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The target audience of the journal is all scientists working in the field of health, graduate students and researchers in this field.

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Middle Black Sea Journal of Health Science

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Author Contributions: Concept: …….., Design: …….., Literature search:……..... Data Collection and/or Processing: ……..., Analysis and/or Interpretation:……, Writing - …….

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Levine WC, Pope V, Bhoomkar A, Tambe P, Lewis JS, Zaidi AA, et al. Increase in endocervical CD4 lymphocytes among women with nonulcerative sexually transmitted diseases. J Infect Dis. 1998;177(1):167–174.

Chapter in Edited Book: Hornbeck P. Assay for antibody production. In: Colign JE. Kruisbeek AM, Marguiles DH, editors. Current Protocols in Immunology. New York: Greene Publishing Associates; 1991. p. 105-32.

Book with a Single Author: Fleiss JL. Statistical Methods for Rates and Proportions. Second Edition. New York: John Wiley and Sons; 1981. p. 105-32.

Editor(s) as Author: Balows A. Mousier WJ, Herramaflfl KL, editors. Manual of Clinical Microbiology. Fifth Edition. Washington DC: IRL Press. 1990. p. 105-32.

Conference Paper: Entrala E, Mascaro C. New structural findings in Cryptosporidium parvum oocysts. Eighth International Congress of Parasitology (ICOPA VIII); October 10-14; Izmir-Turkey: 1994. p. 1250-75

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Methods

Results

Discussion

Conclusion

Acknowledgements

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Whole text should not exceed 4500 words except for resources and English summary.

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Key Words

Introduction

Methods

Results

Discussion

Conclusion

Acknowledgements

References (most 20)

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Structure

Title

Abstract (average 100-300 word)

Key words

Introduction

Case report

Discussion

Conclusion

Acknowledgements

References (most 20)

Whole text should not exceed 2200 words except for resources and English summary.

d) Review articles

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Key words

Introduction

The compilation text also including appropriate sub-headings,

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Abstract

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Key words

Surgical technique

Conclusion

References (most 15)

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Structure

Cover Letter

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Abstract (average 100-150 word)

Key words

Topics related to the subject.

Conclusion

References (3-5 inter)

h) Original Images: Rarely seen annotated medical images and photographs in the literature.

Structure

300 words of text and original images about the subject

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Structure

Topics related to the subject.

References (3-5 inter)

i) Questions and Answers: Are the texts written in form of questions and answers about scientific educative –instructive medical issues.

FEBRUARY 2022 **VOLUME 8** **ISSUE 1**

CONTENTS

EDITORIAL

With Strong Steps…

We are happy to be together with interesting and covid-19 articles during the normalization process.

We would like to express our sincere thanks to all the researchers who contributed.

Our journal will grow even more with your efforts.

Hope to meet in other issues ...

PhD, Assoc. Prof. Ülkü KARAMAN

Editor

Middle Black Sea Journal of Health Science / Mid Blac Sea J Health Sci **February 2022; 8(1):1-8**

RESEARCH ARTICLE **DOI:** 10.19127/mbsjohs.979585

Evaluation of Gross Alpha and Beta Radioactivity Concentrations in Tooth Samples

Zerrin Unal Erzurumlu[1](ID), Arzu Sahin[2](ID), Cigdem Guler[3](ID), Mehmet Melih Omezli[4](ID), Mehmet Emin Korkmaz[5](ID), Osman Agar[6](ID), Soner Cankaya[7](ID)

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Received: 06 August 2021, Accepted: 03 November 2021, Published online: 25 February 2022

Abstract

Objective: Teeth are used as an important data source to estimate radioactivity accumulation in individuals. This study aimed to evaluation the gross alpha (GA) and gross beta (GB) radioactivity concentrations in tooth samples.

Methods: Mandibular permanent first molar teeth of individuals living in the Middle Black Sea region were used for the study to ensure standardization. The teeth samples were divided into 4 groups according to the age factor (Group 1: 6-15 years, Group 2: 16-30 years, Group 3: 31-45 years, and Group 4: 46-65 years). Each group was divided into two subgroups according to gender factor. Measurements were completed with a nuclear spectroscopic system containing a gas-flow proportional counter. Data were analyzed statistically.

Results: While a statistically significant difference was detected among groups for GA radioactivity concentration ($p<0.05$), no significant difference was detected among groups for GB ($p>0.05$). Mean GA value was higher in Group 1 (6-15 years) compared to the other groups. There was no statistically significant difference between the genders in both GA and GB radioactivity concentrations for all groups ($p>0.05$).

Conclusion: While the GA radioactivity concentration was affected by the age factor, it was not affected by the gender factor.

Keywords: Teeth, gross alpha, gross beta, radioactivity, radiation

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INTRODUCTION

Radiation is a natural part of our environment and is defined as "energy traveling through the environment". Radiation is investigated under two main headings of ionizing radiation and non-ionizing radiation according to the amount of energy transported. Radiation with real importance in terms of human health and the environment is ionizing radiation (1,2).

The human body is exposed to natural and artificial sources of ionizing radiation. Natural radiation sources comprise the largest portion of radiation exposure every year and may be classified in two broad categories as cosmic and terrestrial contributions. High-energy cosmic rays and secondary radiation formed in the atmosphere comprise the cosmic contribution. Radioactive nuclides produced during the earth's formation and still found in the crust comprise the terrestrial contribution. Exposure to Radon (^{222}Rn) forms the most significant contribution to total dose (1,3,4). Artificial sources are due to human activities involving industrial and nuclear technology including medical applications, nuclear reactors, atmospheric nuclear tests and accidents, and traditional mining operations. Though it may vary in different regions in the world, it is considered that an individual is exposed to about 2.4 mSv of natural radiation each year. The maximum dose permitted professionally is 20 mSv annually. Annual exposure to artificial radiation sources comprises a relatively lower amount of the dose. Just as the human body is exposed to external radiation due to pollution of air, soil, water, and plants by radioactive elements, it may be exposed to internal radiation with transport of radioactive material into the human body and accumulation in certain regions of the body (5,6).

Radioactivity is the process of spontaneous fission or decay of unstable atoms or elements to gain more balanced nuclear structure. Unstable elements have natural radioactivity. Stable elements are made radioactive as a result of core bombardment in nuclear reactors to create artificial radioactive elements which produce radiation as a result of radioactive decay (5,7,8).

Alpha particles comprise two neutrons and two protons; as a result, the electrical load is positive. Alpha radiation comes from naturally formed elements like uranium and radium and from some human-made elements. Due to their load and heavy mass, alpha particles densely ionize matter and rapidly lose their energy. They cannot pass the first layer of the skin; however, if a material releasing alpha particles is eaten as food or taken in through the airway, they may affect body cells (9). Beta particles are rapidly moving electrons or positrons emitted from an atom. They may travel several cm through skin or water. They can be stopped by thin aluminum or plastic sheets. GA and GB activity concentrations are defined as total radioactivity from all alpha and beta emitters (10,11). GA and GB' measurements have the quality of indicators, with radioactivity of radioactive material releasing alpha or beta rays determined in Becquerels (Bq) (10,11).

Due to their slow metabolism and retraction, teeth have recently been used for biological modeling. The presence of trace elements in dental structures covers a wide range of fields from archeology to environmental studies, and biomedicine. Teeth provide important scientific data about some

substances found in the individual's body. Recently, it has become popular to use human teeth for both radioactivity measurements and fundamental analysis studies (5,10).

Teeth have been used as an important data source in determining the accumulation of radioactivity of individuals (4,12-14). Teeth have been investigated for GA and GB radioactivity concentrations in different region from Turkey (4,5,15-17). However, the work done in the Black Sea Region is limited (15,17). The aim of this study is to determine the GA and GB concentrations in permanent tooth samples belonging to individuals living in the Central Black Sea region. The null hypotheses tested were that (1) the age factor does not affect GA and GB radioactivity concentrations values, and (2) gender factor does not affect GA and GB radioactivity concentrations values.

METHODS

The Clinical Research Ethics Committee of Ordu University approved this study (2017/100). This study follows the Helsinki Declaration. In addition, informed consent was obtained from patients, giving permission to use the teeth for the study purposes after removal.

For creation of study groups and determination of sample size in the groups, Mangano et all's (18) study was used as a guide. Accordingly, with alpha=0.05 and Power=0.80, the minimum sample number required per group is 23. The sex distribution in each group was assigned so as not to create a statistical difference.

A total of 97 mandibular permanent first molar teeth were used for the study. The teeth samples were obtained from individuals between the ages of 6-65 and living in the Middle Black Sea province, who were decided to have a tooth extraction for any reason at Ordu University Faculty of Dentistry. In addition, teeth samples with any restoration, teeth samples of individuals who smoked, had previous exposure to any imaging method involving radiation for the head-neck region, or and radiotherapy were not included in the study.

Preparation of samples and groups

The teeth samples were divided into 4 groups according to the ages of the individuals as Group 1: aged with 6-15 years (n=25), Group 2: aged with 16-30 years (n=25), Group 3: aged with 31- 45 years (n=23), Group 4: aged with 46-65 years (n=24). Additionally, they were investigated according to the gender of the individual.

Each sample was stored in physiological saline (Osel/ İstanbul/ Turkey). They were mechanically cleaned with a hard brush and weights were recorded. They were dried in an oven for 120 min (Mipro – MLF, Turkey). Then pressed and ground for 60 seconds. The powdered samples were transferred to stainless steel planchettes. All samples had GA and GB activity concentrations counted with a nuclear spectroscopic system containing gas-flow proportional counters (MPC-9604-ASC-950-DP, USA) (4,19-22). The system was calibrated for alpha and beta energies. Standard samples with equal concentrations were preperated. To calibrate the alpha and beta energies in the system 241Am (3.78 kBq) and 90Sr (3.76 kBq) were used. Count efficiency for the system was 38-40 % for alpha and 95-99 % for beta radiation. Each sample was counted three times. The results are given as arithmetic mean with standard error (4,19).

Statistical analysis

GA and GB radioactivity concentration values obtained in the research with the aim of revealing differences according to research groups and individual gender, firstly had the normality assumption checked with the Shapiro-Wilk test ($p<0.05$). Based on the results of the normality test, differences among the age groups in terms of measurement values were determined with the Kruskal-Wallis and Dunn's multiple comparison tests. Differences according to gender were determined with the Mann-Whitney U test. The correlation between ages of individuals with GA and GB values was determined with the Spearman's rho correlation coefficient. Research findings are given as n, mean, standard deviation, median and IQR values. All statistical calculations were performed in the SPSS V. 22.0 statistical program. Research findings had significance level of $p<0.05$ accepted as significant.

RESULTS

The distribution of GA and GB concentrations is presented in Table 1. Statistically significant difference was detected among groups for GA radioactivity concentration ($P<0.05$). Mean GA value was higher in Group 1 (6-15 years) compared to the other groups ($P<0.05$). However, there was no statistically significant difference between the groups for GB radioactivity concentration ($P>0.05$). There was no significant correlation identified between age and GA and GB radioactivity concentrations ($r = -0.173$, $P=0.090$ and $r=0.022$, $P= 0.828$, respectively).

The mean GA and GB radioactivity concentrations values were 0.167±0.102 Bq/g and 0.459±0.805 Bq/g, respectively. The minimum and maximum GA radioactivity concentrations values were 0.056 and 0.610 Bq/g. The minimum and maximum GB radioactivity concentrations values were 0.043 Bq/g and 2.799 Bq/g.

The mean GA and GB radioactivity concentrations for male and female individuals in the study according to age groups are given in Table 2. There were no significant differences between the genders for both GA and GB radioactivity values in groups ($P>0.05$). When all tooth samples are assessed according to the gender of individuals, the mean GA and GB values in female were 0.159±0.100 Bq/g and 0.552±0.889 Bq/g, the mean GA and GB values in male were 0.177±0.105 Bq/g and 0.346±0.683 Bq/g, respectively.

Table 1. Distibution of GA and GB radioactivity concentrations

Groups		n	Mean	Std. Deviation	Median	IQR	P*
Gross Alpha	Group 1	25	0.249[a]	0.157	0.149	0.271	**0.002**
	Group 2	25	0.129[b]	0.053	0.119	0.058	
	Group 3	23	0.129[b]	0.027	0.140	0.041	
	Group 4	24	0.159[ab]	0.061	0.144	0.069	
Gross Beta	Group 1	25	0.531	0.897	0,099	0,061	0.657
	Group 2	25	0.308	0.688	0.093	0.021	
	Group 3	23	0.460	0.713	0.096	0.056	
	Group 4	24	0.539	0.920	0.097	0.087	

Different superscripts **a** and **b** show statistically significant difference among groups ($P<0.05$)
P*=Kruskal-Wallis Test

Table 2. GA and GB radioactivity concentrations for genders according to groups

	Gender	n	Mean	Std. Deviation	Median	IQR	P*
				Group 1			
Gross Alpha	Male	13	0.270	0.145	0.205	0.270	0.183
	Female	12	0.226	0.173	0.144	0.226	
Gross Beta	Male	13	0.280	0.658	0.094	0.033	0.341
	Female	12	0.803	1.061	0.101	2.102	
				Group 2			
Gross Alpha	Male	8	0.110	0.034	0.108	0.062	0.336
	Female	17	0.138	0.058	0.120	0.088	
Gross Beta	Male	8	0.154	0.197	0.091	0.058	0.749
	Female	17	0.380	0.822	0.093	0.015	
				Group 3			
Gross Alpha	Male	8	0.146	0.019	0.144	0.006	0.098
	Female	15	0.119	0.027	0.130	0.052	
Gross Beta	Male	8	0.531	0.800	0.097	1.243	0.651
	Female	15	0.421	0.689	0.096	0.022	
				Group 4			
Gross Alpha	Male	15	0.148	0.055	0.141	0.035	0.310
	Female	9	0.176	0.069	0.149	0.112	
Gross Beta	Male	15	0.406	0.822	0.096	0.034	0.493
	Female	9	0.762	1.079	0.116	1.694	

P*= Mann-Whitney U test

DISCUSSION

The human body is exposed to external radiation due to pollution of air, soil, water, and plants by radioactive elements. Humans may be exposed to internal radiation due to intake of radioactive material through different routes including the respiration system, digestive system, or dermal absorption. These elements accumulate in different sections of the organism linked to the chemical properties (5). As a result, it is very important to analyze individuals for some radioactive material with properties of accumulating in the body. Total exposure to natural or artificial ionizing radiation sources may be determined by investigating teeth. There are previous studies examining GA and GB values in drinking water and teeth (1,4,5,17,23). Therefore, in present study, GA and GB values were examined in dental samples.

In the current study, the effect of age and gender factors on GA and GB values was evaluated in permanent first molar tooth samples. Considering our results, while a statistically significant difference was detected among groups for GA radioactivity concentration, no significant difference was detected among groups for GB. Therefore, the first null hypothesis was partially rejected. In addition, no statistically significant difference was found between the genders in both GA and GB radioactivity concentrations for all groups. Therefore, the second null hypothesis was accepted.

We are exposed to many adverse effects due to exposure to artificial radiation for a variety of reasons during our lives and because of natural radiation affecting our bodies in nature. Radioactivity measurements are important to assess the effect of radiation on the environment and living organisms. This type of analysis may assist in preventing some health problems that may be experienced by of variations occurring from the first stage of life until the end in humans. As radionuclides (226Ra, 228Ra, 210Po, 40K) are similar to Ca in terms of structure

and precipitation properties, in the body accumulation occurs especially in bones and teeth (5,24,25).

There are limited numbers of studies about GA and GB activity measurement in teeth in the literature. Penna-Franca (26) reported the radionuclide concentration in teeth from HLNRA inhabitants in Brazil was 0.76±0.30 Bq/kg (ash). Yamamoto et al (13) measured 226Ra activity in permanent teeth and bones of those living in different places in Japan. They reported that there was no appreciable difference in concentration of 226Ra between various permanent tooth samples in different age groups in Tokyo (13). Sogut et al. (4) measured GA and GB activity concentrations in human tooth and stated GA and GB have different values for different age groups. The findings of our study are partially compatible with the findings of Sogut et al. (4). In our study, a significant difference was found between age groups for GA radioactivity concentration, and no significant difference was found between age groups for GB value. Different results may have been due to the regional and nutritional differences or the differences in the type of tooth used and the sample size. In addition, permanent first molar teeth may carry traces related to exposure doses during both intrauterine life and after birth. The use of natural and artificial foods such as breast milk and formula may also have caused the difference in results.

There are studies examining the mean GA and GB values in teeth in Turkey (4,5,17). Sogut et al. (4) reported the GA and GB values were 0.203-0.534 Bq/g and 0.010-0.453 Bq/g for females, 0.009–1.168Bq/g and 0.071–0.204 Bq/g for males, respectively in a study from Adıyaman in Turkey. Taskin et al. (5) reported the mean GA and GB values were 31.0-47.8 Bq/kg and 71.2-89.2 Bq/kg for females, 52.7-82.1 Bq/kg and 114.0-154.4 Bq/kg for males, respectively in a study from Istanbul, Turkey. Ugur et al. (17) compared GA and GB radioactivity in the Black Sea region and Cukurova region in their study and reported values were higher in the Black Sea region. In our study, the mean GA and GB values for teeth samples from females were 0.159±0.100 Bq/g and 0.552±0.889 Bq/g, males were 0.177±0.105 Bq/g and 0.346±0.683 Bq/g, respectively. Different results in the literature may be due to environmental conditions, eating habits and use of different sample sizes.

This study is considered to have some limitations. First, lack of personal information like occupation and diet of patients. Second, only permanent first molar teeth were examined. Different results can be obtained when different type of the teeth was included in the study. Third, tooth samples belonging to the individuals over 65 years of age were excluded from the study because the target n number in the group could not be reached. Finally, the sample size was limited due to the long duration of the analysis and the high cost. Data obtained in our study analyzing radioactivity in permanent first molar teeth from the Central Black Sea region provide valuable contributions to the literature. However, additional studies should be conducted to evaluate the effects of different parameters on GA and GB.

CONCLUSION

- Statistically significant difference was detected among groups for GA radioactivity concentration ($p<0.05$).
- Mean GA value was higher in Group 1 (6-15 years) compared to the other groups.

• No statistically significant difference between the genders in both GA and GB radioactivity concentrations for all groups ($p>0.05$).

Ethics Committee Approval: Ethics committee approval was received for this study from Ordu University Clinical Research Ethics Committee (2017/100)

Peer-review: Externally peer-reviewed.

Author Contributions: Concept: Z.U.E., A.S., C.G.; Design: Z.U.E., A.S., C.G.; Literature search: Z.U.E., A.S., C.G. M.M.O.; Data Collection and Processing: Z.U.E., A.S., C.G. M.M.O.; Analysis or Interpretation: Z.U. E., A.S., C.G., M.M.O., M.E.K., O.A., S.C.; Writing: Z.U. E., A.S., C.G., M.M.O., M.E.K., O.A., S.C.

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RESEARCH ARTICLE

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Covid-19 Fear and Compliance with Protective Measures of Students Who Continue Face-to-face Education During the Pandemic

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Abstract

Objective: This research was conducted to determine the conditions of Covid-19 fear and compliance with protective measures of students who continue face-to-face education.

Methods: The research was descriptively conducted between November 12-20, 2020. The universe of the study consisted of secondary and high school students in a province in The eastern black sea region of Turkey, and the sample consisted of 188 students who were reached by the snowball sampling method.

Results: In the study, the average score of the Covid-19 fear scale of the students was 18.88±6.66. 89.4% of the students said they regularly used masks, 86.7% said they regularly washed their hands and 67.6% said they regularly followed social distance rules. The educational status of the students' fathers (β= -0.314; p = 0.000), their families catching Covid-19 (β = -0.178; p = 0.012), and their anxiety about their families being sick (β= 0.195; p = 0.007) were found to be a significant predictor on the Covid-19 Fear Scale.

Conclusion: In the study, it was determined that most of the students have knowledge about the methods of protection against Covid-19. Students' fears of Covid-19 were found to be moderate. It is recommended that school health nurses increase their awareness by educating students about Covid-19 disease and preventive measures.

Keywords: Covid-19, Fear of Covid-19, Health, Nursing, School, Student

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INTRODUCTION

Covid-19 pandemic is an important public health problem affecting the entire world (1). With the increasing number of cases, Covid-19 has caused various difficulties for both countries and societies (2). One of these difficulties has been experienced in the field of education. According to UNICEF data, 56.6% of the students worldwide (990,324,537) were affected by the pandemic. According to the course of the pandemic, it is seen that schools apply different methods such as closed, partially open, open and interrupting education at the country level (3). Face-to-face education is continued in some countries by evaluating the risk level in the society (4). The first case of Covid-19 recorded in Turkey was observed on March 10, 2020. After the first case was seen, face-to-face education was suspended at all levels on March 16, 2020, and the distance education process started. Face-to-face education started gradually at some grade levels (kindergarten, primary school, middle school and high school) on 21 September 2020. As of November 17, 2020, due to the increase in the number of cases, face-to-face education was suspended again, and the distance education process started at all levels (5).

To minimize the transmission of the virus in schools that continue face-to-face education during the pandemic process, students, teachers, school staff and families should take comprehensive protective measures (1). Students, who have an important place in society, may be exposed to risk in terms of Covid-19 with face-to-face education (6). Studies show that children escape the disease lightly (7,8), and that contamination is minimized when children comply with social distance, masks, and personal hygiene rules, especially in the school environment (9). In this process, compliance with protective measures in the school environment is very important for the control of the pandemic. Students should follow protective measures such as wearing masks, hand hygiene, and paying attention to social distance rules (3,10).

The reasons such as continued uncertainty about the treatment of Covid-19 in society, an instant increase in case and death rates, and constant news about the pandemic in the media create fear (11). Studies show that mental health of individuals is affected due to the pandemic, and that emotions such as fear, panic, anxiety, stress and hopelessness are experienced (12-15). In the process of a pandemic, fear is an important emotion that activates a person to cope with an existing situation. However, the degree of fear is important. A high level of fear may cause a person's mental health to be negatively affected, and a low fear may cause protective measures to be ignored (16).

Determining the status of students' compliance with protective measures with Covid-19 fears is important for the course of the pandemic in schools. It is stated that determining students' covid-19 fears is especially important in terms of research and applications (12,17). In this context, it is necessary to make great efforts to effectively address the problems that may occur in "emergency" situations such as pandemics that affect the whole world and to avoid the long-term negative effects of these experiences such as anxiety and fear, especially on the psychosocial development of children (15). When the literature is examined, it is emphasized that the studies on students attending school are limited and that evidence should be created by making studies in

this field (18). School health nurses play an important role in preventing and controlling the spread of infectious diseases in the school environment (19). It is important for this study to be conducted by nurses, who are experts in the field of public health, to reveal the current situation and to provide suggestions to school health nurses. This research was conducted to determine the conditions of Covid-19 fear and compliance with protective measures of students who continue face-to-face education during the Covid-19 pandemic.

Research Questions

1. What does the nature of Covid-19 fear of students who continue their education face-to-face during the Covid-19 pandemic process?
2. Do the socio-demographic characteristics affect the fear of Covid-19 of the students who continue their education face-to-face during the Covid-19 pandemic?
3. What are the mask usage behaviors of students who continue face-to-face education during the Covid-19 pandemic process?
4. What is the hand washing behaviors of students who continue face-to-face education during the Covid-19 pandemic process?
5. What are the behaviors of students who continue their education face-to-face during the Covid-19 pandemic to obey the social distance rules?

METHODS

This research was descriptively conducted on students who continued face-to-face education during the Covid-19 pandemic in a province in the Eastern Black Sea region of Turkey between November 12-20, 2020. The universe of the study consisted of middle school (5th and 8th grades) and high school (9th and 12th grades) students who continued face-to-face education during the Covid-19 pandemic. The sampling consisted of 188 students who were reached using the snowball sampling method. The criteria for participating in the research are volunteering, obtaining parental consent, using a web-based smart device, and continuing face-to-face education.

Measures

The data of the study were collected using the "Information Form" and "Covid-19 Fear Scale".

Information Form: This form was prepared by researchers in line with the literature (11,12,15,20). The form consists of two parts. In the first part, there are 14 questions that determine the socio-demographic characteristics of the students (age, gender, class, family type, mother education, father education, monthly income level, knowledge about Covid-19, information source, catching Covid-19, family's catching Covid-19, worrying about the family in terms of the illness, thinking that they can be protected from Covid-19 and being knowledgeable about the methods of protection from Covid-19). In the second part, the practices of students on protection methods from Covid-19 were prepared within the framework of mask (14 questions), hand washing (8 questions) and social distance (17 questions) measures (21,22). Questions about protective measures are rated as yes-no-sometimes. After this form was prepared, it was finalized by taking the opinions of 5 experts.

Covid-19 Fear Scale: The scale developed by Ahorsu et al. (2020) was adapted to Turkish by Bakioglu, Korkmaz and Ercan (2020). The scale, consisting of seven questions, is a 5-point Likert (1: Strongly disagree, 5: Strongly agree) type. The scale

consists of one dimension. The scores that can be obtained from the scale range from 7 to 35. The total score obtained from all items of the scale reflects the level of Covid-19 fear experienced by the individual. A high score means experiencing a high level of fear. Cronbach's Alpha value of the scale is 0.88 (23,24). In this study, Cronbach's Alpha value was found to be 0.85.

The data collection procedures

In this study, data were collected through an online form. The form consists of two parts; the first part includes the consent form, and the second part includes survey questions. In the first section, there is a section containing the consent of the parents of the students. In this section, families of the students were asked to read the informed consent form carefully and fill in the questionnaire for the study of their children, if they found it appropriate. The consent form contained detailed information about the purpose, benefits and process of the study. With the approval of the parents, the students who volunteered to participate in the study were included in the study by answering the questionnaire questions. In this way, the consent of the children and parents who participated in the study and answered the questionnaire questions was obtained. The time given to the participants for each form is approximately 15 minutes. Within the scope of the data protection law, anonymity has been provided, personal data are kept and not shared with second parties.

Statistical analysis

The data of the study were analyzed in the SPSS 20.0 package program. The compliance of the data to normal distribution was evaluated with the Kolmogorov-Smirnov Test. The data were evaluated by descriptive statistics (number, percentage, arithmetic mean, standard deviation, minimum and maximum) and linear regression analysis. The significance level in the study was accepted as $p<0.05$.

RESULTS

It was determined that the average age of the students was 13.22 ± 2.92 (Min: 10; Max: 18), 60.6% were girls, 16.0% had an extended family, 34.0% had a primary school graduate mother, 28.7% had a university graduate father, and 51.6% had a family whose expenses were equal to the income. It was found that 2.1% of the students had no knowledge of Covid-19, 40.4% were informed by means of television, 2.1% caught Covid-19, families of 30.9% of the students had Covid-19, 77.1% were worried about their family being sick, 93.1% thought that they could protect themselves from the disease and 87.8% had knowledge about prevention methods. The average score of the Covid-19 Fear Scale of the students within the scope of the study was found to be 18.88 ± 6.66 (Min: 7; Max: 35) at a moderate level (Table 1). Students' age, gender, class, family type, mother and father education, monthly income, catching Covid-19, having Covid-19 in their family, worrying about their family being sick, thinking that they can be protected from Covid-19 and having knowledge about protection methods from Covid-19 produces a meaningful relationship with the Covid-19 Fear Scale ($R=0.477$, $R2=0.227$, $F(12,175)=4.290$, $p<0.05$).

Table 1. Distribution of Students' Socio-demographic Characteristics (n=188)

Descriptive Characteristics		**X±SD**	
Covid-19 Fear Scale		18.88±6.66 (Min:7; Max:35)	
Age		13.22±2.92 (Min:10; Max:18)	
		n	**%**
Gender	Male	74	39.4
	Female	114	60.6
Grade	5	82	43.6
	8	49	26.1
	9	6	3.2
	12	51	27.1
Family Type	Nuclear Family	149	79.3
	Extended Family	30	16.0
	Broken Family	9	4.8
Mother Education	Not literate	4	2.1
	Literate	3	1.6
	Primary School	64	34.0
	Secondary School	35	18.6
	High School	44	23.4
	University	38	20.2
Father Education	Not literate	1	0.5
	Literate	3	1.6
	Primary School	41	21.8
	Secondary School	38	20.2
	High School	51	27.1
	University	54	28.7
Monthly income	Less income than expenses	54	28.7
	More income than expenses	37	19.7
	Income is equivalent to expenses	97	51.6
Having knowledge about Covid-19	Yes	184	97.9
	No	4	2.1
Covid-19 Information Sources	Family	43	22.9
	Friend	2	1.1
	Internet	29	15.4
	School Staff	5	2.7
	Healthcare Professionals	14	7.4
	Social Media	13	6.9
	Television	76	40.4
	Other	6	3.2
Catching Covid-19	Yes	4	2.1
	No	184	97.9
Having Covid-19 in the family	Yes	58	30.9
	No	130	69.1
Worrying about family getting sick	Yes	145	77.1
	No	43	22.9
Thinking that protection from Covid-19 is possible	Yes	175	93.1
	No	13	6.9
Being knowledgeable about methods of protection from Covid-19	Yes	165	87.8
	No	23	12.2

These characteristics of the students explain 23% of the total variance of the Covid-19 Fear Scale. When the t test results regarding the significance of the regression coefficients were examined, it was found that the students' fathers' educational status (β= -0.314; p = 0.000), their families' catching Covid-19 (β = -0.178; p = 0.012), and their anxiety about their families' illness (β = 0.195) ; p = 0.007) appear to be a significant predictor on the Covid-19 Fear Scale. The fact that the students' fathers are university graduates reduces their Covid-19 fears 4.6 times, that their families catching Covid-19 decreases their

Covid-19 fears 2.6 times, and the fear for family members getting sick with Covid-19 increases their Covid-19 fears 3.1 times (Table 2).

Table 2. Regression Analysis Related to the Prediction of Socio-demographic Characteristics of Students for Covid-19 Fear Scale Scores

	Unstandardized Coefficients		Standardized Coefficients	t	p	95.0% Confidence Interval for B		Collinearity Statistics	
Variable	**B**	**Std. Error**	**Beta**			**Lower Bound**	**Upper Bound**	**Tolerance**	**VIF**
Constant	21.894	5.197		4.213	0.000	11.638	32.150		
Age	-0.114	0.294	-0.049	-0.388	0.699	-0.695	0.467	0.274	3.656
Gender	-1.346	0.928	-0.099	-1.451	0.149	-3.178	0.485	0.949	1.054
Grade	1.056	1.684	0.079	0.627	0.531	-2.268	4.380	0.280	3.577
Family Type	2.144	1.131	0.131	1.896	0.060	-0.088	4.377	0.927	1.079
Mother Education	-1.322	1.238	-0.080	-1.068	0.287	-3.766	1.121	0.789	1.267
Father Education	-4.613	1.088	-0.314	-4.240	**0.000**	-6.761	-2.466	0.805	1.243
Monthly Income	0.935	0.902	0.070	1.037	0.301	-0.845	2.715	0.960	1.042
Catching Covid-19	2.047	3.248	0.044	0.630	0.529	-4.364	8.458	0.888	1.126
Having Covid-19 in the family	-2.562	1.012	-0.178	-2.531	**0.012**	-4.560	-0.564	0.892	1.121
Worrying about family getting sick	3.081	1.123	0.195	2.744	**0.007**	0.865	5.297	0.877	1.140
Thinking that protection from Covid-19 is possible	-2.186	1.851	-0.083	-1.181	0.239	-5.840	1.467	0.884	1.131
Being knowledgeable about methods of protection from Covid-19	-1.844	1.378	-0.091	-1.339	0.182	-4.563	0.875	0.957	1.045

R= 0.477 R^2=0.227 $F_{(12.175)}$=4.290 p=0.000

In the study, it was found that 89.4% of the students used masks wherever they were not alone and could not maintain social distance, 92.0% used medical masks, 96.8% wore masks to cover their mouth and nose, 55.3% washed their hands before wearing the mask and 27.67% stated that they carried a spare mask with them (Table 3).

