amount of COG sway during the rise to stand and for the first five seconds following the rise. COG sway velocity during and immediately after the rise should be minimal. Therefore, low scores indicate good balance control and high scores are worse.

2.3. Statistical Analysis

Variance Inflation Factor (VIF) and regression correlation matrix for Klein Goldberger model were used to assess the collinearity among independent variables, after Shapiro–Wilk test and histograms were conducted to evaluate the normality of data.

Pearson correlation analysis was used for identifying association between Balance Master scores and independent variables. The characteristics of participants are provided by sex to enable meta-analyses and sample size calculations for future studies. The outcomes of interest, Balance Master

scores were regressed against two independent variables: FTM and LBM. The regression analyses were mixed men and women as the distributions of key variables were not vastly different (23). All statistical analyses were performed using R statistical. software (packages of 'olsrr'and 'lubridate' Version 3.6.0, St. Louis, Missouri, USA) was used (24).

3. RESULTS

The demographic and clinical characteristics of the subjects were illustrated in Table 1. There were significant correlations between FTM, LBM and STS parameters (RI, WTT and COG). There was a strong negative relationship between FTM and RI (r: – 0.423, p=0.047). Also, the correlation between LBM and RI are significantly positive (r: 0.628, p=0.028). The relationships between FTM and COG (r:0.343, p=0.102), FTM and WTT (r: – .288, p=0.141), LBM and COG (r: – 0.136, p=0.216), LBM and WTT (r: – 0.330, p=0.119) were not statistically significance (Table 2).

Table 1. *Demographic and clinical characteristics of the subjects*

	Subjects (n=49)		
Sex	**Male: 18 (% 36,74)**	**Female: 31 (% 63,26)**	**All Subjects**
Age (years)	53.38 ± 5.83	52.61 ± 8.10	52.83 ± 7.39
Weight (kg)	94.38 ± 9.41	92.31±20.07	94.52 ± 16.77
Height (cm)	173.33 ± 6.30	159.35 ± 5.32	164.22 ± 8.57
BMI (kg/m^2)	31.38 ± 2.54	36.84 ± 6.83	35.56 ± 5.71
FTM (kg)	24.88 ±4.83	39.29 ± 12.85	34.68 ± 12.54
LBM (kg)	69.45 ± 6.44	53.54 ± 7.62	59.15 ± 10.47
STS-WTT (sec)	0.47 ± 0.30	0.45 ± 0.21	0.44 ± 0.22
STS-RI (% Wt)	24.17 ± 10.64	18.90 ± 6.31	21 ± 8.68
STS-COG sway velocity (deg/sec)	4.11 ±1.25	4.27 ± 1.32	4.25 ± 1.25

FTM: Fat Tissue Mass, LBM: Lean Body Mass, STS: Sit to Stand, WTT: Weight Transfer Time, RI: Rising Index, COG: Center of Gravity, Wt: Weight

Table 2. *Correlation analysis between each predictor and balance master scores indicators*

	OUTCOMES (BALANCE MASTER SCORES)					
	RI		COG		WTT	
Predictors (range)	r	p	r	p	r	p
FTM	-0.423	**0.047***	0.343	0.102	-0.288	0.141
LBM	0.628	**0.028***	-0.136	0.216	-0.330	0.119

*FTM: Fat Tissue Mass, LBM: Lean Body Mass, COG: Center of Gravity, WTT: Weight Transfer Time, *p<0,05 (statistically significant)*

Overall, the regression models could explain 10-21% of the variabilities in STS parameters: rising index (21%), COG sway velocity (11%), the weight transfer time (10%). FTM was significantly associated with rising index (β: – 0.287, p=0.040), but not with COG sway velocity (β:0.270, p=0.073) and weight transfer time (β: – 0.038, p=0.802). LBM was significantly related to rising index (β:0.435, p=0.003); yet, not with COG sway velocity (β: – 0.100, p=0.066), weight transfer time (β: – 0.092, p=0.549). The results of regression analyses are presented in Table 3.

Table 3. *Multiple regression analysis: relationship between each predictor and balance master scores indicators*

	OUTCOMES (BALANCE MASTER SCORES)					
	RI		COG		WTT	
Predictors (range)	β	p	β	p	β	p
FTM	-0.287	**0.040***	0.270	0.073	-0.038	0.802
LBM	0.435	**0,003***	-0.100	0.066	-0,092	0.549
R^2	**0.21**		**0.11**		**0.10**	

*FTM: Fat Tissue Mass, LBM: Lean Body Mass, COG: Center of Gravity, WTT: Weight Transfer Time, R: Regression, *p<0,05 (statistically significant)*

4. DISCUSSION

The aim of the current study was to investigate to what extent FTM and LBM are associated with movement strategies of STS task in individuals with obesity. Up to date, few studies investigating the STS task in obese individuals have been reported in the scientific literature, although it is the most frequently used task in daily living (16).

The results of the current study revealed that FTM and LBM scores have a significant role in the STS task for individuals with obesity. The main finding of the current study was the observed relationship between the rising index with both FTM and LBM values. Rising index was found to be significantly related with FTM negatively and LBM positively. It shows that higher and lower rising indexes seen in obese individuals were a consequence of higher LBM and FTM, respectively. Since the rising index is considered to be an important indicator of lower extremity extensor muscle strength, this finding could also result from lower leg strength relative to mass (15). It has already known that a relative reduction in muscle strength observed in obese individuals from the studies comparing the relative strength of the trunk, knee and hand in obese and non-obese individuals (17). Muscle morphology determined by FTM and LBM may appear to be the major determinants of obesity-related differences in muscle strength. On the other hand, fat tissue has a great role in the secretion function of adipocytokines that have a catabolic effect on muscles by means of muscle mass and strength. Schaap et al. also speculated that these adipocytokines mediate the linkage between higher FTM and loss in muscle strength (18). Unfortunately, we did not measure lower extremity muscle strength in the current study. But the both significant negative correlation between FTM and rising index and positive correlation between LBM and rising index supported this opinion. In addition, Deforche et al. conducted a study in adolescence and indicated a lower rising index in obese boys during the STS test compared with their normal-weight counterparts (19).

The findings of the current study indicated that FTM was also positively related with COG sway velocity which is an indicator of postural balance control during functional tasks. The postural balance control during STS movement is one of the fundamental requirements to achieve the proper task. STS is commonly investigated by dividing the movement into two critical events as rising and standing phases. Rising phase starts at the onset of COG progressing forward and

ends at the first point where COG is greater than 90% of the end COG position. Standing phase is determined by the completion of COG forward progression. Postural balance control should be maintained until the task is completed. STS movement presents a challenge for balance control and stability since this transition from a sitting to a standing position changes the base of support from three points to two points of support (20). The previous study revealed that obese adolescence had greater sway velocity during STS task, especially in standing phase. It was considered that their participants had difficulties in decelerating the forward trunk motion to rise the body based on the results of previous study (19). Sibella et al. showed that obese adults rose from the chair by limiting their forward trunk flexion and moving the feet posteriorly from their initial position compared to normal weighted adults from a biomechanical point of view (13). Together with inferior lower extremity strength (concluded from observed lower rising index) and possible kinematic deviations could have impaired postural balance control of the obese individuals with higher FTM participated in the current study.

Both FTM and LBM of the obese individuals in the current study were not related with WTT during STS. WTT is the other measured parameter in STS test since it provides insight for performance of the movement (21). This period is defined as a preparation for standing which usually occurs very quickly; the time from the seat to the arrival of the COG over the feet (10).

Therefore, WTT is an independent parameter from lower extremity strength. A WTT has been suggested to be an indicator of higher postural and directional control (22). The Deforche et al. mentioned about slower transfer time to complete multiple sit to stand tests in obese boys but they did not design their study by investigating FTM or LTM of their subjects (19). We can conclude that obese individuals in this study performed WTT during STS task regardless of their fat or lean body mass.

The comparison of our results with the limited number of studies related with the obesity and STS task is difficult because of methodological differences the studies had. For instance, Deforche et al used the Balance Master system to test STS task but the characteristics of their subjects were totally different from our subjects. Sibella et al. investigated STS task in obese adults but they performed 3D motion analysis to reveal differences in kinetic and kinematic variables during STS task. They also compare the data of obese adults with non-obese ones. Furthermore, presentations of the results differ largely. Up to date, the current study is the only one that investigated what extent FTM and LBM were associated with movement strategies of STS task in individuals with obesity. It can be concluded that there is limited information regarding the impact of FTM and LBM on functional tasks in obesity, despite its considerable importance for participating in any kind of physical activity. Further studies are warranted on these topics.

STS task was chosen due to its high repeatability in daily living and its property as a being prerequisite activity for participating in any physical performance. Our findings may be useful to develop proper interventions to improve obese individual's performance during functional tasks such as changing posture from sitting to standing. Also, the results of this study promote the literature as a research used an objective method to assess balance and body composition. Our study has cross sectional design which allows to look at FTM and LBM in relation to STS skills only at one point in time. This limitation caused researchers were not able to determine at the time order of changes in the STS skills of individuals with obesity. Further research needs to find out whether training on FTM and LBM will improve STS skills of individuals with obesity in the longitudinal designs.

5. CONCLUSION

This study highlights yet other factors, such as FTM and LBM, that may influence the ability of obese individuals to perform STS task in their daily routine. FTM and LBM measured in the current study can explain the significant percent of the variation in rising index during STS task, meaning a decrease in FTM and an increase in LBM provided a support to rise up during STS. Moreover, it was revealed that an increase in FTM deteriorated the postural stability. Minimizing the FTM and optimizing the LBM together may help to improve rising index and postural balance skills during STS task. Improving lean tissue mass and decreasing fat tissue mass would be an effective strategy to improve STS in obese population to increase their agility and could encourage physical activity participation as well.

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Clinical and Experimental Health Sciences

Evaluation of Foveal Thickness and Macular Choroidal Thickness with Optical Coherence Tomography in Behcet's Disease

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ABSTRACT

Objective: To evaluate the foveal thickness and macular choroidal thickness on patients who were diagnosed with Behcet's Disease (BD).

Methods: A total of 60 patients were included in this prospective cross-sectional study. Patients were divided into two groups. Group 1 consisted of 30 patients who were diagnosed with BD and Group 2 consisted of 30 healthy controls. Detailed ophthalmological examination was performed on both groups and foveal thickness and macular choroidal thickness were measured with Spectral-Domain Optical Coherence Tomography (SD-OCT). To measure the choroidal thickness enhanced depth imaging OCT (EDI-OCT) technique was used.

Results: Mean foveal thickness in BD patients was 216.06 ± 53.14 µm and mean subfoveal choroidal thickness was 363.21 ± 85.22 µm. Mean foveal thickness and subfoveal choroidal thickness in healthy controls was 211.65 ± 16.60 µm and 352.83 ± 87.11 µm respectively. There was no statistical significance between patients with BD and patients of the control group regarding foveal and subfoveal choroidal thickness. However, anatomical deformation of Ellipsoid Zone structure in OCT had the most effect on visual acuity (p=0.001).

Conclusion: This study shows that there was no statistically significant difference in terms of foveal thickness and macular choroidal thickness in patients with BD.

Keywords: Behcet's disease, optical coherence tomography, choroidal thickness, inflammation.

1. INTRODUCTION

Behcet's disease (BD) is a systemic immune-mediated occlusive vasculopathy whose etiology and pathogenesis are not fully elucidated. Oral aphthous stomatitis, genital ulcerations, skin lesions, and ocular disease are evaluated as major findings (1). Ocular involvement is seen approximately in 60-80% of the patients. Anterior and posterior ocular involvement often proceed to iridocyclitis with hypopyon and retinal vasculitis (2). Hence, uveitis seen in BD is shown to be affecting choroid due to diffuse infiltration of inflammatory cells into the choroid (3). Retinal vasculitis with anterior, posterior involvement, or panuveitis are characteristics of the disease. Fundoscopic changes due to posterior segment involvement can significantly affect visual acuity (4-8). Besides clinical examination, the evaluation of the posterior segment involvement in BD can be practiced by fundus fluorescein angiography (FFA), indocyanine green angiography (ICA), ultrasonic biomicroscopy (UBM), multifocal electroretinogram (mfERG), and SD-OCT (9-13). The choroid, which is crucial for the retina to function properly, has up to 85% of the ocular blood flow. A great quantity of diseases including central serous chorioretinopathy, age-related macular degeneration, and chorioretinal inflammatory diseases has an impact on choroidal thickness (14, 15). Enhanced depth imaging (EDI) technique has been a good turn for physicians evaluating choroidal tissue with OCT. Since this imaging technique is widely accepted and used by physicians all over the world, understanding the morphological changes in choroid are easier not only in healthy population but also pathological diseases and conditions such as central serous chorioretinopathy, high myopia, polypoidal choroidal vasculopathy, age-related macular degeneration and Vogt-Koyanagi-Harada (VKH) disease (16-20). Furthermore, Park et al. revealed long term changes in choroidal thickness in Behçet's disease following up patients at least 24 months. According to that study, choroidal thickness decreased over time in BD patients and it was associated with the length of active inflammation (21). This present study was conducted

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to measure foveal thickness and macular choroidal thickness using Enhanced Depth Imaging technique of spectral domain OCT (SD-OCT) in patients diagnosed with Behcet's disease and to compare it with healthy controls in the same age group.

2. METHODS

In this prospective cross-sectional study, 60 eyes of 30 BD patients with active, inactive, and no ocular involvement older than 18 years of age and 60 eyes of 30 age and sex-matched healthy controls were included. All individuals agreed to sign an informed consent. This study was conducted in accordance with the principles of the Helsinki Declaration. Patients who had a history of intraocular surgery, glaucoma, or any other co-existing ocular pathologies and systemic disease and patients who had a spherical equivalent refractive error of more than ±5.00 diopters were excluded from this study. This study was approved by the Clinical Research Ethics Committee of Cumhuriyet University School of Medicine on 11.11.2014 and numbered as 2014-11/03. Complete ophthalmological examination of patients including best corrected visual acuity (BCVA), slit-lamp biomicroscopy, non-contact tonometry to measure intraocular pressure, fundoscopy after pupil dilatation, and Spectral Domain-OCT (SD-OCT) scanning with RS-3000 Advance (Nidek Co., Ltd, Gamagori, Japan) was performed. All OCT measurements of the patients were performed between 9 and 12 am. Macular anatomy was evaluated with SD-OCT. The presence of ERM, internal and external retinal layers, especially ELM, Ellipsoid Zone, RPE-BM complex were examined, foveal thickness and subfoveal choroidal thickness was measured as well as choroidal thickness of nasal and temporal of the fovea. To evaluate the macular anatomy, an area of 12 mm was examined by selecting the ultrafine quality in Macula Line choroidal mode of the OCT device. With the Tracing HD plus feature, 120 sections of the Scanning Laser Ophthalmoscope (SLO) image was captured. Using Enhanced Depth Imaging OCT (EDI-OCT), subfoveal, nasal, and temporal macular choroidal thickness was measured manually with the measurement tool of built-in software based on the distance between the lowest part of the RPE / BM complex and the choroidoscleral junction. Manual method was used to measure foveal thickness by marking the distance between the lowest part of the RPE-BM complex and the foveal pit. In this study, the demographic data, clinical ophthalmological examination findings, macular anatomy, observing the structural integrity of the Ellipsoid Zone and RPE-BM complex with SD-OCT and their effects on BCVA were evaluated alongside the evaluation of foveal thickness and subfoveal, 1000 µm nasal and temporal choroidal thicknesses with OCT in both groups.

2.1. Statistical Analysis

The data analysis of this study was performed using the SPPS version 22 (IBM Statistical Package for the Social Sciences Statistics; New York, USA). In independent groups, the significance test of the difference between the two means was used when the parametric test assumptions were fulfilled. Kruskal-Wallis test, the Mann Whitney U test, and the Chi-square tests were used when the parametric test assumptions were not fulfilled. The mean value of the continuous variables is presented as mean ± standard deviation (SD). A value of $p<0.05$ was considered statistically significant.

3. RESULTS

Of 30 Behcet's patients, 11 (36.7%) were male and 19 (63.3%) were female. The mean age of the patients was 36.16 ± 11.85 years (19-60 years). The mean age of diagnosis with BD was 28.60 ± 8.83 years. The control group consisted of 30 healthy subjects. Of the 30 patients in the control group, 15 were male (50%), 15 were female (50%), and the mean age was 35.10 ± 7.58 years (20-65 years) in the control group. Demographics and treatment modalities are presented in Table 1. Regarding mean age and gender, no statistical significance was found between groups ($p\geq0.05$). All 30 patients with BD (100%) were receiving systemic medical treatment at the time of participation in the study. Twenty-nine patients (96.6%) were on colchicine, 11 were on azathioprine (36.6%), 10 (20%) were on steroids and 5 (23.3%) were on cyclosporine. The right eye of 4 patients (13.3%), the left eye of 5 patients (%16.6) were involved leading to unilateral ocular involvement in 9 patients (30%) in total. Seven patients (33.3%) had bilateral ocular involvement.

Table 1. *Demographic characteristics of BD patients and control group*

	BD group (n=30)	Control group (n=30)	P value
Age (Mean ± SD)	36.16±11.85	35.10±7.58	p=0.68
Sex (male/female)	11/19	15/15	p≥0.05
Mean Age of Diagnosis (Mean ± SD)	28.60±8.83	-	-
Treatment			
Colchicine	96.6% (n=29)	-	-
Azathioprine	36.6% (n=11)	-	-
Corticosteroids	20% (n=10)	-	-
Cyclosporine	23.3% (n=5)	-	-

BD: Behçet's Disease

Best corrected visual acuity and SD-OCT measurements of the groups are shown in Table 2. The mean BCVA of all BD patients was 0.92 ± 0.23. There was 1 eye (1.66%) with BCVA lower than 0.1, 3 eyes (5%) with BCVA between 0.1-0.3, 2 eyes (3.33%) with BCVA between 0.4-0.6, and 54 eyes with BCVA equal or higher than 0.7. There was no statistical difference between genders regarding BCVA ($p>0.05$). All eyes in the control group had normal visual acuity. When

the BCVA of the two groups was compared, the difference between groups was statistically significant (p=0.012), but the difference was not significant when subfoveal, nasal, temporal choroidal thickness, and foveal thickness were compared. Comparison of BCVA regarding OCT measurements revealed a statistically significant difference (p<0.05). The difference between eyes with normal OCT findings, eyes with Ellipsoid Zone defect, and eyes with both Ellipsoid Zone and RPE-BM defects were found to be statistically significant (p=0.001). The difference between eyes with normal OCT findings, RPE-BM defect, and ERM was not statistically significant (p>0.05).

Table 2. *Comparison of best corrected visual acuity and SD-OCT values in patients with Behcet's disease and control group*

	BD group (n=30)	Control group (n=30)	P value
BCVA	0.92±0.23	1.00±0.00	p=0.012*
Subfoveal choroidal thickness (µm)	363.21±85.22	352.83±87.11	p=0.51
Nasal choroidal thickness (µm)	331.61±81.06	329.63±84.04	p=0.90
Temporal choroidal thickness (µm)	344.40±82.49	328.83±79.52	p=0.30
Foveal thickness (µm)	216.06±53.14	211.65±16.60	p=0.54

BCVA: Best Corrected Visual Acuity BD: Behçet's Disease. Values are presented as Mean ± Standard deviation.

When the patients with BD were evaluated with structural SD-OCT findings, two eyes had epiretinal membrane (ERM), 4 eyes (6.7%) had RPE-BM defect, 2 eyes (3.3%) had Ellipsoid Zone defect, 2 eyes (3.3%) had both Ellipsoid Zone and RPE-BM complex defect.

Mean foveal thickness in patients with BD was 216.06 ± 53.14 µm and mean subfoveal choroidal thickness was 363.21 ± 85.22 µm. Mean foveal thickness in the control group was 211.65 ± 16.60 µm and mean subfoveal choroidal thickness was 352.83 ± 87.11 µm. No statistically significant difference was observed between the two groups regarding foveal and subfoveal choroidal thickness (p>0.05 for both). Comparison of best corrected visual acuity and SD-OCT measurements in BD patients and control group are presented in Table 2. There was no statistically significant difference between foveal thickness, subfoveal choroidal thickness, 1000 µm nasal and temporal choroidal thickness in terms of BCVA in BD patients.

4. DISCUSSION

BD is a chronic vasculitis of the arteries and veins involving multiple systems and has high morbidity due to ocular involvement. In 70% of patients with BD, inflammatory eye findings are observed (22). Eye involvement is more frequent and more severe in young adults and especially in males and is less common in females and the elderly (23). Optical Coherence Tomography may reveal some indiscernible changes which can not be seen with fundoscopy in patients who have posterior segment involvement related to Behcet's disease. In this current study, patients with BD had an increased foveal and macular choroidal thickness compared to the control group.

Although there are publications in the literature indicating BCVA is affected more in young male patients, the mean BCVA of male BD patients was 0.94 ± 0.18 in this study. In literature, BCVA was below 0.1 in 20-33% of eyes. In this study, only 1 (1.66%) eye had BCVA under 0.1.

Many factors may affect OCT measurements. Most reported causes are age, ethnic origin, diabetes mellitus, hypertension, myopia, axial length, central serous chorioretinopathy, and history of intraocular surgery (24,25). In a few studies, OCT measurements revealed significant diurnal variation between measurements. In these studies, the choroidal thickness increased towards midnight and was measured thinner at noon. The difference between these measurements varies between 30 and 60 µm (26,27). As mentioned before, to minimize the effect of diurnal variations on OCT measurements, we have taken all measurements at the same time of the day.

Choroidal thickness in BD in the inactive phase was found to be thicker compared to the healthy population. Also, patients who had posterior segment involvement in the inactive phase had significantly higher subfoveal choroidal thickness compared to the fellow healthy eye. There was a 15.3% decrease of mean subfoveal choroidal thickness in BD during the inactive phase. Along with the increase in subfoveal choroidal thickness in the acute phase of posterior uveitis in BD, vascular leakage has increased, but these findings regressed after the acute aggravation phase of posterior uveitis. This same study showed that choroidal thicknesses of BD patients in the inactive phase were found to be thicker than the healthy population. The cause of this thickening in the choroid is due to leakage in the vascular structures. No statistically significant correlation was found between the duration of uveitis and the severity of anterior or posterior inflammation and subfoveal choroidal thickness (28). Besides, some studies revealed that BD patients with posterior segment involvement had higher subfoveal choroidal thickness measured by EDI-OCT compared to the healthy population. Kim et al. reported that BD patients with posterior segment involvement in the active phase had significantly higher subfoveal choroidal thickness than in BD patients who had posterior segment involvement in the inactive phase (28). Studies evaluating BD patients who had posterior segment involvement during the inactive phase, EDI-OCT showed that subfoveal choroidal thickness and retinal thickness were significantly thinner in BD compared to the healthy population and this thinning progressed over time. Among the causes of thinning of subfoveal choroidal and retinal thickness, choroidal atrophy triggered by affected choroidal circulation secondary to recurrent posterior uveitis and choroid, which provides oxygen and metabolite support to the retina, failing to fully function was shown (29,30).

In the literature, there are some studies evaluating the Ellipsoid Zone with OCT, which has been shown to have a close relationship with BCVA. These studies evaluated the relationship between Ellipsoid Zone structural integrity and visual acuity in patients with retinal vein occlusion, retinal detachment, and macular hole (31-33). In a study by Unoki et al., the effect of Ellipsoid Zone and ELM on BCVA was evaluated in Behcet's patients during the remission phase and only the relationship between Ellipsoid Zone and BCVA was observed but the same relationship could not be demonstrated with ELM (34).

In histopathological studies, the choroidal thickness of the posterior pole was reported to be approximately 220 µm (35). In a study by Karampelas et al., retinal and choroidal imaging was performed with OCT in patients with idiopathic panuveitis. In that study, OCT images revealed the effects of duration of the disease and accompanying cystoid macular edema on visual acuity and retinal and choroidal changes. Also, that study revealed retinal and choroidal thickness and BCVA are not related (36). In a study by Iaccarino et al., no correlation between BCVA and choroidal thickness in patients who had posterior uveitis secondary to Behcet's disease was found (37). In another study, where 21 eyes of 21 patients with inactive idiopathic panuveitis were compared with the healthy group, choroidal thickness was correlated with the severity of the disease. However, the average choroidal thickness of affected eyes was thinner in contrast to the control group. The reason for this thinning was the thinning of the Haller's layer and hyporeflectivity as a result of loss of luminal spaces in choroidal vasculature (36). Histopathological studies have shown diffuse and focal infiltration of inflammatory cells such as CD4+ T cells, macrophages, and immunoglobulin and complement accumulation in choroidal tissue (3,38-40). Various clinical features may be observed with conventional imaging systems including FA and ICGA in patients with Behcet uveitis (9,41,42). As a result of leukocyte infiltration in choroidal vascular inflammation, choroidal hyperfluorescence, dye leakage or choroidal vessel wall staining may be seen (43,44). As a result of the accumulation of exudative material in the stroma, edema, and fibrosis or choroidal vascular obstruction, hypofluorescence and choroidal filling defects may be seen (42,43,45). Furthermore, the relationship between increased blood flow and vascular resistance and ocular perfusion pressure and choroidal thickness may also cause choroidal thickening in the active phase of inflammation (46,47). Thus, the accumulation of exudates due to changes in ocular blood flow caused by choroidal vascular inflammatory reaction might also lead to choroidal thickening (28). In this current study, we observed that the pathophysiological changes in choroidal tissue may cause choroidal thickening as indicated in some studies in the literature and we found that choroidal thickness was increased in Behcet's patients.

5. CONCLUSION

Inclusion of only a small heterogenous, cross-sectional group of Behçet's patients, some patients receiving medical treatment prior to the participation in the study, and SD-OCT measurements being taken without considering any diurnal variations are amongst the limitations of this study. Further studies with larger sample sizes are needed to elucidate the relationship between foveal thickness, macular choroidal thickness, and BCVA. In conclusion, even though patients with BD had an increased foveal and macular choroidal thickness compared to the control group, we observed no statistically significant difference in terms of foveal thickness and macular choroidal thickness.

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Clinical and Experimental Health Sciences

The Comparison of the Effectiveness of Local Ice and Manual Pressure Applications in Decreasing Pain Related to Intramuscular Injection

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ABSTRACT

Objective: Because of the pain they cause, intramuscular (IM) injection applications can constitute a negative experience for both the patients and the nurses performing the application. This study was planned to compare the effectiveness of local ice and manual pressure applications in decreasing the injection pain experienced by patients.

Methods: This study performed a university hospital in Turkey. One hundred and thirty five patients, 45 in the local ice group, 45 in the manual pressure group and 45 in the control group, met the inclusion criteria and completed the study. The local ice group received cold ice application to the injection area before injection. The manual pressure group received pressure applied by the researcher to the injection area before injection. The control group received routine injection. Study data was collected using the Wong-Baker FACES Pain Rating Scale (WBS) and the Visual Analog Pain Scale (VAS).

Results: As a result of the study, no difference was found between the groups in which manual pressure and local ice applications were applied. However, a statistically significant difference was found between the experimental groups (manual pressure and local ice) and the control group. The mean ± standard deviation WBS and VAS scores of the control group (2.22±0.84 and 13.13±13.49, respectively) were statistically significantly higher than the groups in which manual pressure (1.82±0.80 and 8.11±9.13, respectively) and local ice (1.80±0.69 and 7.26±4.98, respectively) were applied.

Conclusions: It was concluded that local ice and manual pressure applications before IM injections were effective in decreasing the injection pain of patients.

Keywords: Injections, injection pain, local ice, manual pressure, pain control.

1. INTRODUCTION

Injections are considered the gold standard in the parenteral application of various drugs (1). Intramuscular (IM) injection, which is one of the parenteral applications, is used worldwide commonly. IM injection is often preferred in the application of drugs such as antibiotics, vitamins, and painkillers (2). However, if the area is not appropriately determined in IM injection treatments or if the injection is not performed with the appropriate technique, serious complications may arise (3). The most common among these complications is pain, and this may arise as a result of not choosing the appropriate area, the injector penetrating the skin, and the mechanic and chemical effects of the drug during and after injection (1,4).

Pain, which is an unwanted experience for any patient, is defined as the fifth symptom of life and thus its management is important regardless of the pain being acute or chronic (5,6). IM injection pain not managed properly can cause fear of injection to arise in patients. As a result, the quality of life of the patient can be negatively affected or patients may delay seeking medical attention (6,7). Additionally, painful injections can harm the relationship between patients and nurses (8,9) For this reason, it is important for nurses to manage injection pain with appropriate interventions (10). In order to manage pain properly, nurses first need to know the pain, the factors affecting the pain, genetic or ethnic predilection, and pain tolerance. It is important for nurses to evaluate their patients, choose the most appropriate evidence based intervention, apply it to the patient, and observe the results (6).

The right to ease pain is one of the most basic human rights (10). Many different methods have been tried throughout the centuries to ease injection pain. Applications of pressure and ice are also among these methods (11,12). In pressure application, the pressure applied has been

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reported to cause beta endorphin to be released into the bloodstream in the area, easing pain. According to the door control theory, pain senses in the back horn of the spinal cord are inhibited by pressure, decreasing pain (13). In ice application, the conduction speed of the nerves in the area is decreased, slowing down the conduction of pain signals, increasing the pain threshold, and causing a decrease in pain intensity (12,14). These interventions, which can be used by nurses to decrease pain during injection, can be sued in clinical application without any additional cost or loss of time (11).

Applications towards easing pain can help patients to cope with this situation better. There are studies in the literature showing that pressure (10,11,15,16) and ice applications (8,12,14) care effective in decreasing injection pain. However, no studies comparing the effectiveness of manual pressure and ice applications could be found. For this reason, this study was planned to compare the effectiveness of local manual ice and pressure applications in decreasing the injection pain experienced by patients.

2. METHODS

2.1. Aim of the Study

This is a non-randomized (quasi-experimental) study planned to compare the effectiveness of local ice and manual pressure applications in decreasing the injection pain experienced by patients.

2.2. Setting and Sample

The universe of this study, which was performed between September 10th 2016 and March 10th 2017, consisted of the inpatients in the obstetrics service of a university hospital. The sample size of the study was calculated using the power analysis method. In the calculation performed by taking into account the parameters of the groups, 126 patients were found to be sufficient with a 0.80 power rating, a 0.05 error rate, and a 0.95 effect level. Taking possible losses into account, assigning 45 patients each to the local ice, manual pressure, and control groups was found appropriate.

Factors that may affect the pain experience of the individuals were taken into consideration in the selection of the sample. In order to eliminate the effect of gender on the pain experience of the patients and to standardize the application, only female patients were studied. Because the biological and psychosocial conditions of the individuals may affect the intensity, frequency and duration of the pain, patients with communication problems, very fat or thin patients, lesions at the injection site, and severe pain before injection were not included in the study. Patients who received the same treatment were selected for the study in order to standardize other factors that may affect the individual's perception of pain, such as injection speed, needle temperature and the content of injected fluids. And all patients were performed under the same conditions as a single operator. In addition, the ventrogluteal region was preferred because it is a reliable IM injection site away from nerves, bones and blood vessels. In this context, the sample of the study consisted of patients who were on IM diclofenac sodium treatment in their routine treatment, who were older than 18 years of age, who had no communication problems, were not too fat or thin (body mass index 18-30), had no lesions at the injection site, did not have severe pain before injection (VAS score <8), and were willing to participate in the study. Also, 9 patients who were obese (n=6) and had a preoperative pain score greater than 8 (n=3) were not included in the study.

2.3. Study Hypotheses

Hypothesis (H_0)1: There is no difference between manual pressure application and local ice application in reducing pain associated with intramuscular injection application.

Hypothesis (H_1)1: There is a difference between manual pressure application and local ice application in reducing pain associated with intramuscular injection application.

Hypothesis (H_0)2: Local ice application is not effective in reducing pain associated with intramuscular injection application.