In the study, it was found that 86.7% of the students always washed their hands with plenty of water and soap for 20 seconds, 81.4% avoided touching their eyes, nose and mouth with their hands, 84.6% disinfected their hands while entering school building or classroom and 86.7% disinfected their hands while leaving school building or classroom, and 88.8% avoided touching surfaces that were frequently touched at school (Table 4). In the study, it was found that 67.6% of the students obeyed the social distance rules, 73.9% paid attention to keeping at least 1 meter distance from others while going to school, 75.0% while going home from school, 78.7% while entering the school building, 78.2% while leaving school, 79.8% in the common places of school, 77.7% during transportation to school, 76.6% in the classroom and 78.2% paid attention to always staying at home when they were not at school (Table 5).

Table 3. Distribution of Students' Characteristics Regarding the Use of Masks

Mask Usage Characteristics		n	%
Do you wear a mask wherever you are not alone and cannot maintain social distance?	Yes	168	89.4
	No	7	3.7
	Sometimes	13	6.9
Do you use a medical mask all the time?	Yes	173	92.0
	No	5	2.7
	Sometimes	10	5.3
Do you always hold the strings when putting on and taking off your mask?	Yes	154	81.9
	No	7	3.7
	Sometimes	27	14.4
Do you wear your mask so that it covers the mouth and nose completely?	Yes	182	96.8
	No	1	0.5
	Sometimes	5	2.7
Do you touch the inner surface of your mask after putting it on?	Yes	8	4.3
	No	155	82.4
	Sometimes	25	13.3
Do you always wash your hands before putting on your mask?	Yes	104	55.3
	No	19	10.1
	Sometimes	65	34.6
Do you always wash your hands after removing your mask?	Yes	153	81.4
	No	10	5.3
	Sometimes	25	13.3
Before putting on your mask, do you disinfect your hands if you cannot wash them?	Yes	135	71.8
	No	17	9.0
	Sometimes	36	19.1
After removing your mask, do you disinfect your hands in case you cannot wash your hands?	Yes	151	80.3
	No	10	5.3
	Sometimes	27	14.4
Do you replace your mask with a new one when it gets wet, moist and dirty?	Yes	172	91.5
	No	2	1.1
	Sometimes	14	7.4
Do you always throw your mask into the trash when it gets dirty?	Yes	181	96.3
	No	4	2.1
	Sometimes	3	1.6
Do you open your mask while sneezing and coughing?	Yes	19	10.1
	No	155	82.4
	Sometimes	14	7.4
Do you always carry a spare mask with you?	Yes	125	66.5
	No	11	5.9
	Sometimes	52	27.7
Do you keep your spare mask in a clean and dry place?	Yes	176	93.6
	No	8	4.3
	Sometimes	4	2.1

Table 4. Distribution of Students' Handwashing Characteristics

Hand Washing Characteristics		n	%
Do you wash your hands often?	Yes	176	93.6
	No	1	0.5
	Sometimes	11	5.9
Do you always wash your hands with soap and water for 20 seconds?	Yes	163	86.7
	No	-	-
	Sometimes	25	13.3
When you cannot wash your hands, do you disinfect them with hand sanitizer?	Yes	171	91.0
	No	6	3.2
	Sometimes	11	5.9
Do you avoid touching your eyes, nose and mouth with your hands?	Yes	153	81.4
	No	7	3.7
	Sometimes	28	14.9
Do you disinfect your hands every day when entering the school building or classroom?	Yes	159	84.6
	No	12	6.4
	Sometimes	17	9.0
Do you disinfect your hands every day when leaving the school building or classroom?	Yes	163	86.7
	No	12	6.4
	Sometimes	13	6.9
Do you avoid touching surfaces that are frequently touched in schools (such as door handles, stair handrails, electric switches)?	Yes	167	88.8
	No	6	3.2
	Sometimes	15	8.0
Do you touch the handrails and walls while using the stairs at school?	Yes	12	6.4
	No	154	81.9
	Sometimes	22	11.7

Table 5. Distribution of Students' Characteristics Related to Social Distance Rules

Social Distance Rules		n	%
Do you always follow the social distance rules?	Yes	127	67.6
	No	8	4.3
	Sometimes	53	28.2
Do you make sure that there is at least 1 meter distance between you and people when you go to school from home?	Yes	139	73.9
	No	9	4.8
	Sometimes	40	21.3
When going home from school, do you pay attention to keeping at least 1 meter distance from people?	Yes	141	75.0
	No	9	4.8
	Sometimes	38	20.2
When entering the school building, do you make sure that there is at least 1 meter distance between you and other students?	Yes	148	78.7
	No	8	4.3
	Sometimes	32	17.0
Do you pay attention to keeping a distance of at least 1 meter from other students when leaving the school building?	Yes	147	78.2
	No	11	5.9
	Sometimes	30	16.0
Do you pay attention to keeping a distance of at least 1 meter from other students in the common areas of the school (such as corridor, garden, canteen, meeting room)?	Yes	150	79.8
	No	9	4.8
	Sometimes	29	15.4
Do you always sit at the same table in class?	Yes	151	80.3
	No	13	6.9
	Sometimes	24	12.8
Do you always sit in a diagonal seating arrangement in the classroom?	Yes	132	70.2
	No	30	16.0
	Sometimes	26	13.8
Do you make sure that you are at least 1 meter away from other students and teachers in the classroom?	Yes	144	76.6
	No	12	6.4
	Sometimes	32	17.0
Do you speak loudly and shouting in class?	Yes	9	4.8
	No	145	77.1
	Sometimes	34	18.1
Do you play games that require contact with your friends during breaks?	Yes	10	5.3
	No	151	80.3
	Sometimes	27	14.4
Do you regularly air your classroom during breaks?	Yes	162	86.2
	No	1	0.5
	Sometimes	25	13.3
Do you exchange food, drinks and equipment with your friends?	Yes	9	4.8
	No	149	79.3
	Sometimes	30	16.0
Do you enter other classrooms, teachers' rooms and administration rooms at the school?	Yes	46	24.5
	No	111	59.0
	Sometimes	31	16.5
Do you make sure that there is at least 1 meter distance between you and people in transportation to the school (such as school buses, public transportation)?	Yes	146	77.7
	No	23	12.2
	Sometimes	19	10.1
Do you go to school when you have problems such as fever, cough, respiratory distress?	Yes	2	1.1
	No	177	94.1
	Sometimes	9	4.8
When you are not at school, do you always make sure that you stay home?	Yes	147	78.2
	No	10	5.3
	Sometimes	31	16.5

DISCUSSION

The findings of the study conducted to determine the fear of Covid-19 and the compliance with protective measures of students who continue their education face-to-face during the Covid-19 pandemic are discussed in this section in line with the literature. It was found that the Covid-19 Fear Scale mean scores of the students within the scope of the study were moderate. Similarly, Gencer (11), Duman (20), Lorca et al. (25), Reznik et al. (26) and Doshi et al. (27) found that Covid-19 fear was moderate. However, in a study conducted with university students after the Covid-19 Outbreak in China, it was determined that 0.9% of the participants experienced intense anxiety symptoms, 2.7% moderate anxiety symptoms and 21.3% mild anxiety symptoms (12). On the other hand, in the studies conducted by Ahorsu

et al. (2020) and Sakib et al. (2020), it was determined that fear was high (23,28). In children, prolonged exposure to stress factors such as fear of infection, disappointment and boredom, insufficient information, lack of face-to-face contact with friends and teachers and lack of personal space in the home environment, direct and indirect consequences of financial losses of family affect mental health (15). People may be afraid because Covid-19 is contagious and deadly, and the disease does not have a proven treatment or vaccine. It is stated that one of the mental health problems experienced in school-age children against the pandemic is fear (29). Similar to the literature, in our study, it is seen that the fear of Covid-19 in students is at a moderate level.

In the study, it was found that the education status of students' fathers, students' concerns about their families having the illness and about their families being sick were a significant predictor of the Covid-19 Fear Scale. It was found that students' fathers' being a university graduate reduced their fear of Covid-19 by 4.6 times, the illness of their families reduced Covid-19 fears 2.6 times, and their fear of family members being sick increased their fear of Covid-19 3.1 times. In a study conducted by Mertens et al. (30) to determine the predictors of Covid-19 fear, it was found that gender, being knowledgeable about the disease, and worrying about the illness of loved ones affected fear but having the disease did not. Doshi et al. (27) stated that the fear of Covid-19 was higher in women, married people and people with low education levels. Perz et al. (17) stated that there was a positive relationship between anxiety and fear of Covid-19 in university students. Soraci et al. (28) and Sakib et al. (31) stated that there was a relationship between the Covid-19 fear scale and anxiety about the disease. Duman (20) stated that the loss of relatives due to illness affected the fear of Covid-19. Bakioglu et al. (24) stated that the illness of one of his relatives did not affect the fear of Covid-19. Cao et al. (12) stated that having a disease in family or close relatives increased anxiety, living in the city center, family income and living with the family reduced anxiety. Gencer (11) stated that gender, age and marital status affected the fear of Covid-19 and educational status did not. Gritsenko et al. (32) stated that gender affected the fear of Covid-19 and Broche-Pérez et al. (33) stated that the fear of Covid-19 was 3.13 times higher in women. In our study, it was found that fathers' being more effective on students due to the patriarchal structure of the Turkish society is important for the fact that Covid-19 fears of the students whose fathers are university graduates are low. It was also seen that fathers' high education status positively affected the financial status and social security of families, and students believed that they would receive treatment in better conditions in case of an illness. It was also thought that the better awareness of the students, whose fathers had high education status, of the disease and protective measures decreased the Covid-19 fears. In case of a family member's pulling through the illness, it is thought that learning techniques to cope with Covid-19 is effective in reducing the Covid-19 fears and in case of anxiety for family members being sick increasing the Covid-19 fears, it is thought that students have a fear due to the risk of infecting their loved ones.

When the applications of students for protective measures were examined in the study, it was seen that

89.4% used masks wherever they were not alone and could not maintain social distance, 92.0% used medical masks, 96.8% wore masks to cover their mouths and noses, 86.7% always washed their hands with plenty of water and soap for 20 seconds. 81.4% stated that they avoided touching their eyes, noses, and mouths with their hands, 67.6% stated that they always obeyed the social distance rules and 78.2% stated that they always paid attention to staying at home when they were not at school. Similarly, in a study conducted by Dardas et al. (34) on Jordanian adolescents, it was reported that majority of the adolescents exhibited effective protective behaviors to prevent Covid-19 from spreading. On the other hand, in a study conducted by Chen et al. (35) on primary school students, it was found that 42.05% of the children showed good hand washing behavior and 51.60% showed good mask wearing behavior. In schools, it is very important for students to comply with social distance rules, to wear a mask to cover the mouth and nose, and to comply with personal protective measures such as washing their hands with water and soap for at least 20 seconds in terms of preventing contamination in Covid-19 disease (3,10). In our study, it is seen that most of the students obey protective measures similar to the studies conducted on adolescents.

Limitations

This study contains some limitations. This study was conducted on students of 5th, 8th, 9th and 12th grades who continued face-to-face education with the approval of the Ministry of Education in Turkey in the Covid-19 pandemic process. Therefore, research results represent these classes. In addition, due to the increase in cases in Turkey, face-to-face education was suspended in all classes shortly after this study began to be implemented. Therefore, the small number of students in the study sample is an important limitation in terms of generalizability of the results.

CONCLUSIONS

In the study, it was found that the students' Covid-19 fears were moderate. It was found that the students' fear of Covid-19 was predicted by their fathers' education status, their families catching the illness, and their anxiety about their families being sick. In the study, it was determined that most of the students paid attention to masks, hand washing and social distance rules at school, and some did not. In line with these results, to prevent the transmission and spread of Covid-19 disease, it is important for school health nurses to provide training in cooperation with families on protective measures for students, to inform students about the disease and to increase their awareness, taking into account the students who do not comply with protective measures. At the same time, it is important that school health nurses provide mental support for students to cope with the fear of Covid-19. In addition, taking into account the prevalence of social media use among young people, informative content and applications about Covid-19 should be included on the internet and various social media platforms

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RESEARCH ARTICLE **DOI:** 10.19127/mbsjohs.1008275

The Role of St. John's Wort Oil (Hypericum Perforatum and Olive Oil) in the Prevention of Peritoneal Adhesion in a Rat Model: An Animal Study

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Abstract

Objective: We aimed to investigate Hypericum Perforatum (St. John's Wort Oil) and pure olive oil with respect to their effect on preventing intra-abdominal adhesions after abdominal surgery.

Methods: This was an animal study carried out by the Giresun Faculty of Medicine, Department of General Surgery between August 10, 2020, and September 10, 2020. In the study, intra-abdominal adhesion development was examined macroscopically and microscopically on the 14th day after experimental abdominal surgery in three groups [(i) Control, (ii) olive oil application, (iii) St. John's Wort oil application] each consisting of 7 female Wistar Albino rats. Majuzi classification and Zuhlke's microscopic adhesion classification was used to evaluate adhesions.

Results: Macroscopically, fibrous bands were not observed in 1 rat in the control group, 2 rats in olive oil recipients, and 1 rat in St. John's Wort oil recipients. A significant difference between the groups was identified in terms of Zuhlke's microscopic adhesion scores ($p = 0.026$). Accordingly, the adhesion level was significantly reduced in olive oil recipients compared to controls ($p = 0.002$). There was no significant difference in terms of adhesion between all groups ($p>0.05$). The Majuzi adhesion classifications in the control group, olive oil group and St. John's wort groups were also similar ($p = 0.308$).

Conclusion: In rats who underwent abdominal surgery, it was determined that intra-abdominal olive oil application reduced the level of adhesion, while St. John's Wort oil application had no effect on adhesion formation.

Keywords: Abdominal Surgery, Adhesion, St. John's Wort Oil, Olive Oil

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INTRODUCTION

Abdominal surgery frequently results in intra-abdominal adhesions which can cause infertility and chronic pain among other effects. Difficulties in re-operations, bleeding problems, organ injuries, and other effects may also develop due to adhesion. In addition, the economic burden of hospitalizations and reoperations due to adhesions is quite high (1,2).

The main causes of adhesion formation in the abdomen are peritoneal trauma, ischemia and foreign bodies (3). Laparoscopic and minimally invasive techniques have been adopted to reduce trauma occurrence during surgical intervention. Laparoscopic surgery is associated with less intra-abdominal adhesion formation than classical open surgery; however, postoperative adhesion is still observed in patients who underwent laparoscopic methods (4). Therefore, only changing the surgical technique does not appear to be sufficient to reduce postoperative adhesions and related complications. In order to prevent adhesions, besides choosing surgical techniques that can minimize peritoneal damage, it is necessary to reduce the inflammatory response, inhibit coagulation, stimulate fibrinolysis and protect surfaces that may cause adhesion (5). Studies aimed at preventing adhesions have targeted the pathophysiological mechanism of adhesion formation. In this regard, various agents such as those suppressing inflammation and/or oxidation have been explored in addition to anti-fibrinolytic and/or anti-coagulant compounds. However, there have been no studies showing compound that can be used to prevent the development of adhesion (5-8). In addition to the antidepressant, anti-inflammatory and antibacterial properties of St. John's Wort [Hypericum Perforatum (HP)] shown in experimental studies (9-12), the positive effects of topical application of HP oil on wound healing have been shown in both animals and humans (13,14). Likewise, the anti-inflammatory, antibacterial and antioxidant properties of olive oil, which is another inexpensive and easily accessible herbal product, have been shown in various studies (15-17). Considering the mechanism of adhesion, HP and olive oil have many properties that might make them suitable for the prevention of peritoneal adhesions.

Our aim was to examine the effects of HP and pure olive oil on the formation of intra-abdominal adhesions following abdominal surgery.

METHODS

Animal Characteristics and Study Groups

In the study, 24 female Wistar Albino rats (weighing between 250 and 350 g) were included. Rats were fed with standard chow and tap water. Rats were housed in standard cages and were kept in light/dark cycles of 12 hours before and after the study (at a standard temperature of 22 °C). All animals included in the study were observed for at least 48 hours to ensure normal behavioural characteristics before inclusion into the study. Rats were weighed after 12 hours of fasting and were divided into three groups–each comprising 8 rats.

Control group: Laparotomy was performed and after palpating the ileum and cecum, the abdomen was closed.

Olive oil group: 1 ml of pure olive oil (Komili, Ayvalik, Turkey) was administered intraperitoneally after laparotomy, immediately before the abdomen was closed.

St. John's Wort group: 1 ml of pure St. John's Wort oil (Luba, Gonen, Turkey) was administered intraperitoneally after laparotomy, immediately before the abdomen was closed.

Laparotomy was performed on the rats 14 days after the procedure, and the formed adhesions were examined macroscopically and histopathologically. Since one rat in each group died after surgery, the examinations were performed on 7 rats in each of the groups.

Surgical Procedure

Experiment preparation procedures were carried out similarly in all rats. Anaesthesia was achieved by injecting 80 mg/kg ketamine HCl and 10 mg/kg xylazine HCl intraperitoneally. After shaving the abdominal skin of the subject, it was cleaned with povidone iodine and appropriate positioning was ensured in a standard heat bed used for animal surgeries. In order to provide analgesia during and after the procedure, 0.02 mg/kg fentanyl was administered subcutaneously as needed. With a 3 cm incision made from the median line, the abdomen was entered and the cecum was brought out on a wet sponge. Serosal petechiae were created on the cecum by rubbing dry sponge, and the laparotomy process was completed. In group 1, the ileum and cecum were palpated and the abdomen was closed. In group 2, laparotomy was performed and 1 ml of pure olive oil was administered intraperitoneally before the abdomen was closed. In group 3, laparotomy was performed and 1 ml of St. John's Wort oil was administered intraperitoneally before the abdomen was closed. During abdominal wall closure, the fascia was sutured with 2/0 polydioxanone suture and the skin was sutured with 3/0 silk. A single dose of cefazolin (20 mg/kg) was administered intramuscularly for postoperative antibiotic prophylaxis. In the postoperative period, normal oral feeding was achieved by all rats. The rats were sacrificed on the 14th postoperative day and evaluated macroscopically and microscopically in terms of adhesion development.

Macroscopic Evaluation

Postoperative intraperitoneal adhesions were ascertained using the Majuzi classification [Grade 0: lack of adhesion, Grade 1: small irregular adhesions, Grade 2: medium density but easily separable, Grade 3: Dense but irregular and cannot be separated easily, Grade 4: Almost complete, regular, cannot be separated easily]. An experienced surgeon blinded to groups evaluated macroscopic adhesion.

Histopathological Evaluation

Samples were obtained from fibrotic bands located between the peritoneum and cecum. A pathologist blinded to rat groups performed the histopathological examination. After the cecum samples taken from the subjects had been fixed in 10% formaldehyde, they were made into paraffin blocks and cut into 5 µm sections. Finally, staining was performed with haematoxylin and eosin, and histopathological examination was performed under light microscopy. Interstitial fibrosis and inflammatory cell reaction were evaluated in the examination. Zuhlke's microscopic adhesion classification was used to evaluate adhesions.

Zuhlke's microscopic adhesion classification (Figure 1):

- Grade 0: No adhesion, no interstitial reaction.
- Grade 1: Weak connective tissue, rare cell, old and new fibrin, thin reticulin fibrils.

- Grade 2: Connective tissue with few cells and capillaries.
- Grade 3: Thicker connective tissue, dense cells, denser and thicker-walled vessels, rare elastic and smooth muscle fibres, rare collagen fibres.
- Grade 4: Thick or nodular granulation tissue, dense collagen fibre and smooth muscle fibres.

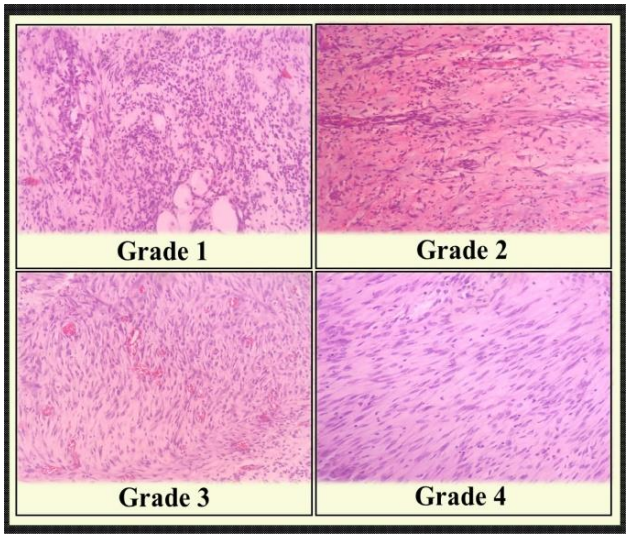

Figure 1. Zuhlke's microscopic adhesion classification histological image samples (H&E stain 20x100)

Statistical analysis

Statistics and analyses of results were performed on the 21.0 version of SPSS (IBM, Armonk, NY, USA). For the normality check, the Kolmogorov-Smirnov test was utilized with Lilliefors correction. Data are given as median (minimum - maximum) for continuous variables, and as frequency for categorical variables. Between-groups comparison of these variables were performed by analyzing differences between measurements with the Kruskal-Wallis test. The Bonferroni correction was used for pairwise comparisons. P values of <0.05 were defined to demonstrate statistical significance in all analyses.

RESULTS

Since one rat in each group died after surgery, no examination could be performed in terms of adhesion in these rats. Macroscopically, fibrous bands were not observed in 1 rat in the control group, 2 rats in olive oil recipients, and 1 rat in St. John's Wort oil recipients. A significant difference between the groups in terms of Zuhlke's microscopic adhesion scores was found (p = 0.026). Accordingly, the levels of adhesion were significantly lower in the olive oil group compared controls (p = 0.002). Adhesion degrees were similar between all groups (p>0.05). (Figure 2).

The comparison of Majuzi adhesion classification findings between the control, olive oil and St. John's Wort groups also yielded non-significant results (p = 0.308) (Table 1).

Table 1. Adhesion grade with regard to group

	Control (n = 7)	Olive oil (n = 7)	St. John's Wort oil (n = 7)	*p-value*
Zuhlke's microscopic adhesion classification	3 (2 – 4)[a]	1 (0 – 2)[b]	2 (1 – 3)[ab]	0.003
0	0 (0%)	2 (28.6%)	0 (0%)	
1	0 (0%)	2 (28.6%)	1 (14.3%)	
2	1 (14.3%)	3 (42.9%)	3 (42.9%)	
3	4 (57.1%)	0 (0%)	3 (37.5%)	
4	2 (28.6%)	0 (0%)	0 (0%)	
Majuzi adhesion classification	2 (1 – 3)	2 (0 – 3)	2 (2 – 3)	0.310
0	0 (0%)	1 (14.3%)	0 (0%)	
1	2 (28.6%)	0 (0%)	0 (0%)	
2	4 (57.1%)	3 (42.9%)	4 (57.1%)	
3	1 (14.3%)	3 (42.9%)	3 (42.9%)	

Data are given as median (minimum – maximum) for continuous variables and as frequency (percentage) for categorical variables.
[a,b]: Same letters denote the lack of statistically significant difference between groups

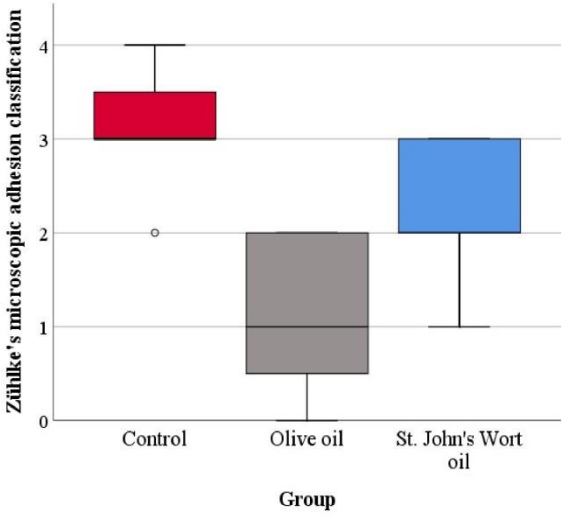

Figure 2. Zuhlke's microscopic adhesion classification with regard to group

DISCUSSION

Advances in the understanding of intra-abdominal adhesion mechanisms has led to use of many substances aimed at preventing adhesion formation. The pathophysiology of adhesion includes tissue damage and the subsequent inflammatory response, and there are many studies that have sought to prevent adhesion formation with agents targeting these factors (18,19).

Many studies have reported that HP has anti-inflammatory, antioxidant and antibacterial properties (9-12). These properties of HP are attributed to its various components, including quercetin, I3, II8-biapigenin and hypericin (20,21). In our study, considering that the development of adhesion after abdominal surgery was due to similar pathophysiological mechanisms, intra-abdominal HP was applied to rats that underwent abdominal irritation and the development of adhesion was examined. However, in the analyses performed, it was determined that the level of inflammation and adhesion formation in the St. John's Wort oil group was indifferent when compared with the controls and olive oil recipients group. Similar to our study, in an animal study investigating olive oil, St. John's Wort oil and control groups, Hızlı et al. reported that adhesion, inflammation and fibrosis levels were not different in the St. John's Wort oil group compared to other groups. Consistent with our study, the adhesion level in the olive oil group was lower than that of the control group, while it was found to be similar to the St. John's Wort oil group (22). Although other studies drew attention to St. John's Wort oil, in our study, it was observed that although the adhesion in St. John's Wort oil recipients was relatively lower compared to controls, statistical significance was not present. This may be due to the low number of animals per group in our study.

In various studies examining the properties of pure olive oil, it has been determined that it has anti-inflammatory, antibacterial, antioxidant and antineoplastic properties (15-17). It has also been shown that it can improve wound formation with its various properties (23). Currently, it is being suggested that olive oil can prevent adhesion with respect to its hydroflotation feature resulting from its high viscosity value (24). In addition, it has been stated that squalene, beta sitosterol, erythrodiol and some other components in olive oil have anti-inflammatory activity (25). As a result, we observed that adhesion formation occurred at a lower frequency in rats that had received pure olive oil application. When studies focusing on adhesion investigations are examined, various outcomes can be observed throughout the literature. In an animal study conducted with a model similar to ours, Ural et al. (24) applied 5 ml of pure olive oil to rats, for which

they created an abdominal surgery model, and reported that no adhesion formation could be identified in the intra-abdominal region 30 days after the operation. The authors attributed this finding to anti-inflammatory effects and properties that support tissue regeneration. Hızlı et al. (22) also stated that they found lower adhesion olive oil recipients relative to controls. The results of these studies are in support of our findings. Although no examination was made on olive oil content and mechanism of action in our study, it was thought that the anti-inflammatory components shown in other studies may have an adhesion-reducing effect (24,25). In experimental models with more animals, it may be feasible to suggest long-term follow-up of rats with intra-abdominal pure olive oil application, thereby enabling longer-term comparisons and elucidation of possible side effects, which may, in turn, lead to studies examining the utility of olive oil application for adhesion prevention in humans.

The primary limitations of our study are animal count per group and the short postoperative follow-up period in terms of adhesion development. In addition, one animal died in each surgical group before measurements could be performed. The cause of death in these animals may be due to the application of foreign agents, or may be a direct result of surgical stress, and therefore, such effects should be investigated in larger series.

CONCLUSION

In this animal study, in which the effects of St. John's Wort oil and olive oil were examined with regard to adhesion formation after intra-abdominal surgery, it was determined that St. John's Wort oil (HP) did not alleviate adhesion, whereas olive oil had protective properties and reduced the degree of adhesion. In future studies, the effect of olive oil and St. John's Wort oil on adhesion can be revealed in more detail by including more animals, applying different doses, and examining longer-term results.

Ethics Committee Approval: Ethics committee approval was obtained from Giresun University Rectorate, Faculty of Health Sciences Dean's Office, Animal Experiments Local Ethics Committee Directorate (Number: 12763492-770-E.32531, Date:24.07.2020).

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Conflict of Interest: No conflict of interest was declared by the authors.

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Antibacterial Activity of a Series Engineering Nanoparticles Against Oral Anaerobic Periodontal Pathogens Species in Vitro

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Abstract

Objective: Periodontal disease is an essential phenomenon in human health. Oral pathogens can cause severe break which may show the way to serious issues in human disease like chronic obstructive pulmonary disease and cardiovascular diseases. Therefore, the aim of this study is to evaluate the antibacterial effect of a series nanoparticles on oral pathogens.

Methods: In this study, antibacterial activity of a series of nanoparticles such as MWCNT, CuO2, CaCO3, SiO2, Al2O3, MgO and ZrO2 against oral pathogens such as *Porphyromonas gingivalis* (Pg) and *Aggregatibacter actinomycetemcomitans* (Aa) was demonstrated. We evaluated the bactericidal effect of the nanoparticles to perio pathogens by measuring the inhibitor zone region. Antimicrobial experiments were conducted in five replicates.

Results: As a result, we confirmed that engineering nanoparticles exhibited good bactericidal activity. SiO2 nanoparticle was the most effective on Pg. CaCO3 nanoparticle was the most effective on Aa. The order of the nanoparticle types in which the Pg is most sensitive is SiO2> MgO> Al2O3> ZrO2> CuO> MWCNT> CaCO3. For Aa order is CaCO3> SiO2>MgO> ZrO2> CuO> MWCNT> Al2O3.

Conclusion: Our results suggest that engineering nanoparticles have a significant inhibitory effect on Aa and Pg. And, these effects are increased with increasing concentrations of nanoparticles. These results can be further clarified with new studies.

Keywords: Antibacterial activity, *Aggregatibacter actinomycetemcomitans*, engineering nanoparticles, *Porphyromonas gingivalis*

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INTRODUCTION

Recently, nanotechnology offers superior advantages in various fields of science and technology. Pharmaceutical nanotechnology with these advantages has begun to attract the attention of many researchers (1,2). Because highly ionic nanoparticulate metal oxides are particularly interesting as antimicrobial agents, they can be prepared with unusual crystal morphologies that have a large number of surfaces and corners and other potentially reactive sites (3,4). Thus, metal-containing nanomaterials have the potential to be used for infection control in dentistry, but little is known about their antibacterial properties. (5,6). In particular, the molecular mechanisms of the inhibitory effect of silver ions in silver nanoparticles on microorganisms have been described. Accordingly, the expression of DNA loses its ability to proliferate, and that other ribosomal subunit proteins and other cellular proteins and enzymes required for it are lost and ATP production is disabled (4,7,8). Therefore, it is foreseen that metal oxide nanoparticles with antimicrobial activity (nanoanthibiotics) may provide a good alternative to reduce and / or control the growth of bacteria in the oral cavity (4,9). Gingivitis is a gingival inflammation due to microbial dental plaque accumulation in gingival margin. Periodontitis is the most common chronic inflammatory disease in the society characterized by loss of gums and bone, which can develop when gingivitis is not treated (10). Bacteria in the microbial dental plaque on one hand directly damage the host tissue with the products they secrete, while at the same time, they induce tissue destruction by activating the host tissue immune system (11). In this respect, the quantitative and qualitative reduction of the bacteria in the plaque is essential for the health of the periodontal tissues (12). In addition, proliferation of pathogenic bacteria in the mouth leads to periodontitis, an inflammatory disease that is a risk factor for other systemic diseases such as chronic obstructive pulmonary disease and cardiovascular diseases (9,13).