Hypothesis (H_1)2: Local ice application is effective in reducing pain associated with intramuscular injection application.

Hypothesis (H_0)3: Manual pressure application is not effective in reducing pain associated with intramuscular injection application.

Hypothesis (H_1)3: Manual pressure application is effective in reducing pain associated with intramuscular injection application.

2.4. Measurement

Study data was collected using a General Information Form, The Wong-Baker FACES Pain Rating Scale (WBS), and The Visual Analog Pain Scale (VAS).

2.4.1. The General Information Form

This form was prepared by the researcher according to literature (11,14,17), and consisted of demographic characteristics such as age, gender, marital status, pain tolerance, fear of injection, as well as vital findings (blood pressure, and pulse)

2.4.2. The Wong-Baker FACES Pain Rating Scale (WBS)

The WBS was developed by Wong and Baker in 1988. This is scale where facial expressions rated between 0 and 5 are used to determine the pain levels of the patients. In the scale, "0" terms "No pain", "1" terms "a little pain", "2" terms "more pain", "3" terms "moderate pain" "4" terms "intense

pain" and "5" terms "The most intense pain possible". In the scoring performed using facial expressions, the expressions change with increasing scores, which in turn terms an increase in pain levels (18).

2.4.3. The Visual Analog Pain Scale (VAS)

This scale, which is used to evaluate the pain experienced by patients, consists of a horizontal line scored between 0 and 10. The value of 0 terms no pain while the value 10 terms the most intense pain possible.

2.5. Data Collection

The patients, who were being treated in the service where the study was conducted and would undergo IM diclofenac sodium treatments by doctor's orders, were informed on the aim, context, duration, and method of the study. After being informed, the patients who volunteered to participate in the study gave written consent and were included in the sample. Among the inpatients, the first patient was assigned to the local ice application group, the second patient to the manual pressure application group, and the third patient to the control group. The patients were introduced to the VAS before injection, taught how to mark the VAS, and their blood pressures and pulses were measured by the researcher and noted on the general information form. In the injection application, the ventrogluteal area was preferred since it is the safest injection area (3,19). All injection applications were performed by the researcher. For data reliability, two observers were present in each application. The following steps were used for data collection.

The preparation of the diclofenac sodium before injection: The solution, in the form of a 75 mg/3 mL ampoule, was prepared using a 5 mL, 21 gauge, 38 mm injector. The injector tip was changed after drawing the drug into the injector.

The local ice application group: Patients in this group underwent cold application to the injection area before injection for 30 seconds using a 3x3x3 cm ice cube. The area was then wiped with an alcohol swab, and injection was performed after the area dried (8,20).

The manual pressure application group: Patients in this group underwent 10 seconds of pressure applied by the researcher to the injection area before injection with the thumb of the passive hand at a strength sufficient to feel resistance. The area was then wiped with an alcohol swab, and injection was performed after the area dried (11,14,21).

The control group: No application was performed before injection.

After the injection: The patients were asked to evaluate their pain using the VAS. The pain levels of the patients were evaluated by the researcher and the two observers using the WBS.

2.6. Ethical Considerations

Before the study, written permission from the institutions where the study was conducted and ethical approval from the Namık Kemal University School of Medicine Non-Invasive Clinical Studies Board of Ethics were received (2016/61/04/10). Institutional permission from the hospital where the study would be conducted was taken, as well as written consent from the patients who agreed to participate in the study.

2.7. Data Analysis

The analysis of the data obtained from the study was performed using the SPSS (Statistical Package for Social Science) 22.0 package program. Descriptive statistics, such as mean, standard deviation (SD), number, and frequency, were used to characterize the research participants. Kolmogorov-Smirnov test was used for normality distribution of variables. Chi-square and one-way ANOVA tests were used to evaluate the similarity of the groups. One-way ANOVA and Tukey tests were used to determine the difference between groups. A p value of < 0.05 was considered statistically significant.

3. RESULTS

The mean±SD age of the patients who participated in the study was 36.64±12.18 (range: 18-65). 93.3% of the patients were married and 63.0% were elementary school graduates. 55.6% of the patients stated that they had middle levels of pain tolerance, 69.6% stated that they did not fear IM injection, and 85.2% stated that they never had a negative experience regarding IM injection applications. The mean±SD pulse of the patients was 79.62±8.32 beats per minute, their mean±SD systolic blood pressure was 108.00±10.05 mmHg, and their mean±SD diastolic blood pressure was 67.81± 7.21 mmHg. No statistically significant difference regarding these characteristics was found among the groups, showing that the patients in the three groups were distributed similarly ($p>0.05$) (Table 1).

When the mean±SD WBS and VAS scores of the control (2.22±0.84 and 13.13±13.49, respectively), manual pressure (1.82±0.80 and 8.11±9.13, respectively), and local ice (1.80±0.69 and 7.26±4.98, respectively) groups were compared, a statistically significant difference among the groups with regard to mean WBS and VAS scores was found. The difference in the WBS and VAS mean scores was found to be between the control group and the study groups, where the control group received a higher score compared to the groups which underwent pressure and ice applications ($p<0.05$) (Table 2).

Table 1. *Comparison of the descriptive characteristics between manuel pressure, local ice and control groups (N= 135)*

Characteristic	Control Group (n:45) N %	Manuel Pressure Group (n:45) N %	Lokal Ice Group (n:45) N %	Total (N:135) N %	χ2* F** p
Marital Status					
Married	43 95.6	44 97.8	39 86.7	126 93.3	5000
Single	2 4.4	1 2.2	6 13.3	9 6.7	0.083*
Education					
Literacy	7 15.6	3 6.7	6 13.3	16 11.9	
Elementary school	27 60.0	29 64.4	29 64.4	85 63.0	2.177
High school	5 11.1	6 13.3	5 11.1	16 11.9	0.533*
University	6 13.3	7 15.6	5 11.1	18 13.2	
Tolerence to Pain					
High	8 17.8	15 33.3	10 22.2	33 24.4	3.146
Middle	27 60.0	22 48.9	26 57.8	75 55.6	0. 354*
Low	10 22.2	8 17.8	9 20.0	27 20.0	
Fear of Injection					
Yes	14 31.1	17 37.8	10 22.2	41 33.4	2.592
No	31 68.9	28 62.2	35 77.8	94 69.6	0.278*
Bad Experience with Injection					
Yes	8 17.8	6 13.3	6 13.3	20 14.8	0.470
No	37 82.2	39 86.7	39 86.7	115 85.2	0.795*
Age (year) Mean±SD (min-max)	36.64±12.21 (21-65)	34.51±11.58 (19-63)	38.77±12.63 (18-65)	36.64±12.18 (18-65)	1.400 0.253**
Pulse number/minutes Mean±SD (min-max)	78.44±7.75 (64-96)	80.06±7.62 (67-98)	80.35±9.53 (60-98)	79.62±8.32 (60-98)	1.063 0.506**
Systolic Blood Pressure (mmHg) Mean±SD (min-max)	107.11±10.57 (90-130)	107.55±10.47 (90-130)	109.33±9.14 (80-130)	108.00±10.05 (80-130)	0.703 0.544**
Diastolic Blood Pressure (mmHg) Mean±SD (min-max)	65.88±6.84 (50-80)	68.00±7.93 (50-90)	69.55±6.46 (50-80)	67.81± 7.21 (50-90)	2,843 0.053**

** Chi-square Test; **One-way ANOVA*

Table 2*. Intergroup comparison of WBS and VAS mean scores of experimental and control groups (N = 135)*

	Control Group (n:45) Mean± SD	Manuel Pressure Group(n:45) Mean± SD	Lokal Ice Group (n:45) Mean± SD	Total (N:135) Mean± SD	F p
WBS	2.22±0.84	1.82±0.80	1.80±0.69	1.94±0.80	4.112 0.019* 1>2 ve 3**
VAS	13.13±13.49	8.11±9.13	7.26±4.98	9.50±10.10	4.676 0.011* 1>2 ve 3**

** One-way ANOVA. ** Tukey Test; WBS: The Wong-Baker FACES Pain Rating Scale VAS: The Visual Analog Pain Scale, 1=Control Group, 2= Manuel Pressure Group, 3= Local Ice Group*

4. DISCUSSION

IM injection is and invasive and painful drug treatment (8). It is the nurse's responsibility to apply a good injection technique and the best approach to pain management to prevent and alleviate injection-related pain (22). Different methods can be used to reduce the pain associated with injection. In this study, the effects of manual pressure and local ice application on injection pain were compared. As a result in this study, the pain levels of the patients were evaluated both through the observations of the researchers (WBS) and the self-reports of the patients (VAS). In the evaluation based on researcher observation and patients self-reports, no statistically significant difference between the study groups could be found with regard to the pain experiences of the patients, while a statistically significant difference between the study groups and the control group was found. Local ice and manual pressure applications were found to be effective in decreasing the pain levels of patients compared to the control group. According to these results, it was concluded

that local ice and manual pressure applications before IM injection were effective in decreasing the injection pain levels of patients.

When the literature on local ice application is examined, it is seen that the results are similar. In a study conducted by Hasanpour et al. with 90 child patients undergoing intramuscular penicillin injections, the patients were separated into local ice, distraction, and control groups, and the pain levels of the children were measured using the Oucher Scale. As a result of the study, the pain experiences of the distraction and local ice groups were concluded to be less compared to the control group, and non-pharmacological pain management methods were found to be effective (16). In a study where Farhadi and Esmailzadeh examined the effect of local cold application before intramuscular penicillin injection on pain intensity, adult patients in the study group underwent local ice application before injection. As a result of the study, where the pain experiences of the patients were evaluated using the VAS, the injection related pain of the patients who underwent local ice application was found to be significantly lower. It was thus concluded that applying ice locally before penicillin injections could play an important role in decreasing pain (8). In the study conducted by Ramadan et al. on adult patients, it was found that the group who had 30 seconds of local ice application before IM injection had statistically lower pain score due to injection than the patients who did not apply ice (23). In another study conducted by Ramadan et al., it was found that patients who had ice application before IM injection had a decrease in pain due to injection, and ice application was recommended before IM injection (24). In another study, it was stated that cold application for 5 seconds before IM injection was effective in reducing pain due to injection (25). Similarly, in another study by Bilge et al., they used cold spray for ice effect. After the application, they found that the cold spray was an effective attempt to reduce the pain associated with IM injection (26). Additionally, it has been reported in literature that beside its pain decreasing effects, cold applications could cause vasoconstriction and delays in the absorption of the drug, and that this should be taken into consideration in patients where the absorption of the drug needs to be fast (27).

When the studies on manual pressure were examined, the results were found to be similar. In studies conducted by Nasiry et al. with adult patients and Derya et al. with children, the effect of manual pressure application on IM injection pain was evaluated. Manual pressure was applied to the injection area before intervention and the pain levels of the patients were evaluated using the VAS. As a result of those studies, manual pressure application was found to be effective in decreasing the pain perceived by both children and adults compared to the routine application, and this method was suggested for routine use (11,19). In a study where Öztürk et al. evaluated the effect of manual pressure application on injection pain in university students, 123 students underwent IM Hepatitis A and B vaccine applications. Students in the study group underwent 10 seconds of manual pressure application to the injection area before injection and the pain experiences of the students were evaluated using the numerical rating scale. As a result of the study, students who underwent the manual pressure application were reported to experience less pain, and the application was suggested for use in adults before IM injection (21). In another study conducted by Çelik in patients who received IM penicillin, manual pressure was found to be effective in reducing injection-related pain (28).

5. CONCLUSION

Although there are studies in the literature evaluating the effectiveness of manual pressure and local ice applications, no studies comparing the effectiveness of those methods could be found.

In the present study, unlike the literature, the efficiency of the two applications was compared and it was found that there was no difference between the two applications. However, a significant difference was found between the intervention groups and the control group. According to these results, it can be suggested that nurses should utilize local ice and manual pressure applications before IM injection treatments to decrease the pain levels of patients. These physical pre injection applications are thought to be preferable for no additional cost or loss of time, ease and safety of use, and not requiring special training or skill. Performing applications that would minimize the pain of patients in painful interventions such as IM injection would positively affect patient satisfaction, quality of life, and comfort.

Since this study was conducted with a specific group of patients in a single clinic with a small sample size, the results of the study cannot be generalized for all patients. In this study, it was impossible to accomplish a true double – blinded study with manual pressure, local ice therapy or routine injecting as it was obvious to the patients which intervention they were receiving. Pain data being collected not through objective measurements but through patient self-reporting and observation constitutes another limitation of the study. Repeating the study with larger groups to confirm the results is thus suggested.

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Clinical and Experimental Health Sciences

The Relation Between Emphatic Tendency and Level of Compassion among Midwifery Students

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ABSTRACT

Objective: In this study, it has been aimed to determine the relation between the empathic tendency and compassion level in the students of midwifery department.

Methods: The study is a descriptive and analytical study. The data were collected by self-reporting method using "Empathic Tendency Scale" and "Compassion Scale". The study was conducted with a total of 335 midwifery students studying at university in Turkey.

Results: The students' empathic tendency score was found to be 67.38 ±5.86. The students' compassion score was found to be 94.63±11.58. The empathic tendency level of the students studying in the first grade is significantly higher than other grades. There is a positive correlation between the empathic tendency level and the sub-dimensions of the total compassion score, kindness, common humanity, and mindfulness.

Conclusion: It has been determined because of the study that the empathic tendency and compassion levels of the students of midwifery are high. Classes about empathy and compassion should be included in the midwifery curriculum for the students to graduate with this point of view.

Keywords: Midwifery, students, empathy, compassion

1. INTRODUCTION

Midwifery is a professional group providing care to the women, newborns, and their families in a delicate period such as pregnancy and birth. In this delicate period, the midwives should approach the pregnant and their families with an empathic viewpoint and in a compassionate way during the care they provide. Though it is concept hard to understand, empathy is defined as a mirror in our brain enabling us to put ourselves in someone's shoes and the main objective is to be able to completely understand the opposite person (1). Clinic empathy is the ability of understanding the state, viewpoint, feelings and actions of the patient based on their perceptions in an auxiliary or therapeutic way (2). When a care is provided to the patients with this point of view, the performances of the health professionals increase and their chance of experiencing burnout decreases (3, 4). Moreover; the quality of the care and patient satisfaction increase (5). Empathic communication in birth services confronts us as a part of the sentimental support. Women also expect sentimental support as much as the physical support from the midwives in the birth process (6). Empathy and compassion are a very important part of the sentimental support given to the women and are always in interaction with each other (7). However, as different from empathy, behavior is also added to the feeling and thought in the compassion. Compassion also contains the wish for easing the pain of others, the cognitive process related to understanding the resource of the pain and the behavioral process related to performing compassionate actions (8). Compassionate midwifery care, empathy, communication, motivation to support those in need, empowerment of women, negotiation and pain relief activities with knowledge and skills. It also has a positive effect on maternal and child health (9). International Confederation of Midwives (ICM) also asserts that the midwifery care should be respectful for the human rights and compassionate (10). There is a need for the determination of the empathy, compassion levels of the midwifery students and the factors affecting them in the process before their graduation for a qualified midwifery care. However, there are few studies conducted with midwifery students (11, 12). In the study, it has been aimed to determine the empathic tendency and compassion levels of the students in midwifery department and the relation between these two concepts.

2. METHODS

2.1. Study Design

A cross-sectional, descriptive, and analytical study was conducted. The study was carried out in one midwifery

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department at University in Central Anatolia, Turkey. All students who can speak and write Turkish were included in the study. Before the lesson, the students were visited by the researchers and asked to fill in the questionnaire form. It took about ten minutes to fill out the form.

Research Questions

- What is the empathic tendency level of students in midwifery department?
- What is the compassion level of students in midwifery department?
- Is there any relation between the empathic tendency and compassion levels of the students in midwifery department?

2.2. Sample

The population of the study consisted of all 389 midwifery students who studied in the academic year 2019-2020. The study was completed with a total sample of 335 students (86% response rate, failure to complete collection forms or other reasons).

2.3. Instruments

Student Description Form

This form was prepared by the researchers in according with the literature (11, 12). The form includes questions such as the class they studied, the high school they graduated from, and their marital status.

Empathic Tendency Scale (ETS)

The scale prepared regarding the measurement of the sentimental sensitivity of the individual against the phenomena about himself/herself was developed by Dokmen in 1989 (13). The highest score to be obtained from the scale is 100 and the lowest score is 20. Cronbach's alpha value was not found in the original study. In this study, the Cronbach Alpha coefficient of the scale was found to be 0.61.

Compassion Scale (CS)

Compassion Scale was developed by Pommier (2011) and its Turkish validity and reliability were performed by Akdeniz and Deniz (2016) (14, 15). The scale consists of 24 questions in total. It consists of the sub-dimensions such as kindness, indifference, common humanity, separation, mindfulness, and disengagement. The subscales of indifference, separation and disengagement are reverse scored. The compassion level increases as the score attained from the scale increases. Cronbach's alpha internal consistency reliability coefficient for the whole scale was found to be 0.85. When the internal consistency reliability coefficient is calculated for the sub-dimensions, it is 0.73 for kindness, 0.64 for indifference, 0.66 for common humanity, 0.67 for separation, 0.70 for mindfulness, 0.60 for disengagement. In this study, the Cronbach's alpha coefficient for the whole scale was found to be 0.91. Internal consistency reliability coefficients for the sub-dimensions were 0.69, 0.76, 0.66, 0.51, 0.69 and 0.50, respectively.

2.4. Ethical Considerations

Permits have been taken for the conduction of the study from Selcuk University Faculty of Health Sciences Ethics Committee (2019/14367) and from the institutions the study has been conducted. The verbal and written approvals of the students have been taken after they have been informed about the study.

2.5. Data Analysis

The licensed SPSS 20.0 was used for the data analysis. Non-parametric tests have been used in the analysis because the empathic tendency and compassion scale total scores and the affecting factors have not shown normal distribution according to Shapiro wilk test. Spearman Correlation analysis has been applied for the purpose of determining whether there is any relation between the empathic tendency and compassion level of the students. Mann-Whitney U test, Kruskal-Wallis H test and Spearman correlation analysis have been used in the analysis of the data.

3. RESULTS

A total of 335 students have participated in the study and the average age of the students is 20.18±1.67 (min: 17, max:33). The students' mean empathic tendency score was found to be 67.38 ±5.86 (Table 1). Also, 22.6% of them are at their first year, 24.7% are at their second year, 27.4% are at their third year and 25.3% are at their fourth and more years (Table 2). The graduated high school, marital status, social security, and the education of the students about the empathy do not affect the empathic tendency level ($p>0.05$) (Table 2). The students' mean compassion score was found to be 94.63 ±11.58. It has been found that the compassion scale score is only affected from the marital status, the compassion level of the single students is significantly higher than the married students ($p<0.05$). When the sub-dimension score median values and the affecting factors are considered, it has been determined that the year the student has been educated only affects the sub-dimension of the common humanity ($p<0.05$). This difference stems from the fact that the points of the students at the first year of their education are significantly higher. The sub-dimension points median values of indifference, separation, mindfulness, and disengagement show differences depending on the graduated high schools of the students. It has been determined that this difference in all four sub-dimensions stems from the fact that the scores median values of the students who graduated from science high schools are high. The kindness and common humanity sub-dimensions score median values of the students with social security are higher than those of the students with no social security ($p<0.05$). When the marital status of the students has been considered, the mindfulness sub-dimension

score of the single students is significantly higher than that of the married students. The education status related to the empathy are similar in terms of the compassion scale sub-dimensions score median values (p>0.05).

Table 1. *The empathic tendency and compassion scale total and sub-dimension scores*

Variable	Mean	Sd	Median	Q1*	Q3**
Empathic Tendency Scale Total	67.38	5.86	68.0	64.00	71.00
Compassion Scale Total	94.63	11.58	96.00	88.00	104.00
Kindness Sub-Dimension	4.05	0.70	4.00	3.50	4.50
Indifference Sub-Dimension	4.10	0.70	4.00	3.75	4.75
Common Humanity	3.86	0.76	4.00	3.25	4.50
Separation Sub-Dimension	4.02	0.65	4.00	3.50	4.50
Mindfulness Sub-Dimension	3.89	0.68	4.00	3.50	4.50
Disengagement Sub-Dimension	3.71	0.43	3.75	3.50	4.00

**Interquartile range 1 (25th percentiles)*
*** Interquartile range 2 (75th percentiles)*

Spearman correlation analysis shows that there is a positive relation between the empathic tendency level of the students and the sub-dimensions of total compassion score, kindness, common humanity, and mindfulness (Table 3).

Table 3. *Compassion scale total point and the relation between empathic tendency level and sub-dimensions*

Variable*	Empathic Tendency Level	
	r	p
Total compassion score	0.114	0.036
Kindness sub-dimension	0.230	<0.001
Indifference sub-dimension	-0.033	0.542
Common humanity sub-dimension	0.126	0.021
Separation sub-dimension	-0.039	0.474
Mindfulness sub-dimension	0.157	0.004
Disengagement sub-dimension	0.066	0.227

** Spearman correlation analysis*

4. DISCUSSION

The study gives information about the empathic tendency and compassion levels of the students in midwifery department and the relation between them. Students' empathic tendency levels are generally high. It is significantly higher in the first-year students when compared to the students in other grades and decreases as the year of education increases. In a study conducted with the students of midwifery department in Turkey, the empathy skill levels of the first year students have similarly been found as higher when compared to the students in upper classes (11). Demirel et al. have found that the cognitive empathy and compassion levels of the first year students have been higher than the fourth grade students in their study with the students in midwifery department (12). The empathy level of the medicine students also decreases during their educations and shows a sharp decrease especially in the third year of their education (16). In another study conducted in countries with different cultural structures, it was found that the medical faculty students studying in the USA have shown a decreasing trend of empathy levels over the years and there has been a reverse tendency of increase in Far East (17). Because of this difference among countries, it is thought that the empathy levels of students are affected by sociocultural factors.

One of the factors affecting the level of empathic tendency is gender. Quince et al. have reported that sentimental empathy level has decreased in men and not in women during medical education (18). Women studying in the medical school have higher empathy levels than men; and students with higher empathy level have a tendency to choose a more human-oriented specialty (19, 20). In paramedic students, it has been reported that male students could not have empathic communication with patients with drug addiction, whereas female students have had a much higher level of empathy than their male counterparts for all the patients regardless of their medical condition (21). Among the nursing students, empathy levels of female students have been found higher than male students (22). The fact that this study contains only the female students is thought to affect the empathic tendency level positively. The graduated high school, marital status, social security, and education status about empathy do not affect the level of empathic tendency. It is a thought-provoking situation that the level of empathy is inversely proportional to the year of education in a profession group that is educated in the field of health and is expected to have emotional support as well as physical support after graduation.

The compassion scale score has been found as 94.63±11.58 among all midwifery students. Ergin et al. have found the compassion scale score of midwives working in the delivery high (23). Total compassion point is influenced by the professional factors such as total compassion point, number of patients, rotating shift work, number of traumatic births and job satisfaction (23). In this study, it has been found that the total point of compassion scale has been affected only by the marital status; and the compassion levels of the single students have been significantly higher than those of the married students. Regarding the sub-dimensions of the scale, common humanity is higher in the first-grade students and higher in the students with social security than those without the security. In the students graduated from science high schools; indifference, separation, mindfulness, and disengagement sub-dimension points are higher than other students. The results obtained about the compassion level of the students are like the level of empathic tendency. The level of the common humanity decreases with the year of education. Students are expected to communicate better and be more sharing as they get to know each other. However, the emergence of the opposite situation is interpreted as a reflection of the competitive environment on student life.

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Table 2. *The comparison of some properties of the students and their empathy scale total score, compassion scale sub-dimensions and total scores*

Properties	N (%)	Empathy Scale Total Score Median (Q1-Q3)	Compassion Scale Total Score Median (Q1-Q3)	Kindness Sub-Dimension Score Median (Q1-Q3)	Indifference Sub-Dimension Score Median (Q1-Q3)	Common Humanity Sub-Dimension Score Median (Q1-Q3)	Separation Sub-Dimension Score Median (Q1-Q3)	Mindfulness Sub-Dimension Score Median (Q1-Q3)	Disengagement Sub-Dimension Score Median (Q1-Q3)
Education Year*									
First year	76 (22.6)	72.50***(69.00-77.00)	98.50(92.00-105.00)	4.25 (3.75-4.75)	4.25 (3.50-4.75)	4.25***(3.75-4.68)	4.25 (3.50-4.68)	4.00 (3.75-4.50)	3.75 (3.50-4.00)
Second year	83 (24.7)	71.00 (68.00-76.00)	94.00(84.00-102.00)	4.00 (3.50-4.50)	4.25 (3.75-4.75)	3.75 (3.25-4.25)	4.00 (3.50-4.50)	4.00 (3.25-4.25)	3.75 (3.50-4.00)
Third year	92 (27.4)	72.00 (67.25-75.00)	96.50(85.25-104.00)	4.00 (3.75-4.50)	4.25 (3.50-4.75)	4.00 (3.50-4.50)	4.12 (3.50-4.50)	4.00 (3.50-4.25)	3.75 (3.50-4.00)
Fourth year and more	84 (25.3)	71.00 (68.50-74.50)	96.00(90.00-103.00)	4.25 (3.62-4.75)	4.00 (3.75-4.50)	4.00 (3.25-4.50)	4.00 (3.50-4.50)	4.00 (3.75-4.50)	3.75 (3.50-4.00)
		p:0.017	p:0.184	p:0.120	p: 0.915	**p: 0.003**	p: 0.610	p: 0.156	p: 0.615
Graduated High School									
*		72.50 (66.75-78.25)							
Medical High School	34 (10.1)	74.00 (72.50-77.00)	96.00 (87.00-103.25)	4.25 (3.50-4.75)	4.50 (3.75-4.75)	4.00 (3.50-4.50)	3.75 (3.50-4.25)	4.00 (3.43-4.31)	3.75 (3.50-3.81)
Science High School	6 (1.8)	72.00 (69.75-75.25)	104.00(100.00-109.25)	4.25 (3.68-4.75)	4.50*** (4.18-5.00)	4.25 (3.81-4.56)	4.62*** (4.18-4.81)	4.50*** (4.25-4.81)	4.00***(3.93-4.25)
Anatolian High School	202(60.3)	72.00 (68.75-76.00)	94.00 (88.50-104.00)	3.87 (3.68-4.50)	4.37 (3.75-4.75)	4.00 (3.18-4.50)	4.25 (3.50-4.75)	4.00 (3.00-4.50)	3.75 (3.68-4.00)
General High School	22 (6.6)	70.00 (66.00-74.00)	94.00 (88.00-104.25)	4.00 (3.75-4.56)	4.00 (3.75-4.75)	4.00 (3.25-4.50)	4.25 (3.50-4.50)	4.00 (3.75-4.50)	3.75 (3.50-4.00)
Other	71 (21.2)	p: 0.627	95.00(86.00-100.00)	4.00 (3.50-4.50)	4.00 (3.50-4.25)	4.00 (3.50-4.50)	4.00 (3.25-4.50)	4.00 (3.50-4.25)	3.75 (3.25-4.00)
			p: 0.088	p: 0.740	**p: 0.017**	p: 0.849	**p: 0.024**	**p: 0.010**	**p: 0.030**
Social Security Status**									
Yes 302(90.2)		72.00 (68.00-76.00)	96.00 (88.00-104.00)	4.00 (3.75-4.75)	4.25 (3.75-4.75)	4.00 (3.25-4.50)	4.00 (3.50-4.50)	4.00 (3.50 – 4.50)	3.75 (3.50-4.00)
No	33 (9.8)	69.00 (67.00-73.00)	94.00(88.00-100.00)	4.00 (3.25-4.25)	4.25 (3.50-4.50)	4.00 (3.25-4.50)	4.00 (3.62-4.32)	4.00 (3.25-4.50)	3.75 (3.50-4.00)
		p: 0.239	p: 0.200	**p: 0.031**	p: 0.295	p: 0.505	p: 0.637	p: 0.387	p: 0.748
Marital status**									
Married	9 (2.7)	70.00 (68.00-73.50)	88.00 (73.00-98.50)	3.75 (3.00-4.12)	4.00 (3.62-4.12)	3.75 (2.62-4.50)	3.75 (3.00-4.50)	3.75 (2.50-4.00)	3.75 (3.25-3.87)
Single	326 (97.3)	72.00 (68.00-76.00)	96.00 (88.00-104.00)	4.00 (3.68-4.75)	4.25 (3.75-4.75)	4.00 (3.43-4.50)	4.00 (3.50-4.50)	4.00 (3.50-4.50)	3.75 (3.50-4.00)
		p: 0.754	**p: 0.048**	p: 0.109	p: 0.171	p: 0.306	p: 0.230	**p: 0.016**	p: 0.232
Education about empathy**	58 (17.3)	72.00 (66.50-76.25)	100.00 (90.75-103.00)	4.25 (3.75-4.75)	4.37 (3.75-4.75)	4.00 (3.50-4.50)	4.00 (3.50-4.50)	4.00 (3.68-4.50)	3.75 (3.50-4.00)
Yes	277 (82.7)	71.00 (68.00-76.00)	95.00 (87.00-104.00)	4.00 (3.50-4.50)	4.25 (3.75-4.75)	4.00 (3.25-4.50)	4.00 (3.50-4.50)	4.00 (3.50-4.25)	3.75 (3.50-4.00)
No	**335 (100)**	p: 0.949	p: 0.22	p: 0.145	p: 0.149	p: 0.496	p: 0.706	p: 0.341	p: 0.927
Total									

Kruskal-Wallis test, **Mann-Whitney U test, * The group from which the difference is due according to the post hoc test, Bold values: Results are significant if p<0.05*

Another result is that the level of empathy and compassion affects each other. For this reason, it is necessary to focus on how the empathy and compassion level of the students could be supported and nurtured in practice and education. Compassion and empathy are difficult to learn for clinicians (24, 25). There are not enough data on how to teach this concept in midwifery education (26). Ding has stated that simulation-supported education has developed empathy, communication skills and professional identity in pediatric nursing students (27). Donald (2019) has given a compassion-based care course to healthcare professionals and determined that the course has a positive effect on the participants (28). It has been determined in a study conducted with medical students that role modeling and compassion-based education are an ideal teaching method to gain compassion in clinical education (27). In line with all these data, similar interventions should be applied throughout midwifery education, the effects of these interventions on the empathic tendency and compassion level of the students should be determined and interventions determined to be effective in this direction should be added to the midwifery curriculum.

5. CONCLUSION

As a result of the study, it has been determined that the levels of empathic tendency and compassion of midwifery students have been good. However, the level of empathic tendency decreases as the year in which students receive education increases. A positive relationship has been found between the level of empathic tendency and the level of compassion. From an ethical point of view, a compassionate midwifery care is essential for qualified midwifery care. Classes about empathy and compassion should be included in the midwifery curriculum for the students to graduate with this perspective.

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Clinical and Experimental Health Sciences

Effect of Different Crown Removing Procedures on the Implant Stability Quotient and Removal Torque Values of Dental Implants

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ABSTRACT

Objective: To investigate the effects of different crown-removal methods on the osseointegration of dental implants in implant-retained single crowns.

Methods: Two implants were inserted in each tibia of each New Zealand rabbit's rear legs (total of 32 implants were used). After 28 days, resonance frequency analysis was performed on the implants to detect the degree of osseointegration; 24 hours later, the sacrificed tibias were divided into 3 groups according to different crown-removal methods: crown removal with a diamond bur, the use of a spring-loaded crown remover, and the use of a pneumatic crown remover. Following the crown-removal procedures, the implants' resonance frequency analysis (RFA) values and removal torque values were measured.

Results: No significant difference in implant stability quotient (ISQ) was measured after crown removal for either group of diamond bur or group of pneumatic crown remover (p=0.677 and p=0.918, respectively). However, there was a statistically significant difference in implant stability quotient after crown removal for group of spring-loaded crown remover (p=0.008). Moreover, no significant difference was detected between the groups' removal torque values (p>0.05).

Conclusion: The crown-removal procedure has significantly unfavorable effect on the implant stability quotient values of the implants, whereas removal torque values of the implants was not affected crown-removal procedures.

Keywords: Dental implant, crown, resonance frequency analysis.

1. INTRODUCTION

Implant-supported fixed prosthesis is a well-documented and highly predictable treatment option with a high rate of success for replacing single or multiple missing teeth. There are two retention types for fixating a prosthetic superstructure on implant abutments: cementation and screw retention (1-6).

Cement-retained prostheses can be fabricated by conventional laboratory procedures and can be fixated on the abutment just like crowns for teeth (7,8). According to a systematic review, cement-retained implant-supported fixed prosthesis presented fewer technical problems but more biological problems (such as implant failures and marginal bone loss) when compared to screw-retained implant-supported fixed prosthesis (4). In another systematic review, cement-retained implant-supported fixed prosthesis resulted in better preservation of marginal bone, fewer prosthetic complications, and higher implant survival rates when compared to screw-retained implant-supported fixed prosthesis (3).

In clinical studies, the dental implant survival rates are 89.4% for implant-supported single crowns and 86.7% for implant-supported fixed prosthesis (9-12). Thus, implant-supported fixed prosthesis need to be removed and renewed when mechanical or biological complications occur, including fracturing of the veneering ceramic or gingival recession in the aesthetic zone.

Various procedures are utilized to remove implant-supported fixed prosthesis. Conventional methods involve applying physical force on the cervical margin of the restoration with impact delivering devices (7). Manual or spring-loaded back-action instruments, spring-loaded semiautomatic or automatic devices, and pneumatic devices are used for this purpose (13). Another removal procedure is to divide a crown into two parts (mesial and distal) with cutting burs. However, there is no guideline for the clinician as to how crown removal affects the osseointegration of dental implants. Although there is no data in the literature, many prosthodontics advise

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that prostheses should be removed by cutting with diamond burs instead of crown removers to eliminate possible adverse effects of bone-implant contact (BIC). Thus, the objective of this study was to investigate the effects of different crown-removal methods on the implant stability quotient (ISQ) and removal torque value (RTV) of implants in implant-supported single crowns. The hypothesis tested was that no difference exists on the impact of the ISQ and the RTV values of dental implants after different crown-removal procedures.

2. METHODS

2.1. Implants and Animals

Thirty-two conical, calcium-incorporated titanium implants (AnyOne, MegaGen Co. Ltd., Kyungsan, South Korea) with length 7 mm and a diameter 3.5 mm were used in this study.

Eight adult male New Zealand white rabbits weighing 3.5 to 4 kg were used in this study. They were supplied by the same certificated center. This experiment was approved by the Animal Ethics Commission of Cumhuriyet University (protocol number: 65202830/134). Animals were operated on and housed in the Experimental Animal Laboratory of the Veterinary Faculty at Cumhuriyet University. Prior to surgery, animals were kept in individual cages on a standard diet (solid ration) with 12-hour cycles of light at a humidity of 55% to 70% and a temperature of 22°C to 24°C for 2 weeks to ensure adaptation to laboratory conditions.

2.2. Surgical Procedure

The rabbits were anesthetized with a combination of 50 mg/kg ketamine (Ketalar, Eczacıbaşı, Istanbul, Turkey) administered intramuscularly and 5 mg/kg xylazine (Rompun, Bayer, Leverkusen, Germany). The rear legs of the rabbits were shaved and washed with a 70% ethanol mixture and an iodine solution. To improve analgesia and control bleeding, 1 mL of local anesthetic (Ultracaine DS Fort, Aventis Pharma, Turkey) was injected locally into the tibia surgical sites.

The surgical sites were exposed with an incision through the skin (Figure 1A), fascia, and periosteum at the medial surface of proximal tibias using sterile surgical techniques (Figure 1B). The osteotomy was performed on a flat surface on the lateral part of the proximal tibia using a low-speed rotary instrument under constant irrigation with sterile saline, according to the recommended surgical protocol supplied by the manufacturer. Two implants were inserted in each tibia of each rabbit's rear legs (Figure 1C). Thus, each animal received four implants, and a total of 32 implants were performed on eight rabbits. In addition, a manual torque meter was used for standardization of insertion torque values, which were within the range 35±3 N. Following the osteotomy, the surgical sites were closed in layers using Vicryl resorbable sutures (Ethicon, Somerville, NJ, USA; Figure 1D). In the postoperative period, antibiotics (Cephaxon, Toprak İlaç, Sakarya, Turkey) and analgesics (Rimadyl, Pfizer, Istanbul, Turkey) were injected intramuscularly for 3 days to prevent postsurgical infection and to control pain.

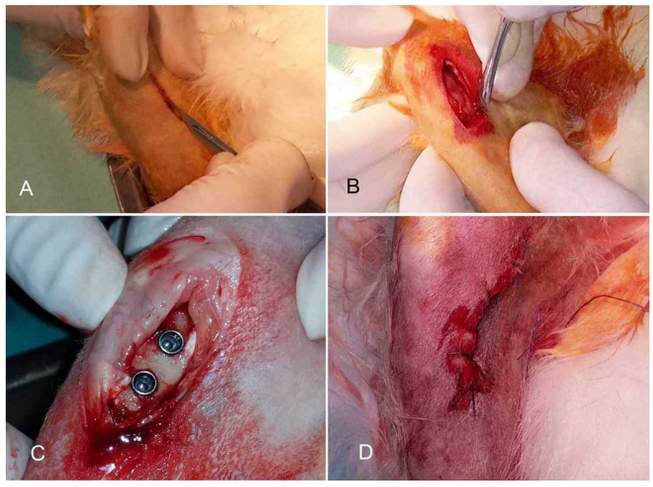

Figure 1. *Surgical procedure.* **A.***Incision through the skin;* **B.** *Elevation of fascia and periosteum;* **C.** *Inserted implants in rabbit's tibia.* **D.** *Closed surgical sites with sutures.*

2.3. Preparation of Crowns

Thirty-two titanium abutments (MegaGen Co. Ltd., Korea) were used in this study; each abutment had a diameter of 4.5 mm and a length of 9 mm (including 3.5 mm gingival length). Cast plastic caps, which enable the production of identical crowns on separate implants, were also used. A buccal extension, which enables the easy placement of crown removers, was added on the plastic caps using casting wax. The conventional casting process was then carried out (Figure 2). Cobalt-chromium alloy crowns were checked on the abutments.

Figure 2. *Production of cobalt–chromium alloy crowns.*

2.4. Resonance Frequency Analysis (RFA)

After 4 weeks, the same surgical protocol was followed and the implants were surgically exposed, and a SmartPeg (MegaGen Co. Ltd., Korea) was screwed into each implant and tightened to approximately 5 N with a special wrench. The implant stability quotient (ISQ) values were measured with MegaISQ (MegaGen Co. Ltd., Korea). For each implant, the probe of the ISQ machine was held stable at a distance of approximately 2 mm from the SmartPeg. Two measurements

were conducted on the mesial and distal parts of the SmartPeg, and mean ISQs were recorded (Figure 3).

Figure 3. *RFA measurement before crown removing.*

2.5. Crown Cementation

Abutments were placed into the implants and fixed with a 25 N·cm torque using a torque wrench (MegaGen Co. Ltd., Korea) according to the manufacturer's instructions. Afterward, the crowns were cemented on the abutments with a dual-cure resin cement (MIS Crown Set, MIS Implant Technologies Ltd, Shlomi, Israel), which came in a plastic syringe and included mixing tips. Finger pressure was applied to the plastic syringe and resin cement was poured into the crowns. They were seated onto the abutments and 1 kg weight was placed onto the crowns. After removing the excessive resin cements, light-cure was applied.

2.6. Crown Removal

After 24 hours to cement the crowns, the animals were sacrificed using an intravenous overdose of ketamine (2 mL) and xylazine (1 mL). Each animal's tibias were removed (Figure 4A) and kept in a 10% buffered formalin solution. The tibias were randomly assigned to 3 groups according to the crown-removal method applied: crown removal with a diamond bur, the use of a spring-loaded crown remover, and the use of a pneumatic crown remover.

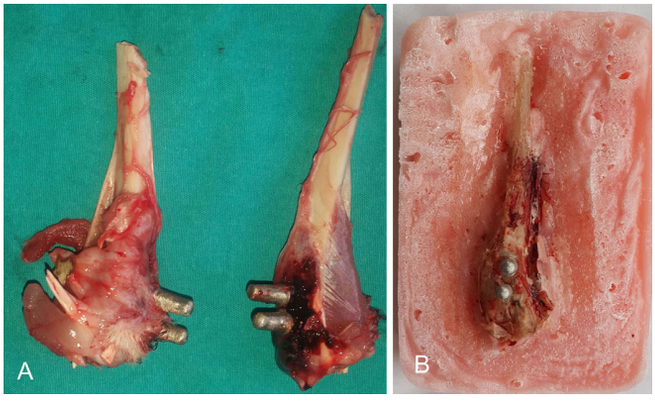

Figure 4. *A. Harvested tibias. B. Embedded tibias into autopolymerizing acrylic resin.*

For the group of diamond bur, the crowns were removed by cutting with a black-belt torpedo diamond bur (MDT Dental, Afula, Israel; Figure 5A). Fission of the crowns was performed at a pressure of 32 psi and under water cooling at a constant speed of 25 mL/min. The maximum bur rotation rate was set at 400,000 ± 2,000 rpm. In addition, each diamond bur was used for one cut only.

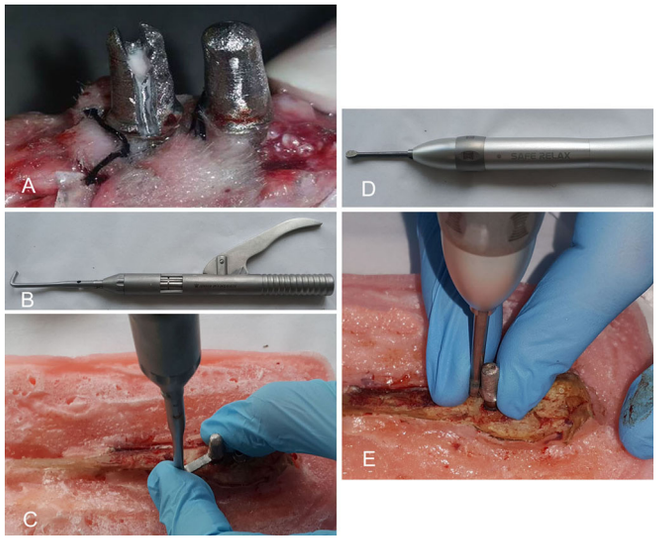

Figure 5. *Crown removing methods. A. Bur-cut; B. Spring loaded back action crown remover; C. Application of spring loaded back action crown remover; D. Pneumatic crown remover; E. Application of pneumatic crown remover.*

For the group of spring-loaded crown remover, the tibias were embedded into auto polymerizing acrylic resin (Meliodent, Bayer Dental Ltd., Newbury, UK; Figure 4B). A spring-loaded, back-action crown remover (Jensen jp-1, Dental Instruments, İslamabad, Pakistan; Figure 5B) was positioned at the buccal extension of the crowns (Figure 5C). Maximum force was adjusted and delivered until the crowns were removed. The reactivation requirement of the crown remover was not needed. During activation, a second researcher achieved the stabilization of the acrylic block by using a clamp from one end of the block to the table and she also applied finger pressure on the other end of the block to prevent the movement.

For the group of pneumatic crown remover, the tibias were embedded into auto polymerizing acrylic resin (Meliodent, Bayer Dental Ltd.). A pneumatic crown remover (Saferelax, Anthogyr, Sallanches, France; Figure 5D) was used to remove this group of crowns (Figure 5E). It was plugged into the dental unit's turbine head housing, which provides compressed air for activation. The maximum force was adjusted, the tip of the remover was placed at the crowns' buccal extension, and force was delivered until removal was achieved. During activation, a second researcher achieved the stabilization of the acrylic block.

After the crowns were removed, a smart peg was screwed into each implant. The ISQs were measured again, and the data were recorded.

2.7. Removal Torque Test

Following resonance frequency analysis (RFA), to evaluate implant stability, a removal torque test (RTT) was performed on the implants (Figure 6). The second researcher stabilized the acrylic blocks, and a digital torque meter (IMADA, Northbrook, IL, USA) was positioned in the direction of the implant axis. The removal torque values (RTVs) were measured until the implant rotated inside the bone tissue, completely rupturing the bone-implant interface. These RTVs were then recorded for statistical analysis.

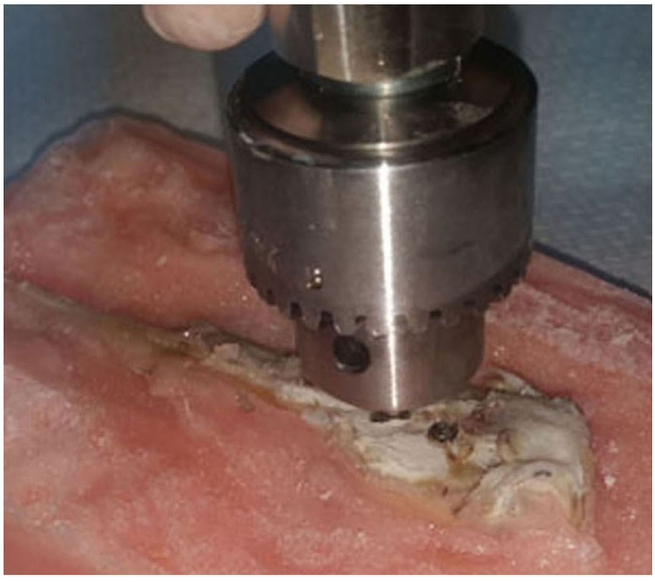

Figure 6. *Application of RTT.*

2.8. Statistical Analysis

The RFA values and RTVs were analyzed using the Kruskal-Wallis and Mann-Whitney U tests; SPSS (version 16.0; SPSS, Chicago, IL, USA) was used for the statistical analysis. Differences in ISQs were evaluated with the Wilcoxon signed-rank test. A correlation analysis (Spearman) was used to determine the correlation of the RFAs and RTVs. Values of *p* greater than .05 were considered statistically significant.

3. RESULTS

The means and standard deviations of the ISQs and RTVs for all groups are presented in Table 1. The highest mean ISQ values was seen in the group of pneumatic crown remover before crown removal (66.9 ± 8.3), and the lowest was detected in group of spring-loaded crown remover after crown removal (51.5 ± 29.09). Analysis of the data also revealed that no significant difference in ISQ values was measured after crown removal in either with a diamond bur or pneumatic crown remover (p=0.677 and p=0.918, respectively). However, there was a statistically significant difference in ISQ values after crown removal in group of spring-loaded crown remover (p=0.008).

Table 1: *Mean and standard deviations (SD) of the ISQ values and RTVs of the groups*

Groups	ISQ values before crown removal	ISQ values after crown removal	Reverse torque values (N.cm)
Group Bur	64.3^{a} (12.43)	64.1^{a} (17.43)	18.7^{A} (7.29)
Group Spring-loaded	65.3^{a} (14.53)	51.5^{b} (29.09)	14^{A} (8.06)
Group Pneumatic	66.9^{a} (8.3)	65.2^{a} (11.6)	18.7^{A} (7.87)

For each horizontal row: values with small letters indicate no statistically significant difference (p>0.05)
For each vertical column: values with capital letters indicate no statistically significant difference (p>0.05).

The lowest RTV was found in group of spring-loaded crown remover (14 N.cm). Furthermore, diamond bur and pneumatic crown remover groups exhibited similar mean RTVs (18.7 N/cm). However, no significant difference in RTVs was detected between the groups according to the Mann-Whitney U test results (p>0.05). Moreover, Spearman analysis revealed a positive correlation between ISQ and RTV (r=0.532).

4. DISCUSSION

Based on the results of the present study, the hypothesis that no difference exists in the ISQ of dental implants after various crown-removal procedures was partially accepted. Because, ISQ values presented significant differences after different crown removing procedures whereas, RTV did not change after crown removing procedures. There is very limited research about crown-removal procedures for implant retained single crowns. Worni et al. (7) carried out crown-removal procedures on 74 crowns that were cemented on dental implants in 21 patients. They found that, regardless of cement type (provisional or definitive), a pneumatic crown remover device can be safely applied for crown removal without technical complications. In addition, Polat Sağsöz et al. (14) investigated the effects of crown-removal procedures on 815 units of fixed partial dentures in 160 patients. They reported that a manual instrument resulted in marginal damage to the restorations. Furthermore, consistent with the results of the Worni et al. study (7), they found that pneumatic crown removers caused less marginal damage than did manual ones. In the present study, unlike the spring-loaded, back-action crown remover, the pneumatic crown remover had no adverse effect on the ISQ of dental implants. Thus, the results of the present study are in agreement with those of Worni et al. (7) and Polat Sağsöz et al. (14).

Nevertheless, in the literature, researchers have tried to establish the correlation between ISQ values and the percentage of BIC. Although RFA was presented as a sensitive method for detecting BIC%, (15) some researchers found no correlation between ISQ and BIC% (16-19). However, a positive correlation between RTVs and BIC% has been found (20).Furthermore, Bischof et al. (21) advocated that RTVs are more reliable than ISQs when evaluating bone-implant interface. Thus, although clinically not applicable, RTT was also used in the present study to assess the implant stability

and osseointegration. Based on the results of the present study, a linear relationship was seen between ISQ and RTV. This result is in accordance with that of Gehrke and Marin (22), who reported a relative correlation between ISQ and RTV for each time period (6, 8, and 12 weeks after implantation) in their groups. Contrarily, Bischof et al. (21) and Cehreli et al. (23) found no linear correlation between ISQ and RTV. At this stage, the important question is which method should primarily be considered. RTT enables measurement of the strength of the interface between bone and implant in terms of shear; RFA detects the stability during bending (24). The bending force simulates the clinical situation more closely than does the shear force based on data about force, direction, and stiffness of the bone-implant junction.

One of the limitations of this study is that metal crowns (instead of metal-ceramic crowns) were cemented on the abutments. Thus, the bur cutting was performed on only one layer—metal. However, a ceramic layer would be more easily removed by burs than a metal layer would. Therefore, this limitation may not affect the results of the present study. On the other hand, future investigations could focus on the effect that the removal procedure has on the ISQ and RTV values of dental implants in FPDs that are retained with multiple implants and those that have a monoblock design.

5. CONCLUSION

Within the limitations of the present study, crown-removal procedure has negative effect on the ISQ values of dental implants. Clinicians may primarily consider using bur cutting method for removing of the crowns because the SL group had a lower ISQ, and lower RTV's than the other 2 groups.

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Clinical and Experimental Health Sciences

Investigation of Fracture Resistance of Zirconia Restorations After Different Surface Treatments

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ABSTRACT

Objective: The purpose of this study was to investigate the effects of the different surface treatments on fracture strength of the zirconia-based ceramic restorations.

Methods: Each of 120 dental implant abutments and analogs were used in the present study. Zirconia core materials were manufactured on dental implants by using CAD/CAM device and they were randomly divided into 6 groups (n=20) according to surface pretreatments; control group (Group C), airborne-particle abrasion (Group AA), silica-coating (Group SC), Nd:YAG laser (Group N), bur-cut from cervical region (Group BC), and bur-cut on the functional tubercule (Group BT). Cementation was succeeded with two different types of cements including a dual-cure resin-cement and a glass ionomer cement. The obtained data were evaluated statistically using one-way ANOVA and Tukey tests (p=0.05).

Results: No statistically significant difference was found between the groups (p>0.05). Similarly, no statistically significant difference was found between the resin cement and glass ionomer groups with respect to fracture strength values (p>0.05).

Conclusion: Within the limitations of the present study, surface treatments and cement have no effect on the flexural strength of zirconia ceramic crowns.

Keywords: Dental implants; dental lasers; fracture strength test; surface treatments, CAD/CAM.

1. INTRODUCTION

Zirconia-based restorations became popular with a high level of flexure strength and fracture toughness, durability, chemical and dimensional stability compared with other all-ceramic restoration systems (1-5). However, a translucent ceramic superstructure should be applied onto the opaque zirconia-substructure to obtain more esthetic restorations (2,4,6,7). Sailer et al. reported that the failure rate of veneered zirconia frameworks was 13.0% and 15.2% after 3 and 5 years and chipping of the veneering ceramic is the one of the main factors responsible for reduced survival rates (8,9). In addition, the bonding between the zirconia core and the tooth is important for the clinical success of zirconia restorations (6,10,11). Thus, there have been considerable efforts by many researchers to modify the surface properties of zirconia, mechanically and chemically by various surface treatments (12,13). Several techniques, especially the airborne particle abrasion with alumina, silica coating, various adhesive monomer and metal primers and CO2, Nd:YAG, and Er:YAG laser treatments (10,12,14,16) have been reported to facilitate the bond strength between resin cement and Y-TZP ceramic.

On the other hand, recent studies have expressed concern about cracking and surface flaws produced by surface pretreatments including grinding, sandblasting, and laser, which may induce the tetragonal to monoclinic phase transformation of zirconia and, thus reducing the strength and toughness, decreasing reliability and increasing the failures in the clinic (17).

However, limited studies on flexural strength testing after surface treatment of the zirconia have been done. In the light of all these data, the purpose of the present study was to investigate the effects of roughening and abrasion procedures (airborne-particle abrasion, silica coating, Nd:YAG laser irradiation, grinding from the cervical line and grinding from functional tubercule) applied to the zirconia surface on the flexural strength of the zirconia-based restorations. The

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hypothesis tested was that surface treatment procedures applied on zirconia result in lower flexural strength of the restorations.

2. METHODS

120 implant analogs and abutments with a diameter of 4.5 mm and a length of 9 mm (including 3.5 mm gingival length) (AnyOne, MegaGen Co. Ltd., Kyungsan, South Korea) were used in this study. Implant analogs were embedded into the acrylic resin using the copper analogs (Figure 1). Abutments were seated on the implant analogs and tightened with the torque values of 30 N cm according to the manufacturer suggestion.

2.1. Fabrication of the Zirconia Specimens

A CAD/CAM system (Yenamak, Yenadent Ltd. Şti., Istanbul, Turkey) was used to design and mill the crowns. Mandibular first molar crowns with a buccolingual width of 8 mm, a mesiodistal width of 10 mm, and an occlusal thickness of 1.5 mm was designed over implant abutments. Of the substructures; 20 were fabricated 0.2 mm longer at the cervical line for the group of bur-cut from cervical region whereas 20 were fabricated thicker at 0.2 mm occlusal to the functional tubercules for the group of bur-cut on the functional tubercule. Milled crowns were finished and polished following manufacturers' instructions. Furthermore, crown dimensions were verified with a digital caliper (Altas 905, Gedore-Altas, Istanbul, Turkey).

Specimens were then divided into 6 experimental groups (n=20) according to the surface treatments applied:

Group C—untreated (control): This group served as the control group, so no treatment was applied to the zirconia surfaces in this group.

Group SB—sandblasted: The bonding surfaces of the zirconia specimens were sandblasted (Ney, Blastmate II, Yucaipa, CA, USA) with 120 µm aluminum oxide (Al_2O_3) for 10 s. The air pressure for sandblasting was maintained at 2 bars. Specimens were mounted in a special holder at a distance of 10 mm between the surface of the specimen and the blasting tip. Then, the specimens were rinsed under running water and dried with oil-free compressed air to remove the remnants.

Group SC—silica-coating: 30 µm silica-modified Al2O3 particles (CoJet Sand) were sprayed on the surface of the specimens with an intraoral airborne-particle abrasion device (Co-Jet, 3M ESPE, St Paul, MN, USA) at 2 bars for 10 s. In order to adjust application distance of 10 mm, a special holder was used.

Group N—Nd:YAG laser irradiated with contact mode: Bonding surfaces of zirconia specimens were irradiated with a Nd:YAG laser (Smarty A10, Deka Laser, Florence, Italy). Laser energy was delivered in pulse mode with a 300 mm diameter laser optical fiber, a wavelength of 1,064 µm at 100 mJ (pulse energy), 10 Hz (repetition rate), 1 W (output power), 300 µs (pulse duration), and 141.54 J/cm^2 (energy density) for 20 s. In addition, only air cooling was used during the laser irradiation of the specimens.

Group BC—bur-cut from cervical region: Cervical region of the zirconia was milled 0.2 mm with a black-belt torpedo diamond bur (MDT Dental, Afula, Israel) under water cooling.

Group BT—bur-cut on the functional tubercule: Functional tubercule of the zirconia was milled 0.2 mm with a black-belt torpedo diamond bur (MDT Dental, Afula, Israel) under water cooling.

Silicone index was used to standardize veneer thickness for all groups. Feldspar veneering ceramic were performed on the zirconia frameworks (VITABLOCS Mark II, VITA Zahnfabrik, Bad Säckingen, Germany) according to the manufacturer suggestions.

2.2. Cementation of the Specimens

The obtained crowns were cemented onto the implant abutments (Figure 2). The specimens of each groups were divided into 2 groups and two different cement materials were used in cementation procedure. For each group, half of the specimens were adapted with a dual-cure resin cement material (Panavia SA, Kuraray, Tokyo, Japan) including MDP while other half of the specimen were adapted with a glass ionomer cement material under finger pressure. A 2 kg force was applied on the crown to standardize the force during cementation. In this manner, it was exposed to light for 2 seconds and pre-hardening was performed. Residual cement fragments were cleaned using a sound and radiation was applied for 20 seconds at each surface of the crown in accordance with the instructions of the manufacturer (Elipar, 3M ESPE, St Paul, MN).

2.3. Fracture Strength Test of the Zirconia-Based Specimens

After cementation procedure was completed, all of the specimens were stored at 37°C distilled water bath device (Nüve BM 302 – Nüve Sanayii Malzemeleri İmalat ve Ticaret A.Ş., Ankara, Turkey) for 24 hours. Then these specimens were subjected to the thermal cycling machine (GM, Gökçeler Makine Tic. ve San. Ltd. Şti., Sivas, Turkey) for 3000 cycles. After aging process, the specimens were attached to a custom jig of a universal testing machine (Lloyd LF Plus, Ametek Inc, Lloyd Instruments, Leicester, UK) and fracture strength test was performed (Figure 3). A 5 mm-diameter metal end was inserted to fit the central fossae of the specimens at a crosshead speed of 1 mm/min to determine their fracture strength in terms of Newton. At the same time, fracture types of the specimens were saved. Fracture types were termed as a crown fracture in presence of fractures in both superstructure porcelain and zirconia or a fracture between superstructure porcelain and zirconia; a cohesive fracture in presence of only fracture of the superstructure porcelain; an adhesive fracture in case of full detachment of

crown and cements from the abutment and finally a mixed-mode fracture if the fracture was both cohesive and adhesive at the same time.

2.4. Statistical Analysis

In evaluating the data, the program IBM SPSS Statistics 22 (IBM SPSS, New York, USA) was used for statistical analysis. Since the assumptions for a parametric test (Kolmogorov-Smirnov) were fulfilled, one-way analysis of variance was used to compare the means obtained from more than two independent groups. Tukey tests were used to find the differences between the groups. The data are stated as the mean and standard deviation at the table, and an error level of 0.05 was used.

3. RESULTS

Mean and standard deviation values of the groups for bonding strength were shown (Table 1). No statistically significant difference was found between the groups ($p>0.05$). Similarly, no statistically significant difference was found between the resin cement and glass ionomer groups with respect to fracture strength values ($p>0.05$). In the resin cement groups; the highest fracture strength was encountered in the specimens which were applied 0.5 mm abrasion from the functional tubercule whereas the lowest fracture strength was found in the specimens of silica-coating group. In the glass ionomer groups; the highest fracture strength was encountered in the specimens which were applied laser irradiation whereas the lowest fracture strength was found in the specimens with abrasion at the cervical line.

Table 1. *Statistical analysis of data in groups*

		Fracture Resistance	
Groups	n	Resin cement	Glass ionomer cement
Group C	10	1230 (382)	1153 (407)
Group AA	10	1195 (288)	1256 (472)
Group SC	10	987 (352)	1092 (315)
Group N	10	1001 (244)	1396 (367)
Group B	10	1280 (448)	1064 (282)
Group O	10	1410 (498)	1338 (515)

4. DISCUSSION

In light of the obtained data, the hypothesis that surface treatment procedures applied on zirconia result in lower flexural strength of the restorations was rejected. In the literature, conflicting results could be seen on the effects of grinding with diamond instruments on Y-TZP's mechanical properties. A positive effect could be met in some studies (18,20), due to the phase transformation toughening mechanism, where grinding triggers a t-m phase transformation, which results in a volumetric expansion of nearly %4 around the superficial defects, inducing compressive stress concentration and consequently arresting crack propagation (21). However, grinding introduces important superficial defects that could be deleterious, decreasing the mechanical properties and resulting in higher risk of catastrophic failures were exhibited in other studies (22,27).

In consistent with the results of the present study, Song, advocated that airborne-particle abrasion and heat treatment of the upper surface, corresponding to the outer surface of a crown, did not influence biaxial flexural strength of the zirconia specimens (6). Similarly, Jian found that veneer porcelain applied directly after routine lab grinding of zirconia ceramic, and liner porcelain application on rough zirconia cores may be preferred to slightly enhance strength reliability (28). In addition, Ozcan advocated that silica-coating has positive effect on the flexural strength of the zirconia ceramic (29). However, Bankoglu Gungor exhibited that surface treatments affected the phase transformation and biaxial flexural strength of zirconia ceramics (30). Furthermore, presented that application of surface treatments (laser and airborne-particle abrasion) at pre-sintered stage may be detrimental for zirconia ceramics in terms of flexural strength (31).

On the other hand, clinicians may choose to use resin cements with lithium disilicate crowns due to several studies showing that glass-based crowns luted with resin cement demonstrated a higher strength than those luted with resin-modified glass ionomer (RMGI) cement. Therefore, in the present study, half of the specimens were luted with glass-ionomer cement and half were luted with resin cement. The present study shows that flexural strength is independent to the cement types. However, Lawson advocated that cement type (resin and resin-modified glass ionomer) affected fracture load of crowns but surface treatment did not (32).

One of the limitations of this study is that fatigue loading was not performed on the zirconia crowns. Therefore, future studies could focus on the effects of surface treatment and cement on the fatigue life of zirconia ceramic crowns.

5. CONCLUSION

Within the limitations of the present study, surface treatments and cement have no effect on the flexural strength of zirconia ceramic crowns.

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Clinical and Experimental Health Sciences

Oxidative Stress in Controlled Hypotension: Assessment with a Novel Oxidative Stress Marker

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ABSTRACT

Objective: The aim of this study was to evaluate the effects of oxidative stress on thiol-disulfide homeostasis caused by hypotensive anesthesia in mastoidectomy-tympanoplasty cases undergoing controlled hypotension.

Methods: Fifty adult patients scheduled for mastoidectomy and tympanoplasty were included in the study. Anesthesia was induced with lidocaine, propofol, rocuronium, and remifentanil. The maintenance of anesthesia was continued with remifentanil infusion (target mean arterial pressure as 60-65 mmHg) along with 2% sevoflurane/40% O2/air mixture. Blood samples were taken 5 times at the t0 (before induction), t1 (intraoperatively after intubation), t2 (first hour) and t3 (second hour of the operation) and t4 (following recovery). Total thiol (TT) and Native Thiol (NT) levels were measured, and thus, Di-Sulphide (SS), Di-Sulphide/Native Thiol (SSNT), Di-Sulphide/Total Thiol (SSTT), and Native Thiol/ Total Thiol (NTTT) values were estimated.