In vitro studies have shown that certain metal nanoparticles inhibit some microbial species. Various nanoparticles, composites and derivatives have attracted great interest for their potential antimicrobial effects. In particular, metal nanoparticles such as silver, silver oxide (Ag2O), titanium dioxide (TiO2), silicon (Si), copper oxide (CuO), zinc oxide (ZnO), gold (Au), calcium oxide (CaO) and magnesium oxide (MgO), have been shown to exhibit antimicrobial activity (14). The two most important parameters affecting the antimicrobial effect of nanoparticles are the type and size of materials used (15,16). The smaller the size of the nanoparticles, the stronger the bactericidal effect is known (14). The size of the nanoparticles is related to the surface / volume ratio and has different properties than the larger size of the same particle with the reduction in particle size (17). The reason for this is that as the size of the nanoparticles decreases, the fraction of the surface molecule significantly increases, improving the properties of the nanoparticles such as heat treatment, mass transfer, dissolution rate, catalytic activity (18). However, although the mechanisms of antibacterial action of the nanoparticles are still not fully elucidated, free metal ion toxicity and reactive oxygen species (ROS) formation and morphological (shape) and

physicochemical properties of the nanoparticles have proven to have an effect on their antimicrobial activities (15). Few studies have been carried out on gram negative anaerobic pathogenic bacteria which are the periodontitis agents of nanoparticles. Although studies focused mainly on the bacterial species found in the oral cavity, gram positive facultative anaerobic bacteria such as Streptococcus mutans were chosen for ease of use. Unfortunately, antibiotic treatments have made these bacteria resistant to conventional antibiotics.

Therefore, the aim of this study was to investigate the effects of various engineering nanoparticles on *Porphyromonas gingivalis* (Pg) and *Aggregatibacter actinomycetemcomitans* (Aa), which are pathogenic bacteria for periodontal diseases.

METHODS

Nanoparticles materials

In this study, multi-walled carbon nanotubes (MWCNT) 90+% purity, 5-10 nm and metal oxide powders (in 99.5+% purity, zirconium oxide (ZrO2) 40 nm, alumina oxide (Al2O3) 20 nm, copper oxide (CuO) 25-55 nm, calcium carbonate (CaCO3) 50 nm, silicon oxide (SiO2) 15-25 nm, magnesium oxide (MgO) 20 nm nanopowders were purchased from Nanography (Ankara, Turkey) to investigate the concentration dependence of the antibacterial effect of engineering nanoparticles.

Strains and growth conditions

The lyophilized gram negative anaerobic species (Aa DSM catolog no. 11123 and Pg DSMZ catolog no. 20709) used in this research were obtained from German Collection of Microorganisms and Cell Cultures (Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH, DSMZ, Braunschweig, Germany). Each inactive bacteria for reactivation were grown under anaerobic conditions and then stored in a bacterial suspension. Briefly, the Aa starin were incubated in CaSo Bouillon (Carl Roth) for 24-48 hours at 37 °C in a 5 % CO2 medium under anaerobic standard conditions. After incubation, the Aa were suspended in Schaedler liquid medium to provide a turbidity equivalent to the 108 CFU/mL-1 McFarland standard. Pg strain was cultured under anaerobic conditions 10% C02, 5% H2 and 85% N2 on Columbia blood agar plates containing 5% sheep blood and 0.5% K vitamin at 37 °C for at least 48 hours.

Characterization and Preparation of Engineering nanoparticles

MWCNT and nanoparticle powders were suspended in chlorhexidine (CHX) prepared with 2% by ddH2O to interact with bacteria. The nanoparticle was left to sonication for 30 minutes to ensure homogenization and dispersion of the suspension. Then, from these stock solutions, test solutions were prepared at concentrations of 1.5, 3 and 6 mg/L for CuO, 4, 8 and 16 mg/L for ZrO2, 0.05, 0.1 and 10 m /L for CaCO3, 5, 10 and 20 mg/L for MWCNT, 12.5, 25 ve 50 mg/L SiO2, 25, 50 ve 100 mg/L for Al2O3 and MgO. The nanoparticle powders were characterized by SEM. These solutions were then autoclaved to eliminate naturally occurring microorganisms and was then sonicated for 20 min. and immediately used for disk diffusion tests.

Antibacterial activity assay

Agar disc diffusion method was used to determine the antibacterial activity of nanoparticles solutions with CHX. 100 µL of the bacterial suspension adjusted according to Mcfarland 0.5 at the

spectrophotometer (0.5 McFarland standard) were impregnated uniformly on the surface of solids containing nutrient agar solid medium for Aa and solid blood agar for Pg. 20 µL of the nanoparticle solutions previously prepared with CHX were impregnated on sterile empty discs (6 mm diameter) and placed at equal distances to the petri dishes. 20 µL 0.2 % CHX was used as positive control and ethanol was used as negative control. The petri dishes were incubated at anaerobically for 72 hours at 37°C. After incubation, the average diameters of the bacterial inhibition growth zones formed around the discs in petri dishes were measured. For each nanoparticle solutions and for each bacterial strain, the mean and standard deviation values were obtained from six replicates.

Statistical analysis

Antimicrobial experiments were conducted in five replicates. Data points were expressed as the mean ± SD. Data were analyzed using analysis of variance (ANOVA) from SAS version 9.1 software (SAS Inst., Inc., Cary, N.C., U.S.A.). Duncan's multiple range tests were used to determine the significant difference of mean values. Unless stated otherwise, significance was expressed at 5% level.

RESULTS

Table 1 shows the mean values of bacterial growth inhibition zone diameters for two bacterial species exposed to multi-walled carbon nanotubes (MWCNT) and nanoparticles (CuO, SiO2, Al2O3, CaCO3, MgO, ZrO2) prepared with CHX based on six repetitive determinations. Disc diffusion test reveals the differences in sensitivity of nanoparticles (CuO, CaCO3, SiO2, Al2O3, MgO and ZrO2) and MWCNT for Pg (DSMZ 20709) and Aa (DSMZ 11123). Aa selected for this study were noted to be the most sensitive species for all nanoparticles and MWCNT. The order of the nanoparticle types in which the Pg is most sensitive is SiO2> MgO> Al2O3> ZrO2> CuO> MWCNT> CaCO3. For Aa order is CaCO3> SiO2>MgO> ZrO2> CuO> MWCNT> Al2O3. In addition, both bacterial species are more susceptible to SiO2 nanoparticles. This means that the nanoparticle type which increases the antibacterial property of CHX is SiO2. In contrast, both bacterial species have shown low sensitivity to MWCNT. When compared CHX (control group) and nanoparticle concentrations, significant differences were observed in all concentration groups of Pg and Aa bacteria ($P < 0.01$). The comparison of all nanoparticle concentrations with CHX resulted in significant differences in the highest concentrations ($P < 0.01$). Generally, the antibacterial effect of the lowest nanoparticle concentrations was lower than the control group (CHX). This means that the addition of nanoparticles to CHX increases the antibacterial activity at high doses and has no effect on low concentrations. In fact, it was observed that the addition of low concentrations of CHX to the nanoparticle reduced the antibacterial activity of CHX. For example, the addition of MgO nanoparticle to CHX at concentrations of 100 and 50 mg/L increased the antibacterial activity of CHX. Another result is stronger antibacterial effect on CHX and nanoparticles than Aa bacteria Pg. Unlike other nanoparticles, ZrO2 and SiO2 nanoparticles increased the antibacterial activity of the control group (CHX) even at the lowest concentrations. This means that even the lowest concentrations of these

nanoparticles to CHX has increased the antibacterial activity of CHX.

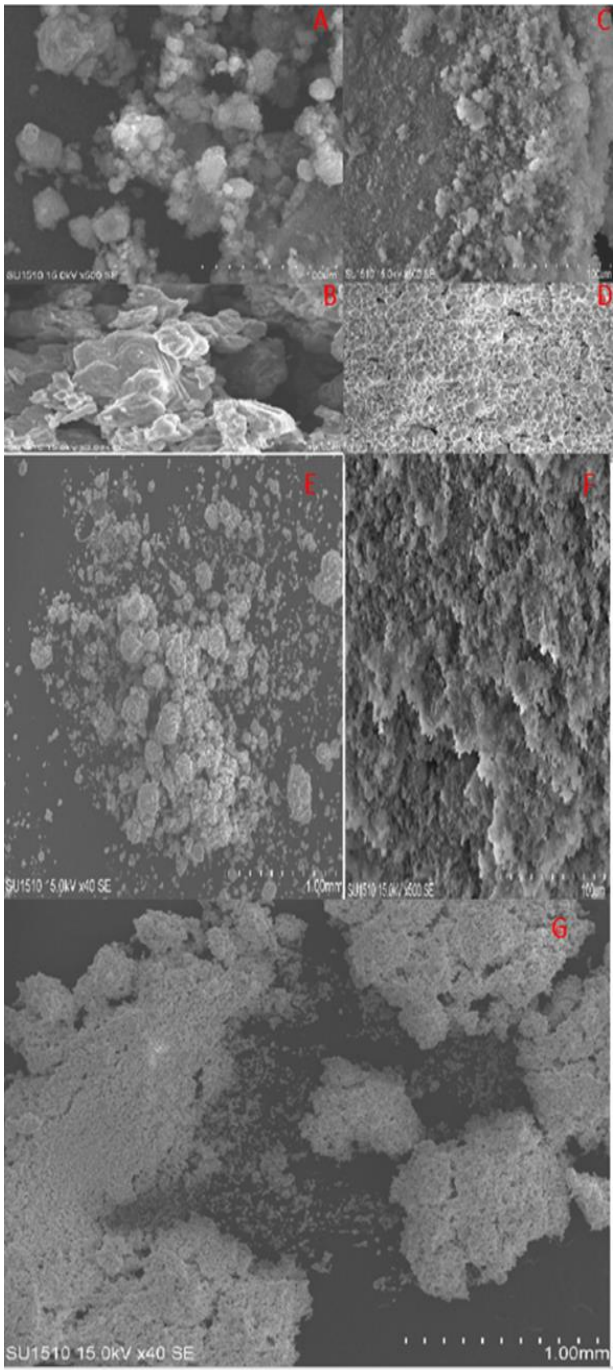

Figure 1. SEM image of nanoparticles, A) MWCNT B) CuO C) SiO2 D) Al2O3 E) CaCO3 F) MgO G) ZrO2

DISCUSSION

Many studies on nanoparticles have increased in recent years. Researchers have focused on environmental impacts or how we can use them in medical studies (19, 20).

Table 1. The mean zone diameters of nanoparticles as measured by disk diffusion method.

Treatments	Pg (inhibition zone) Mean±SD	Aa (inhibition zone) Mean±SD
Control (CHX)	12.00c±0.01	14.35c±0.01
6 mg/L CuO	16.22a±0.01	20.60a±0.01
3 mg/L CuO	12.52b±0.01	18.51b±0.01
1.5 mg/L CuO	10.70d±0.01	14.30d±0.01
Control (CHX)	12.00d±0.01	14.35c±0.01
16 mg/L ZrO2	16.70a±0.01	20.95a±0.01
8 mg/L ZrO2	15.16b±0.01	18.10b±0.01
4 mg/L ZrO2	13.25c±0.01	14.20d±0.01
Control (CHX)	12.00c±0.01	14.35d±0.01
10 mg/L CaCO3	14.11a±0.01	22.33a±0.01
0.1 mg/L CaCO3	12.25b±0.01	19.00b±0.01
0.05 mg/L CaCO3	11.08d±0.01	16.42c±0.01
Control (CHX)	12.00d±0.01	14.35d±0.01
20 mg/L MWCNT	16.26a±0.01	20.55a±0.01
10 mg/L MWCNT	13.72b±0.01	18.80b±0.01
5 mg/L MWCNT	12.85c±0.01	15.00c±0.01
Control (CHX)	12.00d±0.01	14,35d±0.01
50 mg/L SiO2	21.23a±0.01	21.15a±0.01
25 mg/L SiO2	16.83b±0.01	18,45b±0.01
12.5 mg/L SiO2	12.57c±0.01	15.00c±0.01
Control (CHX)	12.00c±0.01	14.35d±0.01
100 mg/L Al2O3	18.25a±0.01	19.75a±0.01
50 mg/L Al2O3	15.00b±0.01	16.00b±0.01
25 mg/L Al2O3	10.48d±0.01	14.78c±0.01
Control (CHX)	12.00c±0.01	14.35d±0.01
100 mg/L MgO	19.00a±0.01	21.00a±0.01
50 mg/L MgO	12.89b±0.01	18.50b±0.01
25 mg/L MgO	10.78d±0.01	16.00c±0.01

**P<0.001
[a,b,c,d] P<0.05. Significant differences between study groups
Each nanoparticle concentration experiment was repeated 5 times.

Major advances in nanotechnology have led to the investigation of nanometer-sized metal oxides as antimicrobial agents. The use of inorganic metal oxide NPs has attracted a great deal of attention due to the biocompatibility of mammalian cells, as well as promising antimicrobial activity, even at low concentrations (21). NPs have been accepted as antibacterial agents and have been used for oral infection control in dentistry (4). The exact mechanisms for the bacterial toxicity of nano-metals have still not been fully elucidated. The possibilities,

however, include free metal ion toxicity resulting from the dissolution of metals from the surface of NPs and the formation of oxidative stress by the production of reactive oxygen species (ROS) on the crystal surfaces of NPs (20). The occurring ROS can then act synergistically in bacteria by attacking polyunsaturated phospholipids and may cause local DNA damage (22). Electrostatic attraction between the negative charge of the bacterial cell membrane and the positively charged NPs showed that it was critical for antimicrobial activity (4). In one study, structural changes resulting in cell death and damage to bacterial membranes have been demonstrated (23). It is estimated that the 3-20-fold decrease in the negatively charged peptidoglycans in the gram-negative species (Pg, Prevotella intermedia, and Aa) will cause differences in sensitivity. Furthermore, the ability of silver, copper and zinc to bind to the basic enzyme sulfhydryl (-SH) groups may produce differences in sensitivity to these metals between anaerobic and aerobic bacteria. For example, the low affinity of zinc for sulfhydryl groups may explain the lack of antimicrobial activity against Pg (4). However, it is still unclear whether NPs have superior antibacterial properties compared to conventional metal salts used in dentistry or other routine antibacterial products for oral cavity such as chlorhexidine used in surgical gargles (4). Most microbial studies with NPs have been made with well-known model organisms such as Escherichia coli (23). However, NP concentration and size are the most important factors affecting the antimicrobial properties of NPs. Therefore, ultrasonic and dispersants are often used to break up NP agglomerates (24). In this study, sonication (20 min) was used to prevent agglomeration of NPs prepared with CHX. In addition, the agar medium is chosen instead of broth, because the NPs in the broth can precipitate and make the estimation of the nominal exposure concentration of NPs difficult (25). NPs greater than 10 nm accumulate on cell membranes, and may compromise cell permeability. This causes leakage of intracellular components and subsequent cell death (26). The nanoparticles smaller than 10 nm can accumulate in the cell by penetration into the membranes, thereby making an effect on the nucleic acid (27). Another mechanism in which the NPs exhibit antimicrobial activity in the presence of oxygen is ROS production. By disrupting normal cellular functions such as breathing chain, NPs trigger ROS formation such as OH^{-}, O2- and H2O2, and can cause death of bacteria (28).

In this study, anaerobic conditions are important in terms of antibacterial properties of NPs. In addition, the SiO2 NPs having the lowest size as mentioned above has the highest antibacterial activity in both bacterial species. In previous studies, the antimicrobial activity of SiO2 NPs has become more important due to increased surface area (14). Although it does not have a strictly toxic mechanism, silica causes a negative change in the biofilm to reduce adhesion and thus the growth of bacteria (22). Among the NPs tested in our study is the most sensitive nanoparticle SiO2 for Pg. For Aa, the most sensitive nanoparticle after CaCO3 was reported to be SiO2 NPs. The results we have obtained have been confirmed by previous studies. However, the previous studies did not use anaerobic pathogens (29).

In several studies, CaO and MgO NPs have been shown to have strong antibacterial activity related to alkalinity and active oxygen species. The antibacterial mechanism of CaO and MgO NPs has been confirmed to provide an increase in pH by the superoxide production on the surface of these particles and also by hydration of CaO and MgO (14). Thus, MgO NPs damage the cell membrane and then cause the intracellular contents of bacterial cells to be destroyed (30). In our current study, the nanoparticle having the least sensitivity in all the NPs tested for Pg was CaCO3. Interestingly, for Aa the most sensitive is the nanoparticle. For MgO NPs, the sensitivity of both species is almost the same.

There is not much literature study on the species used in our study (Aa and Pg). Moreover, the current studies in the literature differ from the nanoparticles we use. For example, Vargas-Reus et al. (28), Ag, Cu2O, CuO, ZnO, TiO2, tungsten oxide (W03), Ag + CuO composite and The activities of the NPs of the Ag + ZnO composite were evaluated against Prevotella intermedia, Pg, Fusobacterium nucleatum and Aa with minimum inhibitory (bacteriostatic) concentration (MIC) and minimum bactericidal concentration (MBC). The NPs evaluated showed that the antimicrobial properties were different according to the bacterial species. Besinis et al. (22), Ag, TiO2 and SiO2 NPs and routine disinfectant CHX compared the toxicity of Streptococcus mutans against oral pathogenic species. All analyzes showed that Ag NPs had the strongest antibacterial activity among tested NPs, and reported that they were 25 times lower than CHX in bacterial growth.

CONCLUSION

This study confirmed that MWCNT, CuO2, CaCO3, SiO2, Al2O3, MgO and ZrO2 nanoparticles against Pg and Aa have antibacterial effect. The results of this study showed that the antibacterial properties of CHX mouthwash increased with these nanoparticles. It has been noted that these effects are increased with increasing concentrations of nanoparticles. Our results suggest that engineering nanoparticles have a significant inhibitory effect on Aa and Pg. These results can be further clarified with new studies.

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Ethics Committee Approval: Since this study was conducted under in vitro conditions, there is no need to obtain an ethics committee certificate.

Peer-review: Externally peer-reviewed.

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Conflict of Interest: The author has no interests to declare

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Evaluating Intervertebral Foramen Measurements for Patients with Anterior Cervical Disc Surgery in Oblique CT

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Abstract

Objective: It is particularly difficult to determine the level of radiculopathy pain. Because radicular pain usually doesn't fit the dermatomal map. unlike the foramen lumbar vertebrae, where the cervical nerve root is exerted, it has a slope of approximately 45 degrees to the vertebrae in the axical plane and 10-15 degrees in the horizontal plane. Due to this structure of cervical foremen, the evaluation of conventional ct results in incorrect or incomplete diagnosis. In our study, we compared the change in cervical foramen patients with anterior cervical discectomy and cage (fusion) to oblique ct reconstructive and preop and postop.

Methods: CT images were acquired in a 64 slice CT system (60–80 mAs, 120 kVp, FC86 reconstruction core and 2.0 mm slice thickness at 2.0 mm intervals). Oblique sagittal images were created with OsiriX Lite v. 12.0.1 version and measurements were performed. For each level, the area has been measured in addition to the short and long axle length of the neural foramens from the pre-op and post-op oblique sagittal images.

Results: In our study, 98 cervical intervertebral foramen oblique CT de preop-postop, long axle, short axle and field measurements were evaluated with 43 patients from 16/01/2019 to 03/02/2020, 3 patients with two levels of anterior ceral discectomy + interbody cage. Right side, long axle, short axle, and area respectively; 13,37%, 5,99%, 16,87% increase. Left side, long axle, short axle, and area respectively, increased by 14,27%, 7,11%, 23,20%

Conclusion: The cage, which is placed on the intervertebral level, will increase the area of the foramen, increase the space of the foramen, and allow the nerve to decompression. This is why it is necessary to insert the material with the highest height of the intervertebral disk level that can be placed during surgery.

Keywords: Surgery, Cervical Intervertebral Disc, Oblique CT

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INTRODUCTION

Cervical Disk heniation due to foraminal and spinal channel shorthand, incompetence in hand movements based on neck pain, myelopathy and radiculopathy, difficulty walking, balance and coordination disorder leads to a loss of power in the extremities with sensory pathologies such as needles in hands and feet – tingling (1). These complaints are caused by the axial loading of the cervical spine and the degenerative process resulting in disc herniation and bone spur formation. In particular, radiculopathy is a clinical form of a neural compression in the intervertebral foramen. The location of the cervical region that caused the complaint is important for the treatment algorithm. It is particularly difficult to perform level determination in radiculopathy. Because radicular pain usually doesn't fit the dermatomal map (2,3). Therefore, it needs EMG and advanced imaging techniques. In his surgery, it is important to keep the decompression of neural elements and the shape of the spine intact.

Anterior Cervical Discectomy and Fusion (ACDF) are the most common surgical method used today. It was first defined by Robinson and Smith and Cloward in 1950 (4,5). It was first used with the fusion agent to use autogenous bone gref, and then went into surgery with the development of interbody cage. High surgical results were found using the anterior interbodycage method used for ACDF (6).

However, unlike the foramen lomber vertebrae, where the cervical nerve root is exerted, it has a slope of approximately 45 degrees to the vertebrae in the axial plane and 10-15 degrees in the horizontal plane (7).C3-C7 is found in a groove where the intervertebral foramen medialde stops the pedincule limit, where the transverse process ends in laterality. In the medial segment of the canal, superior to the nerve root, there is the uncinate process posterolaterally to the peduncle of the adjacent vertebra, and the superior articular process inner point anteromedially. More laterally, after the nerve root is divided, the ventral and spinal nerves continue in the groove, and the posterior surface of the vertebral artery is adjacent to the anterior surface of the superior articular process. (Figure 1.3).

Due to this structure of cervical foramen, the evaluation of conventional ct results in incorrect or incomplete diagnosis. We're in the study we compared the change in cervical foramen measurement of patients we have administered ACDFin obliq ct reconstructive and preop and postop.

Anatomy

Cervical vertebral shows a different structure. Anatomically, especially C1, C2 and C3-C7 are very different. In daily practice, C3-C7 spine pathologies appear more often (Figure1.1)

In cervical vertebral bodies (C3-C7), the spinal canal increases caudally. Abuzayed, B et al., in a study group of 48 healthy volunteers, measurements of the corpus of the cervical vertebrae were made and it was observed that the width gradually decreased between the C3-C7 vertebrae (8). In the same study, it was emphasized that the anterior posterior diameter gradually increased (8) Anteroposterior diameter is especially important in anterior cervical discectomy and guides the neurosurgeon about the corpus borders while performing discectomy. Another important measure is the sagittal and transverse diameter of the cervical spinal canal. In a study by Yu et al., while the

transverse diameter gradually increased between C2-C6, it was observed that the diameter decreased at the C7 level and was measured at the narrowest C3 level (9,10). Torg Ratio is an indicator that can help diagnose patients at risk for cervical spine injury, obtained by dividing the diameter of the spinal canal in a vertebra by the corresponding vertebral body sagittal diameter (11).

Other formations that distinguish cervical vertebrae from other vertebrae are vertebral foramen and uncinate processes in their transverse processes (Figure 1.2). Vertebral arteries pass through the vertebral foramen, and it is vital to consider the vertebral artery neighborhoods in all procedures to be performed on the cervical spine. The uncinate processes, on the other hand, are located dorsilaterally, superior to the corpus of the cervical vertebrae, and form the uncovertebral joint with the caudodorsilateral of the corpus of the lower vertebrae. In cervical discectomy method, partial resection of the uncinate process has an important place in terms of decompressing the nerve root trace and it has been seen that it provides significant benefit in post-op intervertebral foramen enlargement. (7)

Between the two adjacent vertebrae are the intervertebral foramina, from which the nerve roots emerge. The shape of the foramen is considered ovoid. These foramina also contain segmental radicular arteries and sinuvertebral nerves (recurrent meningeal). Nerve endings innervating the annulus fibrosis from the sinuvertebral nerves branch and may be the source of chronic neck pain and discopathic pain (12). Intervertebral foramen borders the intervertebral disc anteriorly, uncinate processes in the trunk and cervical vertebrae, facet joint posteriorly, pedicles above and below (Figure 1.3). The dimensions of the intervertebral foramen in the cervical region, in the MRI measurements of Lantell et al. in 20 healthy people; On average, the height was 11.08 ± 1.88 mm, the width was 5.69 ± 1.91, and the area was 51.61 ± 1.83 mm2 (13). It was reported that the widest area was between C2-C3 and the narrowest area was C7-T1 (13). As the nerve roots leave the intervertebral foramen It exits by running close to the pedicle of the upper vertebra (2). The uncinate process located in front of the intervertebral foramen undergoes osteophytic changes as a result of degenerative processes and causes radiculopathic pain in the patient by compressing the nerve trace. (1) The basic mechanism of osteophytic changes is the deterioration of axial balance and the spine's efforts to develop compensation by hypertrophying the uncinate processes (3).

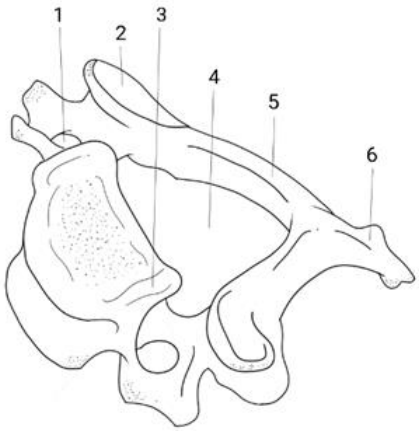

Figure 1.1. 1. Transvers Foramen 2. Superior Articular Facet 3.Uncus 4. Vertebral Foramen 5. Lamina 6. Spinous Process

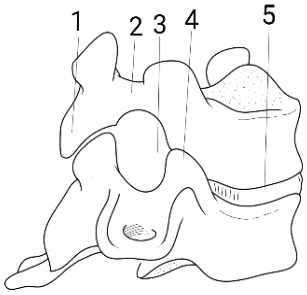

Figure 1.2. 1. Superior Facet Joint 2. Pedicle 3. Intervertebral foramen 4. Uncus 5. Intervertebral Disc

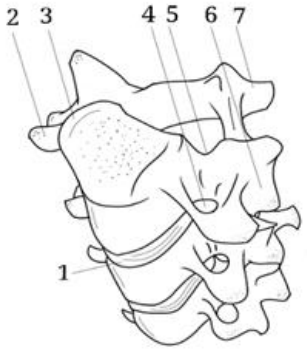

Figure 1.3. 1. Intervertebral Disc 2. Anterior Tubercle 3. Uncus 4. Transverse Foramen 5. Pedicle 6. Inferior Articular Process 7. Spinous Process

METHODS

Unlike the lumbar level, routine axial, coronal and sagittal reformat images are not sufficient in the evaluation of the cervical neural foramen (Figure 2.2). For this reason, oblique sagittal images were created for each level to reveal the neural foramen anatomy and existing pathologies. Information about patient imaging was collected from the picture archiving and communication system (PACS) of our institution. CT images were acquired on a 64-slice CT system (60–80 mAs, 120 kVp, FC86 reconstruction core and 2.0 mm slice thickness at 2.0 mm intervals). Oblique sagittal images were created with OsiriX Lite v.12.0.1 version and measurements were performed (Figure 2.1). In addition to the short and long axis length of the neural foramen, area measurements were made from pre-op and post-op oblique sagittsal images for each level (Figure 2.3).

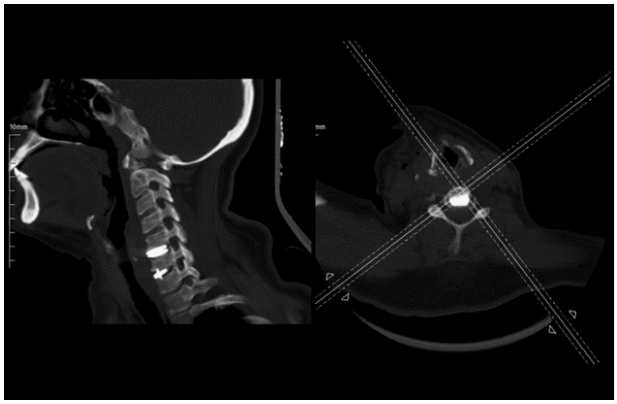

Figure 2.1. Sagittal foramen view in oblique reconstruction

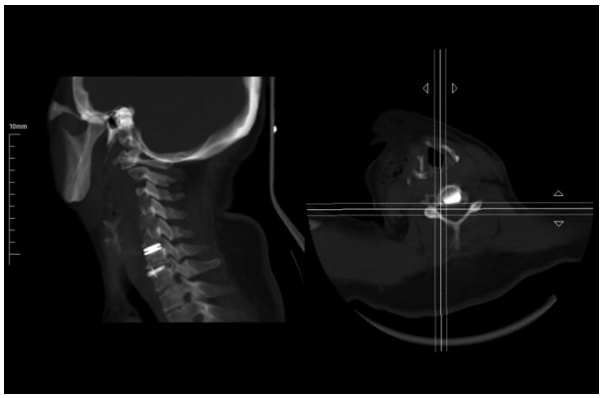

Figure 2.2. Sagittal foramen view in conventional CT

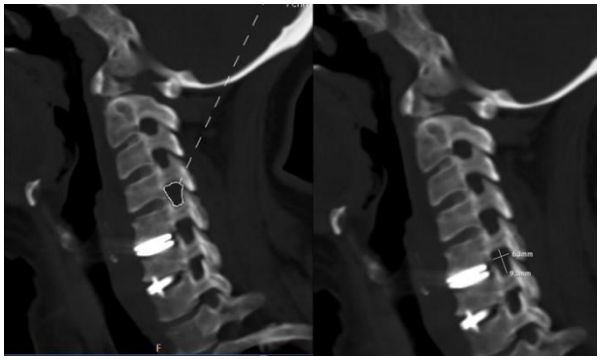

Figure 2.3. Foramen area measurement in oblique sagitt

Statistical analysis

Statistical data IBM SPSS 20.0 software was used. Numerical data were evaluated with histogram and Kolmogorov-Smirnov test. All parameters fit the

normal distribution. Sampled sample t-test was used to compare the data. These data were shown with numbers and numerical data were determined as mean + - standard deviation or median. P < 0.005% was found to be statistically significant

RESULTS

In our study, between 16/01/2019 and 03/02/2020, 43 patients were single-level, 3 patients were two-level anterior cervical discectomy + interbody cage, 98 cervical intervertebral foramen oblique CT performed preop-postop; long axis, short axis and area measurements were evaluated. 21 of the patients were female and 22 were male. Laminoplasty was not added to the operation. Schematic drawings and CT images of the cervical intervertebral foramen are shown below. In the calculations made accordingly; right side long axis preop 8.1204mm (±1.11766mm) postop 9.2061mm (±1.36830mm) (p<0.001), short axis preop 4.5959mm (±1.14782mm) postop 4.8714mm (±1, 24197mm) (p<0.001) and area preop 35.9735mm² (±11.55679mm²) postop 42.0429mm² (±12.89079mm²) (p<0.001). Left side long axis preop 8.1939mm (±1.16412mm) postop 9.3633mm (±1.32251mm) (p<0.001) short axis preop 4.4204mm (±1.14909mm) postop 4.7347mm (±1.20460mm)) (p<0.001) and area preop 34.6732mm² (± 10.97012mm²) postop 42.7203 (±12.66639 mm²) (p<0.001) Right side, long axis, short axis and area, respectively; There was an increase of 13.37%, 5.99%, 16.87%. Left side, long axis, short axis, and area respectively; There was an increase of 14.27%, 7.11%, 23.20%. (Table 1) As a result of this surgical procedure, a statistically significant increase was found in spinal foramen measurements (p<0.005%).

Table 1. Increase rates of long axis, short axis and area of cervical foramen after preoperative and postoperative measurements.

	Long Axle	Short Axle	Area
Right-Side	% 13,37	% 5,99	% 16,87
Left-Side	% 14,27	% 7,11	% 23,20

DISCUSSION

Cervical disc herniation is a disease that is seen frequently in the community and is frequently applied to the outpatient clinic with neck pain, myelopathy and radiculopathy. In the surgical treatment, providing neural foramen (NF) decompression in the control of pain caused by radiculopathy is the main purpose of surgery.

The anatomy of the cervical neural foramen has been described in several studies. Ebrahiem et al. (14) have divided the neural foramen groove into 3 as medial middle and lateral. The medial region is thought to be associated with the intervertebral disc (Picture 1.4). Nobuhiro and colleagues (15) divided the neural foramen into a narrow entrance zone and a large cone-shaped zone where it separates from the dural sac. He stated that the interveretbral disc hernia is associated with the narrow zone.

MR foramen compression is very valuable in the evaluation of cervical disc herniation. However, MRI does not show bone tissue pathologies as well as soft tissue pathologies. Therefore, CT imaging is helpful in surgical planning and in the evaluation of post-operative bone decompression. There are publications that indicate that the source of cervical foramen stenosis is osteophytes rather than soft tissue (16).

In our study, we compared the preoperative and postoperative images of 46 patients who underwent

ACDF in oblique CT. The surgeon did not know that such a study would be done while performing the operations. Therefore, the surgeon did not aim to increase the long axis of the foramen during the operation. He used the anterior cervical discectomy technique, which he used in daily practice. He performed bilateral uncinate process decompression and used the cage material of the maximum size he could distance. With oblique CT, the intervertebral foramen could be evaluated optimally (figure 2.1-2.3). As a result of our measurements and statistical study, the long axis of the neural foramen increased due to the cage we could place. Due to the decompression of the uncinate process, the short axis increased, and the area of the neuronal foramen increased, and the compression due to the bone spur was decompressed.

There are few studies similar to ours in the literature. In their study, Wu et al. showed that the height and area of the intervertebral foramen increased in the measurements they made with conventional CT after the application of intervertebral cage (17). Again, Liu et al. compared the heights of the interforamen in cervical MRI after traction for conservative treatment and showed that the height of the foramen increased as the load placed on the traction increased (15).

Oshina et al. (16) measured interforaninal heights in preoperative and postoperative conventional CT and MR in patients scheduled for cervical disc surgery. Then, they evaluated oblique CT and 3D CT measurements as preop and postop in the same patients and compared these two different measurement techniques. While preoperative CTs did not change the surgical indication, they found differences with conventional imaging techniques in postoperative comparison. However, as seen in these studies, while conventional CT provides information about the long axis, it cannot provide clear information about the short axis and, accordingly, the change in the interforamen area

CONCLUSION

In conclusion, decompression of the long axis of the foramen cannot be performed surgically in anterior cervical disc surgery. Due to the difficulty of reaching this region and its close proximity to important vascular and neural structures, adequate decompression cannot be achieved. However, increasing the long axis of the cage foramen placed at the intervertebral level will help to increase the area of the foramen and decompress the nerve. For this reason, the material with the highest height that can be placed at the level of the intervertebral disc during surgery should be placed.

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Author Contributions:
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Umbilical Cord Seperation Time and Related Factors

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Abstract

Objective: The aim of the study is to determine the methods used in umbilical care, the separation time of the umbilical cord, and the factors affecting it.

Methods: A quantitative longitudinal observational analytical study was conducted between May 2018-May 2019 in an obstetrics clinic of a state hospital in eastern Turkey. The study consisted of a sample of 345 newborns and their mothers. Necessary permissions were obtained before the research data were collected. The data were collected through face-to-face interviews and via telephone. The data obtained were evaluated by percentage distribution, Independent Samples t-test, ANOVA, and Mann-Whitney U test.

Results: The average gestational age of the newborns is 39.11 ± .71 week. 42.6% of the mothers stated that they performed umbilical cord care. The mean separation time of the umbilical cord in newborns was calculated as 7.55 ± 2.64 days. It was observed that the umbilical cord of the babies whose mothers put some application to the umbilical cord fell off in an average of 8.27 ± 2.97 days, while those who did not practice fell off in 7.01 ± 2.22 days ($p < 0.05$).

Conclusion: According to the findings of the study, keeping the umbilical cord open and dry without any application to it shortens the time of umbilical cord falling off.

Key words: Cord practice, Midfiwery, Newborn, Nursing, Umbilical cord

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INTRODUCTION

The navel in newborns is a susceptible area for a bacterial colonization that causes infections such as neonatal sepsis and omphalitis (1-4). Shortly after birth, the umbilical cord encounters non-pathogenic bacteria such as coagulase-negative staphylococci and diphtheroid bacilli(5-7).The World Health Organization claims that one-fourth of the neonatal deaths in the world are due to the infection; 75% of these occur in the first week of life, with the umbilical cord being the gateway (8,9). Therefore, umbilical care is important to prevent infections in the neonatal period (4,10,11).

The umbilical cord is colonized by microorganisms of the vagina, skin, and the obstetrician's hands. Hand washing is the simplest and most effective way to prevent contamination of the umbilical cord. However, since it is not always possible to apply this, it is recommended to use antiseptics in the care of the umbilical cord (7,12-14). When the conducted research are examined, it is seen that antiseptics such as alcohol, triple dye, chlorhexidine, antibiotics (mupirocin, polybactrin, bacitracin, etc.), hexachlorphene containing powder, silver sulphadiazine, and povidone-iodine are used in umbilical care (4,15-20).

It has been observed that the use of topical antiseptics or antibiotics is not predominant in developed countries, but it is effective in areas at high risk for neonatal tetanus or in poor hygienic conditions (2,3,16,19,20). Apart from the fact that antiseptics have negative effects such as its iodine and mercury compounds are absorbed into the blood, having a neurotoxic effect (3), causing burns on the skin (13). It has been also reported that it delays the separation time of the umbilical cord (12,21,22). Delay in the separation of the umbilical cord increases the risk of developing infections. However, the purpose of umbilical care is to keep the cord dry and moisture-free so as not to lead to infection (4,7,11,19,23).

There are different applications in the literature on umbilical cord care according to the development levels of the countries. Especially in developing regions with low socioeconomic levels, antiseptic applications to the umbilical core are observed (5,7,13,19-21,24). The low socio-economic level of the province where the study was planned and the lack of data on umbilical care gives an important role to the health care professionals, especially to the nurses and midwives.

Therefore, the research was carried out to determine the methods used in umbilical care, the separation time of the umbilical cord, and the factors affecting it.

METHODS

Design

A quantitative longitudinal observational analytical study.

Sampling and Setting

The study was conducted between May 2018-May 2019 in an obstetrics clinic of a state hospital in eastern Turkey. The study consisted of a sample of 492 newborns born between the specified dates in the obstetrics and gynecology service of the state hospital and their mothers.345 newborns and their mothers who met the inclusion criteria were included in the research sample. The sample represents 70% of the population.

Inclusion Criteria

"Mothers and babies without mental illness, babies and mothers who do not need intensive care, babies and mothers without abdominal malformations, and mothers willing to participate in the study".

Data Collection Tool

A 45-question form was used. The first part consists of the introductory features of the newborn and the parents (20 questions) as a data collection tool in the research. The second part includes mothers' practices for umbilical care and the separation of the umbilical cord and changes around the umbilical cord area (25 questions).

Data Collection

The purpose of the research was explained to the mothers in the obstetrics clinic after obtaining the necessary legal permissions for the research. After obtaining written consent from the mothers who volunteered to participate in the study, a questionnaire that lasted an average of 10-15 minutes was completed by the mothers. Mothers were asked to check when and how often they bathe their babies, to check the cord area, and record the separation time of the cord. Mothers were called on the 10th day following the birth of the baby. Questions about the umbilical cord were asked to the mothers on the phone and recorded on the form. This process took an average of 5 minutes. The mothers of the newborns whose umbilical cord did not fall off within the first 10 days were called on the 14th day and if it still did not fall off, the data were collected on the 20th day

Statistical analysis

The Statistical Package for the Social Sciences (SPSS) 18.0 software program was used to analyze the data in a computer environment. The data were evaluated with percentage distribution, independent samples t test, Anova and Mann Whitney U test. Normality tests were performed before the variables were analyzed. The t test was used for the normally distributed variables, and the Anova and Mann Whitney U tests were used for the non-normally distributed variables.

RESULTS

57.4% of the mothers with an average age of 29.52 ± 5.17 were high school graduates and 77.1% were not working in an income-generating job.83.5% of the mothers reside in the city center, 85.2% of them stated that their income is equal to their expenses. 43.8% of the mothers who had an average of 1.65 ± .68 children stated that they had their last birth via cesarean section (Table 1).

The average week of gestation of the newborns included in the study was 39.11 ± .71, the average height was 49.83 ± 1.05 cm, the average weight was 3404.78 ± 1769.22 g, 36.8% of them were born in the winter season and 58.8% were male. Although not included in the table, it was observed that the average bathing period of the newborns was 3.47 ± 2.34 days, 43.8% of them were bathed on the third day and 90.4% of them were bathed in a sunken bath (Table 2).

42.6% of the mothers stated that they performed umbilical cord care, 95.4% of them stated that they used 70% alcoholic solution package sold from the pharmacy, 4.1% used povidone iodine, and 86.4% left the umbilical cord open.5.8% of the newborns showed signs of infection, 85.0% of them were applied antibiotic ointment to the umbilical cord, while 15.0% of them received an alcoholic solution.

The umbilical cord of the newborns fell off at an average of 7.55 ± 2.64 days (Table 3).

Table 1. Characteristics of Mothers

Variables	N	%
Age (Year)(X̄±SD)	29.52±5.17	
Age		
Aged 25 and below	77	22.3
Aged 26 and above	278	77.7
Educational status		
Middle school and under	40	11.6
Highschool	198	57.4
University and above	107	31.0
Employment status		
Yes	79	22.9
No	266	77.1
Place of residence		
Centre	288	83.5
District	29	8.4
Countryside	28	8.1
Economic Condition		
Income less than expenses	51	14.8
Income equal to expenses	294	85.2
Route of delivery		
Vaginal delivery	194	56.2
Cesarean section	151	43.8
The average number of children (X̄±SD)	1.65±.68	

Table 2. Socio-demographic Variables of Newborns

Variables	n	%
Gender		
Female	142	41.2
Male	203	58.8
Gestational age(week)(X̄±SD)	39.11±.71	
Height (cm) (X̄±SD)	49.83±1.05	
Weight (gr) (X̄±SD)	3404.78±1769.22	
Season of the year		
Winter	127	36.8
Spring	99	28.7
Summer	67	19.4
Fall	52	15.1

When some factors related to the separation time of the umbilical cord were examined, it was observed that the umbilical cord of the babies whose mothers aged 26 and over fell off in a shorter time (7.52 ± 2.66) compared to the mothers 25 years and younger. It was observed that the umbilical cords of the babies whose mothers put some applications to the cords fell off in an average of 8.27 ± 2.97 days, while the umbilical cords of the babies whose mothers did not put any applications to the cords fell off in 7.01±2.22 days.A statistically significant relationship was observedbetween the practice of an application to the umbilical cord and the time for the cord to fall off(t=4.523, p=.000).While the mean time for the umbilical cord to fall off was 7.30 ± 2.40 days for those who kept the umbilical cord area open to the air, it was calculated as 9.14 ± 3.45 days for those who kept it covered.A statistically significant relationship was found between the practice of an application to the umbilical cord area and the time for the cord to fall off(t=4.571, p=.000).

Table 3. Distribution of Some Conditions Related to the Umbilical Cord and Its Care in the Newborn

Variables	n	%
Application to the umbilical cord		
Yes	147	42.6
No	198	57.4
If yes, the application (n=147)		
Umbilical cord care kit (alcoholic solution)	141	95.9
Povidone iodine	6	4.1
Taking care of the umbilical cord area		
Open	298	86.4
Covered	47	13.6
Signs of infection around the umbilical cord	20	5.8
Yes	325	94.2
No		
If yes, the application [a](n=20)		
Antibiotic Ointment	17	85.0
Cleaning with alcohol	3	15.0
Cord separation time (day) (X̄±SD)	7.55±2.64	

[a]= Number of respondents

The mean time of separation of the umbilical cord in babies who were bathed in the first 2 days after birth was 6.79 ± 2.29 days while it was 7.80 ± 2.46 days for those bathed on the 3rd day and 8.20 ± 2.64 days for those bathed on the 4th day.A statistically significant correlation was observed between the

newborns' first bath time and the separation time of the umbilical cord (F = 8.152,p=.000).It was also found that as the frequency of bathing increased, the separation time of the umbilical cord shortened, but this correlation was not statistically significant (F =2.857, p =.059) (Table 4).

Table 4. Distribution of Factors Associated with the Separation Time of the Umbilical Cord

Variables	Cord separation time (day)	Test/p
Mother Age		
Aged 25 and below	7.67±2.56	t=.447, p=.665
Aged 26 and above	7.52±2.66	
Application to the umbilical cord		
Yes	8.27±2.97	t=4.523,p=.000
No	7.01±2.22	
Taking care of the umbilical cord area		
Open	7.30±2.40	t=4.571,p=.000
Covered	9.14±3.45	
First bath time		
Within the first 2 days	6.79±2.29	F=8.152,p=.000
3rd day	7.80 ±2.46	
4th day and after	8.20 ±2.64	
Frequency of bathing		
Everyday	7.43±2.70	F=2.857,p=.059
Every other day	7.41±2.32	
Other	8.38±3.54	
Signs of infection around the navel		
Yes	8.40±2.56	U=2449.500,
No	7.50±2.64	p=.060

t= t test F= Anova U=Mann-Whitney U

DISCUSSION

The umbilical cord falls off within the first 15 days after birth (25). The delay of the separation time of the umbilical cord by exceeding 1 month suggests bacterial infections and some blood diseases (15). Therefore, evaluation of the separation time of the umbilical cord and related factors becomes important for healthcare professionals. In this study, the separation time of the umbilical cord is 7.55 ± 2.64 (Min = 3 Max = 18) days. The World Health Organization recommends keeping the cord clean and dry (26). A study reports that keeping the area around the umbilical cord dry is a safe, economical, and easy practice (27). However, it is seen that there are different practices regarding umbilical cord care in health institutions and some families (25). 70% of alcohol consumption is recommended for umbilical cord care in the hospital where the study was conducted. However, only less than half of mothers practiced the umbilical cord care. Almost all of the mothers who practice cord care use the alcohol solution recommended by the hospital for the care. Although the number is low, it is seen that mothers also use povidone iodine in cord care. When the literature is examined, the use of alcohol in neonatal umbilical care contradicts the general recommendations and delays the fall of the umbilical cord (9,18). In this study, the fact that almost half of the mothers use alcohol in umbilical care as a routine practice does not coincide with the evidence-based practice approach in nursing. In other studies, it is seen that practices such use of alcohol and chlorhexidine are preferred for cord care in different hospitals (5,7,10,18,24,25). In the research, it is seen that the umbilical cord of the babies that weren't taken care of and left dry and open (7.01 ± 2.22, 7.30 ± 2.40) falls off in a shorter time. A study reported that the umbilical cord of the babies treated with chlorhexidine took 13.28 ± 6.7 9 days to fall off while the mean time for the dry umbilical cord group to fall off was reported as 7.85 ± 2.51 days (15). Also, in another study it was found that the mean separation time of the umbilical cord was 6.36 ± 2.88, and the separation time of the umbilical cords left dry without application was 4.78 ± 1.82 days (28). Quattrin et al.

(25) reported that the umbilical cords applied alcohol fell off in 12.0 ± 4.2 days and those left dry fell off in 10.1 ± 4.0 days. Khairuzzaman et al. (18) stated in his study that the mean cord separation time in chlorhexidine and dry cord care groups were 7.44 ± 3.75 and 4.83 ± 2.05 days after birth respectively. Ozdemir et al. (24) reported that the umbilical cords of babies who were treated with dry care fell off in a short time (average 7 days), and those who were applied 4% chlorhexidine (average 10 days) fell off in a longer time. As seen in this latest study and other studies, the umbilical cord of newborns that were left open and dry without any application fell off earlier. It is observed that mothers who are young, have a high economic level, and reside in the center have a higher rate of practice on the umbilical cord care. In the hospital where the study was conducted, it is recommended not to bathe the newborns until their umbilical cord falls off. However, in this study, it was observed that almost all mothers had their babies bathed before this recommended period. It was observed that the umbilical cord of the babies who were bathed in the first 2 days fell off in a shorter time. Ayyildiz et al. (29) reported that the umbilical cord fell off in 6.1 ± 1.4 days in babies given a sponge bath, and 8.3 ± 2.5 days in those given tub bath. It was reported that 3.9% of babies who were given tub bathing had symptoms of omphalitis. In this last study, 5.8% of mothers reported that newborns had symptoms of omphalitis. Also, it is observed that the separation time of the umbilical cord is delayed in newborns with omphalitis.

Limitation

In this study, the separation time of the umbilical cord and related factors were obtained from the mothers' self-reports. Data are subjective. In addition, the results obtained in the study can be generalized to the study group in which the research was conducted.

CONCLUSION

According to the findings obtained in the study, keeping the umbilical cord open and dry of the newborns and the first bath time shorten the separation time of the umbilical cord. Therefore, unless there is a medical requirement, it is recommended to use "the dry care method (" keep clean and dry "), as suggested by the World Health Organization and America Academy of Pediatrics. In this context, it is recommended that both health professionals and mothers be supported with evidence-based practices in belly care.

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Analysis of Forensic Geriatric Patients Admitted to Emergency Department

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Abstract

Objective: Today, geriatric individuals are experiencing more health problems due to physiopathology changes caused by old age. In this study, demographic properties and diagnosis and treatment process in emergency service of geriatric cases who were admitted to emergency service and filed judicial report.

Methods: In four years (2013-2016), 65 years and older who applied to the emergency department of a university hospital and the data of 737 patients whose forensic reports were prepared were investigated. Data of this study were obtained from patient files and automation system records. Socio-demographical properties (age, gender), reason to admit to emergency service, trauma type, duration of treatment in emergency service, type of treatment outcome, and department of admittance were investigated.

Results: Average age of 737 cases were 73.70±7.54 (Female/Male,309/428). 84% of the cases had come to the service with trauma, and the most common reason for trauma was fall (45.4%). Highest number of the cases were observed in summer and autumn. Most common pathology in the cases was fracture (37.3%). 38% of the cases were admitted to related clinics, 5.6% of the cases died, and 56.4% of the cases had outpatient treatment.

Conclusion: In this study, the most common cause of forensic reports in elderly patients admitted to the emergency department was trauma caused by falls (street or home) and the resulting fracture.

Key words: Elderly, Emergency department, Forensic case, Geriatrics

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INTRODUCTION

World Health Organization (WHO) defined old age as "decrease in adapting to environmental factors" and accepted old age as 65 or above (1). As speed of death had decreased, preventive and medical health services had developed, diagnosing patients became easier with technology, and increased treatment options had extended average life expectancy. Thus, number of geriatric populations around the world had increased (2).

It is clear that geriatric individuals had decrease in adapting to new environment, perceiving events, and applying activities that require attention. As a result, it is also observed that those individuals acted slowly and carelessly (3). Therefore, geriatric patients are subjected to trauma more. Both multiple traumas and physiopathology, metabolic changes related with old age, and comorbid increased the frequency of complications as well as treatment (4). In Turkey, Unal et al. (5) stated that 20% of emergency service patients were geriatric group. In judicial geriatric cases in the hospital, increased mortality and morbidity was visible (6).

In this study, the main objective was to retrospectively determine demographical and clinical properties of 65 years or older cases where judicial report was filed when those individuals came to emergency service. The results of this study will contribute to forming country-based data, and rational, effective diagnosis and treatment protocols can be created for regional geriatric cases.

METHODS

After approval of ethical committee for using the data of patients, cases between 01 January 2013-31 December 2016 in Medical Faculty Hospital emergency service of individuals who are 65 years old or higher were investigated (ethical committee no: 2017/86). This study was planned descriptive and retrospective. Data of this study were obtained from patient files and automation system records. As there were insufficient information in a case file and records, this was excluded form evaluation. Socio-demographical properties (age, gender), type and time they came to emergency service, trauma type, injured body part, duration of treatment in emergency service, treatment outcomes, department of admittance, and mortality rates were investigated. Falls at home and on street were all defined under fall category.

Statistical analysis

Statistical analyses were conducted with SPSS 21.0 program. For numerical variables of descriptive analysis arithmetic average, and standard deviation were represented as number and percentage for category variables. Descriptive statistics were used and the relationship between intergroup and category variables were investigated with Chi-square test. Results were evaluated at 95% reliability rate, and $p<0.05$ was accepted as significant**.**

RESULTS

In 3-years period, 737 cases with judicial report and with individuals 65-years or older were determined in emergency service. 309 (41.9%) were female and 428 (58.1%) males. General average age was 73.70 ± 7.5, average age of female was 75.00 ± 7.5, and average age of male was 73.89 ± 6.6. There was no significant difference with gender for different years ($p=0.466$).

When years and age average relationship was investigated (Table 1), there was significant

relationship between gender and age averages of individuals in 2015 (p=0,001).

Table 1. Relationship between years and age average of female and male

	Female		Male		p value
Year (n)	n	Average age	n	Average age	
2014 (284)	158	73.77±6.5	126	75.76±7.7	0.020
2015 (222)	129	72.34±6.0	93	75.36±7.5	0.001
2016 (231)	90	74.20±7.0	141	72.13±6.7	0.028

38.5% (n=283 people) of all cases applied in 2014, 30.25% (n=223) applied in 2015, and 31.3% (231) applied in 2016. When season applications were investigated the highest values were observed in autumn (31% n=230), and summer (29.5% n=218). In 2014, 30.38 (n=86) applied in summer, 29.32% (n=83) applied in autumn; in 2015, 30.49% (n=68) applied in autumn, 27.35% (n=61) applied in summer; in 2016, 30.30% (n=70) applied in summer, 26.83% (n=62) applied in autumn (Figure 1).

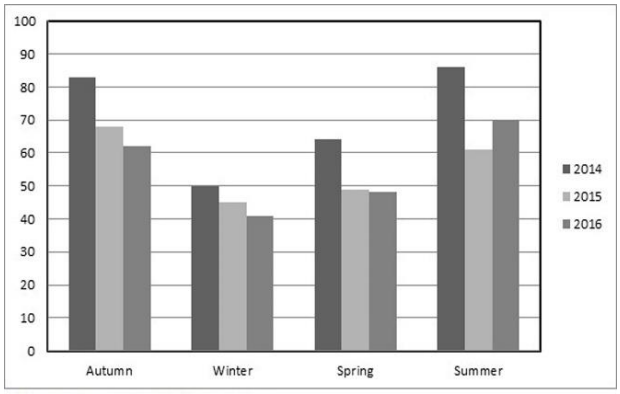

Figure 1. Seasonal distribution of patients

When application reasons of the patients were investigated, most common type was identified as trauma (84% of cases n=620). Most common reason for trauma was 45.4% (n=334) fall, and 20.4% (n=150) traffic accident. For female patients, 56.85% (n=175) had fall, 10% (n=31) had in-vehicle traffic accident, 5% (n=14) had extravehicular traffic accident, and 17.5% (n=54) had poisoning. For male patients, 37.2% (n=159) had fall, 14% (n=60) had in-vehicle traffic accidents, 10.6% (n=45) had extravehicular traffic accident, 15.5% (n=66) had sharp object injuries, and 11% (n=45) had poisoning. In both genders, there was significant difference for motor vehicle accident and fall compared to other trauma types (p=0.001).

When application reasons were investigated on yearly bases, in 2015 there was no significant difference between reasons; in 2016, there was statistically significant difference for motor vehicle accident, fall, and foreign object aspiration, in 2014 there was statistically significant difference for motor vehicle accident, and fall (p=0.0001). Fall had the highest values for all three years (in 2016 33.8% (n=78); in 2015 48.2% (n=107); in 2014 52.8% (n=149)). In 37.3% (n=275) of the cases fracture was observed. Additionally, in multiple trauma cases where two or more systems were affected, the ratio was determined as 70% (n=50), where for three or more systems the ratio was 30% (n=22). In multiple trauma cases where two or more systems were affected, most common was “extremity trauma and thorax trauma” with 40% (n=20), and least common was abdomen trauma and head-neck trauma with 1.4% (n=1). In multiple trauma cases where three or more systems were affected, most common was thorax with 77% (n=17), extremities with 68% (n=14), and head-neck with 45% (n=10). When treatment of the patients after emergency service were investigated 38% (n=279) of patients were admitted to related clinics, 5.6% (n=42) died, and 56.4%

(n=416) received outpatient treatment (Table 2). It was determined that 34% (n=105) of female cases, and 40.7% (n=174) of male cases were admitted to hospital. When gender and emergency service treatment outcomes were investigated, there was no significant difference (p=0.257).

When hospital admittance and application reasons were investigated, most common admittance were caused by 39.8% (n=181) fall, 23.5% (n=107) motor vehicle accident, 17.1% (n=78) poisoning, and 9.2% (n=42) blunt trauma. There was statistically significant relationship between admittance rate and application reasons (p=0.001).

Patients who admitted to hospital were mostly admitted to orthopedy clinic (n=116, 26%), emergency service (n=105, 23.1%), thoracic surgery (n=72, 16%), and brain surgery (n=60, 13.2%) services respectively, and least to otorhinolaryngology (n=2, 0.4%) service. Outcomes of cases were given in Table 2. When the relationship between case outcomes and gender was investigated, there was no significant difference (p=0,257). Most common cause of death among cases was motor vehicle accident (n=20, 48%), and fall (n=17, 41%). When the relationship between death rate of cases and application reasons was investigated, there was significant difference (p=0,001). 25.6% (n=189) of the patients applied to emergency service were operated, 64.4% (n=475) were evaluated with computer tomography (CT), 11.7% (n=86) were evaluated with magnetic resonance (MR), and 95.1% (n=702) were evaluated with direct graphs (Figure 2).

DISCUSSION

Increase in geriatric population is regarded as an important economic and social problem around the world. Fall is the first cause of injury in geriatric patients. In this study that aimed identifying judicial geriatric cases and determining related precautions in our region, it was observed that geriatric trauma ratio was high (n=620, 84%), and most common injury type was fall (n=334, 45.4%). Physiopathology changes in geriatric cases and increased medication use changes outcome, progress, and cost of trauma (7,8). In this study, 37.2% (n=159) of male, and 56.8% (n=175) of female cases indicated fall. Current diseases and decreased muscle and bone mass in geriatric patients increases the frequency of motor skill falls (9). Additionally, transition to elementary family from large family after industrial revolution showed a decrease in number of family members that lived together. Thus, trauma ratio of older people at their home increases. In addition, osteoporosis in female is frequently visible with decreased visual acuity and mobility, while balance loss during walking increases the frequency of falls (6). Tuncay et al. (10) found that fall frequency of geriatric patients was 38.1% within one-year frame. Hawk et al. stated that fall ratio of geriatric patients was 44% within one-year frame (11). Tanrikulu (12) stated that fall in both genders had 82.3% ratio. Durak et al., (13) in their study on patients who applied to the forensic medicine institution, detected trauma at a rate of 94.5%, and the female-male ratio was found to be 2/1. Beating was detected in 65.7% of the admitted geriatric patients and falls were detected in only 1.4% of them. The findings of this study were in line with the literature. We believe that precautions that will prevent geriatric patients to fall, and exercise programs that will develop and protect reflexes will decrease the traumas related with fall.

In our study, among 20.4% (n=150) of all cases, traffic accidents were the second most common trauma after falls. Among all cases, 12% (n=91) experienced in-vehicle traffic accident where 8.4% (n=61) experienced extravehicular traffic accident. Traffic accidents were less common in geriatric patients. However, these patients need more admittance and intensive-care services. It is believed that this relates to decreased driving rates with old age. Additionally, mortality rates related with accident were higher than other adults (14). Bilgin et al (6) and Aktas et al. (15) identified that most common trauma mechanism on geriatric patients were fall and traffic accidents. Bilgin et al (6). found that in-vehicle and extravehicular accident rates were close (in-vehicle 48.6%; extravehicular 46.3%). Yasar and Buken (16) found that 67.81% was in-vehicle accidents where 29.4% were extravehicular accidents. Different from our studies, Kandis et al. (17) found that traffic accident ratio was 69%, and fall ratio was 10%.

In our study, traffic accident was more common in male patients (n=105, 24.6%) compared to female patients (n=45, 14.6%). The reason for more common results in male patients indicated that male drivers are more intense in traffic and live more actively. Decreased visual and audial functions, slow motions during walking, unable to notice vehicles due to old age could be listed among reasons for extravehicular traffic accidents

In our study, 38% (n=279) were admitted to related clinics, and 5.6% (n=42) were dead. Ozturk et al. (2017) found that 68.5% of geriatric patients were admitted to hospital (18). Satar et al. (19) stated that admittance ratio was approximately 59.8% where death ratio was 2% among geriatric patients who come to emergency service. Kandis et al. (12), found admittance at 17% level and Tanrikulum (17) found 12.4%. Dagar et al., (20) identified 11.5% of patients with life-threatening condition and found that 3.2% of these patients died. It is believed that in literature, different death ratios due to trauma was related with trauma region and current conditions of the patients.

When locations of injuries were evaluated, 37.3% (n=275) of the patients had fracture. Most common damage were seen in extremities (34.3%, n=212). The fact that geriatric patients have more osteoporosis or osteoarthrosis explains the frequent occurrence of fractures. Similarly, Bilgin et al. (6) found 33% extremity trauma in their study. Akoglu et al., (21) determined that in both local and multiple trauma patients, most organ injuries were extremities. Tanrikulu (12) found in a study conducted in Erzurum that, extremity trauma ratio was 77%. Durak et al., (13) determined that isolated head trauma (35.2%) and isolated extremity trauma (31.0%) were the most common. Traumatic bone fracture was detected in 31.0% of the patients.

Patients who admitted to hospital were mostly hospitalized in orthopedy clinic (n=57, 26%), emergency service (n=35, 23%), thoracic surgery (n=35, 16%), and brain surgery (n=29, 13.4%) services respectively, and least to otorhinolaryngology (n=8, 0.4%) service. Most common cause of death among cases was motor vehicle accident (n=20, 48%), and fall (n=17, 41%).

In our 3-yearlong study, it was determined that male geriatric patients who applied to emergency service of a university hospital were subjected to more trauma (58.1%, n=428). Findings of our study

were consisted with other studies. It is believed that such high ratio is related with actively working male population, and active involvement to social life. When seasonal distribution of hospital applications was investigated, each 3 years showed similar results, and the highest ratio was observed during winter, and highest ratio was observed during summer and autumn. In the Samsun region, the coastline had temperate climate while the interior region has continental climate. Therefore, due to cold weather conditions during winter, it was seen that geriatric population mostly spent time at home and were inactive. Kandis et al. investigated cases applied to hospital in Kirikkale and found that number of cases decreased during winter and number of cases increased during spring and summer (17). Tanrikulu and Tanrikulu (12) investigated geriatric cases in emergency services in Erzurum and found that highest number of applications to emergency services were during summer and autumn and lowest number or applications were during winter.

In our study, mortality rate of cases that applied to emergency service and judicial reports were filed was determined as 5.6% (n=42). Guneytepe et al. (22) identified mortality ratio as 9.6%.

Emergency services are highly intense departments where first aid is made, and patients are directed to different clinics if necessary. Due to physiognomy, mental and motor system decreases, geriatric patients are more defenseless against trauma and various diseases. Therefore, those patients apply to emergency services with higher admittance and treatment needs. Additionally, since treatment processes of geriatric patients is longer, those patients are subjected to radiological and laboratory processes, and require more complex service. It is extremely important to regulate emergency services in hospitals according to needs of geriatric patients. Therefore, increasing the number of research regarding emergency service application of geriatric patients across the country will be guiding to plan services with high quality.

To help geriatric patients to live healthy and active life, reasons and frequencies of trauma should be determined, preventive precautions should be taken, cost and functionality analysis should be conducted, and emergency service needs should be arranged accordingly. Different corporate regulation is needed for different requirements of geriatric patients to help increasing life quality and decreasing health costs.

CONCLUSION

As a result, in this study, the most common cause of forensic reports in elderly patients admitted to the emergency department was trauma caused by falls (street or home) and the resulting fracture. It was found to be the most common case application in summer and autumn season. Although there are many articles about geriatric patient groups in the literature, geriatrics and forensic cases are a subject that has not been studied much together. We think that our study will contribute to this deficiency.