Results: During the operation, progressive decrease was observed in thiol levels of patients. There was a significant decrease in t3 thiol values when compared with t0 value. Thiol values were observed to have returned to baseline values after recovery from anesthesia ($p>0.05$). SS, SSNT and SSTT levels were found as increased in t1 blood samples, but increase in SSNT and SSTT levels was significant. Throughout the operation, values were observed to have dropped and reverted back to initial values.

Conclusion: Since the measurement of thiol-disulfide blood values is able to show the instantaneous state of oxidative stress, it can be used in anesthesia practice in which every event occurs very quickly.

Keywords: Thiol-disulfide homeostasis, controlled hypotension, oxidative stress.

1. INTRODUCTION

The plasma thiol pool comprises organic compounds containing sulfhydryl group called mercaptans which consists mainly of albumin and protein thiols. In addition, cysteine (Cys), cysteinylglycine, glutathione, homocysteine and γ-glutamylcysteine known as low molecular-weight thiols contribute to the thiol pool (1). Thiol-containing proteins present in the cell play an important role in redox-sensitive reactions (2). Thiols react with oxidizing agents to form thiol-disulfide bonds (3). These disulfide bonds are again reduced to thiol groups when oxidative stress conditions change. Thus, dynamic thiol-disulfide homeostasis is maintained. Dynamic thiol-disulfide homeostasis has an important role in antioxidant protection, detoxification, apoptosis, regulation of enzymatic activities, and cellular signaling mechanisms (4). Thiol disulfide balance was demonstrated to change in such diseases as cardiovascular disease, cancer, and rheumatoid arthritis. This balance is known to chance in numerous diseases and conditions apart from them (5). Plasma thiol levels are mostly measured using Ellman's reagent, 4,4'-dithiodipyridine (4-DPS), or by adopting more complex methods. However, these methods are not suitable for use in automated analyzers. Erel and Neselioglu have developed a new automated method that measures thiol-disulfide homeostasis (5). This new method allows the evaluation of both thiol [total thiol (TT), native thiol (NT)] and disulfide (SS) side of the reaction. The increase in disulfide [disulfide/native thiol ratio (SSNT), disulfide/total thiol ratio (SSTT)] together with the decrease in the amount of thiol refers to the increase in oxidation. In the contrary case, it may be said that reduction increases. It was projected that determining how much thiol-disulfide values change under which conditions would shed light on the pathogenesis of many diseases, and numerous studies have been carried out on this subject (6,7).

Controlled hypotension is a technique used to increase surgical visibility during surgery and to reduce surgical

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complications. It is aimed to keep intraoperative mean arterial pressure between 50-65mmHg or systolic arterial pressure between 80-90 mmHg or 30% of the input value (8). Volatile anesthetics, sympathetic antagonists, sodium nitroprusside, nitroglycerine hydralazine, trimethaphan, adenosine, phenoldopam, α-2 agonists, and some opioid analgesics may be used for the purpose of controlled hypotension. Remifentanil is an opioid analgesic and is a μ-opioid receptor agonist. Due to being metabolized by non-specific esterases having very fast clearance, and its provision of rapid recovery, it is often used in the clinics for the purpose of controlled hypotension (8). However, inadvertent formation of free oxygen radicals is possible during hypotension application (7). Thiol-disulfide homeostasis can be affected very rapidly from oxidative changes, and oxygen radicals are likely to alter hemostasis. In cases where hypoxia or ischemia is possible, blood thiol-disulfide levels of the patient provide valuable information about the state of oxidative stress (9,10). The aim of this study was to evaluate the effects of oxidative stress caused by hypotensive anesthesia on thiol-disulfide homeostasis in mastoidectomy-tympanoplasty cases undergoing controlled hypotension with remifentanil.

2. METHODS

2.1. Hypothesis and Number of Patients

The study hypothesis (H_1) was established as "controlled hypotension creates a significant change in patients' blood thiol and disulfide levels." Since the change of blood thiol and disulfide levels of patients were a dependent variable based on initial value (t0), there was no control group in this study. In other words, since the measured thiol-disulfide blood values were compared with the t0 value, the t0 value constituted the control group.

As a result of power analysis (gPower 3.1.9.2, Franz Paul, Universitat Kiel, 2014, Germany) conducted by assuming that 20% change in time between time slices in blood thiol and disulfide levels was considered to be significant by using study data obtained from normal volunteers [5], it was estimated that the study should include 49 patients (Effect Size 0.5, α=0.05, 1-β=0.82). Fifty patients were planned to be included in the study by taking into consideration the patients that may be excluded from the study due to unforeseen issues.

2.2. Patient Group

The study was conducted following the approval of the Ankara Atatürk Training and Research Hospital Clinical Research Ethics Committee (Approval Date: 14.1.2015, No: 26379996/03). Written informed consents were obtained from the patients included in the study. Adult patients undergoing mastoidectomy and tympanoplasty surgery in ASA I risk group were included in the study. Patients that had any abnormal values in their preoperative routine examinations, patients with known comorbidities, and patients that had continuous drug use were not included in the study. Patients with difficult intubation during anesthesia, allergies or intraoperative acute cardiac or respiratory problems, and other unpredictable anesthesia-related complications were determined as exclusion criteria. The patients were evaluated in the anesthesia outpatient clinic one day before the operation. Patients without any abnormal findings were included in the study.

2.3. Anesthesia Practice

After the patients were taken to the operation room, routine monitoring (5-lead ECG, Pulse Oximeter, and non-invasive arterial blood pressure cuff) and intravenous (IV) access with an appropriate catheter were provided. Intraoperative fluid requirement was satisfied with crystalloid 0.9% NaCl solution as 8-10 ml/kg by also evaluating the fasting status of the patients. Lidocaine 1 mg/kg, Propofol 3mg/kg, rocuronium 0.5 mg/kg and remifentanil 1 μg/kg were administered intravenously for induction of anesthesia following 3 min preoxygenation. Remifentanil infusion was commenced after induction and continued by gradually increasing until the target mean arterial pressure (MAP) value reached to 60-65 mmHg (0.125-0.5 μg/kg/min). All patients underwent invasive arterial blood pressure monitoring with a 22 G cannula from the radial artery (after the Allen test) to ensure frequent drawing of blood and to carry out strict blood pressure monitoring. The maintenance of anesthesia was continued with remifentanil infusion along with 2% sevoflurane/40% O2/air mixture. Ventilation was ensured with an end-tidal CO2 ($ETCO_2$) pressure of 32-36 mmHg. In the event that the heart rate drops below 50/min, 0.5 mg of atropine IV was administered. Mean arterial pressure values that continued below 60 mmHg for 1 minute and above were accepted as hypotension, remifentanil dosage would be halved, and if it would not reach normal values within 5 minutes, it was stopped till mean arterial pressure would reach normal values, and ephedrine 5 mg IV was administered. Remifentanil infusion was continued when normal mean arterial pressure was maintained. For postoperative analgesia remifentanil infusion was terminated with contramal 50 mg IV close to the end of the case (10 min before). The patient was extubated abiding by extubation criteria and was taken to the recovery unit. An intraarterial catheter was withdrawn in the recovery unit and patient was sent to the ward when Aldrete score was sufficient.

2.4. Blood Sampling, Analysis and Interpretation of Results

A total of 5 blood samples were collected, namely, before induction (t0) in the preoperative operation room, after intraoperative intubation (t1), at the 1st hour (t2), at the 2nd hour (t3), and after recovery (when Aldrete score = 10) (t4). Blood samples were centrifuged at 3600rpm for 10 minutes. Serum/plasma samples were separated and stored at – 80°C. Total thiol (TT) and native thiol (NT) levels were measured simultaneously in all blood samples. Disulfide (SS), disulfide/native thiol (SSNT), disulfide/total thiol (SSTT) and native

thiol/total thiol (NTTT) values were also calculated using these parameters. Tests were evaluated by a new technique developed by Prof. Dr. Ozcan Erel (5) and were interpreted by him. Cost of kits and tests were covered by Prof. Dr. Ozcan Erel.

2.5. Collection of Data

Age, sex, height, body weight values of patients, duration of anesthesia, duration of surgery, and blood samples obtained at t0, t1, t2, t3, and t4 time slices were collected as anonymous data. Collected data were recorded using Excel software (Excel 2010© for Windows v14.0.7, Microsoft Corporation).

2.6. Statistical Analysis

The distribution of the data of each parameter was evaluated by Shapiro-Wilk test. The data showed normal distribution. Age, height, body weight data were given in tables by calculating mean and standard deviation. Paired-T test was used to compare TT, SS, NT, NTTT, SSTT, and SSNT values with t0 value at t1, t2, t3, and t4 time slices. $p<0.05$ was considered significant. SPSS 23 software (2015, IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.) was used for statistical estimations.

3. RESULTS

A total of 50 patients in ASA I risk group were included in the study. One patient was excluded from the study due to the fact that the targeted mean arterial pressure values could not be reached during the operation. The mean age of the patients was 37.0±10.7 years, and 57.1% of the patients were male. BMI measurements were 26.0±4.2. Demographic data of patients are given in Table 1.

Table 1. *Demographic data of patients*

Parameter		Value
Age (year)		37.0±10.7
Gender*	Male	28 (57.1)
	Female	21 (42.9)
Height (cm)		169.5±7.0
Weight (kg)		74.9±13.4
BMI (kg/m^2)		26.0±4.2

*Values are presented as mean ± standard deviation of the parameters; *values are presented as number and percent of cases [n (%)]; BMI: body mass index.*

None of the patients included in the study had difficult intubation and any complications of surgery and anesthesia. The mean duration of anesthesia was 119.1±37.1 minutes, and the duration of surgery was 94.5 ± 33.2 minutes. Since the anesthesia time of all patients was 60 minutes or more, t0, t1, t2, and t4 samples could be obtained. However, t3 blood samples were obtained from 25 patients with anesthesia duration of 120 minutes or above. Medications were administered to all patients without any issues within the study protocol, and MAP, ETCO2, and other vital signs were kept at the desired values. None of the patients required Atropine, but 4 (8.2%) patients required the administration of 5 mg ephedrine.

There was a progressive decrease in TT and NT values of patients at all times during the operation (Figure 1), and when all measurement values were compared with t0 values, there was a significant decrease in t3 TT, NT, and SS levels. Thiol values more or less returned to baseline values following recovery ($p>0.05$). The change of TT, NT, SS, SSTT, SSNT, and NTTT values of patients throughout the operation is given in Table 2.

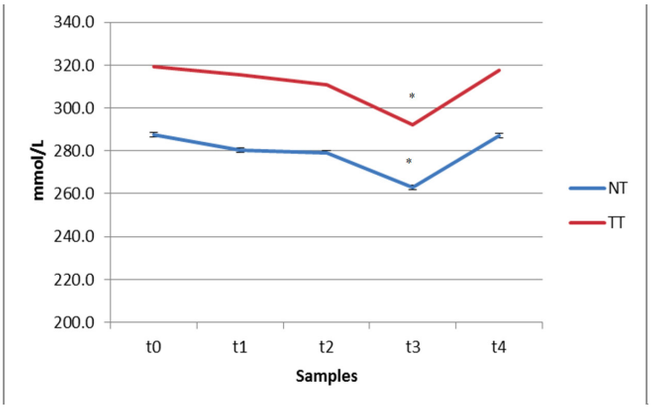

Figure 1. *The change in TT and NT values of the blood samples of patients taken during the operation. NT: Native Thiol, TT: Total Thiol, t0: before anesthesia, t1: after intubation, t2:1st hour, t3:2nd hour, t4: after anesthesia, * p<0.05 statistically significant, t3-t0: paired T-test*

Table 2. *The change of TT, NT, SS, SSTT, SSNT, and NTTT values of patients throughout the operation*

	t0 (n=49)	t1 (n=49)	t2 (n=49)	t3 (n=25)	t4 (n=49)
TT (µmol/L)	319.4±84.1	315.7±65.6	310.9±84.1	292.2±59.8*	317.8±72.6
NT (µmol/L)	287.6±75.1	280.4±60.8	279.3±78.2	263.0±54.0*	287.1±71.1
SS (µmol/L)	15.9±8.3	17.6±7.0	15.8±7.3	14.6±7.6*	15.3±6.0
SSTT (µmol/L)	4.8±2.1	5.6±2.1*	5.2±2.2	5.0±2.4	5.0±2.3
SSNT (µmol/L)	5.5±2.6	6.4±2.7*	5.9±2.8	5.7±3.0	5.7±3.0
NTTT (µmol/L)	90.3±4.1	88.9±4.2*	89.7±4.4	90.1±4.8	90.0±4.6

TT: Total Thiol, NT: Native Thiol, SS: Disulfide, , SSTT: Disulfide/Total Thiol, SSNT: Disulfide /Native Thiol, NTTT: Native Thiol/Total Thiol

It was established in t1 blood samples that mean blood SS levels of patients had an increase, and that these levels started to decrease throughout the operation. The increase in t1 SS values was not statistically significant when compared with baseline values, but the decrease in t3 value was found as significant (Figure 2). It was observed that mean SSNT and SSTT rates in t1 blood samples increased, and that the values decreased and went back to the initial values during the operation. The increase after anesthesia induction was found as statistically significant ($p<0.05$) (Figures 3 and 4).

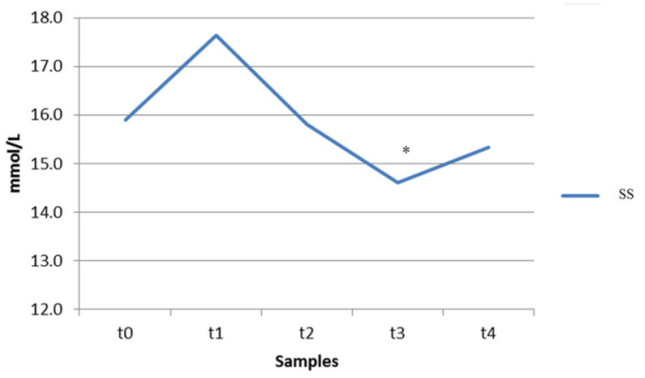

Figure 2. *The change in SS values of the blood samples of patients taken during the operation. SS: Disulfide, t0: before anesthesia, t1: after iIntubation, t2: 1st hour, t3: 2nd hour, t4: after anesthesia., * p<0.05 statistically significant, t3-t0:paired T-test*

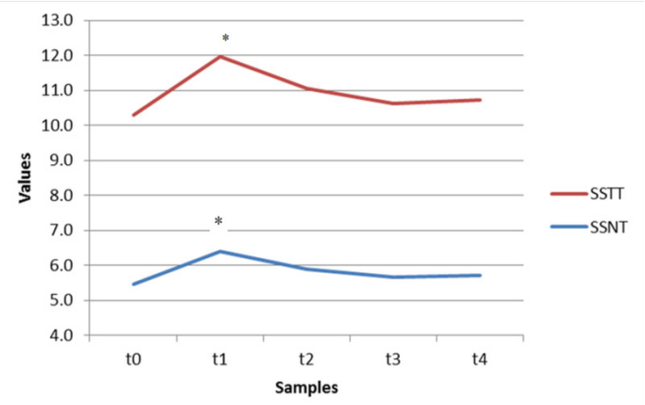

Figure 3. *The change in SSNT and SSTT rates of the patients throughout the operation. SSNT: (Disulfide/Native Thiol)x100 SSTT:(Disulfide/Total Thiol)x100, t0: before anesthesia, t1: after intubation, t2: 1st hour, t3: 2nd hour, t4: after anesthesia, *p<0.05 statistically significant, t1-t0: paired T-test*

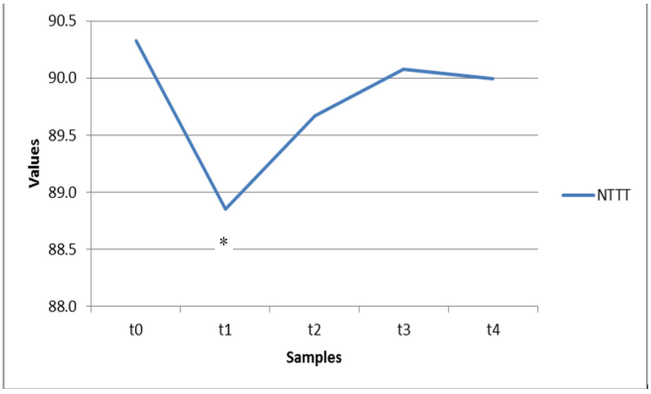

Figure 4. *The change in NTTT rates of the patients throughout the operation. NTTT: Native Thiol/Total Thiol)x100, t0: before anesthesia, t1: after intubation, t2: 1st hour, t3: 2nd hour, t4: after anesthesia, values are presented as mean of the parameters, *p<0.05 statistically significant, t1-t0:paired T-test*

4. DISCUSSION

In our study in which we evaluated the effects of controlled hypotension on dynamic thiol homeostasis reflecting biochemical evaluation of oxidative stress changes, we established thiol-disulfide blood changes accordant with stress factors. In our literature review, we did not find any study examining the effects of controlled hypotension on thiol balance. Therefore, since articles that can be taken as a reference for the evaluation of the results are nonexistent, we assessed our results in the light of studies on the effects of various diseases, general anesthesia, and other interventions on thiol-disulfide balance.

Thiols acting as fast electron acceptors have negative standard reduction potential. When an oxidant interacts with a thiol group, it is neutralized to a relatively less toxic byproduct than the oxidized thiol. Plasma TT (-SH+-S-S-), NT (-SH), and SS (-SS-) levels are more frequently used for routine diagnoses and follow-ups of numerous diseases and metabolic syndromes (5). Thiol-disulfide deposition may occur in extremely oxidative situations. Increased disulfide levels were often associated with increased oxidative stress states (diabetes mellitus, atherosclerosis, cancer, hypertension, etc.) (11-13). Similarly, in their study, Topuz et al. found that thiol-disulfide mechanism plays an important role in acute pulmonary embolism conditions (14).

Controlled hypotension in tympanoplasty cases is a frequently used method for reducing blood loss and providing better visibility in the surgical field. However, controlled hypotension can disrupt the microcirculatory autoregulation by suppressing the autonomic nervous system, thereby leading to end organ damage (15). However, there are no studies on mortality and morbidity except for the very old studies on this subject (16). Disruption of microcirculatory autoregulation may cause oxidative stress in addition to anesthesia and surgical stress response (17,18). Oxidative stress plays an important role in the pathogenesis of numerous diseases. Therefore, the importance of thiol-disulfide balance increases. Thiol disulfide values measured by manual and difficult methods have become very easy thanks to the automated method developed by Erel et al. (5). Thiol balance is a dynamic process that can manifest long-term pathologies as well as detecting momentary abnormalities. In our study, we showed that thiol and disulfide values changed significantly during intubation process. It is a correct approach to benefit from dynamism of thiol-disulfide tests in the field of anesthesia in which bleeding and ischemia, and thus, oxidative stress.

The rapid change of thiol and disulfide blood levels creates difficulty in determining normal values. In our study, we found t0 thiol values close to normal values established by Erel et al. (5) but slightly lower in the preoperative period. We believe that this may be due to thiol value change stemming from preoperative stress, despite our patient group comprised of patients that had no health issues other than the surgical intervention that they would undergo.

Anesthesia triggers inflammatory processes during surgery. The emergence of inflammatory mediators and free radicals also causes membrane damage of peroxidation products (19). Anesthetic agents used in studies have been reported to affect oxidative stress (20-22). In our study, we avoided using thiol containing sodium thiopental as anesthesia induction agent in order not to affect laboratory values, and we opted for using propofol that decreases oxidative stress by reducing lipid peroxidation (23,24). The balance between prooxidants and antioxidants in our body may be temporarily disrupted by volatile anesthetic agents. Studies have shown that sevoflurane is converted to free oxygen radicals by the enzyme CYP2E1 (25,26). Sevoflurane enhances lipoperoxidation in vivo and in vitro by inhibiting antioxidant enzymes (27). In addition to these studies, in their study that evaluated the oxidant and antioxidant effects of sevoflurane, desflurane, and propofol infusions in patients undergoing laparoscopic cholecystectomy, Erbas et al. found the antioxidant effects of sevoflurane and propofol as significantly higher (21).

In this study, a statistically significant increase was established in SSNT and SSTT values of patients after intubation. In our literature review, we found that pre-oxygenation conducted with 100% oxygen during induction period was reported to cause an increase in oxidative stress (28). We also preoxygenated our patients for 3 minutes during induction of anesthesia. In addition, it may be suggested that the formation of inflammatory and catabolic state through stress response during endotracheal intubation contribute to the increase in oxidation, leading to a rise in SS level. In the following periods of the operation, the graph of the SS level was interpreted as oxidative stress continuing albeit in a diminishing manner. When SSNT and SSTT elevation are evaluated in detail, it is observed that the increase in SS level and the decrease in NT level are effective. Our study showed that SS level increased rapidly and NT level decreased in case of stress.

In their study that evaluated thiol-disulfide balance of various pressures and albumin modified by ischemia in 36 child patients that would undergo laparoscopic surgery, Ozgunay et al. (29) did not find any difference in thiol-disulfide balance but established the albumin values that ischemia modified as high. In another study conducted by Polat et al. (30) on laparoscopic surgery, a significant decrease was established in NT, TT, and SS levels during operation. They did not establish any change in SSNT and SSTT levels. Unlike the study by Ozgunay, they did not find any statistically significant difference in ischemia-modified albumin levels. In their study that evaluated open surgery and laparoscopic surgery in previous hernia repair, Polat et al. established changes in sulfhydryl levels in both groups. TT, NT, and SS levels also manifested a decrease (t3) in our study. Unlike the above, increase was observed in SSTT and SSSNT levels in the blood sample drawn at the t1 time in our study. As explained above, post-intubation is associated with the occurrence of TT and NT decrease and SS value increase. Significant decrease of NTTT in t1 suggests that NT is instantaneously affected from oxidative stress. Long-term evaluation showed that SS, TT, and NT values continued to decrease in patients that underwent controlled hypotension. In our study group, since the mean duration of anesthesia was 119.1±37.1 minutes, it was not possible to evaluate the actual effects of controlled hypotension. However, when the graphs are evaluated, it may be foreseen that thiol and disulfide values would decrease in long-term anesthesia.

Due to the fact that there was no previous study on the same subject and that thiol-disulfide blood levels could be affected by numerous individual factors, no control group was formed. As a control group, it was assumed that the change would be more significant compared to preoperative blood values of patients. The ability of anesthesia agents that does not directly affect thiol-disulfide balance to indirectly reduce or increase oxidation makes it difficult to fully understand the effects of controlled hypotension.

5. CONCLUSION

We evaluated in our study the change in thiol and disulfide blood values in tympanoplasty cases that underwent controlled hypotension. We found that the stress response after intubation increased SSNT and SSTT levels and decreased NTTT. We predicted that SSNT, SSTT, and NTTT values can be used in rapidly developing conditions. In addition, we found that NT, TT, and SS values decreased progressively during controlled hypotension. We showed that oxidative stress increased as the duration of controlled hypotension is prolonged. Since the measurement of thiol-disulfide blood values is able to show the instantaneous state of oxidative stress, it can be used in anesthesia practice where every event occurs very quickly.

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Clinical and Experimental Health Sciences

Upper Extremity Functioning in Individuals with Type 2 Diabetes Mellitus: A Comparative Study

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ABSTRACT

Objective: The aim of this study was to evaluate the upper extremity functions of individuals with type 2 diabetes mellitus and to compare them with those of healthy subjects.

Methods: The study included 36 diabetic patients (mean age: 55.05±5.85 years; 21 female, 15 male) and 36 healthy control subjects (mean age: 53.52±7.74 years; 20 female, 16 male). Grip strength was evaluated using a hand dynamometer. Upper extremity endurance was evaluated using the Unsupported Upper Limb Exercise Test (UULEX), and upper extremity disability level with the Disabilities of the Arm Shoulder and Hand Test (DASH-T).

Results: The diabetic patients obtained lower scores of upper extremity endurance ($p<0.05$) and the disability level of the diabetics was found to be higher than that of the healthy control group ($p<0.05$). No significant difference was determined between the groups in terms of grip strength ($p>0.05$).

Conclusion: In individuals with type 2 diabetes mellitus, there is a significant decrease in upper extremity endurance and an increase in the level of upper extremity disability.

Keywords: Diabetes mellitus, disability, muscle strength, upper extremity, physical endurance

1. INTRODUCTION

Diabetes mellitus (DM) is a chronic, metabolic disease and much of its morbidity and mortality is associated with micro and macro vascular complications. DM is also associated with musculoskeletal disorders that can cause loss of function in the hands and shoulders, significantly diminishing the quality of life of patients (1).

Diabetic neuropathy has been shown to play a role in muscular problems and physical functions. Peripheral neuropathy also changes muscle mass, quality and fiber density by affecting not only sensory and motor functions, but also the strength and endurance of muscles in diabetic individuals. Poor muscle quality, decreased muscle strength, exercise intolerance due to lack of physical activity, and obesity are common in people with diabetes, resulting in poor physical function (2,3). There may also be the addition of occupational and psychosocial factors related to upper extremity musculoskeletal disorders in the presence of DM and thus hand and shoulder problems are seen more frequently in the diabetic population (4). For all the above-mentioned reasons, type 2 diabetes increases the disability level of diabetics. This pathological process affects both upper and lower extremity physical functions.

Muscular endurance plays an important role in the accomplishment of daily activities of individuals both with and without disabilities. One of the factors leading to shoulder problems and disability in diabetics is insufficient endurance. This condition decreases the working capacity of these patients (5). Previous studies have elaborated on the neuropathic effect on distal extremities generally and research has mainly been conducted on this issue (6,7). There are numerous studies in literature that have measured the upper extremity disability level and hand grip strength of individuals with type 2 diabetes (8-11). In several studies, upper limb muscle strength has been evaluated but not an evaluation of the extent of the difference from healthy individuals (12-14). However, to the best of our knowledge there are no studies that have investigated the impact of

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muscle endurance of the shoulder girdle on upper extremity functions in diabetics.

The aim of this study was to assess grip strength, endurance, and disability levels of the upper extremities in type 2 diabetics and to compare these values with those of healthy individuals. It was hypothesized that upper extremity function (low limb endurance, higher disability level, low hand grip strength) would be lower in individuals with type 2 diabetes.

2. METHODS

This comparative study was conducted at Near East University Hospital, Department of Internal Medicine during February 2017 and May 2017. The study was approved by the Ethics Committee of Scientific Researches of Near East University (NEU/2017/44-369 on 24/02/2017).

2.1. Participants

This study was conducted on a total of 72 participants, comprising 36 type 2 DM patients (age: 55.05±5.85 years; 21 females,15 males) and 36 healthy control subjects (age: 53.52±7.74 years; 20 females, 16 males). A confirmed diagnosis of type 2 DM was made by an internal medicine specialist. The healthy control group subjects were recruited from volunteers with no diabetes symptoms and normal blood glucose levels. Participants in the age range of 30-65 years who met the inclusion criteria were recruited for both groups. The inclusion and exclusion criteria were defined and applied by a medical doctor and a physiotherapist. The medical diagnosis was made by a relevant medical doctor. All measurements and tests used in this study were performed by an experienced physical therapist.

The inclusion criteria for diabetic group and the control group were;

- Participants diagnosed with type 2 DM who used medication stably for minimum 3 months or longer for the diabetic group
- Participants whose blood glucose values were within normal limits for the control group

The exclusion criteria for diabetic group and the control group were;

- Having an orthopedic and neurologic disorder of the upper extremities for in both group
- Had an operation in the upper extremities for both groups
- Having a communication problem for both groups

The criteria for drop out from the study were;

- Failing to complete all of the tests
- Having an illness during the assessment process
- Having incomplete or missing data
- Having a BMI (Body Mass Index) level of higher than 30 kg/m^2

2.2. Study Design

This was a cross-sectional and comparative study. All participants were informed about the study and provided verbal and written consent for participation. The demographic data of the participants and some characteristics were recorded (Table 1). All measurements were taken on the same day by the same therapist. Initially 82 participants were enrolled and after the exclusion of 10 with BMI >30 kg/m^2, statistical analysis was made of the remaining 72. The participants were separated into two groups: (1) diabetic group (n=36); (2) healthy control group (n=36) (Figure 1).

Table 1. *Demographic and clinical characteristics of the diabetic and control group*

Variable	Diabetic Group (n=36)	Control Group (n=36)
Gender (n,%)		
Female	21 (%58.3)	20 (%55.6)
Male	15 (%41.7)	16 (%44.4)
Age(years)(mean±SD)	55.05±5.85	53.52±7.74
BMI(kg/m^2)	28.58±3.53	27.30±3.74
Exercise Habit (n,%) Yes/No	14 (38,9%) / 22 (61.11%)	15 (%41,7) / 21 (58,3%)
Dominant Hand (n,%) Right/Left	32 (%88.9) / 4 (11.1%)	29(%80.55) / 7(19.44%)
Diabetes Duration	7,78±6,58	–

BMI:Body mass index, SD: Standart deviation

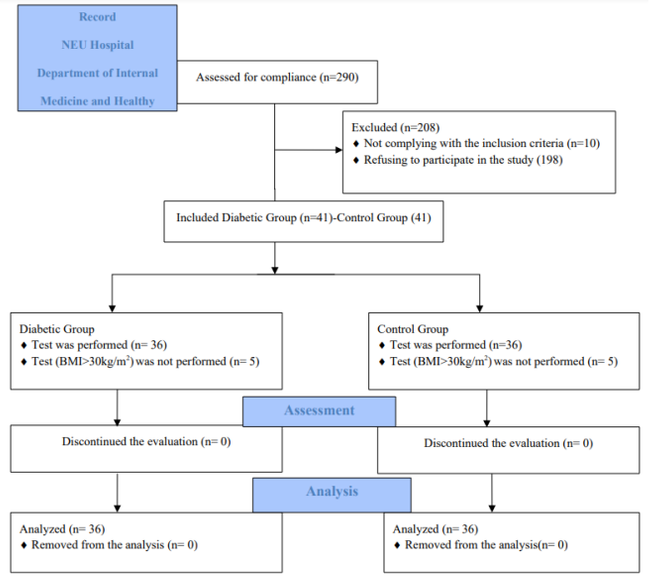

Figure 1. *Selection of the individuals recruited for the study and group formation*

2.3. Assessment

2.3.1. Hand grip strength: grip hand dynamometer (GRIP-D TKK5401)

Hand grip strength was measured with a Grip Hand (TKK 5401 Grip-D; Takei, Niigata, Japan) hand dynamometer. Grip tests were performed in the standard position recommended by

the American Society of Hand Therapists because of the lower possibility of making a difference in hand grip strength values (15). In this standard position, the patients are seated with hips and knees at 90° flexion, shoulders in adduction, forearms in a neutral position, elbows at 90° flexion, wrists at 0 – 30° extension with 0 – 15° ulnar deviation. The measurement was repeated three times with 15 seconds rest between each measurement. The average of the 3 measurements was used in the evaluation (16). The assessments for the right and left hands were made separately, the average was calculated, and a single value was recorded.

2.3.2. The Upper Extremity Endurance: Unsupported Upper Limb Exercise Test

The Unsupported Upper Limb Exercise Test (UULEX) was used for the assessment of upper extremity endurance. The participants were seated on a chair with their knees touching a wall that contained the lines of the UULEX. The lowest line corresponded to the knee level of the subject. The subject held a plastic bar weighing 0.2 kg keeping the arms shoulder width apart, and moved from the hips towards the different levels of the UULEX lines. Each movement started at the hip joint and ended at the hip joint of the participants. The first level was performed for 2 min, and then the upper levels were performed for 1 min. Each level started and ended at the hip joint. The bar was lifted approximately 30 times (rising to the level) per minute as accompanied by a metronome. When the subjects achieved their maximum height, the 0.2 kg bar was exchanged for a bar weighing 0.5 kg. The same procedure was followed until the maximum height was reached for this weight. Subsequently, the weight was increased by 0.5 kg every minute until 2 kg was reached (Figure 2). The subjects were instructed to continue the test until tolerance limitation. The time from the beginning to the end of the test was recorded as the test duration (17,18).