Ethics Committee Approval: Was obtained from the Ondokuz Mayis University Ethical Committee (approval number: OMÜ KEAK 2017/68)

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I.A, M.E, Writing- M.K, L.D, I.A, M.E, Critical Review- M.K, L.D, I.A, M.E.

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RESEARCH ARTICLE

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Comparative Evaluation of Cyclic Fatigue and Corrosion Resistance of Three Different Nickel-Titanium Instruments

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Abstract

Objective: The aims of the study are to investigate the effect of the surface treatment process on prolonging the life of the rotary instruments against cyclic fatigue and the effect of the surface coating process on the corrosion resistance of Ni-Ti files.

Methods: This study was carried out in two stages. In the first one, a total of 120 Ni-Ti rotary instruments (25/.04 taper) from 3 brands (HeroShaper, RaCe, and TF) were selected. Sixty of them were anodized then all of them were tested in simulated root canals with two different curvatures. The time until fracture was recorded, and the number of cycles was calculated for each group. The second stage; the effect of anodization on corrosion resistance was assessed. The file groups tested in 5% NaOCl solution at 37° C. Data were subjected to The Mann-Whitney U test. The significance level was set at P= 0.05.

Results: There was a statistical difference among the rotary systems in terms of cyclic fatigue. Among the file types, TF instruments were the most resistance to cyclic fatigue and RaCe instruments had the lowest results. The effect of anodization process was different among file groups.

Conclusion: Within the limits of this study, the increase in canal curvature reduces the life of the rotary instruments. While the anodization process did not change cyclic fatigue in all file groups in 20° curved canals, it reduced the wear life of RaCe and HeroShaper files and extended the wear life of TF files in canals with 37° curved canals.

Key words: Anodization, Canal curvature, Corrosion, Cyclic fatigue, HeroShaper, RaCe, Ni-Ti, Rotary system files, Twisted File.

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INTRODUCTION

The root canals must be cleaned, shaped, disinfected, and hermetically filled for successful endodontic treatment (1). Recently, nickel-titanium (Ni-Ti) rotary instrument systems have been used for shaping root canals. These systems are exposed to cyclic fatigue and corrosion in the root canal. Sudden breakage of files because of this stress affects the success of endodontic treatment negatively. Metal fatigue results from cyclic fatigue, static torsional fatigue, and dynamic torsional fatigue. Cyclic fatigue is the common cause of breakage in continuous rotary systems (2-4).

In parallel with the developments in the field of engineering, various surface treatments are applied to the files to prolong the life and increase its durability. Among these applications, the most frequently used process is surface coating with anodization. Anodization is controlled oxidation performed to form a protective oxide film or layer on a metal surface that can slow or prevent further oxidation (5).

Effective canal irrigation along with mechanical preparation is also very important for the success of endodontic treatment. Besides their antimicrobial benefits, irrigation solutions also facilitate mechanical shaping. Despite all these advantages, these solutions can have some chemical and electrochemical effects on the canal instruments, causing corrosion on the surface of the canal files, which is manifested by pitting and porosity (6). The studies have reported that the pits and porosity formed on the surface because of corrosion reduce the cutting capacity of the file and decrease the resistance against breakage (6,7). Therefore, it is desirable that Ni-Ti canal files are not affected by the irrigation solution.

The aims of this study are to investigate the effect of the surface treatment process on prolonging the life of the rotary instruments against cyclic fatigue and corrosion tendency of Ni-Ti files and the effect of the surface coating process on the corrosion resistance of Ni-Ti files. The first null hypothesis is that there are not significant differences among the instruments in terms of the number of cycles to file breakage and time to fracture. The second null hypothesis is that the surface treatment process does not affect the life of the rotary instruments against cyclic fatigue. The third null hypothesis is that the surface treatment process does not affect the corrosion resistance of Ni-Ti files.

METHODS

This experimental study is taken from the thesis “Comparative Evaluation of Cyclic Fatigue and Corrosion Resistance of Three Different Nickel-Titanium Instruments” done in 2011 at Atatürk University. This study was approved by the Ethics Committee of the graduate school of health sciences of Atatürk University, Erzurum, Turkey, (2011.3.1/7).

This study was carried out in two stages. In the first stage, the cyclic fatigue test was applied to covered and non-covered RaCe (FKG Dentaire, La-Chaux-de-Fonds, Switzerland), HeroShaper (Micro-Mega, Besancon, France), and Twisted Files (TF) (SybronEndo, Orange, CA). The second stage; the corrosion resistance of these systems in 5% NaOCl was evaluated.

Cyclic fatigue test.

The cyclic fatigue testing block prepared by Atatürk University Engineering Faculty was used in this study. The properties of the canals on the testing block were 16-mm the working length, 5-mm the radius of curvature, and 20°, 26°, 30°, and 37° the angles of curvature, 1 mm the diameter and depth. The canals have 20° and 37° angles of curvatures were used in this study.

Before the test procedures, surface images were taken from the canal files with Scanning Electron Microscopy (SEM) (JSM 6400-Scanning Electron Microscope, Jeol, Tokyo, Japan).

Then, a total of 60 files (20 files from each system) were randomly divided into 6 groups.

1. Group: 25/.04 RaCe files (20° angle of curvature) (n=10)

2. Group: 25/.04 HeroShaper files (20° angle of curvature) (n=10)

3. Group: 25/.04 TF files (20° angle of curvature) (n=10)

4. Group: 25/.04 RaCe files (37° angle of curvature) (n=10)

5. Group: 25/.04 HeroShaper files (37° angle of curvature) (n=10)

6. Group: 25/.04 TF files (37° angle of curvature) (n=10).

X-Smart (Dentsply, Maillefer, Ballaigues, Switzerland) torque-controlled endodontic motor was used with 2 N/cm torque and 500 rpm

The lubricant gel (FileCare gel; Munich, Germany) was applied to the testing canals for each file. The chronometer, 1/100 second sensitivity, was started when the file started to rotate, and it stopped when the file broke. The total working time was recorded for each file.

The lubricant on the surface of the broken files was cleaned by an ultrasonic cleaner. Then, SEM images were taken from the broken surfaces.

Anodization (Anodic Oxidation) process

The coating process was carried out at 25°C, in 2 M acetic acid solution, at 10 V current, for 5 minutes and the surface images were taken by SEM. Then, a total of 60 files (20 files from each system) were randomly divided into 6 groups.

1. Group: anodized 25/.04 RaCe files (20° angle of curvature) (n=10)

2. Group: anodized 25/.04 HeroShaper (20° angle of curvature) (n=10)

3. Group: anodized 25/.04 TF (20° angle of curvature) (n=10)

4. Group: anodized 25/.04 RaCe (37° angle of curvature) (n=10)

5. Group: anodized 25/.04 HeroShaper (37° angle of curvature) (n=10)

6. Group: anodized 25/.04 TF (37° angle of curvature) (n=10)

All the cyclic fatigue procedures mentioned above were done for these groups as well.

In the corrosion test, potentiodynamic scanning was performed using the Gamry G750 (Pennsylvania, USA) block in the Engineering Faculty of Atatürk University.

Corrosion process

A triple corrosion unit consisting of canal file, reference electrode, and counter electrode was set up in a glass container. The reference electrode was Ag/AgCl, and the counter electrode was graphite. After connecting the file and electrodes (according to

the recommendations of the manufacturer), measurements were performed at a scanning speed of 2 millivolts/sec in the potential range of -1 volt / +1 volt.

5% NaOCl (White Med, U.K.) was used as solution and the solution temperature was kept constant at 37°C, which is body temperature throughout the procedure. HeroShaper, RaCe, and TF files, and anodized HeroShaper, anodized RaCe, and anodized TF files were subjected to the corrosion test. The obtained data were recorded.

Statistical analysis

The descriptive analyses for the groups were calculated. The Mann-Whitney U test was performed after the normality and homogeneity tests. The data were analyzed using Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) for Windows, version 15 software. The statistical significance was set at $p < 0.05$**.**

RESULTS

The results of non- covered HeroShaper, RaCe, and TF files in 20°curved experimental setup are shown in table 1. There were significant differences among the instruments in terms of the number of cycles to file breakage and time to fracture in 20° curved experimental setups (Table 2).

Table 1. The means and standard deviations (SD) of the time and the number of cycles to file breakage in 20°curved experimental setup.

	The time to file breakage mean ±SD	The number of cycles to file breakage mean ±SD
HeroShaper	457.66±62.39	3813.83±519.90
RaCe	375.39±55.21	3128.23±464.27
TF	814.99±249.04	6791.61±2075.34

Table 2. *P* values among the groups in 20° curved experimental setups. ($p < 0.05$)

Instruments	HeroShaper	RaCe	TF
HeroShaper	-	0.008	0.000
RaCe	0.008	-	0.000
TF	0.000	0.000	-

Results of non-covered HeroShaper, RaCe, and TF files in 37° curved experimental setup are shown in table 3. There were significant differences between HeroShaper and RaCe (p=0.000). and between TF and RaCe (p=0.000) in terms of the number of cycling to file breakage and time to fracture (p>0.05) (Table 4). However, there were no significant differences between HeroShaper and TF (P=0.121) (Table 4).

Table 3. The means and standard deviations (SD) of the time and the number of cycles to file breakage in 37° curved experimental setup.

	The time to file breakage mean ±SD	The number of cycles to file breakage mean ±SD
HeroShaper	64.39±6.43	536.58±53.55
RaCe	31.02±5.42	258.51±45.22
TF	71.9±12.41	599.19±103.44

Table 4. *P* values among the groups in 37° curved experimental setup ($p < 0.05$).

instruments	HeroShaper	RaCe	TF
HeroShaper	-	0.000	0.121
RaCe	0.000	-	0.000
TF	0.121	0.000	-

Evaluation of the effect of root canal curve

The increase of root curve in the experimental setup was caused significant decrease in the number of cycling and time to file breakage for all instruments (Table 5).

Table 5. *P* values between 20° and 37° non-covered curved canals ($p < 0.05$).

	HeroShaper	RaCe	TF
P (time)	0.000	0.000	0.000
P (number of cycles)	0.000	0.000	0.000

Evaluation of the Effect of Anodization Process

There was no significant effect of the anodization process statistically among the groups for 20° curved experimental setups. The P values are shown in Tables 6.

Table 6. *P* values between covered and non-covered instruments in 20° curved canals.

	HeroShaper	RaCe	TF
P (time)	1.000	0.45	0.07
P (number of cycles)	1.000	0.45	0.07

There was significant effect of the anodization process statistically among the groups for 37° curved experimental setups. The p values are shown in Tables 7.

Evaluation of Corrosion Test

As a result of the corrosion test, it was found that the anodization process had a positive effect on the HeroShaper file group.

In RaCe and TF gruops, the anodization process reduced the corrosion resistance of the files. Especially for RaCe files, this amount of reduction is greater than others. For TF files, on the other hand, the values are very close for non-covered files. (Table 8)

Table 7. *P* values between covered and non-covered instruments in 37° curved canals.

	HeroShaper	RaCe	TF
P (time)	0.000	0.001	0.041
P (number of cycles)	0.000	0.001	0.041

Table 8. Corrosion test results (E corr: corrosion potential, I corr: corrosion current)

	HeroShaper (non-covered)	**HeroShaper (anodized)**	**RaCe (non-covered)**	**RaCe (anodized)**	**TF (non-covered)**	**TF (anodized)**
E corr	-237.0 mV	42.40mV	414 mV	-310 mV	-119 mV	-216 mV
I corr	4.020 uA	14.80 uA	132.0 nA	335.0 nA	801.0 nA	1.070 uA

Evaluation of SEM Images of files

Non-covered HeroShaper and TF files showed traces of manufacturing on their surfaces, while surfaces of RaCe files were smooth. Since the electropolishing process is performed during the manufacturing phase of RaCe files, possible burrs and roughness are eliminated from the file surface. All three file types have particles on them, and especially TF files have bubble-shaped images. The reason for this image is due to differences in the manufacturing stage. Unlike other Ni-Ti files, TF files are produced with R-Phase heat treatment technology. Although this heat treatment creates a porous structure in the metal, it is a production method that increases the durability of the metal. This is also supported by our fatigue test results (Figure1).

Both crusting and smearing appearances were formed, due to the plastic deformation during cyclic fatigue. The crack is marked and obviously it occurred due to the high load. When the breaking section was examined, it was observed that a spongy structure was formed. Crack starting points are evident. (Figure 2A)

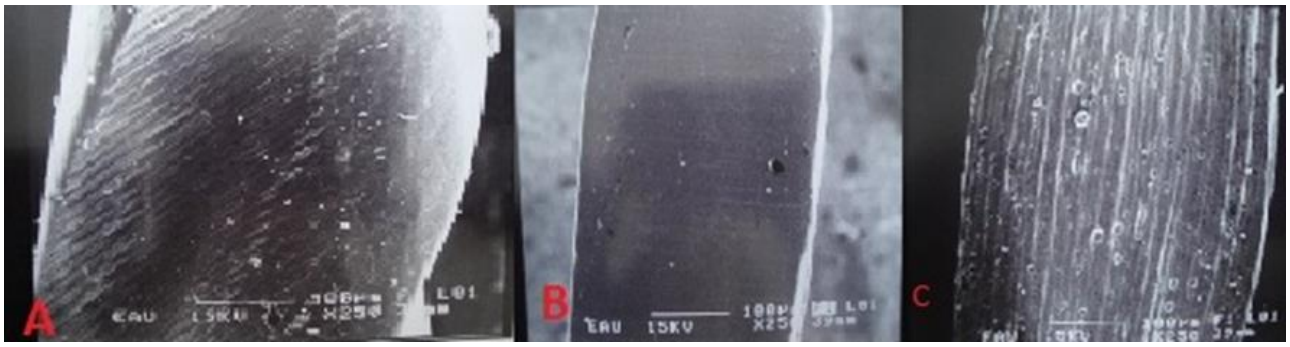

Figure 1. Image of instruments before test procedures A: HeroShaper, B: RaCe, and C: TF *Investigation of Broken Surfaces Non-covered HeroShaper Files*

Figure 2. Image of non-covered instruments after test procedures A: HeroShaper, B: Race, and C: TF

Broken Surface Investigations of non-covered RaCe Files

Traces of plastic deformation are evident on the edges of the file. The crack started from the sharpest point of the cutting-edge part of the file. This suggests that geometrical properties of files in edge designs may be important in terms of metal fatigue.

When the breaking section is examined, it is seen that the crack progresses in the form of tearing. The initial crack origin is smooth. The smoothness of the surface disappeared in the final breaking zone. (Figure 2B)

Broken Surface Investigations of non-covered TF Files

No traces of deformation were observed in the breaking section. The pores from the manufacturing are evident on the surface and most likely caused initiation of the crack (Figure 2C).

Broken Surface Investigations of Covered HeroShaper Files

The breaking images after coating are similar to the breaking images of non-covered files. Again, traces of plastic deformation are evident in the breaking sections. Porous structures were formed on the surface due to the coating, which caused a decrease in fatigue resistance. (Figure 3A)

Broken Surface Investigations of Covered RaCe Files

Plastic deformation is evident in the breaking section. In addition, the porous structure formed due to the coating is especially evident on the sharp edges. (Figure 3B)

Broken Surface Investigations of Covered TF Files

After coating, the surface has become quite rough. Traces of plastic deformation are evident on the sharp edges and are in the form of tearing. The crack started

from the edge and progressed. The crack progression zone is smooth, the other is in the form of tearing. (Figure 3C)

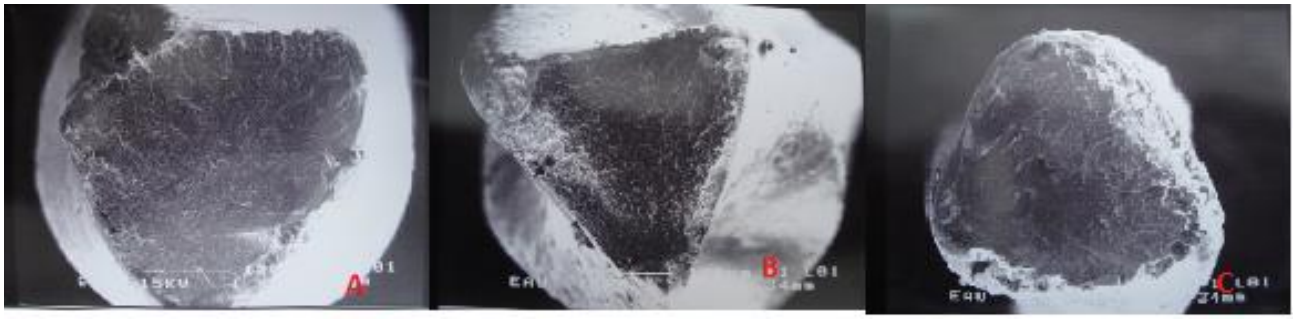

Figure 3. Image of covered instruments after test procedures A: HeroShaper, B: Race, and C: TF

DISCUSSION

The first null hypothesis was rejected for 20° curved experimental setups. There were significant differences among the instruments in terms of the number of cycles to file breakage and time to fracture ($p < 0.05$). The first null hypothesis was partial rejected for 37° curved experimental setups. There were significant differences between HeroShaper and RaCe (p=0.000), and between TF and RaCe (p=0.000) in terms of the number of cycling to file breakage and time to fracture (p>0.05). However, there were no significant differences between HeroShaper and TF (p=0.121). The second null hypothesis was accepted for 20° curved experimental setups. There was no significant effect of the anodization process statistically among the groups. The second null hypothesis was rejected for 37° curved experimental setups. There was significant effect of the anodization process statistically among the groups. The third null hypothesis was rejected. As a result of the corrosion test, it was found that the anodization process had a positive effect on the HeroShaper file group. In RaCe and TF gruops, the anodization process reduced the corrosion resistance of the files.

A specification was determined by American Dental Association (ADA), which includes the physical properties, design features, and mechanical test procedures for endodontic files. The test procedure detailed in this specification No:28 is based on a static module. The tip of the instrument is fixed, then force is applied until breaking occurs, and the breaking resistances of the instrument against the torsional fatigue formed are calculated according to this module. Therefore, this is a reference to determine the resistance of Ni-Ti files to static loading. On the other hand, this specification is not sufficient and suitable for testing the dynamic properties of rotary system Ni-Ti files. In rotary systems, rotary files are used by rotating at a certain speed. Therefore, when testing rotary system files, it should be ensured that the ends rotate freely rather than being fixed.

In addition, since canal curvature is not considered when the test procedures are described in ADA 28 specification; metal fatigue in the instrument while working in curved root canals is not included in the evaluation. Whereas, the repetitive cyclic fatigue event caused by canal curvatures, is perhaps the most important factor in the sudden breakage of rotary

system files. (8,9). In our study, we investigated flexural fatigue that causes breaking due to the preparation of curved root canals.

In our study, we used a different modification of stainless-steel test setup, which is mostly preferred in recent studies (10-12). In this setup, artificial canals are prepared on a stainless-steel block, the file was tested without leaving its orbit during rotation. Thus, undesirable stresses in different directions and intensities due to the sliding of the file during rotation as in pin and tube assemblies were eliminated. Owing to the fiber glass covering the test setup, the file remained in the canal during the rotation, and the breaking moment of the file was clearly observed.

When the instruments are subjected to the fatigue test on the test setup, a lubricating gel is used to prevent friction between the file and the artificial canal and to prevent the heat and stress that may occur as a result of this friction. In some studies, synthetic oils, special oils, and especially in studies using the metal tubes as a test setup, glycerin has been used to prevent friction (10, 12,13,14). In our study, we used FileCare gel produced for Ni-Ti rotary systems for this purpose.

Many studies have reported that the curvature of the canal and the radius of the curvature are an important factor in metal fatigue, which is the biggest cause of instrument fractures during endodontic treatment (12,15,16). The results of these studies, the durability duration of the files decreased as the radius of curvature of the canal decreased. In addition, as the canal curvature increased, the breaking event occurred earlier. These different results obtained were also statistically significant (12,15,16). Our results support those of all these studies. When the results were evaluated, it was observed that the increase in canal curvature significantly decreased the durability of the file for all file groups.

As the curvature of the root canal increases, the stress to which the file is exposed also increases. Each time the file goes round the canal the compressive and tensile forces increase parallel to the canal curvature. Increasing stresses and compressions create larger deformations in the structure of the file, reducing the lifetime of the file.

Studies on metal fatigue have investigated whether there is a difference between the different rotary system files in terms of lifespan (10,17,18).

In a study using Profile, K3, Hero, Mtwo, electropolishing RaCe, and non-electropolishing RaCe files, test parameters were the same for all file groups, canal curvature was determined as 45°, curvature radius as 5 mm, and rotation speed as 300 rpm ((Tripi et al. 2006). Only 25/.06 taper files from each file group were included in the study. Thus, variables such as file thickness and taper angle were kept constants for all experimental groups. When the results were evaluated, the highest value was recorded for Profile files, while the lowest value was recorded for non-electropolishing RaCe files. Since this difference was found to be statistically significant, it was stated that design differences such as cross-section geometry and surface properties are important factors affecting metal fatigue (17). Larsen et al. (10) investigated whether new generation Ni-Ti files have advantages over traditional files in terms of metal fatigue. For this purpose, TF and Profile GT X series files with different production characteristics were compared with traditional Profile and EndoSequence files. As in other studies, all test parameters were kept at the same values for all file groups. It was reported that Profile GT X files were

more durable than all other file groups. 25/.04 TF files were found to be more resistant to breakage than EndoSequence files. However, it was reported that the difference between TF files and Profile files was not statistically significant.

In another study, the effects of different cross-sectional areas of K3, Profile, RaCe and TF files were investigated (19). In this study, 25/.06 files were tested with TF files at 500 rpm and all other files at 300 rpm. The times to breakage were recorded. Since different speeds were used, the number of cycles made by all files was calculated. TF files with the lowest cross-sectional area showed the highest breakage resistance, while K3 files with the highest cross-sectional area were reported to have the lowest breakage resistance. In the statistical evaluation, it was stated that there was a significant correlation between the cross-sectional area and file breakage due to metal fatigue (19).

In another study, Ni-Ti files produced by traditional methods and TF files produced by the twisted method were compared in terms of metal fatigue (Kim et al. 2010). For this purpose, 25/.06 TF, RaCe, Helix and Protaper F1 files were used in this study. The time to fracture was recorded. When the results were evaluated, TF files were reported to show higher resistance to metal fatigue than all other files (18).

In our study, results in 20° and 37° curved canals, the highest metal fatigue resistance was found in TF files. The difference among HeroShaper and RaCe files, and TF files was statistically significant ($p<0.05$). Our results support the results of the above-mentioned studies using TF files. We think that the reason for the high fatigue resistance of TF files is that they are produced with R-phase heat treatment technology.

In a study using RaCe files, RaCe files were reported to have higher resistance than Hero 642 files (17). Whereas, in our study looking at the results in both 20° and 37° curved canals, the lowest resistance to metal fatigue was recorded in RaCe files.

We attribute the reason for this difference between different file systems to the fact that the flexibility and resistance properties of the file differ from each other depending on the geometric shape properties, cross-sectional area, and design differences.

Coating the metal surface with anodization is a method used in the field of implants in dentistry. It is aimed to facilitate osseointegration by coating the implant surface.

In this study, where we investigated whether this surface treatment would make a difference for Ni-Ti files, we recorded different results for different file groups.

In the 20° curved canal, the anodization process increased the wear time of RaCe and TF files while reducing the wear time for HeroShaper files. However, this increase, and decrease was not statistically significant ($p>0.05$).

In the 37 ° curved canal, the wear time of HeroShaper and RaCe files decreased while the wear time of TF files increased. These increases and decreases in the wear time of the files were found to be statistically significant ($p<0.05$).

Evaluating of the results of the corrosion test, the results showed that attention should be paid to anodization applications for files obtained from Ni-Ti alloy. The anodization process may show negative behavior especially depending on the geometry of the file. The complex geometry of the file prevented the

formation of a homogeneous and continuous oxide layer on the surface during the anodization process. This has a negative impact on corrosion resistance.

We think that the reason of different findings exhibited by different file groups may be the design differences of the files and/or the differences in the production phase, caused by the way of production.

The experimental procedures in this study were carried out at room temperature. However, instruments are exposed to body temperature in the clinical condition. The behavior of instruments changes in the different environmental conditions. Also, our experimental setup has only two-dimensional curve. But root canals have three-dimensional curve. The limitations of this study are such as above mentioned.

CONCLUSIONS

Within the limits of this study, increase in canal curvature reduces the life of the rotary instruments. Among the files used, the highest fatigue resistance was recorded in TF files at all curvature. While the anodization process does not change cyclic fatigue in all file groups in 20° curved canals, it reduced the wear life of RaCe and HeroShaper files and extended the wear life of TF files in canals with 37° curved canals.

Ethics Committee Approval: The Ethics Committee of graduate school of health sciences of Atatürk University, Erzurum, Turkey, approved (2011.3.1/7).

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Estimating Height and Body Weight Using Foot Measurements

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Abstract

Objective: Determining the height and weight of the person is the most important factor in forensic cases in which the body integrity is impaired including natural disasters, traffic accidents, wars, murders and decomposition of the body. In this study, it was aimed to obtain linear and multiple regression models and formulas for determining height and weight from foot measurements.

Methods: The relationship between foot measurements and the height and weight of 180 adult individuals (90 males, 90 females) aged 20-65 years were analyzed retrospectively. Foot length and height, malleolar width, calcaneus length and height, 1-5. metatarsal length relationships with height were interpreted. Proximal metatarsal width, distal metatarsal width, 1-5. metatarsal distal end width, proximal end width and corpus width relations with a body weight were evaluated.

Results: For both feet in men, the correlations between height and foot length, height and 5th metatarsal length, and between weight and 2nd metatarsal distal end width were found to be significant. For both feet in women, correlation relationship between height and foot length, 1st metatarsal length, 3rd metatarsal length and in terms of body weight, the correlation relationship between the 1st metatarsal distal tip width, 3rd metatarsal corpus width, 4th metatarsal corpus width, and 5th metatarsal proximal tip width was found to be significant.

Conclusion: In the study, formulas for regression equations, height estimation and body weight were obtained from foot measurements. When the formulas have been developed are used according to gender, they show a deviation of 9-10 cm for height estimation and 11-14 kg for body weight estimation. When our formulas are evaluated by ignoring the gender difference, they show a deviation of less than 6 cm for height estimation and 8-9 kg for body weight. We believe that height and body weight from foot measurements could be predicted by the virtue of our formulas in similar populations. We think that our study results will be beneficial for forensic specialists, archaeologists, criminologists, and researchers who will conduct detailed research on this subject in estimating height and body weight from foot measurements in cases where body integrity cannot be preserved.

Key words: Metatarsal bones, Foot, Height estimate, Body weight estimate

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Note: A section from this research article was previously presented as an oral presentation and a full paper at the 2nd International Congress on Sports, Anthropology, Nutrition, Anatomy and Radiology

INTRODUCTION

In forensic investigations and archaeological researches, determining the age, gender, height and weight of an individual are important factors in the identification of an individual (1). It is not possible to determine the height and body weight of the person in cases such as natural disasters, traffic accidents, wars, murders and decomposition of the body in which the body integrity is impaired (2). Although the usability of long bones such as femur and tibia in estimation of height is reliable, their probability of being found in one piece is very low (3). Foot bones are suitable for evaluation due to their presence in both forensic and archaeological contexts, their small surface area, less exposure to taphonomic factors, and better protection by socks and shoes. Especially small bones such as metatarsal bones can often remain undeformed due to their resistance to postmortem changes (4). Height estimation studies were conducted on foot bones, hand bones, craniofacial bones, femur, tibia, fibula, humerus, ulna, sacrum, coccygeal vertebra, calcaneus and talus measurements in different populations (5-11). Studies on determining body weight in the literature are more limited (12-17). Although the data obtained in studies are specific to the relevant population, it is not correct to completely generalize fully to other populations. Estimation formulas for one population may not be reliable for other populations and ethnic groups. Therefore, regression analyzes for populations and ethnic groups should be performed and formulas should be presented (4). For this reason, it is important to obtain results specific to societies. In this study, it is aimed to examine the relationship between foot measurements, height and body weight, and to obtain linear and multiple regression formulas for estimating height and body weight from foot measurements and compare them with the literature.

METHODS

Research Group

Ethics committee approval was received for this study from the Health Sciences University Samsun Training and Research Hospital Non-Invasive Clinical Research Ethics Committee (07/07/2021, GOKA/2021/13/9). The study was conducted by retrospectively evaluating the bilateral foot radiographs of 180 adults (90 men, 90 women) aged 20-65 years. The inclusion criteria were to be male or female between the ages of 20-65, to have bilateral foot radiographs, and to not have any fractures or deformities in the foot bones. Individuals under the age of 20 and over the age of 65, with unilateral foot radiographs, with fractures or deformities in the foot bones and who did not have height and body weight information in the hospital registry were not included in the study.

In order to determine the sample size, a study titled 'Evaluation of Anthropometric Foot Anthropometric Measurements in Terms of Gender Detection and Height Estimation' was adopted; power and sample size analysis at α (alpha) =0.05 and a test power of 95% were determined as 81 people. A sample size of 180 people was determined in this study (18).

Simple random sampling method was used among patients who applied to the emergency department and orthopedics outpatient clinics of Terme State Hospital (Samsun, Turkey) and had bilateral foot radiography. The measurements were made by a single researcher at different times with an interval of 2 months, and the average results were studied.

Data Collection

The age, gender, height, body weight and background information of the patients were obtained from the hospital registry system.

Foot measurements evaluated by height

1. Foot length: It is the distance between the calcaneara, the rearmost point of tuber calcanei, and the acropodion, the tip of the longest toe.

2. Foot height: The distance from the sole of the foot to the highest point of the talus.

3. Malleolus width: The length between the most medial point of the malleolus mediale and the most lateral point of the malleolus lateralis.

4. Calcaneus length: The length between the most posterior point of the tuber calcanei and the calcaneocuboid joint.

5. Calcaneus height: Perpendicular length between the axis tangential to the calcaneus and the highest posterior point of the tuber calcanei, drawn from the lower posterior end of the tuber calcanei on the lower face of the calcaneus and tangential to the calcaneocuboid joint.

6. 1-5. metatarsal lengths: The length between the most distal point and the most proximal point of the 1-5. ossa metatarsi.

Foot measurements evaluated by body weight

1. Proximal metatarsal width: The length between the most medial point of the basis ossis metatarsale-1 and the lateral point of the basis ossis metatarsale-5.

2. Distal metatarsal width: Length between the most medial point of caput ossis metatarsale-1 and the most lateral point of caput ossis metatarsale-5.

3. 1-5. metatarsal distal end widths: The length between the most medial point and the most lateral point of the midline of the ossa metatarsi 1-5.

4. 1-5. metatars proximal end widths: The length between the most medial point and the most lateral point of the basis ossa metatarsi 1-5.

5. 1-5. metatarsal corpus widths: The length between the most medial point and the most lateral point of the midline of the ossa metatarsi 1-5.

Statistical analysis

IBM SPSS Statistics 22.0 (demo version). program was used for statistical analysis. The conformity of the parameters to the normal distribution was evaluated with the Shapiro Wilks Test and found to be appropriate. In addition to descriptive statistical methods (min, max, SD), Pearson Correlation Analysis was used to examine the relationships between parameters. Linear Regression Analysis (Backward method) was used for a multivariate analysis. Data analysis was performed at a 95% confidence interval and at a significance level of $p < 0.05$.

RESULTS

The mean age of the individuals in our study was 42.99±13.07 years. Their height varies between 149 and 185 cm, with an average height of 166.99±7.03 cm. The weights of individuals vary between 51 and 120 kg, with an average weight of 73.75±11,46 kg. The minimum, maximum, mean and standard deviation values of the measurements of both feet are given in Table 1.