Figure 2. *The unsupported upper limb exercise test*

The Upper Extremity Disability Level: The Disabilities of the Arm, Shoulder and Hand Test (DASH-T)

The DASH test, which is a valid and reliable test, consists of 30 items; 21 items assessing the difficulty experienced during daily life activities, 5 items assessing symptoms (pain, activity-based pain, tingling, stiffness, weakness), and each of the 4 remaining items assessed social function, job, sleep, and self-confidence levels (19). The subject selects the best response to each item on a 5-point Likert system (1: no difficulty, 2: slightly difficult, 3: somewhat difficult, 4: extremely difficult, 5: unable to do it). According to the outcome of the DASH test, a score was obtained in each section in the range of 0-100 (0: no disability, 100: maximum disability) (20).

2.4. Statistical Analysis

The data were analyzed using SPSS vn. 18.0 software. As a result of the power analysis, it was calculated that with 72 patients included in the study (at least 36 patients in each group), 80% power with 95% confidence level for d=0.80 effect size would be obtained (17). Continuous variables were presented as mean ± standard deviation (SD) values, and categorical variables as number (n) and percentage (%). In independent group comparisons, for data conforming to normal distribution, the Significance Test for the Difference between the Two Means was used, and for data not conforming to normal distribution, the Mann-Whitney U Test was used. A value of $p<0.05$ was accepted as statistically significant (21).

3. RESULTS

Figure 1 presents the flow diagram of participants selection. A total of 72 participants, 36 in the diabetes group [male (n=15), female (n=21)], 36 in the healthy group [male (n=16), female (n=20)] completed the study. Exercise habits were present in 14 people in the diabetes group and 15 people in the healthy group. While the right hand was dominant in 88.9% of the diabetes group, it was 80.55% in the healthy group. No significant differences were determined between the groups in respect of age (p=0,41) and BMI (p=0,06) (Table 2). No significant difference in grip strength between the two groups was found (p=0.05). The mean UULEX level (1-8) of the diabetics and healthy control group was 5.97±0.44, and 6.33±0.53 respectively. The mean UULEX weight of the diabetic group and the control group was 1472.20±546.99 gr, and 1944.40±199.20 gr respectively. The mean UULEX duration was 8.98±1.80 min for the diabetic group and 11.45±1.56 min for the healthy control group. When the two groups were compared in terms of sub scores of the UULEX level (p=0.00), weight (p=0.00) and duration (p=0.00), the scores of the diabetic patients were significantly lower than those of the healthy control group. In the comparison of the DASH-T total scores, the scores of the healthy control group (37.25±3.87) were statistically significantly better than those of the diabetic patient group (56.61±18.76) (p=0.00). The findings are summarized in Table 3.

Table 2. *Comparison of physical characteristics of diabetic and control group*

Variable	Diabetic Group (n=36) (Mean±SD)	Control Group (n=36) (Mean±SD)	p*
Age (year)	55.05±5.85	53.52±7.74	0.410
BMI(kg/m^2)	28.58±3.53	27.30±3.74	0.061

**Student t test/ SD: Standart deviation, BMI:Body mass index*

Table 3. *Comparison of the measurement results of the diabetic and control group*

Variable	Diabetic Group (N=36) (Mean±SD)	Control Group (N=36) (Mean±SD)	p
Hand Grip Strength(Kg)	30.21±10.37	34.44±11.00	0.057*
UULEX			
Level(1-8)	5.97±0.44	6.33±0.53	**0.004***
Weight(gr)	1472.20±546.99	1944.40±199.20	**0.000***
Duration(min)	8.98±1.80	11.45±1.56	**0.000****
DASH-T Score	56.61±18.76/150	37.25±3.87/150	**0.000***

**Mann Whitney U test, **Student t test/ SD: Standart deviation, UULEX: Unsupported upper limb exercise test, DASH-T: The Disabilities of the Arm, Shoulder and Hand Test*

4. DISCUSSION

The most important finding of this study was that upper extremity endurance parameters values in diabetic individuals show a significant decrease compared to those of healthy individuals. Although the upper extremity disability level was higher in the diabetic individuals, there was no significant difference in hand grip strength between the two groups.

In a systematic review by Gundmi et al. it was shown that the sample size of all studies was found to be low in general, and as a common result of the studies, it was found that people with type 2 diabetes mellitus had a decrease in hand function. (22). However, based on the grip strength values obtained in this study, no statistically significant difference was determined between the diabetic group and the control group. This unexpected result may have been due to different ratios of dominant extremity between groups, given that the dominant hand is significantly stronger in right-handed people (23). Another factor is that the shorter DM duration in the current study sample may affect the results, although the same results were also found by Akpinar et al (24).

Muscle strength and endurance are the two different components of extremity muscle function: while extremity muscle strength depends on muscle strength generation capacity, extremity muscle endurance indicates the muscle's capability to maintain or repeat a certain task over time. While one repetition maximum (1 RM) method has been mostly used for muscle strength evaluation in various studies, it has also been used for endurance in some studies (25). The 1 RM method is not suitable for diabetic individuals due to the maximum load on the joint, and it is difficult to attain for individuals without training. Furthermore, it is not possible to perform all the movements comfortably in a sitting position. Therefore, there is a clear need for more moderate and safer methods for the evaluation of force and endurance, considering the factors of age and diabetes.

In this study, the UULEX was used to assess upper extremity proximal zone endurance. The first report of UULEX in literature was to assess upper extremity functional level in individuals with chronic obstructive pulmonary disease (17,18). Although UULEX has been shown to be a valid and reliable test for healthy and rheumatoid individuals (26-28), there are no studies in literature illustrating that this test is valid and reliable for diabetic individuals. This can be considered a limitation of this study. However, the method was preferred since it can be performed while seated, it progresses from easy to difficult levels, assesses performance, and can be used for people at any age. In addition, it is easy to use and inexpensive. The UULEX test allows simultaneous evaluation of the upper extremity endurance according to duration, weight, and level.

Shah et al. assessed the distal upper extremity in individuals with type 2 diabetes and measured hand grip endurance (29). In that study, only upper extremity distal region endurance was evaluated, and there was observed to be a significant decrease in the diabetic group compared to the control group. In the current study, the upper extremity proximal region endurance value was lower in diabetics. Park et al. evaluated endurance of the muscles in the forearm and upper arm before and after exercise in diabetic individuals, but provided no information about how the endurance values changed in diabetic individuals compared to healthy individuals, or the endurance of shoulder circumference (25).

Although there are no studies which have assessed proximal upper extremity endurance of shoulder zone muscles, lower extremity proximal endurance has been assessed more often and endurance has been reported to decrease in diabetic individuals. Allen et al. stated that diabetic peripheral neuropathy reduced lower extremity endurance. Lizerman et al. reported that there was a significant reduction in knee flexor muscles endurance in diabetes cases (30,31).

The current study results showed that upper extremity proximal zone endurance was lower in the participants with type 2 DM compared to the healthy participants. According to best of our knowledge this study is the first study assessing upper extremity proximal endurance. Reduction of performance in patients with type 2 diabetes not only in the distal zone but also in the proximal zone is significant for the follow up of these patients and should definitely be assessed.

In a prospective study by Wani and Mullerpatan conducted using the DASH-T questionnaire, functional weakness of the upper extremity was found at the rate of 52.9% in diabetics (32). Laslett et al. investigated shoulder pain, disability and quality of life in diabetic patients and reported that those with higher HbA1c levels or who were receiving retinopathy treatment experienced more severe shoulder pain and disability (33). Another limitation of this study, other than the lack of validity and reliability study of the UULEX test in

patients with type 2 diabetes, is the need of examination level of endurance exposure according to severity and duration of diabetes together with the early effects of diabetes. Further studies are needed depending on the duration and severity of diabetes by using valid and reliable tests in addition to the UULEX test.

The practical implications of the results of this study can be said to be:

1. Future studies are warranted to demonstrate the validity and reliability of UULEX in individuals with type 2 DM.
2. The investigation of the upper extremity functions of diabetic patients and determination of the level of impact is critical.

5. CONCLUSION

Overall, the present study indicated that the endurance and disability levels of patients with type 2 diabetes were affected more substantially than those of healthy individuals. In the light of these outcomes, it is important that not only grip strength but also the upper extremity proximal region should be assessed. Low upper extremity endurance and a high level of disability will cause limitations in daily life activities and injuries due to loading.

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Clinical and Experimental Health Sciences

The Impact of Human Values on Ethical Climate: A Private Hospital Practice

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ABSTRACT

Objective: The aim of this study was to identify the impact of human values on ethical climate. The study also explores the factors affecting either human values or ethical climate.

Methods: The study exploited the data of the staff in a private hospital operating in Istanbul. Accordingly, the data of 178 individuals was obtained in four weeks period starting from March 2019. Human values were measured by Human Values Scale which was validated by Dilmaç (2007). Ethical climate was measured by Ethical Climate Scale which was introduced by Schwepker (2001) and validated by Eren and Hayatoğlu (2011). The study employed one-way variance analyses and Kruskal Wallis tests to understand the variations in human values and ethical climate perception upon socioeconomic factors. Additionally, ordinary least square regression was performed to identify the effect of human values on ethical climate perception.

Results: It was found that better human values were associated with increasing perceptions of ethical climate. Further, the number of children, age and the length of service had considerable impacts on both human values and the perception of ethical climate. Finally, marital status and educational status did not have any significant impacts on human values and ethical climate.

Conclusion: It was identified that the people with better human values were more careful about ethical rules. The findings are important to understand the motivations of ethical climate in a competitive atmosphere. It is believed that further studies investigating ethical climates in public and private organisations comparatively will contribute to the literature.

Keywords: Human Values, Ethical Climate, Values

1. INTRODUCTION

Living in a peaceful society is mostly depend on the harmony between cultural values and the behaviours of the individuals. The values direct attitudes towards people and issues. It is highly possible to experience abuses, iniquities and violence if humanitarian values are not reflected in the behaviours (1). Hence, it can be said that the values have important roles in behavioural attitudes of the individuals. In addition to these, the values considerably enhance not only the vision but also the perception of individuals (2).

The values have been explained in a various way so far. For instance, they have been entitled as the fundamental notion determining the judgement of truth or goodness (3). They have been described as the fact that ensures analysing the issues and determining the behaviours (3). The values have been explained as a concept of organising human-nature and human-human relationships through the judgement of the things desired (and undesired) and determining human behaviours (4). The values have also been described as principles, believes or assets enlighten the preferences about the meaning of the life and shaping the daily life (5). There has been a great deal that the values are not only ideas as beliefs, but also are related to emotions (3, 5, 6). They intertwine with emotions when they gain effectiveness. They are closely related to the aims of individuals and their behaviours in achieving those aims. It can be said that the values are above actions and situations. They function as standards for selecting, changing and directing people, behaviours and events. They can be ranked among themselves according to the importance of their own. Therefore, individuals and cultures can be described according to their priorities of values.

Everything in a society is perceived and compared according to values. People generally adopt the values of the group, society or culture they live in. Besides, they use these values as criteria in their judgements and choices. Thus, they have opportunity to have general judgements like better, more

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appropriate, more accurate, more beautiful, more important and fairer (7).

Ethic means a set of rules and principles or a set of moral principles or behaviours those are accepted socially or individually. From a broader perspective, ethic is the knowledge of what to do (or not to do), what to want (or not to want) and what to have (or not to have) (8). The concept of ethic, that has derived from the Greek word "ethos", is a set of measures examining the values, norms and rules those form individual and social relationships (9).

Ethical issues in terms of business are converged in four categories (10): relations, products, actions and staff. The relations with stakeholders and other partners are gathered in relations category. Products category includes the issues about environmental health, the use of resources and social purposes of the products. Actions category interests in commitments with the values such as truth, honesty, altruism and openness. Finally, staff category bears the issues about the variations of power, wage and ethnic origin among the staff.

Ethical climate is formed by ethical principles and behaviours. It refers the expected behaviours from staff in an organisation. It is originated from human values, policies and actions (11). Ethical climate not only demonstrates the right behaviour but also helps to make the required action in case of ethical issues (12). The frequency of practising expected behaviours among the employees implies that ethical climate is accepted to such an extent (13).

Humanitarian values are generally described as abstract ideals that direct behaviours (14). The impacts of behaviours on organisational climate have been of interest for the last thirty years (15). Human values and ethical climate have important roles in organisations since they (i) promote personal and interpersonal behaviours of the leaders, (ii) contribute to protect fundamental responsibilities and (iii) maintain continuous expansion and improvement of competence (16). Due to their importance in the organisations, this study examines the impacts of human values on the perception of ethical climate. In addition, the study identifies the factors affecting human values and ethical climate perception respectively. By doing this, the study aims to contribute to broader literature investigating the ethical climate by providing the findings from a competitive environment as the study exploits the data obtained from a private hospital operating in İstanbul, Turkey.

There are various studies in the literature examined the ethical climate from different perspectives. Dodd et al. (2018) state that directors who act as servant leaders are more likely to create an ethical work environment in their departments and to be role models that care about the well-being of their followers. It is also highlighted that they prioritize ethical behaviours and positively affect the behaviours of other staff (17). Günel et al. (2015) confirm that ethical leadership positively impacts ethical climate. Soffian Lee et al. (2018) indicate that benevolent and principled climates are positively and significantly associated with organizational commitments (18). Mitonga-Monga and Cilliers (2015) suggest that developing and maintaining a positive ethical climate in an organisation may increase the energy, mental flexibility and the permanence of the staff (19). Amer (2019) highlights that health professionals need greater awareness and training to increase their skills in ethics of integrity and their communication skills, especially in telling the patient the truth about diagnosis and treatment outcomes. Amer (2019) adds that these skills are important as they improve doctor-patient relationships, patients' care satisfaction and patients' health outcomes (20).

Oppong (2019) examines whether ethical decisions and actions are more likely to differ across cultural zone and time, despite the existence of "universal" normative ethical principles. He concludes that values are linked to cultural context within a universal dimension based on common human thoughts (21).

2. METHODS

In this study, a cross sectional and descriptive study design were exploited to identify the impacts of human values on the perception of ethical climate. The research was designed according to total population sampling. The study was conducted with randomly selected 178 volunteers out of 270 individuals working in a private hospital operating in İstanbul. The survey was carried out in four weeks period starting from March 2019.

The questionnaire applied in the study was formed by three sections in total. The first section examined socioeconomic characteristics, second section applied human values scale and the last section applied ethical climate scale.

Both of the scales employed in the study (human values scale and ethical climate scale) were already valid and reliable and widely used in the literature. Human values scale was introduced and validated by Dilmaç (2007). It is a Likert type scale that can be applied individually or in groups. It measures the human values by 42 items in six dimensions (i.e., Responsibility, Friendship, Peacefulness, Respect, Tolerance and Honesty). Higher scores of the scale imply better human values (22).

As for ethical climate scale, it was introduced by Schwepker (2001) and validated by Eren and Hayatoğlu (2011). It is also a Likert type scale measuring ethical climate. Increasing scores of the scale refer higher perceptions of the ethical climate (23).

Cronbach Alpha reliability tests were performed not only for the scales of human values and ethical climate perception and but also for the whole survey respectively. Accordingly, the calculated Cronbach Alpha values were 0.865, 0.912 and 0.858 respectively. Therefore, it was understood that the scales employed in the study were valid and reliable.

Finally, ordinary least squares regression was employed to understand the impact of human values on the ethical

climate perception. The estimation formula can be illustrated as follows:

$$Ethical\ Climate\ Perception_i = \beta_0 + \beta_1 Human\ Values_i + u_i$$

where $Ethical\ Climate\ Perception_i$ is outcome variable, β_0 is constant, $Human\ Values_i$ is the explanatory variable whose impact is of interest, β_1 is the estimated impact and finally u_i is the error term.

3. RESULTS

3.1. Sociodemographic Characteristics of the Respondents

Summary statistics regarding socioeconomic characteristics of the respondents are presented in Table 1. Accordingly, 83% of the participants was female, 64% was married and %67 was over 25 years of age. In addition, 45% held high school or lower degree and 51% worked for five years or shorter. Finally, 34% of the participants did not have any children while 33% of them had one child.

Table 1. *Sociodemographic Characteristics of the Respondents*

Variable		N	%
Gender	Female	148	83.1
	Male	30	16.9
	Total	**178**	**100**
Marital Status	Married	114	64
	Non-Married	64	36
	Total	**178**	**100**
Age	18-25	58	33.3
	26-35	72	41.4
	36-45	44	25.3
	Total	**174**	**100**
Educational Status	High School or Below	80	44.9
	Undergraduate	20	11.2
	Graduate	62	34.8
	Postgraduate	16	9.1
	Total	**178**	**100**
Duration of Service	5 years or Below	90	51.1
	6-10 years	48	27.3
	11-15 years	20	11.4
	16 years or above	18	10.2
	Total	**176**	**100**
The Number of Children	0	62	34.8
	1	60	33.8
	2	36	20.2
	3	20	11.2

3.2. Descriptive Statistics Regarding the Scales

Descriptive statistics of human values and ethical climate perception are presented in Table 2 below. Accordingly mean levels of human values and ethical climate perception were 3.88 and 3.83 respectively while standard deviations of them were 0.34 and 0.66, respectively.

Table 2. *Descriptive Statistics*

Number	Scale	Interval	Min.	Max.	X	S.D.	Skewness	Kurtosis
1.	Human Values	1-5	2.98	4.90	3.88	0.34	0.229	0.491
2.	Ethical Climate	1-5	2.57	5.00	3.83	0.66	0.264	-0.855

X: mean, S.D..: standard deviation

3.3. Variations

In order to understand the variations in human values and ethical climate perception among genders and the individuals with different marital status, t-tests were performed in independent samples. The results are presented in Tables 3 and 4.

Table 3. *The Differences According to Gender*

	Gender	N	Mean	S. D.	t	P
Ethical Climate	Female	148	3.82	0.66	-0.381	0.751
	Male	30	3.86	0.68		
Human Values	Female	148	3.87	0.32	-1.224	0.263
	Male	30	3.94	0.42		

Table 4. *The Differences According to Marital Status*

	Marital Status	N	Mean	S. D.	t	P
Ethical Climate	Non-Married	114	3.94	0.66	3.157	0.002
	Married	64	3.62	0.63		
Human Values	Non-Married	114	3.88	0.28	0.011	0.991
	Married	64	3.88	0.42		

Accordingly, it was identified that human values and ethical climate perception did not vary across genders. On the other hand, human values did not vary upon marital status while ethical climate perception was different among married and non-married samples.

One-way variance analysis (ANOVA) was employed to understand whether human values and ethical climate perception vary upon age while Kruskal Wallis test was performed for the variations upon educational status, the number of children and the duration of service. Accordingly, human values and ethical climate perception significantly differed according to age and the number of children, while there seemed no significant differences according to educational status. As for the duration of service, it was identified that human values significantly differed across the participants with different years of service while ethical climate perception was invariant. The results are presented in Tables 5-8.

Table 5. *The Differences According to Age*

	Age Groups	N	Mean	S. D.	F	p	Difference
Human Values	18-25	58	3.78	0.38	3.431	0.035	B>A
	26-35	72	3.93	0.33			
	36-45	44	3.92	0.28			
Ethical Climate	18-25	58	3.61	0.62	4.875	0.009	C>A
	26-35	72	3.87	0.64			
	36-45	44	4.00	0.70			

A=18-25; B=26-35; C=36-45

Table 6. *The Differences According to Educational Status*

	Educational Status	N	Mean Rank	X^2	P	Difference
Human Values	High School	80	88.85	0.508	0.917	—
	Undergraduate	20	83.70			
	Graduate	62	90.69			
	Postgraduate	16	95.38			
Ethical Climate	High School	80	87.63	1.103	0.776	—
	Undergraduate	20	97.00			
	Graduate	62	87.27			
	Postgraduate	16	98.13			

Table 7. *The Differences According to the Number of Children*

	The Number of Children	N	Mean Rank	X^2	p	Difference
Human Values	0	62	93.31	22.155	0.000	D>A D>B D>C
	1	60	144.70			
	2	36	150.42			
	3	20	198.50			
Ethical Climate	0	62	121.70	51.417	0.000	D>A D>B D>C C>A
	1	60	121.15			
	2	36	145.08			
	3	20	190.70			

A=0; B=1; C=2; D=3

Table 8. *The Differences According to the Duration of Service*

	The Duration of Service	N	Mean Rank	X^2	p	Difference
Human Values	5 years of below	90	77.48	14.982	0.002	B>C B>A
	6-10 years	48	111.38			
	11-15 years	20	78.00			
	16 years or above	18	94.28			
Ethical Climate	5 years or below	90	78.43	7.484	0.058	– -
	6-10 years	48	101.21			
	11-15 years	20	95.10			
	16 years or above	18	97.61			

A=5 years of below; B=6-10 years; C=11-15 years; D=16 years or above

A post-hoc test was performed to identify the differences among age groups in detail. As a result, it was identified that average human values scores of the participants at 18-25 years of age was significantly lower compared to their older counterparts at 26-35 years of age. Additionally, average ethical climate perception scores of the participants in 36-45 age group was significantly higher in comparison with the participants in 18-25 age group.

A post-hoc test was also exploited to identify the differences of human values among the participants with different years of service in detail. Accordingly, average human values scores of the participants with 6 to 10 years of service was significantly higher than the average scores of (i) participants with 5 years of service or shorter and (ii) participants with 16 years of service or longer.

3.4. Correlations Between Human Values and Ethical Climate Perception

The correlation between human values and ethical climate perception is presented in Table 9. There was a positive, linear and weak correlation (r=0,211, p<0,001) between human values and ethical climate perception.

Table 9. *Correlations Between Human Values and Ethical Climate Perception*

Variables (N=178)		Human Values	Ethical Climate
Human Values	R	1	0.211**
	P		0.000
Ethical Climate	R	0.211**	1
	P	0.000	

***r 0.001 significance level*

3.5. The Impact of Human Values on Ethical Climate Perception

Impact analysis of human values on ethical climate perception was performed. Ordinary least squares regression was employed to understand the impact on the perception of ethical climate. The results are presented in Table 10. Accordingly, human values had statistically significant impacts on ethical climate perception (p<0,001). It was understood that one unit of increase in human values scores was associated with approximately 0,2 increase in the scores of ethical climate perception. According to the model which was also understood that statistically significant (F=8,209, p<0,01), human values can identify almost 5% of total variance of ethical climate perception (R^2= 0,045).

Table 10. *Impact Analysis of Human Values for Dependent Variable of Ethical Climate Perception*

Variables	B	Standard Deviation	Beta	T	P
Constant	2.232	0.457		4.887	0.000
Ethical Climate	0.412	0.117	0.211	3.516	0,001

N=178, R= 0.211, R^2= 0.045, Adjusted. R^2 =0.039, F=8.209, p<0.01

4. DISCUSSION

The issues about ethical applications are of interest all over the world. In recent years, unethical behaviours have become an important issue especially in the fields of management. The formal or informal incorporation of morality, human values and ethics into daily lives can be the solution to any problem (24).

An ethical climate is critical to overcome unethical practices in health sector. By originating from the relationship between ethical values and human values, the study was designed to contribute to understanding of improving ethical climates. The study was based on the hypothesis that better human values are associated with improved ethical climates.

Human values have important roles in various things in a society. Wolf et al. (2020) exhibit that human values are

important in tackling with COVID-19 spread. Accordingly, cross-cultural agreement on the importance of human values demonstrate that human values are well placed to develop and adapt effective global interventions to tackle with the spread (25). Crowe (2020) states that human values have notable impacts on human health (26). Several studies in the literature (27-29) suggest that human values are associated with the improvements in professional ethics. In this study, it was identified that human values have important contributions in improving ethical climate. The findings are also important as they provide intuitions for a competitive environment like private hospitals.

Ethical climate is a fundamental aspect of organisational life affecting both individuals and organisations (30). There have been studies examining ethical studies in the literature. Tehraninesat et al. (2020) investigate ethical climate among nurses and conclude that professional values and ethical climate have significant associations with the quality of life (31). Since the ethical behaviours of the employees working at the forefront of customer relations are important, the organisations are required to understand how a strong ethical climate affects attitudes and behaviours in an organisation (32). Yasin et al. (2020) and Nurtatin (2020) demonstrate that improved ethical climate leads to reduced intentions to quit in the organisations. In this study, it was detected that the ethical climate improves in organisations where humanitarian values improve. Hence, the layoffs will decrease in the organisations where humanitarian values are improved (33, 34).

In this study, it was identified that human values and ethical climate perception do not vary according to gender. The finding confirms Karababa ve Dilmaç (2015) suggesting that human values have important roles in experiencing and expressing anger and do not vary upon gender. On the contrary, the finding conflicts with Karagözoğlu (2017) indicating that human values of artisans differ across age and gender groups (1, 35).

It was observed that human values did not vary upon marital status while ethical climate perception was different among married and non-married samples. In addition, human values and ethical climate perception significantly differed according to age and the number of children. Çalışkur et al. (2012) demonstrate a positive and weak relationship between purposeful and instrumental values, and state that “honesty, family security and peace of mind” values are common values seen in all groups. In addition, they detect that participants in different age and gender groups have different purposeful and instrumental values (3).

There were no significant differences according to educational status. It was also identified that human values significantly differed across the participants with different years of service while ethical climate perception was invariant.

Jalali (2013) identify that ethical climate is an important factor affecting work performance and affects the quality of patient care (36). Akdoğan and Demirtaş (2014) demonstrate that ethical leadership directly and indirectly affect ethical climate sub-dimensions (except independence dimension of ethical climate) (37). They add that organizational political perceptions play a mediating role in the indirect effect of ethical leadership (37). Humphries and Woods (2015) conclude that patient flow initiatives and budget policies implemented by institutions have detrimental effects on the ethical practices of nurses. In addition, they indicated that nurses experience moral distress and hence patient care was negatively affected as a result of such policies (38).

5. CONCLUSION

This study examined the impact of human values on the perception of ethical climate. To do this the study employed parametric and nonparametric methods using the data of 178 volunteers working in a private hospital operating in İstanbul. By doing this, the study aimed to provide intuitions towards ethical climate in a competitive environment.

The study also investigated the socioeconomic factors affecting human values and ethical climate perception. Identifying such factors is important since human values and ethical climate have important roles in organisational relations and structures (16).

The study observed that human values have impacts on ethical climate perception. It was identified that better human values were associated with better perception of ethical climate implying that the people with better human values were more careful about ethical rules. Further studies investigating the effects of human values on ethical cultures will make important contributions to broader literature about human values and ethics.

The findings of the study are important to understand the motivations of ethical climate in a competitive atmosphere. It is believed that further studies investigating ethical climates in public and private organisations comparatively will also contribute to the literature of ethical climates.

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Clinical and Experimental Health Sciences

Assessment of The Frequency and Correlation of Carotid Artery Calcifications and Pulp Stones with Idiopathic Osteosclerosis Using Digital Panoramic Radiographs

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ABSTRACT

Objective: The aim of this study was to assess the correlation of carotid artery calcifications (CACs) and pulp stones with idiopathic osteosclerosis (IO) using digital panoramic radiographs (DPRs) to determine whether pulp stones or IO might be possible indicators of the presence of CACs.

Methods: In total, DPRs of 1207 patients (645 females and 562 males) taken within 2018 were retrospectively evaluated to determine the prevalence of CACs, pulp stones and IO according to age and sex. Statistical analysis was performed using chi-square test and Fisher's exact chi-square test.

Results: In total, 287 (23.8%) patients had at least one pulp stone, and 64 (5.3%) patients had CACs. The negative/negative (-/-) status of CACs/pulp stones was significantly higher in the 18–29 years age group than in the 30–39, 40–49, 50–59 and ≥60 years age groups ($p<0.05$). It was also significantly higher in males than females ($p<0.05$). Sixteen (1.3%) patients had IO, which was related to right mandibular molars in all cases. Patients with CACs had a significantly higher prevalence of IO (6.3%) than those without CACs (1%) ($p<0.05$). There was no statistically significant association between pulp stones and the presence of IO and CACs ($p>0.05$).

Conclusion: Within the limitations of this study, pulp stones were not found to be diagnostic indicators of CACs. However, the presence of IO might be a risk factor for CACs.

Keywords: Carotid artery calcification, dental pulp stone, digital panoramic radiograph, idiopathic osteosclerosis.

1. INTRODUCTION

Calcium mineral deposition in ectopic areas and dystrophic lesions can result in pathological conditions, such as arterial atherosclerosis. This mineral deposition occurs in the presence of lesions or plaques, which can be evaluated radiographically. The structure underlying the atherosclerotic calcification shows a connection between bone biology and chronic plaque inflammation, passive mineral deposition and bone formation or remodelling (1).

Although calcification of atherosclerotic lesions is common (1), some previous reports found that the existence and severity of calcification, in addition to long-term vascular events, were correlated with a patient's entire burden of atherosclerotic lesions (2,3). Digital panoramic radiography is one of the most widely used diagnostic imaging methods in dentistry. Due to their wide coverage of the head and neck region, digital panoramic radiographs (DPRs) can capture a large amount of data in a single image. The low radiation dose of DPRs also makes them highly suitable for use in dental clinics (4).

Any calcifications within the lumen of the carotid artery appear as radiopacities on high-quality DPRs. Detection of carotid artery calcifications (CACs) in DPRs is vital due to the significant morbidity and mortality attributable to atherosclerotic lesions (5).

Several studies have examined the effectiveness of radiographic evaluations of CACs using DPRs in various populations (6,7). One study reported that the advantages of digital panoramic radiography for assessing CAC lesions included its non-invasiveness and cost effectiveness (8). Another study concluded that dentists who detect CACs in patient's DPRs should consider a prophylactic specialist examination (9). Following a radiographic diagnosis of CACs, various other diagnostic imaging modalities, such as ultrasonography, magnetic resonance imaging, computed tomography and angiography, with higher resolution capacities are often needed to validate the diagnosis. Following the detection of CACs, a previous study indicated that prompt interventions were needed to combat associated adverse vascular events (10).

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Pulp stones are dystrophic calcifications. Such calcifications may be found in both the coronal and radicular parts of the dental pulp cavity (11). Previous studies demonstrated the ability of both dental radiographs and cone beam computed tomography to detect pulp stones (12-14). Although the etiology of pulp stones is considered idiopathic, some risk factors have been proposed: pulp degeneration, aging, genetics, chronic irritants, trauma, atherosclerosis, cardiovascular diseases, kidney diseases, gallstones and salivary gland stones (15). A previous study suggested that a high level of blood calcium or metabolic dysfunction could be considered etiologies for pulp stones, in the same way that calcifications play a role in the etiology of atherosclerosis (16). Based on a strong correlation between pulp stones and CACs, Yeluri et al. (17) suggested that further evaluations of CACs were required in patients with multiple pulp stones.

Idiopathic osteosclerosis (IO) refers to localized areas of compact bone that evolves within cancellous bone with an unidentified origin. IO is asymptomatic, observed with different shapes and sizes found in both the mandible and maxilla, with a higher frequency in mandibular premolar and molar areas (18). The radiopacity in IO can resemble condensing osteitis, cementoblastomas, hypercementosis, complex odontomas or focal cemento-osseous dysplasia, which are other pathologies of the jaws (19). The diagnosis is established based on an examination of the lesion morphology, along with clinical symptoms and radiographs.

It is unclear whether CACs are associated with an elevated risk of cardiovascular diseases (CVDs). Balbay et al. (20) concluded that the current burden of CVDs in Turkey was significant and that it was projected to increase due to the aging of a large part of the population. They also noted that CVDs were important causes of morbidity, premature mortality and disability in Turkey. Many patients may visit a dentist more frequently than they visit a physician. Dentists can play a role in the early diagnosis of CVDs by detecting the presence of pulp stones and IO on radiographic examinations.

To our knowledge, no study has examined the correlation between CACs, pulp stones and IO in the adult Turkish population. The objective of this study was to assess the potential correlation between the presence of CACs, pulp stones and IO in males and females of different age groups to determine whether pulp stones or IO might be a significant indicator of the presence of CACs.

2. MATERIALS AND METHODS

2.1. Sample Selection

This cross-sectional study used DPRs from patients who visited Biruni University Faculty of Dentistry for dental treatment between January 2018 and December 2018. In total, 2108 DPRs were examined. Of these, the DPRs of 1207 patients (645 females and 562 males aged 18 years or older) fulfilled the following inclusion criteria: for diagnostic purposes, each DPR had to clearly show maxillary and mandibular teeth, in addition to the complete area posterior to the angle of the mandible at the level of the C3-C4 cervical vertebrae, with optimum contrast and density and with no distortion or superimposition of anatomic structures. Low-quality radiographs with incorrect exposure times or angulations were excluded. Regarding the pulp stone evaluation, teeth with fractures, caries and root canal fillings were excluded. The exclusion criteria for the IO evaluations were as follows: condensing osteitis associated with chronic inflammation (teeth with caries, deep restorations or root canal obturations, etc.), mixed radiopaque and radiolucent lesions, benign fibro-osseous lesions, and tori or exostosis. The DPR of each patient that fulfilled the study requirements was evaluated and demographic data in terms of age and sex were documented.

This study complied with the tenets of the World Medical Association Declaration of Helsinki and was approved by the ethics committee of Biruni University (2020/37-16).

2.2. Radiographic Evaluation

A dental radiology assistant took all the panoramic radiographs using a Sirona Galileos panoramic X-ray unit (Sirona, Bensheim, Germany). Each radiograph was analyzed using Picture Archiving and Communication Systems (PACS) software, Version 1.1.1.6 for Windows 10 (Microsoft Corporation, Redmont, WA, USA), on a 28-in Samsung LU28H750UQMXUF monitor (Samsung Electronics, Seoul, South Korea) with 3,840 × 2,160 pixel resolution. Each radiograph was assessed as follows: All original digital images were magnified using the magnification function of the PACS software. The examiner manipulated the images to improve their contrast and brightness to give subjectively the clearest images in the analyzed areas.

One endodontist and one dental radiologist, each of whom had at least 5 years of experience, assessed each image. Before the evaluation of the radiographs, each examiner assessed a series of 30 radiographs that were not associated with the present study for calibration between the examiners. Any disagreement between the examiners in the evaluation was resolved through discussion until agreement was reached. Cohen's kappa was used for inter-observer consensus, which corresponded to very good agreement (value of 0.86).

The diagnosis of CACs was based on heterogeneous unilateral or bilateral nodular, punctate and vertico-linear radiopacities detected posterio-inferior to the angle of the mandible at the level of the C3-C4 cervical vertebrae (Figure 1). The presence of idiopathic pulp stones was characterized as clear radiopaque masses positioned in the coronal pulp chamber, as seen in Figure 1 and Figure 2. Based on these radiological criteria, IO was characterized as well-defined, ovoid, round or irregularly shaped and radiopaque lesions associated with normal bone, with no radiolucent surroundings (Figure 1).

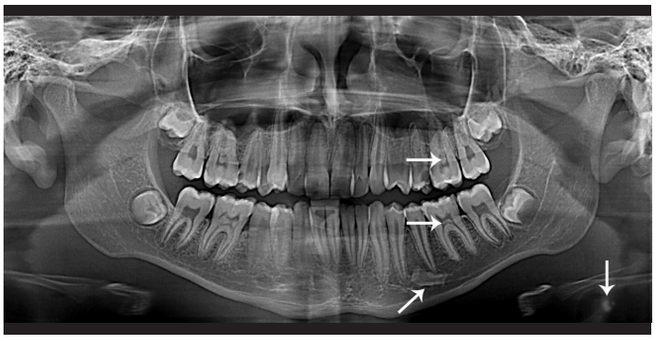

Figure 1. *Panoramic radiograph showing a detectable carotid artery calcification on the left and idiopathic pulp stones within the coronal pulp chambers of the maxillary and mandibular left first molars, with idiopathic osteosclerosis of the left mandibular premolar area (white arrows).*

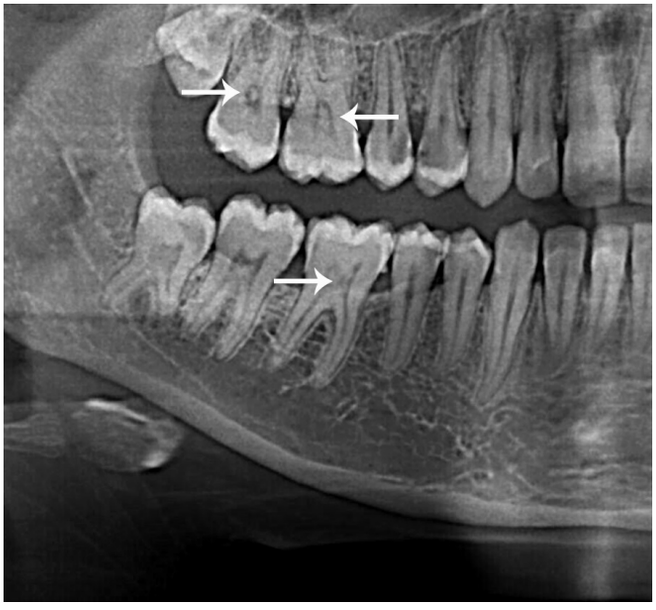

Figure 2. *A close-up view of a panoramic radiograph showing idiopathic pulp stones within the coronal pulp chambers of the maxillary right first and second molars and mandibular right first molar (white arrows).*

2.3. Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics 22 (IBM SPSS, Turkey). A chi-square test and Fisher's exact chi-square test were used to compare differences between the age and gender groups in respect of the presence of CACs, pulp stones and IO. The statistical significance level was set at $p<0.05$.

3. RESULTS

In total, DPRs of 1207 patients were examined. The mean ± standard deviation (SD) age of the patients was 38.15 ± 12.96 years. In the study group, 645 (53.4%) patients were females, and 562 (46.6%) were males. In total, 64 (5.3%) patients had CACs: 53.1% on the right, 21.9% on the left and 25% bilaterally. 287 (23.8%) patients had at least one pulp stone and 16 (1.3%) patients had IO, which was related to right mandibular molars in all cases. The presence of CACs according to age was statistically significant ($p=0.002$). The percentage of patients with CACs in the ≥60 years age group was significantly higher (12.2%) than that in the 18–29 (3%), 40–49 (3.5%) and 50–59 (4.9%) years age groups ($p=0.001$, $p=0.003$ and $p=0.047$, respectively). The frequency of CACs was significantly higher in the 30–39 years (7.1%) age group than in the 18–29 (3%) and 40–49 years (3.5%) age groups ($p=0.021$ and $p=0.045$). Furthermore, the frequency of CACs was significantly higher in females (7.4%) than in males (2.8%) ($p=0.001$) (Table 1).

Table 1. *Descriptive analysis of age and sex and the relation to carotid artery calcifications*

		CACs		*p*
		Absent	Present	
		n (%)	n (%)	
	18-29	325 (97)	10 (3)	0.002[1]
	30-39	339 (92.9)	26 (7.1)	
Age	40-49	276 (96.5)	10 (3.5)	
	50-59	117 (95.1)	6 (4.9)	
	60+	86 (87.8)	12 (12.2)	
Sex	Female	597 (92.6)	48 (7.4)	0.001[2]
	Male	546 (97.2)	16 (2.8)	

[1]*Chi-Square test;* [2]*continuity (yates) test; p<0.05 is statistically significant; CACs: carotid artery calcifications*

The frequency of pulp stones according to age was statistically significant ($p<0.001$). The frequency of pulp stones in the 18–29 years age group was significantly lower (15.8%) than that in the 30–39 (31.2%), 40–49 (25.2%) and 50–59 (25.2%) years age groups ($p<0.001$, $p=0.004$ and $p=0.021$, respectively). In addition, the frequency of pulp stones was significantly lower in the ≥60 years age group (17.3%) than in the 30–39 years (31.2%) age group ($p=0.010$). The frequency of pulp stones was significantly higher in females (28.5%) than in males (18.3%) ($p<0.001$) (Table 2).

Negative/negative (-/-) status for CACs/pulp stones in the 18–29 years age group was significantly higher than that in the 30–39, 40–49, 50–59 and ≥60 years age groups ($p<0.001$, $p=0.027$, $p=0.028$ and $p=0.001$, respectively). The negative/positive (-/+) status for CACs/pulp stones in the 30–39 years age group was significantly higher than that in the 40–49 and ≥60 years age groups ($p=0.002$ and $p=0.010$). The positive/negative (+/-) status for CACs/pulp stones in the 40–49 years age group was significantly lower than that in the ≥60 years age group ($p=0.001$). The – /+ status for CACs/pulp stones was significantly higher in females than in males, and the – / – status for CACs/pulp stones in males was significantly higher than that in females ($p<0.001$) (Table 3).

The presence of pulp stones was not significantly associated with the presence of CACs (p>0.05) (Table 4).

The presence of IO was significantly more common among patients with CACs than without CASs (6.3% vs. 1%) (p=0.008). On the other hand, there was no significant association between the presence of pulp stones and the presence of IO (p>0.05) (Table 5).

Table 2. *Descriptive analysis of age and sex, and the relation to pulp stones*

		Pulp Stones		p^1
		Absent	Present	
		n (%)	n (%)	
	18-29	282 (84.2)	53 (15.8)	<0.001
	30-39	251 (68.8)	114 (31.2)	
Age	40-49	214 (74.8)	72 (25.2)	
	50-59	92 (74.8)	31 (25.2)	
	60+	81 (82.7)	17 (17.3)	
Sex	Female	461 (71.5)	184 (28.5)	<0.001
	Male	459 (81.7)	103 (18.3)	

[1]*Chi-Square test; p<0.05 is statistically significant*

Table 3. *Descriptive analysis of age and sex, and the association between pulp stones and carotid artery calcifications*

		CAC/Pulp Stone				
		-/-	+/-	-/+	+/+	p^1
		n (%)	n (%)	n (%)	n (%)	
	18-29	278 (83)	4 (1.2)	47 (14)	6 (1.8)	<0.001
	30-39	229 (62.7)	22 (6)	110 (30.1)	4 (1.1)	
Age	40-49	210 (73.4)	4 (1.4)	66 (23.1)	6 (2.1)	
	50-59	88 (71.5)	4 (3.3)	29 (23.6)	2 (1.6)	
	60+	71 (72.4)	10 (10.2)	15 (15.3)	2 (2)	
Sex	Female	429 (66.5)	32 (5)	168 (26)	16 (2.5)	<0.001
	Male	447 (79.5)	12 (2.1)	99 (17.6)	4 (0.7)	

[1]*Chi-Square test; p<0.05 is statistically significant; CACs: carotid artery calcifications*

Table 4. *Associations between the presence or absence of carotid artery calcifications and pulp stones*

		CACs		
		Absent (-)	Present (+)	*Total*
		n (%)	n (%)	*n (%)*
Pulp Stones	**Absent (-)**	876 (72.6)	44 (3.6)	*920 (76.2)*
	Present (+)	267 (22.1)	20 (1.7)	*287 (23.8)*
	Total	*1143 (94.7)*	*64 (5.3)*	*1207 (100)*
	p^1		0.149	

[1]*Chi-Square test; p<0.05 is statistically significant; CACs: carotid artery calcifications*

Table 5. *Associations between the presence or absence of idiopathic osteosclerosis (IO) and pulp stones and carotid artery calcifications (CACS)*

		IO		p^1
		Absent	Present	
		n (%)	n (%)	
CACs	Absent	1131 (99)	12 (1)	0.008
	Present	60 (93.8)	4 (6.3)	
Pulp Stones	Absent	906 (98.5)	14 (1.5)	0.385
	Present	285 (99.3)	2 (0.7)	

[1]*Fisher's Exact test; p<0.05 is statistically significant; IO: idiopathic osteosclerosis; CACs: carotid artery calcifications*

4. DISCUSSION

The present study examined the frequency of CACs observed on DPRs in a Turkish population. Many reports have cited the use of DPRs as a valid approach to detect the presence of CACs (2,6). Previous research noted a very high and positive correlation between ultrasonography, Doppler sonography and panoramic radiography in the identification of CACs (2,6,21). Other DPR studies confirmed that CACs could serve as useful indicators of major cardiovascular and arterial diseases (21,22). In the present study, we examined the association of CACs with pulp stones and IO using DPRs. The prevalence of CACs in the DPRs was 5.3% in the present study. Alzoman et al. (23) found a similar prevalence of CACs (5%) in the Saudi population. The frequency of CACs in other studies varied from 2% to 6%, with the frequency altering, depending on the study population's sex, age, ethnic background and life style (24-26). In the present study, the frequency of CACs was higher in females than in males. This finding was similar to that of Santos et al. (24) and Nasseh and Aoun (27). In our study, the highest frequency of CACs was in the oldest age group. This result was consistent with that of previous studies, which found that generally, CACs appeared to be more common in older age groups (both females and males) and that atherosclerosis was common in older people (24,28). In the present study, we detected pulp stones in 23.8% of the patients. This result was higher, lower or close to that of the literature (29-31). The frequency of pulp stones was between 9.9 and 85% some previous studies (30,32). This variation in the results might be due to a number of factors, such as the design of the studies and selection of the cases. In the present study, the frequency of pulp stones in females was significantly higher as compared with that in males. Consistent with our study results, Turkal et al. (33) and Sener et al. (34) found a significantly higher prevalence of pulp stone in females. An increase in the frequency of bruxism in females, as well as sex-related differences in oral care, with females more likely to have restorations and therefore long-term pulpal irritation, can explain these

findings. In contrast to our results, Tassoker et al. (12) found no statistically significant difference in the frequency of pulp stones according to sex. Furthermore, previous studies reported no correlation between age and pulp stones (34,35), whereas we detected the lowest frequency of pulp stones in the youngest age group (i.e. 18–29 years). Factors related to pulp stone formation, such as restorations, caries and parafunctional habits, all of which increase with age according to previous research (34), can explain the low pulp stone prevalence in the youngest age group in this study.

One of the primary aims of the present study was to evaluate the co-occurrence of pulp stones and CACs and to determine whether these anomalies could aid the early diagnosis of other medical conditions, such as CVDs. The results of our study revealed no positive correlation between pulp stones and CACs, in accordance with the finding of similar previous studies (8,36,37). In contrast, a previous study reported a positive correlation between pulp stones, CACs and renal calcifications (17). The differences among these study results may be explained by mechanisms of pathogenesis. The fact that we did not record the presence of CVDs or other medical conditions may also explain the differences.

In the present study, the – / – status for pulp stones/CACs was higher in 18–29 y age group than in the other age groups. Horsley et al. (8) reported that the positive/positive (+/+) status for pulp stones/CACs was higher in those aged 60 y and older than in younger age groups. This finding was in accordance with our result.

Various studies have employed different imaging methods to investigate the IO distribution in different populations (38,39). These studies reported an IO prevalence of between 1.8% and 7.6%, which was higher than that found in our study (1.3%). Variation in the population number, study designs and evaluation criteria might account for the reported differences in IO prevalence. The etiology and pathways of IO are thought to be different than those of pulp stones and CACs (40). Nevertheless, according to our findings, there was a positive correlation between the presence of IO and CACs. This result might contribute to further studies, as, to our knowledge, no published studies have investigated the correlation between these parameters.

A major limitation of this study was the use of DPRs for CAC examinations rather than carotid artery ultrasound, which superior to DPRs in terms of its sensitivity and specificity. An additional limitation is the debate about whether the CACs are associated with an elevated risk of CVDs.

5. CONCLUSION

The results of our study showed that CACs were more common in females, with an increased prevalence among males and females those aged >60 years. Pulp stones were more common in females. In terms of age, they were more common among individuals aged 30–39 years. According to our findings, pulp stones do not serve as a diagnostic component for CACs. However, the presence of IO might be considered a risk factor for CACs. Further studies are needed to evaluate potential correlations among these parameters using different imaging techniques. As DPRs are a fundamental diagnostic component of routine dental examinations, where CACs are detected on DPRs, dentists may refer patients to a specialist for further investigations of possible atherosclerotic diseases.

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Clinical and Experimental Health Sciences

The Effect of Dental Paste with Herbal Content on Remineralization and the Imaging with Fluorescent Technique in Teeth with White Spot Lesion

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ABSTRACT

Objective: To evaluate the effect of Gumgumix herbal toothpaste on remineralization of white spot lesions with a laser fluorescent system called FluoreCam. It is a pilot study.

Methods: The FluoreCam system was used for the fluorescence imaging of the fifteen teeth with white spot lesions. During the study, the patients continued to use the previously owned toothpastes, addition to Gumgumix. Gumgumix was applied on the lesion area with a finger pressure twice a day and was not rinsed mouth after, only a limited spit and was prevented from taking any fluid during 30 minutes. The "Compare" option in the FluoreCam system was used to differentiate the situation before and after the use of the paste; if the marked area were yellow "No Change"; blue "Sound Surface"; green "Improving"; light blue "Mild Improving" and red meant "Worsening".

Results: Of the 13 lesions that were "Suspect Surface" initially, 46% were identified as "Mild Improving", 7% as "Moderate Worsening", 30% as "No Change", and 15% as "Sound Surface". Two of the white spot lesions were recovered totally as 100%.

Conclusion: After use of Gumgumix for one week, remineralization was observed on teeth with white spot lesion. The white spot lesions on two teeth were totally healed.

Keywords: Remineralization, Herbal toothpaste, White spot lesion, Laser fluorescence.

1. INTRODUCTION

Tooth decay is one of the most common chronic diseases in the world and it may cause tooth loss when appropriate treatment is not applied. The modern dentistry concept aims to improve the aesthetic and function of the tooth through the process of remineralization by preventing the progression of caries. Thus, non-invasive treatment of caries lesions without cavity preparation have been developed (1). Demineralization occurs by the dissociation of mineral ions in the dental hard tissues from the hydroxyapatite crystals. Precipitation of hydroxyapatite crystals is called remineralization. Both processes take place on the tooth surface and a large number of hydroxyapatite crystals may be lost before deteriorating tooth integrity. However, gaps are formed on the tooth surface as a result of disintegration of the hydroxyapatite structure. Moreover, demineralization is a reversible process; therefore, partially demineralized hydroxyapatite crystals in the teeth may return to their original size if the conditions for remineralization is provided (2).

Initial enamel caries is the first stage of dental caries and it is possible to control the caries at this stage. It may be treated with a proper regulation of diet, plaque control and application of appropriate antibacterial agents and thus the demineralized enamel may be remineralized (3). Initial caries lesions are limited to enamel and also called "white spot lesions". Caries on the smooth enamel surface is first seen as white spot lesions. These white spot lesions can only be seen when the tooth surface is dried. These opaque surfaces are chalky white and this color is caused by the loss of transparency due to the expansion of the porosity of the sub-surface area as a result of demineralization (4). Remineralization of initial caries lesions without cavitation; easy to apply, short-term, economical, acceptable by the patient, and it is a very convenient conservative method. Many materials are used to prevent demineralization and to remineralize the tooth surface. These are fluoride-containing gels, vernics, mouthwashes, dental floss and toothpastes (5).

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Besides them, some studies showed positive and promising results of remineralization by using herbal tooth creams (6,7).

Ginger is one of these herbal extracts with antibacterial properties. In ginger, there are many active ingredients including terpene and oleoresin called ginger oil (8). Ginger consists of about 1% to 3% of essential oils and non-volatile oleoresin. The main components identified as terpenes are sesquiterpene hydrocarbon and phenolic compounds, gingerol, shogaol and lipophilic rhizome extracts. Potentially active gingerols can be converted to shogaol, zingerone, and paradol (9,10). Ginger and its components show antioxidant activity and prevent damage to macromolecules from free radical and oxidative stress. Ginger also shows antimicrobial activity through gingerol, paradol, shogaol and zingeron (11). Ginger essential oil and oleoresin have shown important antioxidant and antimicrobial activities (12). Gingerol and shogaol have been identified as the most active agents (13). With such properties of ginger, Bilgin *et al* (14) discovered the remineralization effects of ginger and honey mixture on initial enamel caries lesion with 50 micron depth. Afterwards Korkut *et al* (15), studied on remineralization effects of this mixture in herbal toothpaste form (Gumgumix, Beka Ilac, Sultanbeyli, İstanbul, Turkey), reporting the lesions were remineralized quite well compared to the control toothpastes with 1450 ppm fluoride ingredient.

Apart from the remineralization agent it is important to determine the lesions at the early stage and follow the change of the lesion in order to treat demineralization. Thus, it may be evaluated the effectiveness of remineralizing agent applied on the lesion. Traditional caries detection methods are insufficient for the diagnosis and follow-up of the initial caries lesions. For many years explorer has been used for the detection of caries (16). However using explorer may cause defects in the demineralized areas and the cariogenic microflora can be transferred to deeper regions of tooth (17,18). With evolution of technology, non-invasive caries detection methods have been developed (19). Nowadays caries detection methods are able to measure the detected lesions quantitatively and evaluate as numerical data. Numerical evaluation of lesions parameters such as lesion area, lesion depth and mineral loss provides an objective examination (20).

One of the methods used in the diagnosis of initial enamel caries in modern dentistry is laser fluorescence technique (21). The device called FluoreCam, the mineral loss of the tooth can be expressed quantitatively. The FluoreCam system (Therametric, Daraza, Indianapolis, USA) uses the Fluorescence Enamel Imaging (FEI) approach to determine de – or remineralization areas of enamel. The measurements are automatically done by FluoreCam software. This method is simple, fast, repeatable, and able to measure initial caries lesions which may be difficult to diagnose clinically and radiographically. Using FluoreCam as a detection method for mineral changes that have occurred on enamel surface after treatments may increase the patient's confidence to the dentist because it is a painless and non-invasive method (22).

The aim of this pilot study was to clinically visualize any remineralization on the teeth with a white spot lesion by a laser fluorescence system, FluoreCam using the herbal toothpaste, Gumgumix.

2. METHODS

2.2. Study Subjects

A total of 15 teeth with a white lesion from 6 patients with an age range of 14-25 applied to the clinics of Marmara University, Faculty of Dentistry were included in the study from May 2019 to June 2019. Patients allergic to any herbal toothpaste were excluded. Patients with DMFT index 3 or less and with no gingivitis or periodontitis were included.

All patients were informed about the study and a voluntary consent form was signed. All procedures were conducted according to the Declaration of Helsinki. Ethical approval was obtained from the Marmara University, Faculty of Dentistry Clinical Researches Ethics Committee (Reference number: 2019-304).

2.3. Clinical Examination

A standard 'Patient Tracking Form' has been prepared for each patient. In this form, the patient's nutritional details, the frequency of toothpaste and brush usage, the current toothpaste and toothbrush used, how many times he rinsed his mouth after brushing, the use of orthodontic apparatus and the daily meal amount were recorded and the patient's oral examination was performed and air-water spray and eye examination were recorded. The white spot lesions detected were also recorded on the form. Besides, the intraoral view of the white spot lesion was recorded with a mobile phone camera (iPhone 6S).

Five patients with 13 white spot lesions continued using routine toothpaste besides they applied herbal toothpaste Gumgumix (Beka Drug, Sultanbeyli, Istanbul, Turkey) to the lesioned areas twice a day with a finger pressure following tooth brushing for a week as it was a usual application at the in vitro studies. Following use of Gumgumix, they did not rinse their mouth; they only spat and were prevented from taking liquids within 30 minutes. One patient with two white spot lesions kept as control and continued to her routine toothpaste with 1450 ppm NaF, no additional use of Gumgumix toothpaste.

The clinical visualization of remineralization on the teeth with a white spot lesion was carried out by a laser fluorescence system, FluoreCam at baseline and after 1 week from all teeth. The patient's name-surname, age and teeth numbers with white spot lesions were entered into the FluoreCam system. Fluorescence images of the white spot lesioned teeth were obtained with the FluoreCam intraoral camera after drying with air-water spray. Particular attention was paid not to shine the tooth surface while taking the image.

Fluorescence differences within the lesion in the acquired image were confirmed by the parts indicated by the device and field records were made. This area is in a color that FluoreCam automatically determines. If the area is illustrated by blue color, it shows the healthy surface, and the yellow shows the suspected surface with demineralization. FluoreCam system also ranks the suspicious white lesion from Level 1 to Level 3 according to darkness of the area probably the differences in depthness. Lesion sizes and intensities are evaluated in this study. The number extracted for each image represents the cumulative size for all the red outlines on the screen. Size means the area of the lesion which has lesser mineral content. Intensity means the amount of mineral loss. If the size gets bigger, that means the area of the lesion or the areas where there is less mineral content has increased. Intensity always represented as a negative number. If the negative value gets bigger, that means the lesion (mineral content) has worsened. On the contrary if the value gets smaller, that means the lesion has improved. The "Compare" option in the FluoreCam system was used to differentiate the fluorescence intensity disagreement between baseline and 1 week images. If the marked area is yellow, "No Change"; blue is "Sound Surface"; green is "Improving"; light blue is "Mild Improving"; red is considered as "Worsening". The change in lesion size and density is reported in percent on the "Compare" screen. The statistical analysis of the study was carried out by Stata 15.1 (Stata Corp, College Station, TX) computer programme. In the study, density change-gender, size change-gender, density change-carbohydrate consumption, size change-carbohydrate consumption was compared with the Mann-Whitney U test. Moreover, in the change of dimension, "Moderate Worsening" and "No Change" were combined and recorded as "worsened"; "Sound Surface" and "Mild Improving" were combined and recorded as "healthy" and evaluated with Fisher's exact test. Results with a p value below 0.05 were considered significant.

3. RESULTS

According to the measurements obtained in the first session, 13 of 15 lesions were determined as "Level 1" and 2 of them as "Level 2". All lesions were "Suspect Surface" and seen in yellow in the first session. One of the control lesions was Level 1 and the other one was Level 2. According to the measurements done in the second session, 11 of the lesions were recorded as "Level 1", two of them as "Level 2" and two of them as "Sound Surface". One of the lesions determined as Level 1 was Level 2 in the first session. Two of the lesions determined as Sound Surface were Level 1 in the first session. In the comparison made at the end of the second session, six of the lesions (46%), the first session of which was Suspect Surface, were "Mild Improving" and painted in light green color (Figure 1). Four of the lesions (30%) were shown "No Change" and painted in yellow (Figure 2). Two of them (15%) were "Sound Surface" and painted in blue, one of them (7%) were "Moderate Worsening" and painted in pink. According to the percentages seen on the "Compare" screen, eleven of the lesions decreased in size and two of them (15%) increased in size. While the lesion density decreased in seven of them (53%), it increased in six. Two of the white spot lesions were 100% healed. The two control lesions were identified as "No Change". The situation before and after the size was calculated using the Chi-Square test, but since there was only one group in the pre-treatment group, the statistical analysis could not be performed. As a result, out of thirteen lesions initially "Suspect Surface", 46% were identified as "Mild Improving", 7% as "Moderate Worsening", 30% as "No Change", 15% as "Sound Surface". The comparison of the situation before and after the dimension is shown in Table 1.

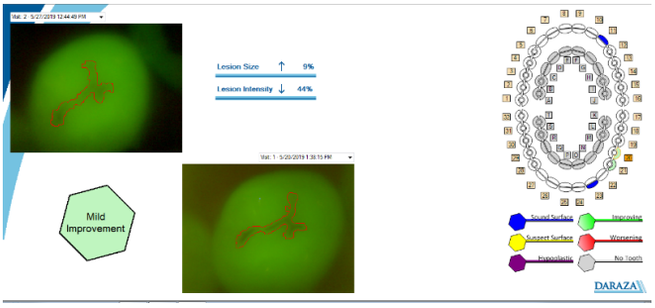

Figure 1. *Image of the lesion which showed "mild improving".*

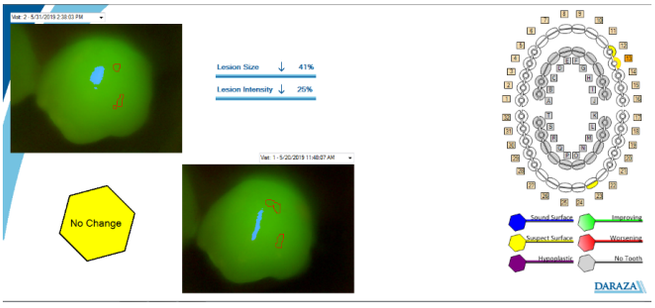

Figure 2. *Image of the lesion which showed "no change".*

Table 1. *Comparison of the before and after of dimensional changes with additionally use of gumgumix toothpaste (difference %).*

Dimension (Before)	Dimension (After)				Total
Suspect surface n (%)	Mild improving n (%)	Moderate worsening n (%)	No change n (%)	Sound surface n (%)	n (%)
13 (100)	6 (46.15)	1 (7.69)	4 (30.47)	2 (15.38)	13 (100)

Density change-gender, size change-gender, density change-carbohydrate consumption, size change-carbohydrate consumption was compared with the Mann-Whitney U test. p values were 0.1564, 0.1069, 0.4972, 0.9060 respectively and no statistically significant results were obtained. In the change of dimension, "Moderate Worsening" and "No Change" were combined and recorded as "worsened"; "Sound Surface" and "Mild Improving" were combined

and recorded as "healthy". Fisher's exact test was used to establish a relationship between change in dimension and carbohydrate consumption (p=0.196) as well as between change in dimension and gender (p=0.685). Due to the small number of patients no statistically significant results were found.

4. DISCUSSION

In today's dentistry, the tendency towards natural and biocompatible products has increased to avoid health problems increasing with the development of technology. Hence researchers have been trying to develop dental products containing mostly natural ingredients (23). For this purpose, herbal extracts and their oils have been used in the pharmaceutical, cosmetic, food and beverage industries. There are plenty of studies that show that plants have properties such as antioxidant, anti-inflammatory, antiviral, antibacterial, antidiabetic and anticarcinogen effect (24). However, apart from the listed effects there are limited number of studies showing the effects of the herbal extracts on the cariogenic bacteria and on remineralization. Recently herbal extracts have been used as antimicrobial plaque agents in medicine to prevent tooth decay and reduce gingivitis and have received special attention as they are not chemical and synthetic (25). Since herbal products are natural, they are safer than synthetic products without showing any side effects. Furthermore, they are economic and available locally.

Herbal toothpaste Gumgumix which is recently produced in dentistry, has antibacterial properties and remineralizing effect due to ginger and honey content which has been observed in various studies (14,15,26). Although a remineralization process occurs on enamel tissue, the mechanism of remineralization by this paste is not known. Remineralizing effect of toothpastes may be achieved by the presence of active agents in the mouth during 30-40 minutes. Unfortunately, in daily routine, people rinse with water immediately and the active agent leaves outside of the mouth. In this way, the anti-caries effect is proportionally reduced with each rinsing with water. In this study, we recommended to apply the active ingredient of the test material herbal toothpaste (Gumgumix) with the finger on the tooth surface for one minute to be more effective and afterwards no rinsing with water.

Göçmen *et al.* compared the effects of NaF, mixture of ginger and honey, mixture of ginger, honey and chocolate, and rosemary oil on the remineralization in vitro and they observed the changes in surface microhardness values statistically significant in all treatments groups and the most significant study group was the mixture of ginger and honey (14). Similar results as demonstrated in Table 1 were obtained in our study.