Table 1. Minimum, maximum, mean and standard deviation values of right and left foot measurements (mm)

	Right		Left	
	Min-Max	Average±SD	Min-Max	Average±SD
1.MDEW	15.39-29.72	21.31±2.27	15.26-29.93	21.29±2.24
1.MPEW	16.13-28.42	22.32±2.38	16.1-28.44	22.25±2.37
1.MCW	8.89-18.76	14.39±1.74	9.2-18.21	14.35±1.69
1.ML	55.36-77.37	65.43±4.5	55.41-77.12	65.38±4.42
2.MDEW	8.32-16.06	12.17±1.49	8.27-15.92	12.13±1.45
2.MPEW	12.63-20.49	16.1±1.58	12.7-21.1	16.05±1.57
2.MCW	6.18-10.19	8.42±0.9	6.17-10.25	8.38±0.87
2.ML	59.8-81.49	70.87±4.86	59.9-81.4	70.78±4.75
3.MDEW	8.13-15.69	11.76±1.46	8.11-15.5	11.75±1.42
3.MPEW	11.22-23.71	16.94±2.02	11.15-23.6	16.89±1.99
3.MCW	5.02-9.99	7.33±0.84	5.11-9.78	7.32±0.8
3.ML	57.05-80.32	68.66±4.87	58.01-79.87	68.6±4.74
4.MDEW	6.61-14.99	10.8±1.66	6.82-14.9	10.76±1.61
4.MPEW	11.77-22.06	16.72±1.99	11.79-21.96	16.67±1.97
4.MCW	5.62-9.64	7.46±0.87	5.73-9.87	7.43±0.83
4.ML	58.95-80.48	68.6±4.57	59.03-79.57	68.52±4.51
5.MDEW	7.13-15.12	11.15±1.46	7.15-15.15	11.12±1.42
5.MPEW	13.21-23.92	18.56±2.28	12.94-23.85	18.51±2.25
5.MCW	5.94-10.6	7.97±0.95	5.89-10.54	7.95±0.94
5.ML	55.33-86.67	67.58±5.15	55.4-85.4	67.61±5.07
FL	225.32-301.12	261.13±17.28	225.46-301.25	261.08±17.2
MW	57.83-84.61	70.54±5.86	58.02-84.31	70.54±5.8
FH	70.3-104.56	84.48±6.12	71.16-104.4	84.5±6
PMW	57.11-99.2	72.64±7.56	57.2-99.67	72.58±7.51
DMW	65.91-105.36	87.67±7.16	66.89-103.88	87.67±7.08
CH	37.7-59.82	48.77±4.18	37.89-59.7	48.71±4.1
CL	67.89-97.36	81.06±6.45	68.15-97.2	81.02±6.4

MDEW: metatarsal distal end width, MPEW: metatarsal proximal end width, MCW: metatarsal corpus width, ML: metatarsal length, FL: foot length, MW: malleolar width, FH: foot height, PMW: proximal metatarsal width, DMW: distal metatarsal width, CH: calcaneal height, CL: calcaneal length

The correlation coefficients between height and right and left foot measurements of men, women, and the study group were evaluated with Pearson Correlation Analysis (Table 2). The highest correlation between height and foot measurements was found with the 5th metatarsal length in men, the 3rd metatarsal length in women, and the foot length in the study group.

Right and left foot measurements were evaluated by Multiple Regression Analysis (Table 3). The “R” value is the correlation coefficient that expresses the relationship between height and foot measurements in

men, women and study groups. The "R2" value is the ratio of variations in height explained by foot measurements in all groups. Accordingly, the relationship between the change in height and right foot measurements was found to be 40.8% in men, 30.7% in women, and 59.6% in the study group. The relationship with left foot measurements was identified as 41.1% in men, 29.4% in women, and 59.9% in the study group.

Table 2. Correlations between height and study parameters

		Height (cm)					
		Men		Women		Study Group	
		r	p	r	p	r	p
Foot length	Right	0.559	0.000*	0.248	0.018*	0.696	0.000*
	Left	0.557	0.000*	0.253	0.016*	0.697	0.000*
Foot height	Right	0.326	0.002*	0.311	0.003*	0.611	0.000*
	Left	0.332	0.001*	0.316	0.002*	0.614	0.000*
Malleolar width	Right	0.350	0.001*	0.208	0.049*	0.654	0.000*
	Left	0.356	0.001*	0.210	0.047*	0.660	0.000*
Calcaneus height	Right	0.356	0.001*	0.255	0.015*	0.606	0.000*
	Left	0.352	0.001*	0.267	0.011*	0.609	0.000*
Calcaneus length	Right	0.457	0.000*	0.368	0.000*	0.688	0.000*
	Left	0.454	0.000*	0.367	0.000*	0.686	0.000*
1st metatarsal length	Right	0.420	0.000*	0.363	0.000*	0.605	0.000*
	Left	0.441	0.000*	0.370	0.000*	0.607	0.000*
2nd metatarsal length	Right	0.493	0.000*	0.316	0.002*	0.568	0.000*
	Left	0.511	0.000*	0.321	0.002*	0.574	0.000*
3rd metatarsal length	Right	0.463	0.000*	0.434	0.000*	0.618	0.000*
	Left	0.452	0.000*	0.413	0.000*	0.611	0.000*
4th metatarsal length	Right	0.535	0.000*	0.298	0.004*	0.608	0.000*
	Left	0.531	0.000*	0.292	0.005*	0.613	0.000*
5th metatarsal length	Right	0.604	0.000*	0.248	0.018*	0.657	0.000*
	Left	0.609	0.000*	0.246	0.019*	0.663	0.000*

Pearson Correlation Analysis, *p<0.05, r: correlation coefficient

Table 3. R, R2, adjusted R2 and standard error values of the estimation as a result of linear regression analysis of right and left foot measurements affecting height in men, women and the study group

	Gender	R	R^2	Adjusted R Square	SEE
Right	Men	0.639	0.408	0394	4.393
	Women	0.554	0.307	0.265	3.741
	Study group	0.772	0.596	0.587	4.515
Left	Men	0.641	0.411	0.397	4.383
	Women	0.542	0.294	0.252	3.776
	Study group	0.774	0.599	0.590	4.499

SEE: standard error of the estimate

Right and left foot measurements affecting height were evaluated with regression analysis. The relationship between height, foot length and 5th metatarsal length in both feet was significant in men ($p<0.05$). In women, the relationship between height and foot length, 1st metatarsal length and 3rd metatarsal length was found to be significant in both feet ($p<0.05$). Although the effects of foot height and calcaneal length parameters were close to statistical significance ($p>0.05$), they were not statistically significant, but these parameters remained in the estimation formula model. In the study group (men and women), the relationship between height and foot height, malleolar width, 3rd metatarsal length and 5th metatarsal length was found to be statistically significant in both feet ($p<0.05$) (Table 4).

According to the results of multiple regression analysis, our formulas for estimating the height of the right and left feet for men, women and the study group are in Table 5.

The correlation coefficients between body weight and right and left foot measurements of men, women, and the study group were evaluated with Pearson Correlation Analysis. The highest correlation between body weight and foot measurements was found with 2nd metatarsal distal end width in men and study group, and 1st metatarsal distal end width in women (Table 6).

Table 4. Regression analysis of right and left foot measurements affecting height

		Unstandardized Coefficients		Standardized Coefficients		
	Model	B	Std. Error	Beta	t	p
Men	(Constant)	104.804	9.446		11.095	0.000*
	RIGHT FL	0.117	0.046	0.281	2.525	0.013*
	RIGHT 5.ML	0.499	0.134	0.415	3.735	0.000*
	(Constant)	104.158	9.502		10.962	0.000*
	LEFT FL	0.114	0.047	0.270	2.425	0.017*
	LEFT 5.ML	0.523	0.136	0.427	3.841	0.000*
Women	(Constant)	119.360	9.898		12.060	0.000*
	RIGHT FL	-0.158	0.061	-0.441	-2.600	0.011*
	RIGHT FH	0.191	0.104	0.181	1.839	0.069
	RIGHT CL	0.233	0.120	0.251	1.951	0.054
	RIGHT 1.ML	0.401	0.171	0.343	2.339	0.022*
	RIGHT 3.ML	0.355	0.126	0.330	2.809	0.006*
	(Constant)	117.105	10.396		11.265	0.000*
	LEFT FL	-0.144	0.061	-0.401	-2.360	0.021*
	LEFT FH	0.198	0.108	0.180	1.832	0.070
	LEFT CL	0.236	0.119	0.253	1.974	0.052
	LEFT 1.ML	0.407	0.176	0.343	2.315	0.023*
	LEFT 3.ML	0.321	0.131	0.287	2.457	0.016*
Study group	(Constant)	80.458	5.567		14.453	0.000*
	RIGHT FH	0.251	0.073	0.218	3.421	0.001*
	RIGHT MW	0.342	0.078	0.285	4.377	0.000*
	RIGHT 3.ML	0.290	0.100	0.201	2.909	0.004*
	RIGHT 5.ML	0.315	0.100	0.231	3.145	0.002*
	(Constant)	79.171	5.669		13.965	0.000*
	LEFT FH	0.262	0.074	0.224	3.528	0.001*
	LEFT MW	0.359	0.078	0.297	4.587	0.000*
	LEFT 3.ML	0.265	0.103	0.179	2.567	0.011*
	LEFT 5.ML	0.328	0.104	0.237	3.156	0.002*

FL: foot length, ML: metatarsal length, FH: foot height, CL: calcaneal length, MW: malleolar width, *p<0.05

Table 5. Height estimation formulas for men, women and study groups

Right/ Left Foot	Men/ Women/ Study Group	Height Estimtion Formulas (cm)
Right	Men	104.804+0.117FL+0.499M5L±9.446
Left	Men	104.158+0.114FL+0.523M5L±9.502
Right	Women	119.360-0.158FL+0.191FH+ 0.233CL+0.401M1L+ 0.355M3L±9.898
Left	Women	117.106-0.144FL+0.198FH+0.236CL+0.407M1L+0.321M3L±10.396
Right	Study Group	80.458+0.251FH+0.342MW+0.290M3L+0.315M5L±5.567
Left	Study Group	79.171+0.262FH+0.359MW+0.265M3L+0.328M5L±5.669

FL: foot length, M5L: 5th metatarsal length, FH: foot height, CL: calcaneus lenght, M1L: 1st metatarsal lenght, M3L: 3rd metatarsal lengt, MW: malleolar width

Table 6. Correlations between weight and operating parameters

		Body Weight (kg)					
		Men		Women		Study group	
		r	p	r	p	r	p
Proximal metatarsal width	Right	0.092	0.391	0.175	0.098	0.268	0.000*
	Left	0.073	0.495	0.190	0.073	0.264	0.000*
Distal metatarsal width	Right	0.159	0.136	0.250	0.017*	0.301	0.000*
	Left	0.158	0.136	0.256	0.015*	0.307	0.000*
1st metatarsal distal end width	Right	0.224	0.034*	0.387	0.000*	0.386	0.000*
	Left	0.217	0.040*	0.392	0.000*	0.385	0.000*
1st metatarsal proximal end width	Right	0.199	0.060	0.240	0.023*	0.334	0.000*
	Left	0.199	0.061	0.228	0.031*	0.331	0.000*
1st metatarsal corpus width	Right	0.187	0.078	0.194	0.067	0.317	0.000*
	Left	0.197	0.062	0.196	0.064	0.323	0.000*
2nd metatarsal distal end width	Right	0.282	0.007*	0.351	0.001*	0.387	0.000*
	Left	0.287	0.006*	0.350	0.001*	0.389	0.000*
2nd metatarsal proximal end width	Right	0.139	0.191	0.194	0.066	0.270	0.000*
	Left	0.152	0.153	0.187	0.077	0.272	0.000*
2nd metatarsal corpus width	Right	0.09	0.400	0.218	0.039*	0.267	0.000*
	Left	0.115	0.280	0.222	0.036*	0.283	0.000*
3rd metatarsal distal end width	Right	0.153	0.149	0.196	0.064	0.255	0.001*
	Left	0.156	0.143	0.206	0.052	0.263	0.000*
3rd metatarsal proximal end width	Right	0.249	0.018*	0.011	0.916	0.255	0.001*
	Left	0.231	0.028*	-0.006	0.958	0.239	0.001*
3rd metatarsal corpus width	Right	0.142	0.180	0.303	0.004*	0.311	0.000*
	Left	0.137	0.197	0.306	0.003*	0.311	0.000*
4th metatarsal distal end width	Right	0.114	0.284	0.274	0.009*	0.285	0.000*
	Left	0.117	0.272	0.291	0.005*	0.293	0.000*
4th metatarsal proximal end width	Right	0.177	0.096	0.117	0.274	0.248	0.001*
	Left	0.15	0.160	0.112	0.291	0.230	0.002*
4th metatarsal corpus width	Right	0.02	0.849	0.104	0.329	0.180	0.015*
	Left	0.039	0.716	0.094	0.378	0.186	0.012*
5th metatarsal distal end width	Right	0.134	0.206	0.371	0.000*	0.313	0.000*
	Left	0.123	0.250	0.391	0.000*	0.320	0.000*
5th metatarsal proximal end width	Right	0.164	0.123	0.355	0.001*	0.296	0.000*
	Left	0.143	0.178	0.351	0.001*	0.283	0.000*
5th metatarsal corpus width	Right	-0.002	0.983	0.245	0.020*	0.222	0.003*
	Left	-0.005	0.961	0.26	0.013*	0.230	0.002*

Pearson Correlation Analysis, *p<0.05, r: correlation coefficient

In terms of body weight, the relationship between the width of the 2nd metatarsal distal end and body weight in both feet was statistically significant ($p<0.05$). The relationship between body weight and 1st metatarsal distal end width, 3-4. metatarsal corpus width and 5th metatarsal proximal end width was statistically significant ($p<0.05$) in both feet and in women. In the study group, the relationship between body weight and 1-2. metatarsal distal end width, 3-4. metatarsal corpus width and 5th metatarsal proximal end width was statistically significant ($p<0.05$) in both feet (Table 7).

Right and left foot measurements were evaluated by Multiple Regression Analysis (Table 8). The relationship between the change in body weight and the size of the right foot was 8% in men, 24.2% in women, and 23.2% in the study group. The relationship with left foot measurements was 8.3% in men, 28% in women and 22.7% in the study group.

According to the results of multiple regression analysis, our body weight estimation formulas that has been created for men, women and the study group in the right and left feet are in Table 9.

Table 7. Regression analysis of right and left foot measurements affecting body weight

		Unstandardized Coefficients		Standardized Coefficients		
	Model	B	Std. Error	Beta	t	p
Men	(Constant)	44.926	11.652		3.856	0.000*
	RIGHT 2.MDEW	2.509	0.908	0.282	2.762	0.007*
	(Constant)	43.346	11.991		3.615	0.000*
	LEFT 2.MDEW	2.643	0.939	0.287	2.816	0.006*
Women	(Constant)	17.010	13.398		2.970	0.048*
	RIGHT 1. MDEW	1.638	0.622	0.306	2.635	0.010*
	RIGHT 3.MCW	3.751	1.897	0.218	1.978	0.048*
	RIGHT 4.MCW	-3.753	1.762	-0.251	-2.130	0.036*
	RIGHT 5.MPEW	1.174	0.570	0.236	2.059	0.043*
	(Constant)	22.283	13.992		2.593	0.015*
	LEFT 1. MDEW	1.833	0.617	0.340	2.972	0.004*
	LEFT 3.MPEW	-1.162	0.613	-0.194	-1.897	0.061
	LEFT 3.MCW	5.050	1.997	0.282	2.528	0.013*
	LEFT 4.MCW	-3.725	1.803	-0.240	-2.066	0.042*
	LEFT 5.MPEW	1.187	0.573	0.232	2.070	0.042*
Study group	(Constant)	17.595	8.776		2.005	0.047*
	RIGHT 1. MDEW	1.087	0.453	0.215	2.402	0.017*
	RIGHT 2.MDEW	1.643	0.667	0.213	2.463	0.015*
	RIGHT 3.MCW	2.386	1.209	0.175	1.974	0.050*
	RIGHT 4.MCW	-2.632	1.204	-0.199	-2.186	0.030*
	RIGHT 5.MPEW	0.816	0.387	0.163	2.109	0.036*
	(Constant)	16.581	9.037		2.835	0.008*
	LEFT 1.MDEW	1.073	0.454	0.210	2.363	0.019*
	LEFT 2.MDEW	1.688	0.682	0.214	2.476	0.014*
	LEFT 3.MCW	2.518	1.301	0.176	1.935	0.055
	LEFT 4.MCW	-2.542	1.277	-0.184	-1.991	0.048*
	LEFT 5.MPEW	0.773	0.394	0.152	1.964	0.050*

MDEW: metatarsal distal end width, MCW: metatarsal corpus width, MPEW: metatarsal proximal end width, *p<0.05

Table 8. R, R2, adjusted R2 and standard error values of estimation as a result of linear regression analysis of right and left foot measurements affecting weight in men, women and the study group

	Gender	R	R^2	Adjusted R Square	SEE
Right	Men	0.282	0.080	0.069	11.523
	Women	0.492	0.242	0.207	8.944
	Study group	0.482	0.232	0.210	10.182
Left	Men	0.287	0.083	0.072	11.505
	Women	0.529	0.280	0.237	8.772
	Study group	0.477	0.227	0.205	10.214

SEE: standard error of the estimate

Table 9. Body weight estimation formulas for men, women and study groups

Right/Left Foot	Men/Women/Study Group	Body Weight Estimation Formulas (kg)
Right	Men	44.926+2.509M2DEW±11.652
Left	Men	43.346+11.991M2DEW±11.991
Right	Women	17.010+1.638M1DEW+3.751M3CW-3.753M4CW+1.174M5PEW±13.398
Left	Women	22.283+1.833M1DEW-1.162M3PEW+5.050M3KG-3.725M4CW+1.187M5PEW±13.992
Right	Study Group	17.595+1.087M1DEW+1.643M2DEW+2,386M3CW-2.632M4CW+0.816M5PEW±8.776
Left	Study Group	16.581+1.073M1DEW+1.688M2DEW+2.518M3CW-2.542M4CW+0.773M5PEW±9.037

M1DEW: 1st metatarsal distal end width, M2DEW: 2nd metatarsal distal end width, M3CW: 3rd metatarsal corpus width, M3PEW: 3rd metatarsal proximal end width, M4CW: 4th metatarsal corpus width, M5PEW: 5th metatarsal proximal end width

DISCUSSION

Determining the height and body weight of an individual in cases where body integrity is impaired is the most important factor in forensic cases (1). The small surface area of the foot bones and their ability to be evaluated due to their resistance to deformations are suitable for metric measurements. Estimation formulas created for one population may not be reliable for other populations, datas obtained in studies are specific to related and similar populations (4). During the comparison of the averages of height, body weight, foot length and foot width measurements in this study between other studies datas, differences were detected between the populations, and the mean measurement values were found to be significantly higher ($p<0.05$) in men than in women, similar to the literature (3,4,12,15).

As a result of multiple regression analysis, the correlation (R) between height and right foot measurements was found to be 0.554 in women and 0.639 in men. Correlation between height and left foot measurements was 0.542 and 0.641, respectively. R2 values showed that 30.7% of the foot measurements affecting height in women were caused by the right foot and 29.4% by the left foot measurements. Although these rates were higher in men, they were 40.8% and 41.1%, respectively. The remaining percentages depend on gender, age, population, hereditary and environmental factors (2). In the study group in which gender discrimination was ignored, the R value was 0.772 for right foot

measurements and 0.774 for left foot measurements. R2 values showed 59.6% for right foot measurements and 59.9% for left foot measurements. We found that among the multiple regression equations which has been created for height estimation, the standard estimation error (SEE) rates were the least in the study group. While SEE was 9.44-10.39 cm in the formulas created for the male and female groups for height estimation, it was less than 6 cm in the study group. Apart from being specific to societies, these changes are due to differences in height and foot anatomy depending on nutrition, physical activity level, working conditions, climatic conditions and innate factors (2,18).

In a study investigating the relationship between height and foot length on the Indian population, the correlation coefficient between height and foot length was 0.63-0.92, and the correlation coefficient between height and foot width was between 0.41-0.54 (20). In our study, the correlation coefficients between height and foot length were found to be 0.24-0.69. In a study conducted in Turkey that evaluated the correlation between height and four different foot sizes: foot length, malleolar height, foot width and navicular height, the highest correlation coefficient was found to be foot length. In the results of their multiple regression analysis, they reported that SEE values were 9-10 cm in men and women, and below 4 cm in the study group (2). These values are quite similar to the SEE rates in our study. We also evaluated the correlation coefficients between height and 10 different foot measurements, and we have found that the highest correlation coefficient was with foot length in men and the study group, and with the 3rd metatarsal length in women.

In another study conducted in South Africa, 1-4. metatarsal length measurements, 5th metatarsal functional-physiological length measurements and height measurements were analyzed out of 226 skeletons of South African natives and European-South Africans (19). They reported that the highest correlation with stature was 0.73 in the 1st metatarsal length in South African women of European descent, and the lowest correlation was 0.44 in the 4th metatarsal length in South African native men. As a result of their multivariate equations, they obtained SEE in the range of 3.81–5.07 cm (19). In a study carried out in Turkey, formulas were developed to estimate height and gender from foot and shoe measurements with logistic regression analysis (21). The correlation coefficients between foot length and height are 0.579 to 0.614 for men and 0.490 to 0.500 for women. These values are higher than our correlation coefficients. In the study group of our study in which gender discrimination was excluded, the correlation coefficient between height and foot length was 0.696 and 0.697, which is higher. Their result of the regression formulas they created, the SEE rates were 31,410 cm for the right foot and 31,607 cm for the left foot (21), which are considerably higher than the SEE rates in our study.

When the correlations between body weight and foot measurements were evaluated in our study, the highest correlation was between the 2nd metatarsal distal end width in men and the study group, and 1st metatarsal distal end width in women. As a result of multiple regression analysis, the correlation (R) between body weight and right foot measurements was found to be 0.492 in women and 0.282 in men. Correlations between body weight and right and left

foot measurements were 0.529 and 0.287, respectively. R2 values showed that 24.2% of the foot measurements affecting body weight in women were caused by the right foot and 28.0% by the left foot measurements. Although these rates were lower in men, they were 8.0% and 8.3% based on right and left foot measurements, respectively.

In a study evaluating the relationship between foot and footprint measurements and body weight. Researchers found that the measurements showing the highest correlation with body weight were between the surface measurements of the first and fifth metatarsal bone heads and the foot width they measured (R men: 0.555 and R women: 0.545). This is followed by heel width (R men: 0.523 and R women: 0.535). They reported 8,923-9,538 kg SEE rates in the estimation equations they created (13). Similar rates (8,776-9,037 kg SEE) were obtained in this study. In another study conducted in India, the correlation values between body weight and foot length (R men: 0.419-0.364, R women: 0.227-0.121) and the correlation between body weight and foot width (R men: 0.348-0.338, R women: 0.158- 0.138) was reported to be higher (14). In a study conducted in Malaysia there was a statistically significant relationship between body weight and foot width in both genders, and the correlation values (R) between them were reported as 0.094-0.121 in men and 0.103-0.180 in women (17). These correlation values are lower than those in our study. The study groups consisted of students between the ages of 17-20, therefore we think that the results cannot be generalized to large populations. In the study conducted in India, which estimated body weight from footprint measurements, they found correlations between 0.70 and 0.71 between body weight and distal metatarsal width in the right and left feet, respectively, and reported rates of 3.05-4.10 in their estimation equations (16). In another study conducted in UK, body weight estimations were made with the measurements of the 1st metatarsal bone (22). In their study, they reached 4.144 and 4.251 kg SEE values in the body weight estimation formulas they created using the 1st metatarsal dorsoplantar diameter and mediolateral diameter. These SEE rates are lower than the SEE values in our study (8,776-9,037 kg).

CONCLUSION

The accuracy of a regression equation in estimating height depends on the value of the standard estimation error. It is defined as a measure of the expected accuracy of a regression equation in estimating the height of an individual from the same population group from which the equation was originally derived. Regression equations derived from combinations of measures offer higher accuracy than univariate formulas. A high value for SEE means low accuracy and vice versa (5).

When the formulas we have developed are used according to gender, they show a deviation of 9-10 cm for height estimation and 11-14 kg for body weight estimation. When our formulas are evaluated by ignoring the gender difference, they show a deviation of less than 6 cm for height estimation and 8-9 kg for body weight. We believe that our formulas can predict height and body weight from foot measurements in similar populations.

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RESEARCH ARTICLE

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An Analysis of Youtube Videos on the Topics of Coronavirus and Dentistry

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Abstract

Objective: The World Health Organization declared a COVID-19 pandemic in March 2020. Dentists and their patients are at a particularly higher risk of infection, emphasizing the need for implementation of measures preventing the spread of the virus during emergency dental treatments. YouTube, a digital platform where anyone can upload videos and get feedback from other users about their content, represents a significant resource for accessing information. The aim of the current study was to analyze the content quality and reliability of YouTube videos on the topics of coronavirus and dentistry.

Methods: The keywords "coronavirus" and "dentistry" were used to identify relevant videos on YouTube. Approximately 120 videos uploaded between March and November 2020, were reviewed by two independent researchers. Of these, 91 videos fulfilled the inclusion criteria and were scored for content quality and reliability.

Results: The majority of videos analyzed were uploaded by public institutions, associations, or hospitals (35.2%) and had a target audience made up of the general population (79.1%). The coronavirus index and total index scores of the videos uploaded by public institutions were significantly higher than those uploaded by dentists ($p = 0.017$; $p < 0.05$; $p = 0.006$; $p < 0.01$). The mean modified DISCERN (mDISCERN) score, used to assess the reliability of the videos, was 2.88 ± 1.08.

Conclusion: The results of this study suggest that specialist physicians should play a more active role in sharing accurate educational videos. Although YouTube, a popular video streaming site, is a valuable resource for accessing useful and accurate information, it also contains large amounts of incomplete and incorrect information which is a significant disadvantage as it can confuse the general public and healthcare professionals and prevent identification of videos produced or verified by authorized healthcare professionals.

Key words: Coronavirüs, communicable diseases, dental education, public health dentistry, social media.

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INTRODUCTION

In December 2019, a sudden rise in the incidence of pneumonia of unknown origin in Wuhan, China, led to the discovery of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a novel human coronavirus that causes COVID-19. The World Health Organization declared a pandemic in March 2020, and rapid global transmission of the virus resulted in approximately 91 million cases of COVID-19 and 2 million associated deaths globally by the 15th of January 2021 (1,2). The first case of COVID-19 in Turkey was detected on the 10th of March 2020 (3,4).

Transmission of the virus may occur through direct contamination, inhalation of droplets produced during coughing or sneezing, or face-to-face contact with carriers of the virus or infected individuals or surfaces (2). The most common symptoms of COVID-19 include fever, cough, fatigue, shortness of breath and, in severe cases, pneumonia and respiratory tract disorders (5,6). According to the Occupational Safety and Health Administration (OSHA), healthcare workers such as dentists are at a higher risk of contracting SARS-COV-2 and becoming potential carriers of the virus as they work in close proximity to the patient's oral cavity and dental procedures often involve the use of aerosol-generating hand-pieces and rotary instruments (5). Therefore, a clearer understanding of the nature of the virus, its potential routes of transmission, its clinical characteristics, and the testing methods used are essential for effective prevention of transmission between healthcare workers and patients (7).

Dental procedures involve a high risk of cross-infection between patients and clinicians. The ways of transmission of this virus are through droplet inhalation or direct contact with the mucous membranes of the mouth, nose and eyes. High-speed handpieces used during dental treatments create aerosols from oral secretions, saliva and blood to the environment and can also be contaminated (8). Unfortunately, the symptoms of this disease are nonspecific and can progress to severe pneumonia while asymptomatic (9-11). Postponement of non-emergency procedures has been recommended during the COVID-19 pandemic. Effective infection control measures should be taken in response to emergencies (8,12). Precautionary measures such as measurement of body temperature using a thermometer; referral of patients with suspected infections to the nearest health institution; postponement of non-urgent dental treatments; incorporation of tele-dentistry where necessary; effective management of dental appointments; active screening of dentists and patients; and social distancing should be implemented before, during, and after all dental appointments. Additionally, all dental staff and patients should receive adequate training on the prevention of transmission and facial coverings should be utilized during dental appointments. The dental team should use personal protective equipment; pay special attention to hand hygiene; and administer antimicrobial mouthwash in the patient’s oral cavity prior to commencing treatment. During dental appointments, rubber dams, high-volume dental suctions, and extra-oral dental radiographs should be used where possible and aerosol-generating procedures should be avoided. Lastly, the workplace should be ventilated and thoroughly cleaned and disinfected on a regular basis (6,13).

Currently, digital platforms such as YouTube, a popular video-sharing website with an estimated monthly view of 1 billion, represent the most accessible sources of health-related information for the general population (5, 14). With the rapid increase in national and international use of YouTube for the purpose of accessing information on diseases, treatment options and protocols, prognoses, and patient experiences, evaluation of the extent to which this information may be misleading, inaccurate, or biased is essential (15). The density and complexity of information obtained through social media often makes it difficult for users to effectively recognize the quality and accuracy of this information, which can affect the treatment process (7,16).

The terms “coronavirus” and “COVID-19” were the most searched words on Google and YouTube in the first four months of 2021 (17,18). Establishment of efficient online resources providing high-quality accurate information on SARS-COV-2 is essential for effective counseling of patients (14). Therefore, the aim of this study was to analyze the content and quality of Turkish YouTube videos on the topics of “coronavirus” and “dentistry”.

METHODS

A new YouTube account was created for the study, and the terms "Dentistry" and "Coronavirus" were searched based on upload date sorting and saved to the account. 120 videos with Turkish content uploaded from March 2020, when the pandemic appeared in Turkey, to November, were listed. Inclusion criteria for the videos were containing Turkish narrators, lasting 1-90 minutes, and being compatible with the search terms. Of the 120 results, only one of the videos that were the same was recorded in the list to be evaluated. Those that do not contain a narrator or are not in Turkish were excluded from the list. The URLs of 91 content that met the inclusion criteria were electronically saved to prevent daily changes. All videos were analyzed by two different specialist dentists for inter-observer reliability. The first researcher examined 44 contents uploaded (videos published in the last half of November, October, September, August, July, June, and May), while the second researcher examined 47 contents (videos published in the first half of March, April, and May). For inter-observer reliability, the first observer re-evaluated 47 videos reviewed by the second researcher (Figure 1).

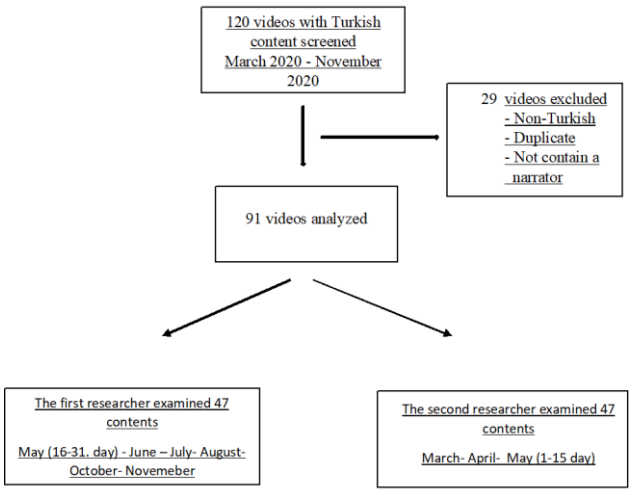

Figure 1. Flowchart of the study

Evaluation of video content

The broadcast date, duration in seconds, number of likes, broadcast source (dentist; news source; public institutions, associations or hospitals), target audience (e.g., dentists, general population), Coronavirus Index score, Dental Index score, Total

Index score, and modified DISCERN (mDISCERN) scores were recorded for each video.