One of the ingredients in Gumgumix is honey, which is a mixture of sugars mainly fructose and glucose. Recent studies showed that honey is an antiseptic and antibacterial agent as containing hydrogen peroxide (H_2O_2), methylglyoxal and bee defensin-1 (27,28). Additionally, Patel et al. reported ginger and honey are more effective than gentamycin on S. Mutans (29). As supporting views, Premkishore et al. used ginger with honey against Streptococcus mutants in an in vitro study and reported considerable antibacterial effect against S. mutants in antibiotic sensitivity test (5). In another study, ginger extracts are used to inhibit the S. mutants and it is reported that the experimental group with the ginger extract showed significantly higher reduction of the S. mutants concentration (30). Besides antibacterial properties, ginger has an effect on saliva and apatite stimulation, in this way ginger is a potential natural agent to treat enamel demineralization (31).

In this study the effect of herbal toothpaste, Gumgumix, on remineralization of enamel was evaluated by FluoreCam system. The Fluorecam system does not contain X-ray which is the biggest advantage. On the other side there are some aspects should be careful with when using the FluoreCam. During the process of image taking, there might be some shining areas on the surface, may cause the existing lesions not to be detected. In this case, the image should be repeated. However, FluoreCam have some disadvantages such as the inability on having a differential diagnosis in deep caries with exposed pulp, failure in the diagnosis of secondary caries in the teeth with restoration and adjacent to restoration, and detecting discoloration or plaque on the tooth surface as a fluorescence loss (false positive value).

In present study one of the patients had the initial enamel lesion, which was not visible due to the orthodontic brackets. The patient with the bracket gave a false positive response as if there was a lesion in the presence of plaque. It was observed that there was no lesion after removing the plaque. Also, it gave false positive answers in the restoration area of the teeth with restoration. However, it was able to detect the initial enamel lesions, which were determined or not determined with the naked eye, on clean surfaces at the stages with a white lesion or before the white lesion. Both white spot lesions that healed completely were small lesions located on the upper lateral. Ease of application of the agent on the surface, lack of fissure and small initial lesion size are likely to be effective in healing. It was determined that 46% of the lesions were "Mild Improving" in the second appointment, they were larger than those which completely healed and some of them had initial fissure caries causing reduction on the recovery rate.

Another point to consider is that the images taken in the first and second appointments should be on the same angulation. If the image is taken from a different angle in the second appointment, the change in lesion size may be reported incomplete. While taking the image, the unit' light should be off and the tooth surface should be dried.

Korkut *et al.* reported that FluoreCam can detect lesions around the orthodontic brackets and achieved a successful remineralization with ginger-honey mixture and demonstrated that it is possible to measure demineralization around orthodontic brackets and to detect the weekly mineral

content alterations by using FluoreCam device (15). Similar results have been found in our study. The daily application of the herbal toothpaste Gumgumix containing active ingredient ginger and honey demonstrated inhibitory effect on demineralization and have enhanced remineralization on enamel (Table 1).

In present study only one lesion showed "Moderate Worsening" at the end of the second appointment. According to the information received from that patient, she did not use Gumgumix regularly.

Due to few patients as a pilot study, no statistical results could be obtained. However, the difference between p50 values coincides with the results obtained in the clinical studies (14,15,26). Also, according to the data obtained in comparing the lesion sizes before and after, it was determined that 61% of the lesions had improvement. We think that our study might yield statistically significant results if the number of patients were higher than the present.

According to the results derived from this study, the daily application of Gumgumix provided enhanced remineralization just in a week. We think that mineral content and antibacterial effect of ginger in Gumgumix may have some role on remineralization process. We also suppose that regular use of Gumgumix may reduce cariogenic microflora which may lead to reduced demineralization. Due to its content, Gumgumix may create an environment which favors for remineralization. Applying Gumgumix on the tooth surfaces helps to repair demineralized areas by preventing further mineral loss and enhancing increased mineral intake.

5. CONCLUSION

Under the conditions of this in vivo study, the herbal toothpaste Gumgumix was determined as an effective agent on preventing and also reversing the demineralization. Even though the remineralizing mechanism of Gumgumix has not been known, additional research on this herbal-based toothpaste is required to identify its potential benefits and efficacy for its regular use in the oral hygiene products. FluoreCam caries detection device is found as useful for determining mineral density and lesion size changes occurring in enamel lesion even within a week. With this promising results, herbal toothpaste Gumgumix containing ginger and honey may safely be used in daily routine as preventive agent and treatment of initial enamel caries lesions in oral hygiene.

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Clinical and Experimental Health Sciences

Retrospective Evaluation of Different Shade Selection Methods in the Context of the Vital Bleaching Technique

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ABSTRACT

Objective: This retrospective study was performed to evaluate the correspondence between digital image analysis and spectrophotometry tooth shade results.

Methods: The study population consisted of 10 patients. Office bleaching was performed using an in-office whitening. Tooth shade was analysed by spectrophotometry and image analysis of digital photographs at baseline, and at 1-week and 3-month follow-up visits. The correspondence between the two methods was evaluated based on the total color change (ΔE), calculated using lightness, chroma, and hue (LCH) values for spectrophotometry and lightness, red-green, blue-yellow (LAB) values for digital image analysis. The Mann–Whitney U, Wilcoxon signed rank and Kruskal–Wallis tests were used for the statistical analyses ($p<0.05$). The correspondence between digital image analysis and spectrophotometry results was determined using the intraclass correlation coefficient (ICC).

Results: At the 3-month follow-up, there were no significant differences in tooth shade results between the spectrophotometry and digital image analysis methods ($p=0.855$), which showed strong agreement (ICC=0.983).

Conclusion: Digital image analysis may be a useful alternative to spectrophotometry for tooth shade selection.

Keywords: Bleaching, Digital image analysis, Shade Selection, Spectrophotometer

1. INTRODUCTION

Dental esthetics is an important issue for all dental practices. Well-aligned white teeth are desired by the majority of both women and men. People desire the “perfect smile”, and dental bleaching represent the initial step towards this goal.

Vital bleaching techniques have proven efficacy, either in the office or at home under professional supervision. Home and in-office bleaching techniques utilize peroxide at different concentrations (1). In-office whitening agents use a higher concentration of peroxide and provide more rapid results. Therefore, patients frequently request in-office bleaching. Clinical application often involves a combination of two bleaching techniques for rapid whitening with less dental sensitivity (2).

High concentrations (25–40%) of hydrogen peroxide (H_2O_2) enhance tooth colour (3). In-office whitening performance is related to the ability of H_2O_2 to diffuse into the hard tissues of the teeth, although deeper penetration is associated with a higher risk of pulp damage. Improvements in whitening techniques could decrease the detrimental effects on pulp tissue with no decrease in efficacy (4).

Shade selection is done using visual or instrumental techniques. The visual technique is the most commonly used for shade selection by dentists but is subjective and depends on numerous environmental factors and the vision of the clinician (5). Instrumental techniques using colorimeters, spectroradiometers, spectrophotometers and digital cameras are objective and convenient for shade selection in clinical practice (6).

Spectrophotometry, which measures the transmittance curve or spectral reflectance of a specimen, quantifies the amount of light reflected from the surface in the visible spectrum at each wavelength and is the most appropriate method for shade selection. Spectrophotometers are unaffected by metamerism and have a longer working life than colorimeters (7).

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Digital image analysis is a shade selection method based on digital photography. Shade selection using this method can simplify communication between the technician and the dentist. Digital image analysis requires an appropriate software program to analyse colour values in an appropriate format. Digital image analysis is a cost – and time-effective method compared to spectrophotometry and colorimetry, although its validity has not yet been proven (8).

In the present study, consistency between spectrophotometric and digital image analysis tooth shade selections, at 1 week and 3 months after in-office bleaching, was evaluated. The null (h_0) hypothesis was that the digital image analysis and spectrophotometric measurements would not be consistent.

2. METHODS

This retrospective clinical study was carried with approval from the Marmara University Faculty of Dentistry Ethics Committee (Istanbul, Turkey; registry no. 2020-383).

The data of patients treated with in-office bleaching procedures at Marmara University, Faculty of Dentistry, Restorative Department, between January 1, 2019, and January 1, 2020 were analysed. The study population in this retrospective analysis consisted of 10 patients aged between 20 and 35 years. Participants were examined in the context of the exclusion/inclusion criteria.

The inclusion criteria were regular attendance of follow-up appointments, caries-free anterior teeth, no restorations on the labial surface, and good general and oral health. The exclusion criteria were pregnant or lactating women, active carious lesions, dentine exposure, endodontic treatment of anterior teeth, internal tooth discolouration, and current smoking.

The bleaching procedure was performed using Opalescence Xtra Boost (Ultradent Products, South Jordan, UT, USA) in two 20-minute sessions, conducted in accordance with the manufacturer's instructions.

Tooth shade was assessed based on follow-up appointment data. Total colour change (ΔE) was denoted by ΔE_1 (baseline and 1 week) and ΔE_2 (baseline and 3 months) and assessed using both spectrophotometry and digital image analysis. Measurements were performed for teeth numbers 11 and 13, from the middle third of the labial surface.

2.1. ΔE Measurements Obtained with Spectrophotometry

Shade selection was performed by one clinician using a Vita Easyshade V spectrophotometer (Vita Zahnfabrik, Bad Säckingen, Germany). The device was calibrated for each measurement according to the manufacturer's instructions (Figure 1). Lightness, chroma and hue (LCH) values from CIELAB colour space were determined and ΔE was calculated (9).

2.2. ΔE Measurements Obtained with Digital Image Analysis

A Canon EOS 700D digital single lens reflex (DSLR) digital camera (Canon, Melville, NY, USA), macro lens (100 mm; Canon), and macro twin flash (Yongnuo YN-24EX/TTL; Shenzhen Yong Nuo Photographic Equipment, Shenzhen, China) were used for the study. Lightness, red-green, blue-yellow (LAB) values were determined with Adobe Photoshop CC software (Adobe Systems Inc., San Jose, CA, USA; Figure 2) and ΔE values were then calculated using a previously described formula (9).

$$\Delta E = \sqrt{[(L_1^* - L_0^*)^2 + (a_1^* - a_0^*)^2 + (b_1^* - b_0^*)^2]}$$

The normality of the data was analysed using the Kolmogorov–Smirnov test. The two methods were compared with the Mann–Whitney U test. Measures were compared among three appointments using the Wilcoxon signed rank test. The intraclass correlation coefficient (ICC) was used to evaluate the agreement between spectrophotometry and digital image analysis tooth shade results ($p<0.05$).

Figure 1. *Determination of LCH values with spectrophotometer*

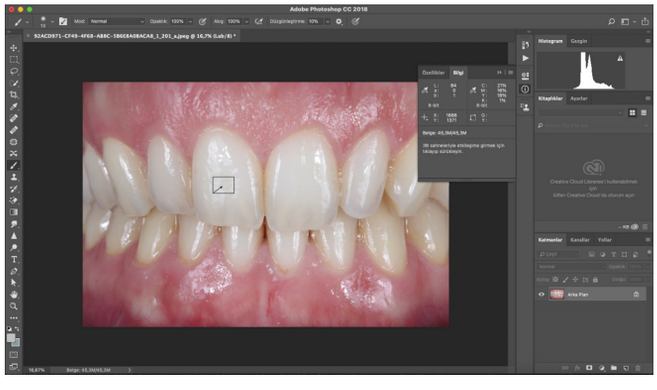

Figure 2. *Determination of LAB values with digital image analysis*

3. RESULTS

The shade selection accuracy was compared between the digital image analysis method and spectrophotometry.

The difference in ΔE values between spectrophotometry and digital image analysis was not statistically significant (p=0.855) (Table 1). The two methods showed a high degree of agreement (ICC=0.983).

Table 1. *ΔE Values of two different methods for all measurements*

	Mean±SD	Median	Q1 – Q3	*p*
Digital Image Analysis	4.00±2.01	3.43	2.53 – 4.84	0.855
Spectrophotometer	4.08±1.99	3.66	2.54 – 5.07	

There were no statistically significant differences between the median spectrophotometric and digital image analysis ΔE_1 values (p=0.808) or ΔE_2 values (p=0.957) (Tables 2 and 3).

The 1-week and 3-month follow-up data were analysed separately. The mean ΔE value obtained using spectrophotometry at the 3-month follow-up was 4.58. Values equal to or above the ΔE threshold of 3.3 are considered noticeable by clinicians (10), so the colour change was clinically detectable in this study.

Table 2. *ΔE1 values of two different method*

	Mean±SD	Median	Q1 – Q3	*p*
Digital Image Analysis	3.13±1.04	3.06	2.4-3.4	0.808
Spectrophotometer	3.30±1.26	2.88	2.4-3.7	

Table 3. *ΔE2 Values of two different method*

	Mean±SD	Median	Q1 – Q3	*p*
Digital Image Analysis	4.88±2.36	4.53	3.28-6.84	0.957
Spectrophotometer	4.88±2.30	4.58	3.27-6.6	

4. DISCUSSION

The present study was performed to determine whether there is a linear relationship between spectrophotometry and digital analysis tooth shade results. The main objective was to investigate the practical utility of digital colour analysis systems in dentistry. Both methods have their own algorithm for colour analysis, and separate ΔE values were obtained for each method. The ΔE values were subjected to correlation analysis, and the h_0 hypothesis that the digital image analysis and spectrophotometric measurements would not be consistent was rejected (i.e. high correspondence was found between the two methods).

Patients' expectations regarding esthetic outcomes are increasing, and esthetic treatments are being performed more widely, including bleaching (11). Tooth colour was not measured immediately after the bleaching session in this study, because dehydration of the tooth can affect the measurements. Thus, shade analysis was performed 1 week and 3 months after the bleaching treatment. The effectiveness of bleaching increases with the application of highly concentrated H_2O_2 products over two sessions (12). Clinically significant colour improvement is also observed. Visual shade selection is the most commonly used method by clinicians. However, this technique is affected by a number of variables and is subjective (13). Therefore, an instrumental alternative method was developed in the late 1990s. Shade detection instruments, such as colorimeters and spectrophotometers, have subsequently been introduced into dentistry. Researchers have reported equivocal outcomes when using colour-measuring devices, with some authors suggesting that these devices do not provide reliable results (14), and others reporting good accuracy (15).

A number of dental photography and software systems have been developed, and digital photography has started to be used for shade selection (16). Digital images can be analysed using convenient software programs that allow all pertinent details to be recorded. This represents a major advantage over contact-type instruments. However, the factors affecting the results obtained with this method, such as the digital camera parameters, reproducibility of digital images, and lighting conditions, should be investigated. More research is also required for standardization of the measurements. The CIELAB colour space is three-dimensional, with L*A*B* axes. A colour stimulus is indicated by chromatic A* (red/green), B* (yellow/blue) and L* (achromatic) values. Shade differences can be quantified using the CIELAB formula based on Euclidean intervals, which has been used widely to determine colour differences in both dentistry and the industrial sector. CIE created a new colour formula, known as CIEDE2000, which is more complex than the CIELAB colour space. However, both of these formulae are convenient for use in clinical practice (17).

Browning et al. reported a Yonghua significant correlation between CIELAB and CIEDE2000 ΔE values (18). On the other hand, while Oliveria et al. reported that CIELAB and CIEDE2000 ΔE values were similar, they nevertheless showed some differences, attributed to the use of two different formulae (19). The CIELAB formula was used in the present study.

There have been few reports comparing digital image analysis and spectrophotometry tooth shade results. Further research is therefore needed.

5. CONCLUSION

Within the limitations of this retrospective clinical study, we showed that spectrophotometry and digital image analysis yielded similar tooth shade results. Thus, digital cameras can be used for shade analysis and selection and can also facilitate communication between dentists and technicians.

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Clinical and Experimental Health Sciences

The Relationship Between the Learning Styles and Academic Performance of Medical Faculty Students

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ABSTRACT

Objective: Medical students have with different learning styles and different educational backgrounds. While the curriculum is being prepared, the success of students this situation should be considered. This study is designed to reveal the learning styles of the second-year medical students and to compare their academic performance with their learning style.

Methods: One hundred and four students of 2nd-year Bezmialem Vakif University Medical School are included in the study. To reveal the learning styles, Kolb's Learning Styles Inventory applied to all students. Also, the academic performance of each student was listed. We compared the statistical relationship between gender and academic performance with students' learning styles.

Results: Of the 104 students' there was 59 female, 45 male in gender. According to the questionnaire, most of the female and male students were assimilators (abstract-passive learners) (%58.5) and divergers (concrete –passive) (%28.8). Students' academic performance results were between 75-80. We did not find a statistically significant difference between gender and students'learning styles and academic performance results (p>0.05).

Conclusion: Identifiying and monitoring of students' learning styles in the universities especially in medical schools is neglected. However, we should know students' learning style in order to recognize their learning habits shaped by previous learning experiences and to improve their success. Moreover, it is important to improve students' performance by using learning strategies and methods suitable for different learning styles.

Keywords: Learning, Academic Test Performance, Education, Medical

1. INTRODUCTION

Learning is one of the most important abilities of human beings and takes place by constructing the information encountered by the individual in their own mind. One of the effective theories in professional education is the experimental learning theory proposed by David Kolb (1). Accordingly, learning is a process, and knowledge is created by the transformation of experiences. The source of thinking and reflections are appropriate cognitive and affective experiences; these ideas are organized and concentrated with pattern and concepts, new actions arise forintellectual transformation. According to Kolb this learning process represents a learning cycle that touches all the bases through the students' active experience, reflection and conceptualization. Therefore learning is not only cognitive, but also an adaptive process between the individual and their environment (2). In addition to these, it is important to know individual differences in the process of information processing. This situation, which is accepted theoretically but neglected in practice, has been the subject of various studies. Although it is accepted theoretically, this situation, which is neglected in practice, has been the subject of various studies (2-6). Learning style is one of the most important concepts that reveal individual differences in the learning process. Knowing a person's learning style enables learning to be orientated according to the preferred method**.** It is necessary to understand whether they are active or reflective when processing information, analytical or holistic while understanding information. Until today, different learning styles have been defined by many scientists and different scales have been developed to determine them. Among these, the most widely used is Kolb's learning styles scale (1-3). In this scale, each learning style has a different way of learning. In this respect, different levels and learning styles of students should be taken into consideration in educational practices (1-3, 8).

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In order to define the learning style, it is necessary to determine whether they prefer active or reflective processing for information, analytical or holistic prefer or intuitive way, visual or auditory tools while learning information, and to understand whether they are performing analytical or holistic processing. Until today, different scales for learning styles have been developed by many author. Among these, the most widely used is Kolb's learning styles inventory. Each learning style on the scale has a different learning pathway. The results of these studies brought attention to the fact that different levels and learning styles of students should be taken into consideration in educational practices (1-3, 8).

If teaching and learning environments are organized according to different cognitive and learning styles, targeted learning outcomes can be achieved. As different results have been obtained in studies conducted for this purpose, the relationship between the academic performance of the individual and the learning environment and the student's cognitive and learning style can be evaluated (5,8,10). This study was planned to investigate the learning styles of Bezmialem Vakif University Medical Faculty (BVUMF) 2nd grade students and to evaluate the relationship between students' gender and academic performance with learning styles.

2. METHODS

One hundred four students attending the BVUMF as 2nd year students were included in the study. Kolb Learning Styles Inventory, which was created by D. Kolb and translated into Turkish by Askar and Akkoyunlu and whose validity and reliability study was conducted and applied in order to determine the learning styles of the students (1). The scale includes for sub – dimensions and 12 guestions in each them, a total of 48 items. For the four sub-items in each question, students are asked to give a score (between 1 and 4 points), giving 4 for the most appropriate option and 1 for the least appropriate. The scale is evaluated by collecting the 1st sub-items as "concrete experinece", 2nd sub-items "reflective observation", 3rd sub-items "abstract conceptualization", and 4th sub-items "active experimentation".

In this way, a score between 12-48 is obtained for 4 sub-items. The next step is to acquire the reunited scores. With the help of 4 points obtained at this stage, two points of 4 are obtained (between – 36 and +36) with the process of "abstract conceptualization – concrete experience" and "active experimentation – reflective observation". With the help of 4 points obtained at this stage, two points of 4 are obtained (between – 36 and +36) with the process of "abstract conceptualization – concrete experience " and "active experimentation – reflective observation". Based on these points, the learning style of the person is determined according to the intersection of the two points. Matrix view of Kolb's learning styles is shown in Table 1.

Table 1. *Kolb learning styles inventory*

	Doing (Active Experimentation-AE)	Watching (Reflective observation – RO)
Feeling (Concrete Experience-CE)	Accomodating (CE/AE)	Diverging (CE/RO)
Thinking (Abstract Conceptualization-AC)	Converging (AC/CE)	Assimilating (AC/RO)

2.1. Diverging (feeling and watching – CE/RO):

These people are able to look at things from different perspectives. They prefer to watch rather than do, tending to gather information and use imagination to solve problems. These people like to gather information and brainstorming and prefer to work in groups.

2.2. Assimilating (watching and thinking – AC/RO):

People who prefer this way wants good clear explanation rather than practical opportunity. They prefer logical approach and more interested in ideas and abstract concepts. People with this style prefer readings, lectures, exploring analytical models

2.3. Converging (doing and thinking – AC/AE):

These people prefer technical tasks and they are best at finding practical uses ideas and theories. They like to work with practical applications and solve problems by finding solutions to questions and problems.

2.4. Accommodating (doing and feeling – CE/AE):

They are attracted to new challenges and experiences. These people prefer to work in teams to complete tasks. This style learners tend to rely on others information than carry out their analysis. Action and initiative roles are required.

2.5. Statistical analysis

The distribution of the data was analyzed using the Shapiro Wilk test. The Kruskal Wallis test was used for comparing three or more groups that did not show normal distribution. Post hoc comparison of variables were found significant in the Kruskal Wallis test was made by Dunn's test. Pearson Chi-square or Fisher's Exact test was used for comparison of categorical data. Mann Whitney U test was used to compare variables that do not have a normal distribution between the two groups. Descriptive statistics of the data are given as median (minimum-maximum) and frequency (percentage). All statistical analyzes were carried out and reported in IBM SPSS Statistics 20.0 program and at $\alpha = 0.05$ significance level.

3. RESULTS

Considering 104 students, distribution of the learning styles was found as 58 (55.8%) "assimilating", 30 (28.8%) "diverging", 11 (10.6%) "converging" and 5 (4.8%) "accomodating".

According to gender, forty five of 104 students were male and 59 of them were female. The distribution of learning styles according to gender, is shown in Table 2.

Table 2. *Distribution of Learning Styles by Gender*

Learning Style	Male	Female
Accommodating	4 (8.9%)	1 (1.7%)
Converging	8 (17.8%)	3 (5.1%)
Diverging	11(24.4%)	19 (32%)
Assimilating	22(48.9%)	36 (61%)
p-value	0.054	

Averages of yearly academic performance was given as success score. Success score according to *Accomodating, Converging, Diverging and Assimilating* learning style was found as 75, 78, 80 and 75 respectively. No statistically significant difference was found between the learning styles and academic performances of the second grade students of the medical school ($p > 0.05$).

The results of students' success score and learning styles by gender is given in Table 3. Statistically significant relationship was not found between the learning styles of male and female students and their academic performance ($p > 0.05$).

Table 3. *Students' success score and learning styles by gender*

Gender	Accommodating	Converging	Diverging	Assimilating	p-value
Success Score in Male	67	70	74	70	0.706
Success Score in Female	76	74	75	71	0.412

4.DISCUSSION

Individuals develop appropriate learning strategies and styles through formal and social learning experiences (1-3,11). According to Dunn, who has conducted many studies on this subject, learning styles are "each student's use of a different and individual's self-directed way while learning and remembering new and difficult information" (12). Medical Students come from different educational environments and bring the habits they have gained with them. Inconsistencies between students the learning style and teaching style may negatively affect the students motivation, required effort, and learning outcomes (3-5,8,11).

In our study, it was determined that more than half of the students were in the assimilating group in terms of learning styles. This was followed by the diverging group. In a study by Gürpınar et al. (3), the learning styles of students in different medical faculties were evaluated and it was found that they focused on the type of assimilating and diverging. These results are consistent with other studies on the subject. The characteristic of the assimilating group is that they prefer to learn by getting the information from its expert, and they prefer to learn by listening and watching to their instructors. In Bezmialem Vakif University Faculty of Medicine, the fact that education is mainly conducted in the form of teacher-centered lectures and this situation is compatible with the learning style of the assimilating group and it is not surprising that there is no difference between the academic performance of this groups. There is also no difference between the learning styles of other groups and their academic performances. Different learning styles, even if they are less in number, should be adopted to curriculum. This approach increases the success and flexibility of the education system, positively affects the student's self-confidence and participation in the learning process (3, 4, 8). It is known that affective, visual and sequential learning features are predominant in medical students. Torrano et al revealed that those who were close to the sensing learning were more concrete-minded and prone to factual memorization in the lecture based teaching (5).

Students start their academic studies with different patterns of learning strategies; the charactersitics of these patterns change during their academic life and regarded as lifelong learning. Fabry et al noticed that most of the changes happen during the first term (11). As soon as they started to medical education, they study according to their prior learning experiences. Further changes refer to learning with colleagues. They learn how to be succesfull from their new learning environment. It is emphasized that this change can take place especially between 3-7 years. It has been shown that the students who have an assimilating style at the beginning of medical school can change their learning styles by active learning over the years. (2,3,11). Gürpınar et al. also showed that, although some of the students have a distinctive learning style, according to curriculum and learning methods, students tend to learn more systematically (3). The relationship between learning styles and academic performance has been studied, mostly have shown no difference (5, 9, 10,13). While the learners with reflective observation were successful in teamwork in problem solving, the intuitive learners were found to be more successful in basic medical sciences and clinical pathology than the others. In the study related to the success in anatomy lesson, the sensory style was found to be more dominant than the intuition. This result is not surprising, while sensory learners are better at memorizing and lab work (5). In our study, although most of the students have an assimilating learning style, statistically significant difference was not found between the academic performance and their learning styles. The students' average achievements are close to each other in all learning styles. This situation evaluated both in the annual course committee exams and final exams. In this case, we considered that regardless of their prior learning experiences and presumptions, they adapted to system with their new learning environment as Fabry et al indicated. Meantime, most of them contribute to the assimilating learning style and being passive listener. And as soon as they realize that they are successful in multiple-choice exams, their learning styles change. In the study of Lynch et al, a relationship was found between multiple choice questions and learning styles, but no difference was

found between learning style and success in the clinical performance exams (13). It is not easy to predict what the result would be, if they were asked to analyze and synthesize the knowledge in the exams assessed clinical reasoning. In our study, no difference was found between the learning styles and gender. The assimilating learning style were used mostly in both genders. In addition, there is no difference between learning styles and academic performances for both gender. In some studies, while no difference was found in learning style between genders, Fabry et al have found that male students learn more visually (2,5,14).

In our study, the research is a cross-sectional study that includes only second grade students and teacher-centered learning activities. Considering that learning styles can change with different teaching strategies and learning methods added to the curriculum, it can be thought that the research design to monitor the success and learning styles of these students over the years will give more detailed results for the purpose of the study.

5. CONCLUSION

In conclusion, program designs and teaching strategies that will provide opportunities for all different learning styles in education should be included to curriculum. Accordingly, assessment systems should be arranged in accordance with the principles of diversity, validity, reliability and equity according to the teaching strategy and learning areas.

The main goal should be to provide learning opportunities that will enable students not only to memorize factual information, but also to use what they have learned to solve different problems through analysis and synthesis.

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Clinical and Experimental Health Sciences

The Effect of Probiotic and Omega-3 Supplements on Total Oxidant and Total Antioxidant Levels in Experimental Colitis

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ABSTRACT

Objective: Treatment of inflammatory bowel disease (IBD) usually involves medical therapy. For this reason, it is recommended to seek alternative treatment methods such as nutritional therapy. The aim of the study is to evaluate the effects of probiotics and omega-3 fatty acids on total oxidant and total antioxidant levels in an experimental colitis model.

Methods: Mice were randomly divided into five groups (n= 10/group) as healthy group, colitis group, group treated with probiotics (VSL#3), group treated with omega-3 (w-3), and group treated with both probiotics and omega-3. To induce experimental colitis, 200 mg/kg dinitrobenzene sulfonic acid (DNBS) + 30% ethanol combination was rectally administered to anesthetized mice. Total oxidant (TOS) and total antioxidant (TAS) levels were measured at the tissue level.

Results: Lower concentrations of TOS were observed in the probiotics groups (2.11±0.23 mmol H2O2 Eq/L), probiotics+omega-3 (2.56±1.18 mmol H2O2 Eq/L), and omega-3 (3.02±1.88 mmol H2O2 Eq/L) groups compared to the colitis group (3.11±0.91 mmol H2O2 Eq/L) ($p>0.05$). Higher TOS and TAS level were observed in the control colitis group compared to other groups; however, the differences were not statistically significant.

Conclusion: Our findings showed that TAS and TOS levels were positively affected by the use of probiotic supplements in IBD. It was determined that using w-3 alone was ineffective in decreasing TOS levels. Studies with higher dosages and longer treatment periods are needed to better observe the effects of nutritional supplements on TOS and TAS parameters in inflammatory bowel diseases.

Keywords: Probiotics, omega-3 fatty acids, total antioxidant level, total oxidant level, colitis, inflammatory bowel diseases

1. INTRODUCTION

Inflammatory bowel disease (IBD) is a systemic disease with an unknown etiology, believed to arise from the interaction between genetic, environmental and intestinal immune factors (1). It is suggested that IBD is caused by an imbalance between pro-oxidant and antioxidant mechanisms (2). Excessive production of oxygen-derived free radicals creates a negative effect on various biological systems (3). Inflammation is directly related to oxidative stress. Conditions such as the increase in the production of free radicals, the inefficacy of the antioxidant defense system cause oxidative stress by disturbing this balance (4,5). Oxidative stress is defined as a condition that causes damage to the organism as a result of the deterioration of the balance between oxidants and antioxidants. It can also occur as a result of an increase in the amount of reactive hydrogen and nitrogen species (RONS) formed by the activation of phagocytic cells. (6,7). Substances produced by oxidative damage are defined as oxidative stress markers. Malondialdehyde (MDA), the final product of lipid peroxidation, is one of these substances (8,9). Lipid peroxidation caused by hydroxyl and superoxide radicals is the key reaction that damages the intestinal mucosa (10). Various animal models and human studies reveal an inverse relationship between antioxidant (AOX) enzyme (11,12) and MDA levels (13). There are many markers used for the evaluation of oxidative stress and antioxidant status (14). However, measuring these markers separately is both

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time-consuming and expensive (15). Consequently, in recent years total oxidant level (TOS) (16) and total antioxidant level (TAS) have been measured (17).

Treatment of inflammatory bowel disease (IBD) usually involves medical therapy and aggressive therapeutic applications are recommended to control inflammation (18). The drugs used can pose a risk to the patient as it can trigger the development of opportunistic infections (19). As a result, it is recommended to seek alternative treatment methods such as nutritional therapy or nutritional support (20). Probiotics are living microorganisms that have a health benefit to the host when taken in sufficient amounts. It was shown that probiotics, especially bifidobacteria, affect cytokine release and reduce mucosal inflammation in IBD animal models (21,22). It is known that w-3 fatty acids, which are among long-chain fatty acids, have strong anti-inflammatory properties (20). The aim of this study is to evaluate the effects of probiotics and w-3 fatty acids on total oxidant and total antioxidant levels in an experimental colitis model.

2. METHODS

2.1. General Plan of the Study

In this study, BALB/c mouse (n=50, aged 6-8 weeks) with weights ranging from 20-30 g were used. The mice were given ad libitum fresh drinking water and standard laboratory chow, in a room where the temperature was 21±2°C'. Their natural night-day cycle was protected. Mice were randomly divided into five groups (n= 10/group) as healthy (non-colitis) group, colitis group, group treated with probiotics (colitis induced mice treated with probiotics), group treated with omega-3 (colitis induced mice treated with w-3), group treated with probiotics+omega-3 (colitis induced mice treated with both probiotics and w-3). Some of the mice died during the study due to diarrhea, aspiration, etc. Analysis was conducted on 29 remaining mice. Ethical Committee approval was taken from Istanbul Medipol University Animal Experiments Local Ethical Committee dated 05/12/2014, numbered 38328770/83.