The Coronavirus Index scoring evaluated the quality of information provided on the symptoms of the disease, methods of virus transmission and prevention of the disease, and the benefits to health services, while the Dental Index scoring assessed information provided on dental emergencies, tele-dentistry, and dental infection control measures. Each item was assigned 1 point, and scores ranged from 0 to 4 for each index. Using individual index scores, the videos were classified into less useful (0–1 points), moderately useful (2–3 points), and very useful (4 points). The Total Index score was calculated by summing the two indexes and was then categorized into less useful (0–2 points), moderately useful (3–5 points), and very useful (6–8 points).

Reliability was evaluated using the mDISCERN score which assesses the references cited, sources of information used, indications of uncertainties, clarity (title-content compatibility), and objectivity of the video. Each component of the mDISCERN score was evaluated using a 5-point Likert scale ranging from 1 (low quality) to 5 (high quality).

Statistical analysis

Statistical analyses were carried out using the NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA) program, and the data were presented using descriptive statistical methods (mean, standard deviation, median, frequency, ratio, minimum, maximum). The Shapiro–Wilk Test was used to evaluate distribution, and the Mann–Whitney test was used to compare quantitative data between two groups that did not exhibit normal distribution. The Kruskal–Wallis test was used to compare three or more groups that did not exhibit normal distribution, and the Wilcoxon test was used to determine differences between the page viewers. Spearman's correlation analysis was used to determine the relationship between quantitative variables, and a p-value <0.05 was considered statistically significant.

RESULTS

The majority of broadcast sources for the 91 videos evaluated between 19th March and 29th November, 2020, were public institutions such as associations or hospitals (35.2%), followed by dentists (31.9%) and news sources (30%) (Table 1). The mean duration of the videos was 1177.4 ± 1425.75 seconds (range: 60 to 5260 seconds), while the mean number of likes was 17.48 ± 42.87 (range: 0 to 367) (Table 2).

Table 1. Distribution of videos by broadcast source and target audience

		N	%
Broadcast sources	**Dentist**	29	31.9
	News sources	30	33.0
	Public institutions	32	35.2
Target audiences	**Dentist**	19	20.9
	General population	72	79.1

The mean, standard deviation, and median values of the two indices and the mDISCERN score have been shown in Table 2.

Spearman's correlation analysis showed a highly significant positive correlation between the Coronavirus Index and Total Index scores (r= .795, p= 0.000); a moderately significant positive correlation between the Coronavirus Index and mDISCERN scores (r= .412, p= 0.000); a highly significant positive correlation between the Dental Index and Total Index scores (r = .659, p= 0.000); a weakly significant positive correlation between the

Dental Index and mDISCERN scores (r = .210, p= 0.045) ; and a moderately significant positive correlation between the Total Index and Mdıscern (r = .210, p= 0.045) scores (Table 3).

The first researcher reported significantly higher Coronavirus Index scores compared to the second researcher (p= 0.011). The Dental Index (p= 0.083), Total Index (p= 0.398), and mDISCERN scores (p= 0.388) did not significantly vary by the researchers (Table 4).

The length of the videos, number of likes, and Dental Index scores did not significantly differ by the broadcast source (p= 0.225). In contrast, the Coronavirus Index (p=0.017) and the Total Index scores (p= 0.006) were significantly lower for videos broadcasted by dentists compared to those broadcasted by public institutions, associations, or hospitals (Table 5).

The duration of videos with a target audience of dentists was significantly higher than those targeting the general population (p= 0.001), while the number of likes (p= 0.190) did not vary significantly by the target audience. The Coronavirus Index (p= 0.039) and mDISCERN scores (p= 0.001) were significantly higher for videos targeting dentists compared to those aimed at the general population. In contrast, the Dental Index scores (p= 0.230) did not vary significantly by the target population (Table 6).

Table 2. The mean, standard deviation, and median values of the two indices and the mDISCERN score

	Mean±Sd	***Min-Max (Median)***
Duration (sn)	1177.4±1425.75	60-5206 (408)
Number of likes	17.48±42.87	0-367 (8)
Coronavirus Index	1.05±1.1	0-4 (1)
Dental Index	2.41±0.94	0-4 (2)
Total Index	3.46±1.47	0-7 (3)
mDISCERN	2.88±1.08	0-5 (3)

Table 3. Correlation analysis of the "Coronavirus Index" and other variables

1. Coronavirus Index	r	1			
	p	.			
2. Dental Index	r	0.125	1		
	p	.239	.		
3. Total Index	r	.795**	.659**	1	
	p	.000	.000	.	
4. mDISCERN	r	.412**	.210*	.435**	1
	p	.000	.045	.000	.

Spearman's *p<0.05 **p<0.01

Tablo 4. Comparison of indexes by researchers

		2. Researcher	***1. Researcher***	***p***
Coronavirus Index	***Mean±Sd***	0.77±0.81	1.36±1.28	***0.011****
	Min-Max	0-3 (1)	0-4 (1)	
	(Median)			
Dental Index	***Mean±Sd***	2.57±0.83	2.23±1.03	0.083
	Min-Max	0-4 (3)	0-4 (2)	
	(Median)			
Total Index	***Mean±Sd***	3.34±1.31	3.59±1.65	0.398
	Min-Max	1-7 (3)	0-7 (3)	
	(Median)			
mDISCERN	***Mean±Sd***	2.79±0.98	2.98±1.19	0.388
	Min-Max	1-5 (3)	0-5 (3)	
	(Median)			

Wilcoxon Testi *p < 0.05

Table 5. Comparison of Scales by broadcast source

	N		*Mean±Sd*	*Min-Max (Median)*	*p*
Time	***Dentist***	29	796.59±1139.48	79-4882 (302)	
	News Source	30	858.73±1066.77	60-5206 (533)	0.225
	Institutions-Association-Hospital	32	1821.25±1732.75	85-4924 (1632)	
Number of Likes	***Dentist***	28	28.96±71.11	0-367 (12)	
	News Source	29	9.66±12.51	0-47 (3)	0.241
	Institutions-Association-Hospital	32	14.53±22.03	0-114 (8)	
Coronavirus İndex	***Dentist***	29	0.62±0.82	0-3 (0)	
	News Source	30	1.07±1.01	0-4 (1)	***0.017****
	Institutions-Association-Hospital	32	1.44±1.27	0-4 (1)	
Dental Index	***Dentist***	29	2.17±0.71	0-3 (2)	
	News Source	30	2.4±1.13	0-4 (3)	0.149
	Institutions-Association-Hospital	32	2.63±0.91	1-4 (3)	
Total Index	***Dentist***	29	2.79±1.05	1-5 (3)	
	News Source	30	3.47±1.55	0-7 (3,5)	***0.006****
	Institutions-Association-Hospital	32	4.06±1.52	2-7 (4)	
mDISCERN	***Dentist***	29	2.66±0.97	1-5 (2)	
	News Source	30	2.77±1.1	0-5 (3)	0.156
	Institutions-Association-Hospital	32	3.19±1.12	2-5 (3)	

Kruskal Wallis Testi *p<0.05 **p<0.01

Table 6. Comparison of Scales by Target Audience

	N		*Median±Sd*	*Min-Max (Median)*	*p*
Duration	***Dentists***	19	3088.47±1365.11	132-4924 (3165)	***0.001****
	General Population	72	673.08±932.23	60-5206 (275)	
Number of Likes	***Dentists***	19	40.39±87.64	0-367 (9)	0.190
	General Population	72	11.68±16.61	0-114 (6)	
Coronavirüs İndex	***Dentists***	19	1.68±1.49	0-4 (2)	***0.039****
	General Population	72	0.89±0.91	0-4 (1)	
Dental İndex	***Dentists***	19	2.21±0.98	0-4 (2)	0.230
	General Population	72	2.46±0.93	0-4 (2,5)	
Total İndex	***Dentists***	19	3.89±1.97	0-7 (4)	0.242
	General Population	72	3.35±1.31	1-7 (3)	
mDISCERN	***Dentists***	19	3.89±1.2	0-5 (4)	***0.001****
	General Population	72	2.61±0.88	1-5 (2)	
	N		***Ort±Ss***	***Min-Max (Median)***	***p***

Kruskal Wallis Testi *p<0.05 **p<0.01

DISCUSSION

Although the Internet represents one of the easiest and most widely preferred methods of accessing information, it is known that uploading data directly without applying any standard quality control causes serious information pollution, especially about medical facts (20,21). The responsibility of maintaining the scientific accuracy and quality of the information presented rests entirely with the uploader (22,23). The coronavirus pandemic has led to massive amounts of data being made public daily via social media networks, which often play a mediating role in connecting individuals with useful information. However, the lack of content and quality assessment strategies often results in the dissemination of large amounts of incorrect and unnecessary information, causing confusion among individuals seeking useful data (7,17). It is thought that technology and the internet will become an indispensable part of our daily life in the coming years, and even within a few years, the internet will be the primary source of information gathering. As the role of technology and the internet continues to expand, ensuring access to high quality videos on digital platforms is critical (24-26).

While previous studies have individually analyzed the quality and reliability of YouTube videos on the topic's coronavirus and dentistry (20,22,23,25-27) few have examined them together and the majority of these videos have been in English (7,16). To the best of our knowledge, this is the first study to assess the quality and reliability of YouTube videos with Turkish content on the topics of Coronavirus and Dentistry together. The majority of videos included in this study were published within 9 months of the start of the pandemic and were targeted at dentists and dental patients.

Previous content analyses of YouTube videos on the topic of SARS-COV-2 used various indexes (16,20,22) such as the Medical Information and Content Index score (15,23), defined by Nagpal et al. (19) during the Ebola epidemic, or those proposed by the Center for Disease Control and Prevention (CDC) (23).

Yuce et al. (16) evaluated YouTube videos containing information on dentistry and the coronavirus pandemic by creating relevant categories for scoring and then adapting the total score to the Global Quality Scale (GQS) scoring system. Ozdede et al. (7) designed a usefulness index consisting of eight questions which were assigned scores ranging from least useful to very useful and used this to evaluate YouTube videos that combined the terms dentistry and COVID-19. In the current study, we designed a scoring system that can be used as an alternative to those employed in previous studies. We evaluated 91 videos and scored them using 3 categories, namely, the coronavirus index, the dental index, and the total index. Our results showed that 74.8% of the videos were less useful and only 4.4% were very useful when evaluated using the coronavirus index, while 12.1% were less useful and 11.0% were very useful when using the dental index. Finally, 27.5% of the videos were considered less useful and 9.9% were very useful when assessed using the total index. Yuce et al. (16) found that 43.6% of the 55 videos analyzed were of poor quality and were deemed useless, while Ozdede et al. (7) reviewed 116 videos and found that 24.1% were less useful and 47.4% were useful.

In the current study, the mean mDISCERN score was 2.88 ± 1.08, indicating low reliability, and this was similar to the findings reported by Yüce et al. (16) who observed a mean mDISCERN score of 2.77 ± 0.99. Khatri et al. (20) reported mean values of 3.12 for videos with English content and found that 20% of the videos considered to be useful had mDISCERN scores < 3. Ozdede et al. (7) used the video information and quality index (VIQI) score to evaluate content quality and reliability and reported a mean value of 3.93 ± 0.97. The VIQI score, like the mDISCERN index, is not just specific to the field of health and can be used to detect reliability of all video content in general.

Institutions, government departments, and health professionals use social media on a daily basis as it is an easy way to reach large numbers of people at the same time. YouTube provides a unique platform where anyone can upload videos and get feedback from other users about their content. (24). Many YouTube videos focus on the topics of health and science and the platform has grown to represent a significant resource for information, particularly in the context of the Zika, H1N1, and swine flu epidemics and, more recently, the coronavirus pandemic (18,19,29). The uploaded videos can have a wide range of information sources, including news

agencies, public institutions such as universities and hospitals, specialist physicians, or individuals (17, 20). Previous studies examining video content during epidemics found that the majority were created by news agencies. Paraphoi et al. (17) examined content on coronavirus published in January, February, and March 2020 and found that the most common sources of information were news centers, and a very small proportion of videos were created by public institutions. Khatri et al. (20) reported similar results, with the vast majority of evaluated videos citing news agencies as the major source of information, followed by public institutions and organizations. Ozdede et al. (7) found that dentists were the most common sources of information in their study (%45.7), followed by public institutions and news agencies (%27.6), and this was similar to the study by Yuce et al. (16) who found that over 50% of the videos examined by them had dentists as the major sources of information (%58.2), followed by news agencies (%10.9).

In the current study, public institutions, associations, and hospitals were the major sources of information, followed by news sources and dentists. The coronavirus index and total index scores of videos broadcasted by dentists were significantly lower than those of videos broadcasted by public institutions. Ozdede et al. (7) reported that video quality differed significantly by the sources of information, with the VIQI scores of videos shared by public institutions being significantly higher than others. Yuce et al. (16) reported significantly higher GQS scores for video content from dental health centers compared to those produced by news agencies. Approximately 79.1% of the videos evaluated in the current study targeted the general population and 20.9% were addressed to dentists, and the mDISCERN and coronavirus index scores of the latter were significantly higher than the former. While Yüce et al. (16) did not take the target audience into consideration in their study, Ozdede et al. (7) divided them into two categories (dentists and patients) and found that the usefulness and VIQI score of videos targeting dentists were significantly higher.

Studies exploring coronavirus-related video content uploaded on YouTube during the pandemic period identified this social platform as an important resource for the dissemination of information on public health issues such as viral infection outbreaks (17,22,23). Researchers have suggested that international health and academic institutions should continue to publish more videos containing information on the recognition and detection of coronavirus (23). The videos included in the current study scored poorly on the Coronavirus Index, which assessed content on the routes of transmission, clinical symptoms and prevention of the disease, and the associated benefits to health services during the pandemic, highlighting the need for more information on these issues. In contrast, the videos scored moderately on the Dental Index, which evaluated information on precautions to be taken for the prevention of dental infection, dental emergency treatment protocols, preventive dentistry practices, and tele-dentistry. YouTube videos shared by public institutions and organizations had more accurate information and were of higher quality, suggesting that it would be beneficial if experts, universities, and other institutions uploaded scientific content of sufficient duration onto YouTube, especially during the pandemic. Based on the findings of the current study, we believe that video content shared on the internet, particularly in the field of health, should be

subjected to institutional approval and quality control systems. Reviewing and removing videos of poor quality and those containing unnecessary/false information would help improve the educational use of these videos for both healthcare professionals and patients.

CONCLUSIONS

The flow of information on social media platforms is an ongoing process. YouTube videos are constantly changing and renewed in terms of content and quality within the framework of current issues. Therefore, in our study, only videos from a certain time interval could be evaluated from the beginning of the pandemic. These videos, which are only in Turkish, have led us to obtain results in a limited area in terms of both time and language. However, the fact that there are only two studies published so far that evaluates videos with English content on the topics of Coronavirus and Dentistry together makes our study valuable. Within the limitations of this study, it can be suggested that dentists should take a more active role in educational information given on social media, especially on YouTube, to create more useful content for dentists and society. Further studies are needed to evaluate the content and quality changes of existing YouTube videos overtime during and after the pandemic.

Ethics Committee Approval: This study was approved by the Ministry of Health of the Republic of Turkey (No: 2020-11-20T14_31_34).

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The Relationship Between Kawasaki Syndrome and Viral Infections

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Abstract

Objective: This study aimed to investigate the relationship between Kawasaki syndrome and viral infections.

Methods: The data of the Kawasaki syndrome cases diagnosed between January 2017 to December 2019 were reviewed from hospital records retrospectively.

Results: Among eighteen cases ten were boys, and eight were girls. Their average age at diagnosis was 38.28 ± 28.38 (3-113 months). Seven cases were in winter, eight in spring and autumn, and three in summer diagnosed. The mean length of stay in the hospital was 7.41±3.34 (3-17 days). All patients presented with fever, and the mean duration of fever was 6.94 ± 1.63 days. Six cases were classified as typical KS (33.3%), and twelve as atypical KS (66.7%). Laboratory examinations revealed a leukocyte count of 16507 ± 61817 /mm³, C-reactive protein 8.59 ±5.87 mg/dl, erythrocyte sedimentation rate (ESR) median value 58 mm/hour (18-102). Fourteen patients had cardiac involvement (pericardial effusion, mitral insufficiency), and six had small coronary artery involvement. Both cardiac and coronary artery involvement rates were higher in the atypical KS. In only six cases (33.3%) were the pathogens detected. The detected infectious agents were: Parainfluenza type 4, Parainfluenza type 3, Respiratory syncytial virus, Group A streptococcus, Epstein-Barr virus, Ochrobactrumanthropi, Rubella, Cytomegalovirus.

Conclusion: Detection of infectious agents in only one-third of the cases and the presence of different factors suggest that the Kawasaki syndrome is not related to a specific pathogenic agent. Coronary involvement was not found to be associated with pathogenic agents. However, atypical KS needs more attention for cardiac involvement.

Key words: Kawasaki syndrome, vasculitis, viral infections

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INTRODUCTION

Kawasaki Syndrome (KS) is a systemic vasculitis of childhood that begins acutely, progresses with fever, has an unknown etiology, and is important in terms of complications that could affect small to medium-sized vessels. It occurs especially between the ages of six months and five years and is an important cause of acquired heart diseases in children (1). Approximately 20-25% of untreated patients have coronary artery abnormalities, including an aneurysm, while this rate is less than 5% in patients treated with intravenous immune globulin (IVIG). For this reason, early diagnosis of the disease and timely treatment are extremely important in terms of preventing the development of complications (1-3). The cause of KS has not been fully elucidated. The fact that young children are affected, the fluctuating geographic distribution of the disease, the self-limiting nature of the acute febrile disease, and some epidemiological and clinical features such as enanthema, conjunctival involvement, cervical lymphadenopathy supports that the disease may have an infectious cause (4-7).

In this study, we aimed to investigate the relationship between KS and viral infections. For this reason, medical records were evaluated retrospectively, including demographic data, clinical and laboratory findings of patients who were followed up after discharge at the pediatric cardiology outpatient clinic.

METHODS

A retrospective cross-sectional study was conducted at the University of Health Sciences in the Zeynep Kamil Maternity and Children's Research and Training Hospital, Istanbul, Turkey. This center is one of the largest referral perinatal centers for pregnant women and children in Istanbul. Participants were enrolled from January 2017 to December 2019. The study was approved by the local ethics committee and written informed consent was obtained from the participants' legal guardians (Ethics committee approval: 05.05.2021, 2021/107). The study was performed by the Declaration of Helsinki.

Study Design

Patients who were diagnosed with KS in the pediatric department and followed up at the pediatric cardiology outpatient clinic were included in the study. Parents of all children willing to participate in the study signed informed consent. Detailed clinical history was recorded from the patients' files. The age, gender, time of admission, clinical and laboratory findings, duration of hospital stay, treatments, and short-term complications of the patients were collected, retrospectively. Children with genetic disorders, failed to consent, incomplete clinical laboratory or cardiac examinations were excluded.

The diagnosis of KS was performed according to the presence of four of the five basic findings in addition to fever lasting four days or longer (Table 1). Fever is characteristically high in KS and responds not to antibiotic treatments. Without treatment, fever may continue for about 1-2 weeks and lasted up to 3-4 weeks in affected cases. Patients were classified according to their findings as typical (classical) or atypical (incomplete) KS. Children with persistent fever and less than four characteristic clinical findings were classified as atypical or incomplete KS (8). In the algorithm by McCrindle et al. in 2017 is reported that patients with two or three clinical criteria in addition to fever lasting at least five days and at least three or more accompanying laboratory findings were

classified as atypical KS. Treatment is also recommended if laboratory findings are less than three, and positive findings are detected in the echocardiography (ECHO) examination. These patients also belong to the atypical KS group (9) (Table 1).

The diagnosis of KS in our study was performed according to the KS criteria of the American Heart Academy (9) (Table 1). In addition to American Heart Academy Criteria fever lasting more than four days, patients meeting four or more of five criteria were defined as typical KS. Children who had persistent a fever but had less than four criteria, met three or more supportive laboratory findings, or showed signs of coronary artery involvement by echocardiography were considered as atypical KS and were also treated. As laboratory findings; complete blood count, acute phase reactants like C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), liver and kidney function tests like alanine aminotransferase (ALT), anti-streptolysin O (ASO), sodium (Na), serology of Toxoplasma immunoglobulin M and G, Rubella immunoglobulin M and G, Cytomegalovirus (CMV) immunoglobulin M and G, Parvovirus immunoglobulin M and G, Herpes simplex type1 immunoglobulin M and G, Herpes simplex type2 immunoglobulin M and G, Epstein Barr virus (EBV) viral capsid antigen immunoglobulin M and G, Strep A rapid antigen test, respiratory tract viral panel examination results were recorded.

Cardiac investigation results including transthoracic echocardiography (ECHO), electrocardiographs (ECG) performed by the pediatric cardiology unit of our hospital were noted. Coronary artery diameters were also evaluated in the parasternal short axis. According to the Z-scoring adapted classifications to height and weight of the cases; Large and giant aneurysms were diagnosed if Z-score> 10 absolute size> 8 mm and above, middle aneurysm if Z-score between 5 and 10 (coronary artery diameter <8 mm), small aneurysm if Z-score between 2.5 and 5, Z-score 2 to 2.5. If Z-score <2, and only dilatation is detected no involvement was recorded. Additionally, 1.5 times coronary artery diameter exceeding the adjacent segment was accepted as coronary artery involvement (8,9).

Table 1. Kawasaki syndrome classical diagnostic criteria (8,9).

In addition to the presence of fever for at least four days

1. Changes in hands and feet: In the acute phase, edema in the palm, soles of the feet. In the subacute phase (2nd and 3rd weeks), peeling of the fingers and toes
2. Changes in the lip and oral mucosa: Erythematous and chapped lips, strawberry tongue appearance
3. Bilateral bulbar conjunctivitis
4. Cervical lymphadenopathy (usually unilateral greater than 1.5 cm in diameter)
5. Rash: Polymorph exanthema (non-vesicular and non-bullous)

Laboratory findings supporting Kawasaki disease

In the presence of fever lasting longer than four days, if two or three criteria are met, c-reactive protein > 30 mg/L and / or erythrocyte sedimentation rate > 40 mm/h

Those who provide 3 or more of the following laboratory findings are diagnosed with KH (incomplete).

1. Anemia (assessed according to the patient's age)
2. Thrombocytosis (> 450.000 /mm³ after the seventh day)
3. Albumin < 3 g/dL
4. Alanine aminotransferase (ALT) elevation
5. Leukocyte count (WBC) > 15.000 /mm³
6. Leukocyte> 10 /high-power field in urine (in every field at large magnification under a microscope)

Statistical analysis

Data were analyzed using IBM SPSS for Windows (Release 20.0, SPSS Inc, Chicago, IL). Data were tested for normality with the Kolmogorov–

Smirnov test. Qualitative variables are expressed as percentages and frequencies, normally distributed continuous variables as means (standard deviations, SD), and non-normally distributed variables as medians (interquartile range [IQR] p25-p75) according to the Kolmogorov-Smirnov test.

RESULTS

Among eighteen cases ten were boys, and eight were girls. Three patients were excluded because of other reasons. The average age at diagnosis of the study population was 38.28±28.38 months (3-113 months). Seven cases were in winter, eight in spring and autumn, and three in summer diagnosed. The mean length of stay in the hospital was 7.41±3.34 (3-17 days). Of the studied cases, four were over five years and fourteen were under five years old (Table 2). The mean age of the patients at diagnosis was between 38.28 ± 28.38 (3-113 months).

All patients presented with fever. The mean duration time of fever was 6.94 ± 1.63 days. In addition to fever for five days or more, the most common accompanied findings were changes in oropharynx and lips (n=12, 66.6%), and nonpurulent conjunctivitis (n=10, 55,5%) (Table 2). Six cases were classified as typical Kawasaki (33,3%), and twelve as atypical Kawasaki (66,7%). Laboratory examinations revealed a leukocyte count of 16507 ± 61817 /mm³, C-reactive protein 8.59 ± 5.87 mg/dl, erythrocyte sedimentation rate (ESR) median value 58 mm/hour (18-102), platelet count 374176 ± 112.182 /mm³, hemoglobin value 10.7 ± 1.09 gr/dl, sodium value was 134.18±3.15 mg/dl. Hyponatremia was present in 47.3% of cases.

Fourteen patients (n=14, 77.7%) had cardiac involvement (pericardial effusion, mitral insufficiency), and six had small coronary involvement. The cardiac involvement rate was 66.6% (n=4) in typical KS and 83.3% (n=10) in the atypical form. Coronary artery involvement was observed in one (16,6%) patient of typical KS and in five (41,6%) cases of atypical KS.

The pathogen was detected in only six cases (33.3%) in viral studies of the respiratory tract. The detected infectious agents were: Parainfluenza type 4, Parainfluenza type 3, Respiratory syncytial virus, Group A streptococcus, Epstein-Barr virus, Ochrobactrumanthropi, Rubella, Cytomegalovirus. Ochrobactrumanthropi, Rubella and CMV factors were detected together in one case. Other factors detected in individual cases were listed on Table 3. However, coronary artery involvement was not found to be associated with pathogenic agents.

Intravenous immune globulin treatment was used in all cases in the first ten days after diagnosis of KS. Orally acetylsalicylic acid (ASA) with a dosage of 80 mg/kg/day divided into four doses and simultaneously 2 g/kg intravenous immune globulin (IVIG) was administered with intravenous infusion in twelve hours in all cases. Patients were followed closely in terms of side effects during the IVIG infusion period. No IVIG-related side effect was detected. Decrease of fever 48-72 hours after treatment was accepted as clinical treatment response. The dose of ASA was reduced in children to 3-5 mg/kg/day single dose a day after 48 hours of fever-free follow-up and control transthoracic echocardiography. Patients with fever after 48-72 hours despite ASA and IVIG treatments were accepted as unresponsive KS and an additional IVIG treatment was applied in these with a dosage of 2

mg/kg/day. All patients had the standard treatment protocol for KS. Recovery of cardiac involvement was observed in most of cases (83,3%). Nobody needs infliximab or other therapies. No side effects were reported due to IVIG and ASA treatments.

DISCUSSION

Kawasaki syndrome is common in children below five years of age and men gender (10). In our study, four of the cases were above five years of age, and fourteen were under five years. The male/female ratio was 1.25 consistent with the literature. Studies have found increase in the frequency of KS with seasonal changes. The highest incidence in Japan and Korea was detected in January (winter) and July (summer) (10). The highest incidence in Europe was detected in the winter season (11). In our study, the cases were mostly diagnosed in the winter season and the second most frequently seasons were spring and autumn. Because the seasonal variability and clinical findings used in the diagnosis of KS can also be seen in viral infections, it brings to mind the questions that infectious agents may cause KS. However, definite clear results cannot be shown in the studies conducted on the etiological ground.

Table 2. Age, gender, and clinical manifestations of kawasaki syndrome

	n (%)
Kawasaki syndrome cases	18 (100)
Age	
<5 years	14 (77.7)
>5 years	4 (22.2)
Gender	
Female	8 (44.4)
Male	10 (55.5)
Clinical Findings	
Fever	18 (100)
Oropharynx changes and lip findings	12 (66.6)
Nonpurulent conjunctivitis	10 (55.5)
Cervical lymphadenopathy	9 (50)
Rash	8 (44.4)
Limb change	7 (38.8)

Table 3. Infectious agents, case laboratory and echocardiography findings

INFECTION AGENT	**ADMISSION MONTH**	**AGE**	**LEUKOCYTE NUMBER (UNIT / MM3)**	**CRP (MG/DL)**	**HEART ATTACHMENT**
PARAINFLUENZA TYPE4	SEPTEMBER	2.19 MONTHS	9340	6.68	LEFT CORONARY ARTERY EXPANSION
RSV	DECEMBER	9.5 AGE	9870	0.2	MINIMAL PERICARDIAL EFFUSION
PARAINFLUENZA TYPE3	AUGUST	11 MONTHS	10900	8.4	TRIVIAL MITRAL INSUFFICIENCY
GROUP A STREPTOCOCCUS (GAS)	JUNE	3 AGE	23400	15.9	MILD MITRAL INSUFFICIENCY
EBV	MAY	1.11 YEARS	14400	0.32	NORMAL
OCHROBACTRUM ANTHROPI	NOVEMBER	1.1 AGE	25000	2.3	RIGHT CORONARY ARTERY EXPANSION
RUBELLA	NOVEMBER	1.1 AGE	25000	2.3	RIGHT CORONARY ARTERY EXPANSION
CMV	NOVEMBER	1.1 AGE	25000	2.3	RIGHT CORONARY ARTERY EXPANSION

Another reason why an infectious trigger is considered is that the syndrome is rarely seen in babies younger than three months, possibly as a result of antibodies transmitted from the mother, and the syndrome is almost absent in adults due to the development of immunity due to previous encounters

(7). It was stated in a study by Rowley et al. an agent that could stimulate the immune system may cause KS in genetically susceptible individuals (12). This hypothesis constitutes the basis of examining viral respiratory tract panels and viral antigens in blood during hospitalization. The infectious agents detected in the cases in our study were Parainfluenza type 4, Parainfluenza type3, RSV, GAS, EBV, Ochrobactrumanthropi, Rubella, and CMV. While Ochrobactrumanthropi, Rubella, and CMV were identified together in one case. Other agents were detected from individual patients. In a study conducted in 2013, fourteen different viruses were detected in the polymerase chain reaction and serological tests from clinical samples, and it was thought that they could be associated with KS (13). In another study by Kikuta et al. (14) Epstein Barr virus DNA sequences were obtained in 83% of KS patients and 18% of the control group. Although it is thought that viral infections may cause KS in different reports, more researches should be performed to elucidate the cause and relationships of KS with viral infections. An infectious agent which causes excessive inflammation in predisposed children is a widespread hypothesis, but no specific pathogen has been identified yet. The mystery over KS remains (12-14).

The KS has also a geographic and ethnic origin. Asia is the continent in which KS is most commonly reported. Japan has the highest incidence in this region. In a study conducted in 2014, the rate of KS in children under five years of age in Japan is 308 in 100.000 children (15). South Korea takes second place with 199.7 per 100.000 children in the same age range (16). Although there is no clear data, the rate in our country is 9% among all vasculitis diseases (17).

Kawasaki syndrome is a serious disease with acute vasculitis involvement in childhood. Coronary artery aneurysms are reported in 20% of untreated children. Untreated children and can lead to coronary stenosis, myocardial infarction (MI), or sudden death syndrome (18). In our study had 77.7% of patient cardiac involvement (pericardial effusion, mitral insufficiency), and 33.3% had small coronary involvement. The coronary artery involvement rate was a bit higher than in the literature. We speculated that this result might be related to the fact that study patients were recruited from the pediatric cardiology outpatient clinic. The geographic localization of our country may also affect this high incidence. The cardiac involvement rate was 66.6% in typical KS and 83.3% in the atypical form observed. Coronary artery involvement was detected in one (16.6%) patient of typical KS and in five (41.6%) cases of atypical KS. Both cardiac and coronary artery involvement rates were higher in the atypical KS in our study.

Maggio MC et al. reported adenovirus identification in siblings diagnosed with KS and coronary artery aneurysm (19). However, some studies in the literature could not find a relation between coronary artery involvement and viral etiology (20,21). Similar to the literature our study results could not demonstrate a relationship between a specific viral agent and coronary artery involvement.

It has been shown that early diagnosis and treatment with intravenous IVIG and ASA decreases this risk to 5%, but the medium to long-term prognosis of children with KS is still unknown and a research area (18). All patients had in our study the standard treatment protocol for KS. No side effects

due to treatment regimens were reported. Recovery of cardiac involvement was observed in most of the cases (83.3%) in our study. Nobody needs infliximab or other therapies. However, our study had several limitations. The first limitation is the relatively small sample size, the second limitation is the retrospective design, and the missing of long-term follow-up evaluations of children with Kawasaki syndrome.