2.2. Experimental Colitis Model

The mice were not given any food, they were only given free access to water 24 hours before the experiment. Anesthesia was intraperitoneally injected at a dose of 80 mg/kg ketamine hydrochloride (Ketalar, Parke Davis ve Eczacibasi, Istanbul) and 10 mg/kg xylazine hydrochloride (Rompun, Bayer HealthCare). A mixture of 2-6 mg (200 mg/kg) of dinitrobenzene sulfonic acid (DNBS)+30% ethanol was given rectally to mice under anesthesia to create experimental colitis, except for the healthy group (23). Phosphate-buffered saline (PBS) was given to the healthy group under the same conditions. Figure 1 shows the protocol of DNBS-induced colitis.

2.3. Nutritional Supplementation

Ten days after colitis induction, the groups received probiotics, w-3, probiotic plus w-3 , or PBS alone (control non-colitis and control colitis groups) for ten days (day 14-23). The VSL#3 probiotic mixture was prepared daily for ten days, dissolved in 200 mL drinking water and administered intragastrically to the probiotic and probiotic plus w-3 groups. VSL#3 is a mixture of one billion CFU of freeze-dried probiotics in one capsule, consisting of eight bacterial strains including three strains of bifidobacteria (B longum, B infantis, and B breve), four strains of lactobacilli (L acidophilus, L paracasei, L delbrueckii subsp. bulgaricus, and L plantarum), and Streptococcus salivarius subsp. thermophilus (Sigma-Tau Pharmaceuticals (Gaithersburg, MD, USA). Additionally, mice in the w-3 and probiotic plus w-3 groups received a 300 mg/kg dose of w-3 fatty acids intragastrically for ten days. The w-3 is a soft gel form of w-3 containing 504 mg EPA and 378 mg DHA per capsule (Omega 950, Solgar, Turkey, Inc).

2.4. Collection of Samples

Mice were sacrificed by cervical dislocation, the rectum was removed with median laparotomy and gently cleaned with normal saline. The longitudinally divided colon segment was maintained at – 80°C for determination of total oxidant and total antioxidant levels.

2.5. Tissue Homogenization

Colon material, obtained by the sacrification of experimental animals, was weighed, and RIPA (Santa Cruz) solution was added per sample for lysis at 2 times the mass observed in the weighing; the added RIPA solution also contains a protease inhibitor cocktail. In the next stage, the tissues were subjected to mechanical decomposition manually on the ice. Then samples were centrifuged for 30 minutes at 14,000 rpm at +4°C, and supernatants were collected.

2.6. Determination of Antioxidant Capacity and Oxidative Stress

TAS and TOS levels of colon tissue homogenates were automatically measured by using the Chromate Manager 4300 (Palm City, USA) analyzer. Absorbance levels of dianicidyl radicals formed as a result of the Fenton reaction were determined in TAS measurement. The antioxidant effect in the samples was then calculated for Trolox equivalent (mmol equiv/L) (Rel Assay Diagnostics, Gaziantep, Turkey). In TOS measurement, in the presence of oxidants, the absorbance caused by the ferric ions that consist of the ferrous iono-dianicide complex was determined. Calibration was carried out with hydrogen peroxide, and TOS levels were determined as mmol H_2O_2 Eq/L (Rel Assay Diagnostics, Gaziantep, Turkey).

2.7. Statistical analysis

Quantitative data obtained from mice were tabulated by calculating their mean (mean) and standard deviations (SD). Qualitative data was given as number (n). The distributions of the groups were evaluated by one-sample Kolmogorov-Smirnov test from non-parametric tests. Groups that showed normal distribution were evaluated with one-way ANOVA (post hoc Tukey's HSD test for binary comparisons). Statistical analyses were carried out using the SPSS 15.0 package program, $p<0.05$ expressed statistical significance.

3. RESULTS

As shown in Table 1, lower concentrations of TOS ($p>0.05$) were observed in the probiotics (2.11±0.23 mmol H_2O_2 Eq/L), probiotics+w-3 (2.56±1.18 mmol H_2O_2 Eq/L), and w-3 (3.02±1.88 mmol H_2O_2 Eq/L) groups compared to the colitis group (3.11±0.91 mmol H_2O_2 Eq/L). The lowest TAS level was determined in the probiotic group (1.49±0.32 mmol H_2O_2 Eq/L). Higher TOS and TAS level were observed in the control colitis group compared to the other groups. However, the differences were not statistically significant.

Table 1. *TOS and TAS levels of different groups*

	TOS	TAS
	(mmol H_2O_2 Eq/L)	(mmolTrolox Eq/L)
	Mean± SD	Mean± SD
Healthy Group (n=6)	2.89±1.04	1.53±0.55
Colitis Group (n=6)	3.11±0.91	1.92±0.48
Probiotics Group (n=5)	2.11±0.23	1.49±0.32
Omega-3 Group (n=6)	3.02±1.88	1.85±0.33
Probiotic+Omega-3 Group (n=6)	2.56±1.18	1.50±0.43
p†	0.101	0.264

TOS: total oxidant status, TAS: total antioxidant status, mmol: millimole, H_2O_2: Hydrogen Peroxide, Eq: equivalent, L: Litre

4. DISCUSSION

Oxidative stress occurs as a result of excessive oxidant radical formation or due to the lack of antioxidant defense molecules and has an active role in the pathogenesis of IBD (24,25). An increase in MDA tissue level indicates an increase in free oxygen radicals (26). In this study, we found the highest TOS level and the lowest TAS level in the colitis group. Similarly, it has been reported that serum TOS levels increase in experimental colitis models (14,27). One study reported that TOS was significantly reduced in IBD patients compared to healthy controls (25). Probiotics suppress bacterial translocation and reduce the number of enterobacteria and enterococci in the ileum and cecum. In a study examining the protective properties of kefir in an experimental colitis model created in rats, it was found that the group receiving kefir had statistically significant lower MDA levels compared to the group that did not receive kefir (28). The effect of B. infantis strain was examined in rats with colitis; it was found that the MDA level was significantly lower compared to the colitis group that did not receive probiotic support (29). In accordance with our study, Mane J et al. (30) showed that the group supported by probiotics had lower level of oxidative stress. Some studies have found that probiotic supplementation did not affect oxidative stress level (31,32) just like w-3 supplementation (33). Morampudi et al. (34) reported that w-3 supplementation reduces oxidative stress. In a meta-analysis on inflammatory bowel diseases, the contribution of w-3 supplementation to the oxidation state was controversial. The same meta-analysis reported that w-3 fatty acids were safe but ineffective for the remission of ulcerative colitis (UC) and Crohn's disease (33). In this study, the highest and lowest TOS levels were determined in colitis and probiotic + omega-3 groups, respectively. Decreased TOS levels in groups receiving probiotic supplements showed that probiotics have an important role in oxidant capacity. The use of w-3 together with a probiotic supplement was found to be more effective than using w-3 alone in reducing TOS levels.

Oxidative stress causes damage by affecting biomolecules and organs in the organism. In normal physiological conditions, there is a balance between oxidant and antioxidant mechanisms (24). It was reported that antioxidant enzyme activities (catalase, glutathione, peroxidase, etc.) and glutathione levels, one of the endogenous antioxidants, were decreased in IBD (35). Decreased antioxidant enzyme levels were also observed in previous studies with IBD patients (10,36). Studies showed that TAS was significantly reduced in IBD patients compared to healthy controls (25,37). On the contrary, D'Odorico et. al (38) stated that individuals with the disease had higher antioxidant enzyme levels compared to healthy individuals. In this study, similar to the study of D'Odorico et. al (38) it was determined that the colitis group had the highest TAS level ($p=0.264$). It is thought that the reason for the high level of TAS in the colitis group was increased functioning of cellular antioxidant systems resulting in increased oxidant production.

Probiotics and w-3 are among the current treatment choices for IBD. It has been reported that probiotics have anti-inflammatory effects in the gut (39,40) and increase antioxidant capacity (39) but there is no sufficient evidence for w-3 fatty acids (41,42). In our study, TAS levels were found to be higher in groups that received probiotic or omega-3 supplements compared to the healthy group. The TAS level of the w-3 group was higher compared to the healthy group, but the difference was not statistically significant. Similar to our study, in a study examining the effects of omega supplementation on antioxidant enzyme levels in inflammatory bowel diseases, it was reported that the patient group had higher antioxidant enzyme levels compared to the healthy control group but the difference was not statistically significant (43). Initially, we thought that the lowest TAS level would be in the colitis group but on the contrary, the highest TAS level was found in this group. This suggests that both the dose used and the duration of support may be insufficient

in the supplementation groups. In this study, we measured TOS to determine oxidant capacity and TAS to determine antioxidant capacity using intestinal tissues. However one of the limitations of our study was that oxidative damage markers and antioxidant molecules were not determined to evaluate oxidative stress and antioxidant status.

5. CONCLUSION

It has been suggested that probiotics are effective in decreasing total oxidant capacity and w-3 in increasing total antioxidant capacity. The use of w-3 together with a probiotic supplement was found to be more effective than w-3 use alone in reducing TOS levels. In addition, it has been observed that the combined use of omega and probiotic supplements is more effective in increasing TAS levels than using omega or probiotics alone. Studies with higher dosages and longer treatment periods are required for IBD to observe the effects on TOS and TAS parameters better. It seems that the immune cells, oxidant, and antioxidant systems of IBD patients have not been evaluated in detail in the literature. These mechanisms have not yet been clearly resolved and more research is needed. We suggest that it would be useful to examine the status of TAS and TOS together with oxidative damage markers and antioxidant molecules in future studies.

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Clinical and Experimental Health Sciences

Exercise Program for Covid-19 Survivors: A Telerehabilitation Framework

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ABSTRACT

Coronavirus disease (COVID-19) is a serious acute respiratory syndrome that has been recognized as a pandemic disease caused by Coronavirus 2 (SARS-CoV-2). The complications related to coronavirus itself, physically inactive period due to symptoms of disease and lockdown may also influence the functional capacities of COVID-19 survivors negatively. It may lead to obstructions in engaging with previous activities of daily living. As a physiotherapy intervention, exercise treatment is one of the novel approaches to support these individuals after the COVID-19 treatment. However, there is limited access to physiotherapy and rehabilitation services during pandemic conditions because of lockdown, especially for infected patients. For increasing accessibility to physiotherapy and rehabilitation care, the World Confederation of Physical Therapy has published a report advising the home-based exercise interventions via Telerehabilitation. Up to date, there is no published framework for structured exercise programs for this population, yet. Since the individual differences in functional levels and possible differences in the severity of coronavirus infection, the physiotherapy, and rehabilitation exercise program should be structured individually for COVID-19 survivors. This document suggests a framework for physical therapists to put into practice an exercise training via telerehabilitation in COVID-19 survivors. The proposed framework has consisted of determination of eligible and risky COVID-19 patients for intervention, physiotherapy assessment tools, 6-week exercise prescription based on FIIT-VP principle (frequency, intensity, time, type, volume, and progression) and criteria for ending exercise.

Keywords: COVID-19, Telerehabilitation, Exercise.

1.INTRODUCTION

COVID-19 disease, an infection caused by severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2), was firstly reported in the world on 31 December 2019. COVID-19 contamination occurs easily with contact respiratory droplets, via contact with infected persons, or contaminated objects and surfaces (1,2). The average incubation period of the infection varies between 2-14 days (3).

Up to end of July 2020, 216 countries, areas or territories affected by COVID-19 pandemic with more than 15 million infected cases worldwide have been reported by the World Health Organization. Turkey is one of the most affected countries in the world with the number of 227,982 infected cases (4). While 80% of people with COVID-19 virus have mild to moderate disease-specific symptoms, 6.1% of patients require treatment in the intensive care units (5). Among these cases, 210,400 have recovered and 5,600 have died by the fatality rate of 2,48% in Turkey (4).

After recovery COVID-19 survivors face multifarious health problems. Although the nature of the disease and its long terms effects still require further research, various system involvement including respiratory, cardiac, neurological, muscular systems has been well highlighted by scientific researches (6,7,8). Musculoskeletal system affected by acute peripheral and respiratory skeletal muscle dysfunction accompanied by polyneuropathy and myopathy (8). These activations together result in decreased muscle strength, limited physical activity, impaired functional performance. As a consequence, COVID-19 survivors may suffer from poor quality of life.

Especially the patients who had received the treatment in an intensive care unit have a greater risk of long-term complications. Patients with older age than 65 years old, with comorbidities, having more than 7 days' length of stay in the intensive care unit, and history of mechanic ventilation are considered to be major risk factors related

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to disability and poor quality of life. Besides complications related to coronavirus itself, a physically inactive period due to symptoms of the disease and lockdown may also influence the functional capacities of COVID-19 survivors negatively. It would lead to obstructions in engaging with previous activities of daily living (9).

Exercise treatment is one of the novel approaches to support individuals with loss of functional capacities, having limitations in activities of daily living (10). Quality of life and health behavior of the patients with COVID-19 would be improved by restoring disturbed functions due to coronavirus infection through physiotherapy interventions. However, there is limited access to physiotherapy and rehabilitation services during pandemic conditions because of lockdown, especially for infected patients. For increasing accessibility to physiotherapy and rehabilitation care, the World Confederation of Physical Therapy has published a report advising interventions via home-based exercise programs with telerehabilitation (11). Home-based exercise programs have been proven to be cost-effective and significantly increase the functional capacities of individuals regardless of coronavirus influence in a 4–6-week timeframe (12). Exercise will also help them to recover chronic stress associated with the pandemic disease. All these mentioned parameters together would support the improvement in the immune system of the COVID-19 survivors (13).

Although exercise training is one of the fundamental treatment approaches in improving the quality of life of COVID-19 survivors up to date there is limited published framework for a structured exercise program in the COVID-19 (14, 15).

Since the individual difference in functional levels and possible difference in the severity of coronavirus infection, COVID-19 survivors should be assessed individually before prescribing an exercise program via telerehabilitation. The eligible patients should be well-identified, all risk should be eliminated and a proper exercise program should be developed according to functional levels.

This document suggests a framework for physical therapists to put into practice an exercise training via telerehabilitation in COVID-19 survivors. The proposed framework has consisted of determination of eligible and risky COVID-19 patients for telerehabilitation intervention, physiotherapy assessment tools via telerehabilitation, 6-week exercise prescription based on FIIT-VP principle (frequency, intensity, time, type, volume, and progression) and criteria for ending exercise.

2.METHODS

This framework was suggested by searching reviews and original articles conducted in “Exercise and COVID-19” and “Exercise and Telerehabilitation” and in combination of both keywords in PubMed database.

3.RESULTS

3.1.Exercise Prescription Via Tele Rehabilitation for COVID-19 Survivors

3.1.1. The eligible COVID-19 survivors for exercise program via telerehabilitation

Expert opinion advises that patients with COVID-19 diagnosis should complete their medical treatment 14 days before participating in any exercise program (16).

3.1.2. Risky groups for participating exercise via telerehabilitation in COVID-19

Patients who were hemodynamically unstable and have percutaneous oxygen saturation (SaO2) <95%, fever ≥38◦, stage 4 chronic kidney disease or need for dialysis, dyspnea> 3/10 (according to BORG scale), fatigue level > 3/10 (BORG scale), unstable blood pressure (blood pressure> 140/90 mmHg or <90/60 mmHg), Stage 3-4 heart disease (according to the New York Heart Association), congestive heart failure, myocarditis, ventricular arrhythmia, ischemic/hemorrhagic stroke, pulmonary arterial hypertension, presence of neurodegenerative disease, increased risk for deep venous thrombosis or history for deep venous thrombosis, transplantation history, receiving immunosuppressive therapy, widespread malignancy, Mini-Mental State Examination (MMSE) score<24, advanced level of osteoporosis and fracture, being pregnant may not suitable for exercise program via telerehabilitation (17,18).

3.2.Designing an Exercise program via Telerehabilitation for COVID-19 survivors

3.2.1. Online Assessments

Online assessments must be performed via easy, short, and simple assessment tools before participating in any exercise program. Table 1 suggests sample assessments that can be performed before prescribing an exercise program for COVID-19 survivors. These assessments include testing vital signs, physical activity level, exercise capacity, cardiopulmonary endurance, lower extremity functional muscle strength, depression, and anxiety level measurements.

Table 1. *Online Assessment Tools*

Vital signs: Heart rate, Blood pressure, Respiratory Rate, Fever
Functional Exercise Capacity Tests
2 Minute Walking Test
10 Meter Walking Test
Time Up Go (TUG) test
Sit to Stand Test (Lower extremity functional strength)
Questionnaires
International Physical Activity Questionnaire – Short Form
EuroQoL-5D (EQ-5D)
Self-Anxiety Scale (1-4)
Self-Depression Scale (1-4)

3.2.2. Criteria for ending exercise

Exercise sessions via telerehabilitation must be ended in case of an increase in heart rate above 85% of the predictive value, reduction in systolic blood pressure more than 20 mmHg, decrease in percutaneous oxygen saturation (SaO2) <93%, increase in breathing frequency> 30 breaths/ min, increased dyspnea, the onset of fatigue and pain, bradycardia, severe shortness of breath and feeling dizziness or lightheadedness, nausea or feeling sick, clamminess or sweating, chest tightness. Patients should be informed about these criteria and physiotherapists must be aware of checking these symptoms regularly (19).

3.2.3. Exercise Prescription

COVID-19 survivors have a different course of the disease since the virus can affect multiple systems in the body differently according to individual differences such as having comorbidity, smoking, and exercise habit and older age. Various effects of the virus may cause the COVID-19 survivors to have different exercise capacities following the infection.

Therefore, the classification of the patients according to their exercise capacity is an important approach before prescribing an exercise program. The Borg Scale is one of mostly used tool to measure overall exertion during physical activity. It is widely used to quantify perceived symptoms such as breathlessness and muscle fatigue during exercise (20).

It is suggested by the current paper to classify COVID-19 survivors into three categories such as being a sedentary or trained individual before COVID-19 diagnosis or being elder. Exercise capacity of individuals for both aerobic and resistance training are defined according to the modified Borg Scale (10 points) Baseline measurements would guide prescription of exercise program via telerehabilitation.

Six-week (three non-sequential exercise days per week) aerobic and resistance exercise program via Telerehabilitation is proposed according to the FITT-VP principle (Table 2 and Table 3). Stretching exercises are also included in the exercise design in the scope of warm-up and cool-down periods (21-23).

Table 2. *Aerobic Exercise Program for COVID-19 survivors*

Aerobic Exercise Training	Sedentary	Trained	Elderly
Intensity / Severity	Low (Borg 1-3) Moderate (Borg 3-5) High (Borg 5-8)	Low (Borg 1-3) Moderate (Borg 4-6) High (Borg 6-10)	Low (Borg 1-3) Moderate (Borg 2-4) High (Borg 3-7)
Exercise Type	Walking	Walking	Walking
Time	30-60 minute	30-60 minute	30-60 minute
Frequency	2-3 day/week	2-3 day/week	2-3 day/week
Total time per week	At least 150 minute	At least 150 minute	At least 150 minute
Progression	* Firstly increase in exercise time weekly (approximately 10%) ↓ * Secondly upgrade in intensity according to Borg Scale	* Firstly increase in exercise time weekly (approximately 10%) ↓ * Secondly upgrade in intensity according to Borg Scale	* Firstly increase in exercise time weekly (approximately 10%) ↓ * Secondly upgrade in intensity according to Borg Scale

Table 3. *Resistance Exercise Program for COVID-19 survivors*

Resistive Exercise Training	Sedentary	Trained	Elderly
Intensity / Severity	Extremely easy (Borg 1) Easy (Borg 2) Somewhat easy (Borg 3) Somewhat hard (Borg 5) Hard (Borg 7) Extremely hard (Borg 10)	Somewhat easy (Borg 3) Somewhat hard (Borg 5) Hard (Borg 7) Extremely hard (Borg 10)	Extremely easy (Borg 1) Easy (Borg 2) Somewhat easy (Borg 3) Somewhat hard (Borg 5) Hard (Borg 7)
Exercise Type: Number of Sets / Number of repetitions	Squat: 1-2 sets, 10 reps Push up: 1-2 sets, 10 reps Sit-up: 1-2 sets, 15 reps Walking lunges: 1-2 sets, 5 reps	Squat: 2-3 sets, 20 reps Push up: 2-3 sets, 20 reps Sit-up: 2-4 sets, 20 reps Walking lunges: 2-3 sets, 10 reps	Squat: 1-3 sets, 8-12 reps Push up: 1-3 sets, 8-12 reps Sit up: 1-3 sets, 8-12 reps Walking lunges: 1-2 sets, 5 reps
Frequency	2-3 days / week	2-3 days / week	1-3 days/week
Progression	Firstly, the increase in the number of repetitions, Secondly, the increase in intensity according to the Borg Scale		

4.CONCLUSION

Up to current knowledge, there is no published or suggested an exercise training framework for COVID-19 survivors. This paper would provide a sample exercise framework for physiotherapists who are willing to encourage their COVID-19 patients by means of regaining their functional capacities in their daily life. Moreover, this proposed exercise program via Telerehabilitation would also help them to overcome barriers to get face to face with their COVID-19 patients in the clinical environment during pandemic conditions.

This firstly announced exercise program via Telerehabilitation, actually at home, for COVID-19 survivors would also support public health by preventing crowded environments especially in health care centers.

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Clinical and Experimental Health Sciences

Treatment Approach for Oral Candidiasis: Two Case Reports

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ABSTRACT

Candida infections are acute and / or chronic infections of the skin, mucosa, internal organs and systems which may be seen at any age. The purpose of this study is to present diagnostic and therapeutic approach for patients who applied to our clinic with the diagnosis of pseudomembranous candidiasis. Both patients who referred to our clinic were using inhaler due to Chronic Obstructive Pulmonary Disease (COPD). Intraoral examination revealed pseudomembranous candidiasis localized on both the border of soft palate and through pharynx of a 60 year-old female patient and on the midline of hard palate of a 70-year-old male patient. Cultures were taken for mycological evaluation of the patients after clinical examination. Antifungal treatment was administered to both patients for 10 days. Healing was observed as a result of the treatment. No recurrence was observed at monthly follow-up assessments performed for patients. In cases of oral candidiasis, antifungal agents should be used locally in the form of suspension or pomade, evaluation of mycological culture should be performed to support clinical diagnosis and the etiological factors that may cause the disease should be studied.

Keywords: oral candidiasis, fungal infection, treatment approach

1. INTRODUCTION

The most frequent fungal infection is candidiasis, and it is caused by *Candida albicans*, a fungus present in 20-50% of healthy individuals. Other strains *(Candida tropicalis, Candida parapsilosis, Candida glabrata, Candida krusei, Candida guilliermondii)* are rarely responsible for candidiasis (1). In healthy individuals, without any local predisposing factor, *C. albicans* causes no clinical manifestations. Based on age and predisposing variables, multiple incidences were found (2, 3). Predisposing factors for candidiasis include local ones, such as xerostomia, poor oral hygiene, chronic mucosal trauma, use of local antibiotics, chronic use of inhalational and topical steroids, radiotherapy to the head area, and systemic ones, such as iron deficiency anemia, diabetes mellitus, primary immunodeficiency, HIV infection and AIDS, leukemia and other malignancies, neutropenia, use of steroids and immunosuppressive medication, broad-spectrum antibiotics, hypoparathyroidism, cortical adrenal insufficiency, and other endocrine diseases (1,3,4).

Oral candidiasis is prevalent and underdiagnosed in the elderly, especially in those wearing dentures, and can be avoided in certain instances with a proper mouth care regimen (5, 6). A wide variety of clinical symptoms are found in oral mucosal candidiasis (3-9). The diagnosis is mainly based on the history and clinical features with further investigations required only for difficult cases. Identification and possible resolution of local or systemic causative factors are essential for the treatment of candidal infection. Nystatin and miconazole are the drugs of choice for topical use. Triazoles (e.g., fluconazole, itraconazole) are useful systemic agents. The dosage and duration of treatment largely depends on the type of candidiasis and the presence of predisposing factors (7,8).

2. CASE PRESENTATION

2.1. Case I

A 60-year-old female patient was referred to the Department of Oral Diagnosis and Radiology Clinic of the Marmara University Faculty of Dentistry by a clinician who observed unhealed oral mucosal lesions on hard and soft palate for one and a half month. A medical history revealed that she had Chronic Obstructive Pulmonary Disease (COPD) and she was treated with bronchodilator (inhaler) as a reliever. On intraoral examination, whitish-yellow, slightly elevated spots were observed on her hard palate and soft palatal region (Fig. 1a, b). On scratching, lesions became scrapable and left diffuse erythematous patches. Smear made from lesion scraping was sent for cytological analysis to validate the existence of candidate hyphae (Fig. 2). Final diagnosis of drug-induced

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pseudomembranous candidiasis was performed on the basis of history, clinical appearance and cytological report. For around 10 days, the patient was recommended to use Nystatin suspension about 4-5 times a day. Within 15 days, the patient was witnessed a serious remission of the lesions (Fig. 3).

Figure 1. *Whitish-yellow, slightly elevated scrapable spots underlying erythematous surface (a, b) on the midline of hard palate.*

Figure 2. *Culture of samples obtained from first case showing candidal colonies (C.albicans)*

Figure 3. *Remission of the lesions after antifungal therapy*

2.2. Case II

A 70 – year-old male patient was referred to the Department of Oral Diagnosis and Radiology Clinic of the Marmara University Faculty of Dentistry by a clinician who observed unhealed oral mucosal lesions on hard and soft palate for one and a half month. A medical record showed he was hypertensive and had COPD. The patient was treated with bronchodilator (inhaler) as a reliever. On intraoral examination, whitish-yellow, slightly elevated spots were observed on the midline of hard palate. (Fig. 4). The lesions become scrapable upon scraping and left dispersed erythematous patches. Smear from lesion scraping was submitted to verify the presence of candidate hyphaee for cytological examination (Fig. 5). On the basis of history, clinical presentation and cytological findings, the final diagnosis of drug-induced pseudomembranous candidiasis was carried out. The patient was also advised to use Nystatin suspension around 4-5 times per day for about one week. After the procedure, the patient was tested and displayed a serious remission of the lesions (Fig. 6).

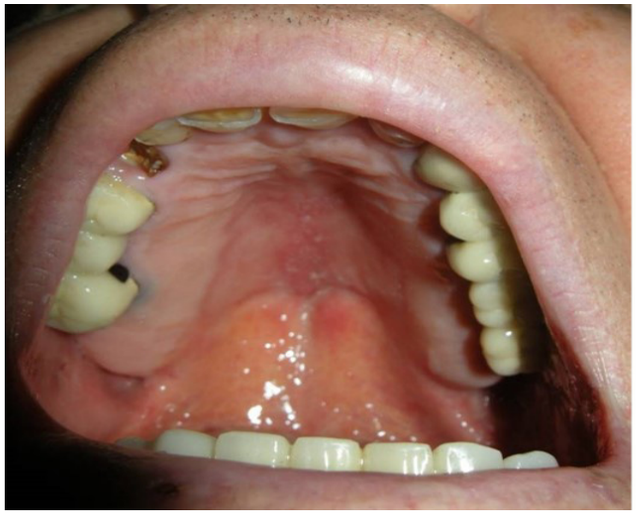

Figure 4. *Whitish-yellow, slightly elevated scrapable spots underlying erythematous surface on the midline of hard palate.*

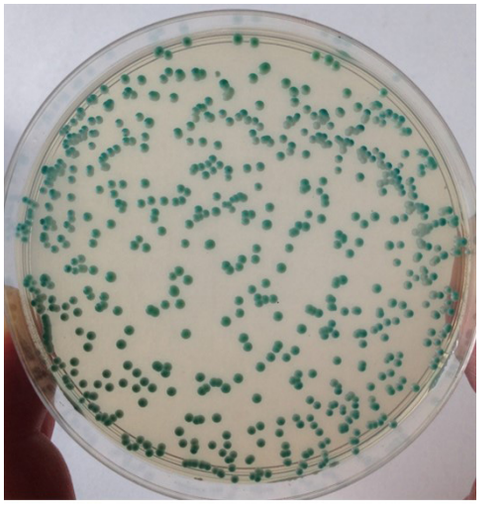

Figure 5. *Culture of samples obtained from second case showing candidal colonies (C.albicans).*

Figure 6. *Remission of the lesions after antifungal therapy.*

3. DISCUSSION

In patients with systemically immunocompromised diseases, fungal human infections caused by distinct *Candida* species vary from such inconsequential conditions such as oral or genital candidiasis to super-infections (9,10). Levels of frequency of *C. albicans* have been recorded as being between 45-65 % and 30-45 %, respectively, in the oral cavity of neonates, healthy children and healthy adults. In comparison, the prevalence figures are 50-65 % of persons wearing removable dentures, 65-88 % of those in acute and long-term care hospitals, 90 % of chemotherapy patients with acute leukemia, and 95 % of HIV patients.

Physiological causes such as old age, childbirth and pregnancy with altered immunity, local trauma, poor dental hygiene, malnutrition, use of broad-spectrum antibiotics, corticosteroids and inhalers, immune deficiencies such as HIV infection, endocrine disorders, malignancies such as leukemia, agranulocytosis, hyposalivation due to autoimmune diseases or head and neck radiation are certain reasons that predispose the host to oral candidiasis (11).

Oral candidiasis treatment should be in the direction for identification and correction of factors that may affect or contribute to the occurrence of oral candidiasis together with a detailed history (12). Any deficiency conditions (iron, folate, vitamin B12 and C) as well as diabetes mellitus or any immunodeficiency state should be investigated. Any pharmacological agent that may contribute to the occurrence of oral candidiasis should be determined and if possible, it should be used instead of an alternative drug. Salivary gland functions should be checked and, if necessary, saliva flow should be measured (13). Adequacy of prostheses in patients with denture stomatitis must also be considered. Oral and prosthetic hygiene should be evaluated and corrected. In addition, patients should be advised not to wear the prosthesis continuously day and night (14). If it is not possible to correct the underlying factors or, if not indicated, pharmacological treatment is required.

The mechanism of action of antifungal agents is to change the metabolism of RNA and DNA or to accumulate peroxide in the cell that is harmful to the fungal cell. Topical polyene or antifungal agents of azole are often effective. In most cases, patients are successful with Nystatin oral suspension (100,000 units/mL-1 mL topically) or nystatin pastilles (100,000 IU) four times a day for 7-14 days. Amphotericin tablets (10 mg) or suspension tablets (100 mg / mL) four times a day for 14-21 days after meals are also realistic. In addition, 2% Miconazole gel, approximately 2.5 mL topically, can be used four times a day after meals for 14-21 days. Miconazole is contraindicated in patients taking warfarin as it potentiates its effects (14,15).

In these reported cases, patients were also analyzed for potential structural factors alongside a proper history and clinical examination. Upon delivery of the final diagnosis, the appropriate therapy was selected by adding the antifungal agent nystatin. Against a large spectrum of yeasts and yeast-like fungi, nystatin is both fungistatic and fungicidal in vitro (9-11,14). In repeated subculture, Candida albicans shows no substantial resistance to nystatin in vitro in increasing nystatin levels and therapy has been adequately successful in healing lesions. When patients were re-evaluated at the follow-up visit, complete remission of the lesions was found.

4. CONCLUSION

The key duties of every dental specialist are diagnosing oral candida lesions together with effective treatment steps. In order to diagnose this clinical issue, proper documentation of medical history is necessary. Where feasible, predisposing factors should be handled or removed. In conclusion, two reports of oral candidiasis triggered by an inhaler have been reported. These forms of reactions are normal in patients receiving an inhaler, so we highly suggest that diagnosis should be carried out immediately. Timely treatments should be carried out and pursued in order to minimize this adverse effect among patients receiving inhaler therapy. Nystatin therapy can be effective in cases of inhaler-induced oral candidiasis.

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