CONCLUSION

The detection of infectious agents in one-third of the cases and different factors suggest that the Kawasaki syndrome is not related to a specific agent. Both cardiac and coronary artery involvement rates were higher in the atypical KS. Atypical KS needs more attention for cardiac involvement. Further prospective multicenter trials with larger sample sizes are needed to evaluate the relationship between viral infections and KS.

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Author Contributions:
Concept – CYG, NE, NUK; Design CYG, NE, NUK; Literature search CYG, NE, NUK; Data Collection and/or Processing – CYG, NE, NUK; Analysis and/or Interpretation – CYG, NE, NUK; Writing – CYG, NE, NUK

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Evaluation of Turkish Cypriots' Knowledge, Attitudes and Behaviours About The COVID-19: A Descriptive Study

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Abstract

Objective: COVID-19 was first discovered in Wuhan in December 2019 and spread all over the world. This study was conducted to evaluate the knowledge, attitudes and behaviours of people living in Northern Cyprus regarding COVID-19.

Methods: This descriptive study designed to evaluate the level of knowledge, attitude and behaviour of participants who are Turkish Cypriots between 7-17 April 2020 after the first COVID-19 case diagnosed in our country. A twenty-nine-item questionnaire was prepared, distributed randomly to participants on social media and took 7-10 min to complete. Data were analyzed with a 95% confidence and $p<0.05$ significance level.

Results: Of the 1192 respondents, 70.8% are between 20-29 years old, 69.8% are women, and 69.1% are university students. The average score in knowledge of all participants about COVID-19 was found to be 47.39, and the general precaution level average score of all participants was found to be 45.97. A statistically significance difference was determined in between the GPL average score and age ($p=0.012$), gender ($p=0.000$), marital status ($p=0.000$), being a university student ($p=0.002$), working status ($p=0.000$), and having a healthcare professional in the family

Conclusion: Both the knowledge and precaution levels of the participants were determined to be at 'good' levels. It was shown that the participants had a high level of knowledge of COVID-19 and a high level of compliance with preventive measures.

Key words: COVID-19; knowledge; attitude; awareness; precaution

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INTRODUCTION

The Novel Coronavirus (SARS-CoV-2) epidemic emerged in the city of Wuhan in China's Hubei province in December 2019 and affected the whole world (1,2). In a short time, more than 800 cases have been confirmed in other provinces of China, Thailand, Japan, South Korea and the United States of America (USA) (3). The Novel Coronavirus outbreak, which the World Health Organization (WHO) named 2019-nCoV on January 12, 2020, was renamed coronavirus disease (COVID-19) on February 11. On March 11, COVID-19 was declared a pandemic by the WHO (4,5).

According to the data of WHO dated 25 August 2021; There have been more than 212.3 million cases worldwide, more than 4.4 million deaths, and more than 4.6 billion doses of vaccination administered (6). Many clinical studies have revealed the signs and symptoms of COVID-19. Among these symptoms, It is possible to count high fever, cough, myalgia, fatigue, expectoration dyspnea, dizziness, diarrhea, nausea and vomiting (7-9).

The first case of COVID-19 in Northern Cyprus occurred on 10 March 2020 in a German tourist. The next day, the spouse of the person who was positive was also announced as COVID-19 positive. The first Turkish Cypriot to infected COVID-19 was announced as the person who returned to the island from England with the same German tourist group (10). As of August 24, 2021, more than 15.3 thousand cases were detected and 50 cases died on the island (11).

Since the beginning of the pandemic, many measures have been taken to prevent the number of cases. At the beginning of these measures were prohibition and/or restriction of entry and exit to countries, restrictions in public activities, interruption of education, quarantine practices, use of masks and gloves, and maintaining social distance. It is known that with the implementation of the right policies and appropriate control measures, it is possible to improve the course of the pandemic. This is closely related to the correct knowledge, attitudes and behaviours of individuals (12,13).

After the increase in cases in Northern Cyprus, various measures were taken in this process and continue to be taken (14). Generally, Measures such as quarantine and limiting entrances and exits to countries, stopping public activities, suspending education, quarantine practices, putting into practice issues such as masks, gloves, and social distance appear during the pandemic period. In this period, it is possible to improve the course of the pandemic with the implementation of the right policies and the right control. This can only be achieved with the right knowledge, attitude and behaviour (13). Based on the importance of correct knowledge, attitude and behaviour, the aim of this study is to determine Turkish Cypriots' the knowledge, attitudes and behaviours about COVID-19.

METHODS

The sample of this descriptive study consisted of 1192 participants who were living in Northern Cyprus. Data were collected online between 07-17 April 2020 and online consent was obtained from each individual who agreed to participate in the study. For the online data collection method, the form created by the researchers considering the literature was prepared online and shared with the participants. Participants who applied the online form between the

specified dates (07-17 April) and met the research criteria were included in the study. After data collection, all data were checked for inclusion criteria. In particular, all individuals whose observation unit (sampling is type) living in Northern Cyprus and over the age of 18 were included in the study (simple random sampling).

The data collection form, which was created by the researchers by examining the literature, consisted of four parts (12,15,16). In the first part, where demographic data were questioned, there were seven (7) questions such as age, gender, marital status, being a student, the department (they were student), their working status and whether there was a health professional in the family. In the second part of the form, there were twenty-nine COVID-19 information questions (general knowledge level part). Each question consisted of three options as 'true', 'false' and 'I don't know'. Aside from these 29 statements were questioned regarding the information using the 3-point Likert Scale, which were graded as follows: Each correct 2 points, incorrect 0 points, and I don't know is "1" point. According to this; the lowest score (min) that the participants can get is 0 (zero), and the highest score (max) is 58 (2point x 29 question). With this scoring system, 'bad' knowledge level is between 0-19 points, 'moderate' between 20-39 points, and 'good' knowledge level between 40-58 points. The result indicates general knowledge (GK).

For the precautions such as wearing a mask, gloves and taking food supplements were questioned in the form (three statements). Precaution questions were answered by the participants in two options: Those who agreed answered 'yes', and those who disagreed answered 'no'. Aside from these 3 precautions, 12 additional statements were questioned regarding the precautions using the 5-point Likert Scale, which were graded as follows: 'very rarely' (1-point), 'rarely' (2-points), 'moderately' (3-points), 'frequently' (4-points), 'very frequently' (5-points). The lowest score is 1 (one), and the highest is 60 (sixty). According to this grading system, scores between 1-20 describes 'bad', scores between 21-40 describes 'moderate', and scores between 41-60 describes 'good' precaution levels. The section was named general precaution level (GPL).

The investigation was conducted in accordance with the principles outlined in the Declaration of Helsinki. To commence the research, necessary permissions were acquired from the Ethics Committee at the Near East University (2020/79). The study participants filled in the data collection form online during the application of the study. Prior to filling in the form, a consent form, containing general information and the purpose behind the research, has been placed, informed of the voluntary nature of their participation in the study, and consent collected from the participants. Moreover, before data collection began, the participants were informed that they could decline to participate in the study at any stage. The data collection form took approximately 7-10 minutes to be filled out by a participant. By scanning the literature, the Cronbach Alpha coefficient of the data collection form developed by the researchers was determined as 0.65.

Statistical analysis

The collected data in this research was analyzed using the Statistical Package for Social Sciences (IBM Corp.; Armonk, NY, USA) (ver. 18.0).

Kolmogorov Smirnov and Shapiro Wilk tests were applied to verify if the data conforms to a normal distribution. Frequency analysis was applied to the socio-demographic features and to some comparisons. In the data comparison, Mann-Whitney U and Kruskal-Wallis H tests were applied, while also taking the number of variables into consideration. The average score of the GK questions and the average score of the GPL were detected using the One-way ANOVA test. Data were analysed with a 95% confidence and $p<0.05$ significance level.

RESULTS

The socio-demographic features of the participants are shown in Table 1. According to this, 70.8% (n=844) of the participants were between the ages of 20-29, 69.8% (n=832) of the participants were women, 82.4% (n=982) of the participants were single, 10.7% (n=128) of the participants were employed in a job that requires a bachelor's degree (officer etc.), 68.9% (n=821) of the participants were university students. 56.7% (n=676) of the university students were studying in a health department; of those, 28.5% (n=340) were studying in a medical faculty. It was found that 57.4% (n=684) of the participants had no healthcare professional in the family (Table 1).

The average score in GK of all participants about COVID-19 was found to be 47.39, and the GPL average score of all participants was found to be 45.97. Based on that, both the GK and GPL of the participants were determined to be at 'good' levels (Table 2).

Table 1. Socio-demographic characteristics of the participants (n=1192)

Characteristic Feature	Number (n)	Percentage (%)
Age		
10-19	72	6.0
20-29	844	70.8
30-39	114	9.6
40-49	76	6.4
50-59	80	6.7
60-69	6	0.5
Gender		
Female	832	69.8
Male	360	30.2
Marital status		
Married	210	17.6
Single	982	82.4
Currently a university student		
Yes	821	68.9
No	371	31.1
Departments (they were students, n=821)	340	28.5
Medicine	138	11.6
Dentistry	98	8.2
Nursing	100	8.4
Vocational School of Health Services		
Other	145	12.1
Working status (n=371)		
Doctor	52	4.4
Health Professional	66	5.5
Officer etc.	128	10.7
Technician etc.	54	4.5
Not working, retired, housewife etc.	71	6.0
Healthcare professional present in family		
Yes	508	42.6
No	684	57.4

Table 2. General knowledge and general precaution level average scores of the participants about COVID-19 (n=1192)

	Number (n)	Av	SD	Min	Max
GK Score Av.	1.192	47.39	3.58	36	58
GPL Score Av.	1.192	45.97	6.87	12	60

GK: general knowledge level, GPL: general precaution level, Av: Average, SD: Standard deviation, Min: Minimum, Max: Maximum

Distribution in the precautions, such as wearing a mask, gloves and taking food supplements, of the participants is shown in Table 3 (attitudes). It was determined that 79.7% (n=950) of the participants wore masks, 58.9% (n=702) wore gloves, and 69.1% (n=824) did not take any food supplement. Participants who wear masks but did not wear gloves or did not took any food supplements were determined to have a higher the GK score (47.58±3.64, 47.72±3.63, 47.50±3.54; respectively). It was significance difference between the GK score and participants who were wearing masks as a precaution (p=0.007). The average score in GPL scores of the participants who wore a mask, gloves and take food supplements were higher than those who did not wear a mask, gloves and did not take any food supplements (46.74±6.71, 47.05±6.61, 47.47±7.05; respectively). It was determined that there was a statistically significant difference between the GPL mean score and the measures to wear masks, gloves, and take food supplements (p<0.00, in all groups; Table 3).

A comparison between the socio-demographic features and the GK average score of the participants is demonstrated in Table 4. The GK average score was noticed to be higher when compared to other variables in participants who were aged between 50-59 (48.97±3.61), female (47.46±3.78), married (48.17±3.45), not a university student (47.91±3.47), medical faculty student (47.91±3.47), working as a doctor (50.38±2.94), and having a healthcare professional in the family (47.47±3.73). There was a significant difference (p<0.05) between the GK average score and age (p=0.028), marital status (p=0.006), being a university student (p=0.012), being a student in a health department (p=0.000) and working status (p=0.001) (Table 4).

Table 3. Comparison between wearing a mask, gloves and taking food supplements against the general knowledge average score and the general precaution level average score (n=1192)

Precaution	Number (n)	Percentage (%)	GK Av± SD	P	GPL Av± SD	P
Wearing a mask						
Yes	950	79.7	**47.58±3.64**	0.007*	**46.74±6.71**	
No	242	20.3	46.63±3.26		42.99±6.73	0.000*
Wearing gloves						
Yes	702	58.9	47.15±3.54	0.094	**47.05±6.61**	
No	490	41.1	**47.72±3.63**		44.44±6.96	0.000*
Taking food supplements						
Yes	368	30.9	47.14±3.67	0.467	**47.47±7.05**	0.000*
No	824	69.1	**47.50±3.54**		45.31±6.69	

GK: general knowledge, GPL: general precaution level, *p<0.05, average score.

Table 4. Comparison between the general knowledge average score against socio-demographic data of the participants about the COVID-19 pandemic

Feature	Number (n)	Percentage (%)	Av Score	SD	Min	Max	P
Age							
10-19	72	6.0	46.19	4.14	36	55	0.028*
20-29	844	70.8	47.30	3.48	36	56	
30-39	114	9.6	47.22	3.52	40	52	
40-49	74	6.4	48.02	3.87	38	54	
50-59	80	6.7	**48.97**	3.61	42	58	
60-69	6	0.5	48.00	4.00	44	52	
Gender							
Female	832	69.8	**47.46**	3.78	36	58	0.762
Male	360	30.2	47.36	3.50	36	56	
Marital status							
Married	210	17.6	**48.17**	3.45	38	54	0.006*
Single	982	82.4	47.22	3.59	36	58	
Currently a university student							
Yes	824	69.1	47.15	3.61	36	56	0.012*
No	371	31.1	**47.91**	3.47	38	58	
Departments							
Medicine	340	28.5	**48.32**	3.62	38	56	0.000*
Dentistry	138	11.6	46.75	3.27	38	56	
Nursing	98	8.2	46.16	3.30	40	54	
Vocational School of Health Services	100	8.4	45.86	3.45	36	52	
Working status							
Doctor	52	4.4	**50.38**	2.94	44	58	0.001*
Health Professional	66	5.5	48.30	3.10	40	52	
Officer etc.	128	10.7	47.04	3.57	39	54	
Technician etc.	54	4.5	47.07	3.44	38	54	
Not working, retired, housewife etc.	71	6.0	47.94	3.20	42	53	
Healthcare professional present in family							
Yes	508	42.6	**47.47**	3.73	38	58	0.846
No	684	57.4	47.33	3.47	36	56	

*p<0.05; GK: general knowledge, Av: Average, SD: Standard deviation, Min: Minimum, Max: Maximum

Table 5 demonstrates the GPL average score of participants according to their socio-demographic features. According to that, participants who were between the ages of 60-69 (48.33±4.50), female (46.83±6.52), married (48.81±5.78), not a university student (47.58±6.61), studying at a nursing department (47.65±5.47), working as a healthcare professional (nursing etc.) (50.18±4.98), did not have a healthcare worker in the family (47.58±6.61) were found higher GPL average score

when compared to other socio-demographical variables. A statistically significance difference was determined in between the GPL average score and age (p=0.012), gender (p=0.000), marital status (p=0.000), being a university student (p=0.002), working status (p=0.000), and having a healthcare professional in the family (Table 5)

Table 5. Comparison between the general precaution level average score against socio-demographic data of the participants about the COVID-19.

Feature	Number (n)	Percentage (%)	Av Score	SD	Min	Max	P
Age							
10-19	72	6.0	46.16	6.07	34	57	0.012*
20-29	844	70.8	45.34	6.84	12	58	
30-39	114	9.6	48.01	5.98	37	58	
40-49	74	6.4	48.13	6.15	34	57	
50-59	80	6.7	47.37	8.79	24	60	
60-69	6	0.5	**48.33**	4.50	44	53	
Gender							
Female	832	69.8	**46.83**	6.52	22	60	0.000*
Male	360	30.2	43.99	7.26	12	57	
Marital status							
Married	210	17.6	**48.81**	5.78	33	60	0.000*
Single	982	82.4	45.37	6.94	12	58	
Currently university student							
Yes	824	69.1	45.26	6.87	12	58	0.000*
No	371	31.1	**47.58**	6.61	24	60	
Departments							
Medicine	340	28.5	42.90	7.26	12	58	
Dentistry	138	11.6	47.08	6.37	28	57	0.002*
Nursing	98	8.2	**47.65**	5.47	37	56	
Vocational School of Health Services	100	8.4	46.68	5.86	28	57	
Working status							
Doctor	52	4.4	43.73	5.24	34	53	0.000*
Health Professional	66	5.5	**50.18**	4.98	38	58	
Officer etc.	128	10.7	46.62	5.69	34	60	
Technician etc.	54	4.5	50.07	7.58	24	58	
Not working, retired, housewife etc.	71	6.0	47.82	8.07	28	57	
Healthcare professional present in family							
Yes	508	42.6	45.26	6.87	12	58	0.002*
No	684	57.4	**47.58**	6.61	24	60	

*p<0.05; GPL: general precaution level, Av: Average, SD: Standard deviation, Min: Minimum, Max: Maximum

DISCUSSION

The Coronavirus 2 agent (SARS-CoV-2), which came up as Coronavirus disease 2019 (COVID-19), causing severe acute respiratory syndrome, became a pandemic. Thus, compliance with the public health precaution measures by the human population of each country had noticeably allowed the respective country to halt the spread of the disease. As mentioned above, the compliance with set precautions as well as the high level of awareness among the population of Northern Cyprus resulted in cessation of new emerging cases by April 17th, 2020 as the last patient receiving treatment was discharged from a hospital on May 11th, 2020. During that period of time 108 cases had been identified (17,18).

Different outcomes had been observed in different countries since the start of the pandemic until today across the world. England, for instance, implemented an alternative strategy; wherein they allowed the virus to disseminate in favour of an increased herd immunity across its population. However, before execution, the country ensured that the elderly population and the population with co-existing comorbidities would receive sufficient protection. This strategy was abandoned shortly in the following period (19).

When looking at examples from Italy, it was noted that the insufficient preparation at the time during the first 2 weeks of the pandemic played an important role in dictating the disease dynamics (20). The first case in Northern Cyprus was seen on March 10th, 2020, and the efforts to raise awareness in the population well in advance had resulted in a positive outcome (10).

In a WEB-based study about COVID-19 carried out on a group comprised of 68% health workers in Asia (30.2% of the participants were doctors, and 29.6% were medical students) it was found out that a significance number of participants had insufficient or weak knowledge on the methods of transmission of the disease and symptoms with a ratio of 61% and 63.6% respectively (21). In our study 65.6% of the participants (n=782) were working as a healthcare professional. The level of general knowledge about the COVID-19 transmission methods, signs and symptoms among the people who worked as a healthcare professional was determined to be 47.55±3.62 during the pandemic.

Among individuals that work in a non-health related field, the GK average scores were determined to be 47.07±3.51. According to this, there was no statistical difference when comparing individuals working in a health-related field and those who did not (p=0.118); both groups achieved ‘good’ GK levels. Once the results were interpreted, the ratio of awareness among the people residing in Northern Cyprus was found to be high during the COVID-19 pandemic. Whether an individual works as a healthcare professional or not carried no significance.

In the study where participants were medical students, it was found that 79.6% of the students had a ‘high’ level of knowledge about COVID-19 (22). It was observed that students who were studying medicine in Northern Cyprus had achieved a higher average GK score when compared to students of other faculties (48.32±3.62). This average illustrates that medical

students have 'good' GK levels surrounding the COVID-19 pandemic.

In a study done in Iran during the pandemic, it was reported that more than half the nurses (56.5%) demonstrated good knowledge levels (23). The overall average scores of individuals working in a health-related field in Northern Cyprus was determined to be 48.14±3.25; with their average GK score at the level 'good'. Among the participants' occupations, the highest average General Knowledge (GK) scores belonged to doctors (50.38±2.94). These results demonstrate that having high GK levels among individuals, both in healthcare professionals/students and other professionals, plays an important role when it comes to the prevention of disease spread.

In a study done in China, at the end of the first month of the outbreak, it was found that the ratio of correct answers in a knowledge survey about COVID-19 was between 70.2-98.6%, and that the mean knowledge level was determined at 90% (24). In our study the ratio of correct answers in the GK questions around the COVID-19 pandemic ranged from 24.5-99.5% and the average percentage was 76.3%. Thus, the society that succeeded in controlling the outbreak which broke out in China had high levels of knowledge and awareness, which was comparable to that of the population of Northern Cyprus.

Myanmar, a country with a population of over 54 million, had faced 378.3 thousand cases by August 2021. Criteria such as hand hygiene, mask wearing, and abidance by social distancing rules demonstrated a compliance ratio of over 80% by the population, indicating a high awareness ratio in the study (25). Similarly, the Hong Kong community, with a population of over 7 million people, demonstrated a 90% awareness ratio (26). It was shown that the compliance ratio to precautions in Northern Cyprus was high (Table 3).

Similar to other research results, our study results emphasize that implementing precautions by the population can be effective in reducing the number of cases. However large the sample of our study is, the results cannot be generalized to all island populations. This is the limitation of the study.

There is a study in the literature confirming the importance of comprehensive approaches combining education and advice in increasing COVID-19 vaccination rates among nurses and midwives in Cyprus (27). Similar to the results of this study, our results emphasize that there is a direct correlation between education level and knowledge scores about COVID-19. It was determined that the knowledge, attitude and behaviour of both healthcare professionals/students and other professionals about COVID-19 were good. The fact that using personal protective equipment due to COVID-19 is an indication that the participants are aware of the pandemic. As a result of the measures taken at the border gates opened as of 30th June 2020, the entrance of the country to be inspected by the RT-PCR test shows that the determined cases in the North Cyprus are import cases. After April 17, no-community-based cases have been identified in people who are living on the island. However, in the ongoing process, cases started to be seen again.

Limitation

This study was limited to participants who agreed to participate and met the research criteria.

CONCLUSIONS

COVID-19 still continues to affect the whole world with positive cases and deaths. For this reason, the necessary information load and importance provide the desired and positive development of attitudes and behaviors.

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YouTube as an educational resource in neurosurgery

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Abstract

Objective: The purpose of this study is to evaluate the contribution of neurosurgery videos on YouTube to the education of medical students, residents and professional medical professionals.

Methods: Members of the Turkish Neurosurgery Association (academic and clinical specialist physicians) and medical students receiving neurosurgery training were asked to respond to a questionnaire via e-mail.

Results: Anatomy (29.1%) was the most watched videos, while vascular, tumor and skull base surgery videos (56.3%) were the most watched surgical videos. While the United States of America is the first among the countries contributing to the videos, our country is the last. It was observed in our study that surgeons watched the operation videos before difficult surgeries and benefited from these videos to increase their experience. It is also undeniable that youtube videos increase the surgical experience of surgeons in underdeveloped and developing countries. has a contribution.

Conclusion: We observed that the training videos were of sufficient quality. In addition, virtual training and surgical videos are increasingly being used for education, especially during the COVID-19 pandemic. It is necessary to increase the diversity of YouTube videos, which have a high rate of viewing among neurosurgery physicians in our country. The training of neurosurgeons can make important contributions to patient care in our country. Considering that such major pandemics may occur in the future, it is certain that more diversification of training and operation videos will be required.

Key words: Neurosurgery, YouTube, virtual education, virtual surgical videos, medical education

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INTRODUCTION

Education is defined as the work of gaining, training and developing knowledge and skills in a certain field or certain subject. Neurosurgery education is the process by which an assistant who has chosen the neurosurgery profession acquires the knowledge and skills to become competent and meet the accepted neurosurgical standards. In general, this training is divided into two branches as clinical and non-clinical application. Clinical education forms the basis of neurosurgery education. In addition to the skills acquired in the operating room, preoperative and postoperative patient care on the wards is an integral part of training for every neurosurgery resident. In our age, medical education benefits greatly from e-learning opportunities. Neurosurgery education has also shifted in this direction, especially during the Covid-19 pandemic period. There are numerous online training tools available to improve residents' understanding of neurosurgery, such as anatomy resources, case illustrations, surgery videos, and various peer-reviewed publications.

Surgical training is a hands-on, experience-built process traditionally supported by textbooks, lectures, cadaver labs, and formal surgical courses. However, the rapid development of technology has led to the emergence of other educational tools such as online lectures and courses, virtual dissections and simulation trainings. The need to emphasize the importance of electronic resources has emerged as the Covid-19 pandemic requires the observance of social distancing measures for a long period of time and reduces the operative experience of surgeons (1-5).

Operative videos have been a painstaking educational tool for both residents and neurosurgeons, especially during the pandemic. Operative videos in neurosurgery can be traced back to the early records of Gazi Yasargil's microsurgery cases; Recording, storing and transmitting videos in high definition (two-dimensional or three-dimensional (3D)) has now become easier. As Robert Spetzler aptly puts it, “Watching a video of a great surgeon will not make you a surgeon, but knowing what is possible and seeing it done will inspire you to become a better surgeon and achieve that goal.” The phrase emphasizes the importance of virtual videos (6).

METHODS

In our study, a questionnaire consisting of 32 questions was sent to 102 neurosurgeons (residents, specialists and academicians). Questionnaires were sent to physicians over the internet, and our study group consisted of members of the Turkish Neurosurgery Association and our close colleagues. The answers given to the questions were evaluated statistically, and the contribution of YouTube videos to neurosurgery education and professional experience, especially during the Covid-19 pandemic were evaluated.

Ethics committee approval of the study was obtained from Lokman Hekim University Ethics Committee (# 2021/0126).

RESULTS

The participants in our study were 93.5% males and 4.5 % females between age 26-69 who were assistants, operators and academicians. Only 29% of them work in a university hospital and 57.5% of the participants are academicians working in an educational institution. 75.8% of the physicians stated that they have more than ten years of professional

experience and 73.8% stated that they spend more than 1 hour a day on the Internet. Neurosurgery operation videos accessed on YouTube were the answer to the most watched video question with 57.4% (Table 1). 96.2% of the participants stated that the videos are educational.

Table 1. Survey questions and the highest rate of answers

QUESTION	ANSWER
Most watched video?	56.3% neurosurgery operation videos
Physicians watching neurosurgery operation video?	84.6% physician
The quality of the videos?	70.9% good
Are the videos educational?	96.4% yes
Most watched operation videos?	29.1% anatomy
Contribution of videos to assistant training?	58.9% sufficient
Time spent online in the Covid-19 pandemic?	increased 87.7%
Contribution of videos to professional experience?	76.8% have

DISCUSSION

In recent years, education has undergone a radical change with the digital revolution. Curriculum has increasingly begun to adopt e-learning, which refers to an approach to teaching and training that uses electronic media to facilitate learning (7,8,9). By adding links to journal articles, virtual lectures, grand tours, 3D anatomical models and dissections, and other educational materials, these resources have been combined with traditional learning styles to create a versatile new form of learning.

Online surgery videos have become a major electronic resource within neurosurgery. These types of videos are an invaluable resource for neurosurgery trainees. As James Rutka said, “If a picture is worth a thousand words, imagine the relative value in words of an operative video!” (14). From this perspective, it is not surprising that many medical students and residents use online videos to supplement their traditional learning and prepare for patient cases (15,16).

Although primarily used by surgical residents, operative videos can also facilitate postgraduate training. Watching videos of surgery edited to continually review the technical steps performed by master neurosurgeons is key to advancing the art of neurosurgery as well as science throughout our careers (14). A survey of neurosurgeons in India (15), 88% of senior neurosurgeons used this technology.

Whether used by neurosurgery residents or neurosurgeons, web-based surgery videos seem to play an important role in education globally, particularly in low-middle-income countries where many surgeons have limited access to journals, cadaver labs, operating theatres/rooms.

A study of neurosurgery in India (15) found that online videos helped 88% of senior neurosurgeons, 91% of junior specialists, and 80% of resident physicians improve their surgical skills. The researchers concluded that e-learning platforms can help provide training opportunities to neurosurgeons in a variety of settings globally. This low-cost resource eliminates the expense associated with journals and textbooks and is readily available to neurosurgeons worldwide.

Given the theoretical usefulness of online surgery videos to facilitate global neurosurgery education, data from the Neurosurgical Atlas shows that such videos are used on a global scale. Between 2016 and 2017, the largest group of people accessing the site was from the United States (29% of viewers). The remainder were from Brazil (6%), India (4%) and various other countries (10). An updated analysis between 2018 and 2019 shows that the overall distribution is similar. 39% of audiences are from the United States, 5% from India, and 4% from Brazil, but users from an impressive 208 different countries accessed the website (17).

In a study, it was revealed that the United States of America contributed to YouTube neurosurgery videos (Table 2).

In our study, it was found that operational videos and educational videos have a high viewing rate. The contribution of our country to such educational videos was found to be low as observed in the literature. The common view is that the quality of the videos is good and their contribution to education is high. Therefore, we should aim to increase use of these videos amongst our neurosurgical trainees.

In a study conducted in India, he said that educational neurosurgery videos contributed to improving the skills of both senior and junior neurosurgeons. However, in this study, the rate of respondents who answered the questionnaire remained as low as 18.84%. This and similar online video sharing videos are very useful for countries with low neurosurgery infrastructure. Enough training equipment is provided to increase the variety of videos (19).

Table 2. Country or region of origin of videos included in the analysis (where specified or extracted)

Country or Region	Frequency	Percentage*
Africa	1	0.6
Australia	3	1.7
Azerbaijan	2	1.1
Brazil	2	1.1
Canada	7	3.9
Egypt	1	0.6
England	1	0.6
Finland	1	0.6
France	1	0.6
Germany	3	1.7
Ghana	1	0.6
India	14	7.8
Indonesia	1	0.6
Iran	1	0.6
Israel	1	0.6
Japan	1	0.6
Malaysia	1	0.6
Mexico	5	2.8
Saudi Arabia	1	0.6
Slovenia	1	0.6
South Africa	1	0.6
Turkey	2	1.1
United Kingdom	3	1.7
United States	123	68.3
Venezuela	2	1.1
Unknown	533	—
Total	713	100.0

*YouTube as a Source of Information on Neurosurgery Nardin Samuel, Naif M. Alotaibi, Andres M. Lozano

Prof. Yasargil was the first neurosurgeon who recorded and collected his microsurgical cases. Many of them were available in compact discs in those days. With the introduction of video-sharing sites like

Vimeo in 2004 and YouTube in 2005, the idea of video sharing became rampant.

In the same study, the rate of watching educational videos was found in the 4th place (Table 3).

Table 3. Cumulative Metrics by Video Category, Sorted by Highest Views

Category	Views	Likes	Dislikes	Comments	Shares
Irrelevant to clinical neurosurgery	44,073,770	549,914	16,371	69,964	6605
Surgical and procedure overview	23,241,074	127,148	3984	29,146	24,942
Patient experience	20,979,639	358,636	5141	47,948	6262
Educational video	1,870,350	8674	362	1327	4743
Promotional video	356,825	1502	63	142	547
Other	24,618	91	10	52	41

*YouTube as a Source of Information on Neurosurgery Nardin Samuel, Naif M. Alotaibi, Andres M. Lozano

Limitations

The limitations of our study are the limited number of neurosurgeons and residents who participated in the survey. We haven't been able to fully represent the entire universe and meet people face-to-face to discuss their answers. By participating in the study with more learners in the field of neurosurgery, the necessary validity and reliability can be ensured and the evaluation of training videos can be more reliable.

CONCLUSIONS

The YouTube training videos on brain tumors, microvascular surgery and anatomy have an undeniable contribution to education. The videos should be more diversified and our country could contribute to this. We will plan studies on this subject are prospectively. While the Covid-19 pandemic has influenced our lives, we have learned that in the coming years physicians should continue to work with online training and congresses to avoid interruptions in medical education.

This study, which we have done, is a pioneer for researching the contribution of YouTube videos to education and for studies to be done on this subject.

Ethics Committee Approval: The non-interventional clinical research titled "YouTube as an Educational resource in Neurosurgery" (Code No 2021107), of which you are the Principal Investigator, was ETHICALLY SUITABLE in accordance with the decision of our Ethics Committee dated 18.10.2021 and numbered 2021/0126.

Peer-review: Externally peer-reviewed.

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Fournier's Gangrene: Our Clinical Experience and Outcomes

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Abstract

Objective: We aimed to present our results and experience related to patients followed with Fournier's gangrene.

Methods: Patient data were retrospectively obtained from patient records. Data from 10 patients attending Ordu University Education-Research Hospital Urology clinic with diagnosis of Fournier's gangrene from April 2017 to April 2021 were used. Cases developing after surgery, with compression wounds, and related to radiotherapy were excluded. Information like patient history, demographic features, comorbid diseases, physical examination findings and treatment outcomes were recorded.

Results: The study included outcomes for 10 patients. Mean age was identified as 71.50±9.09 (51-78) years. All of our patients were male, with no female patient among our cases. Mean body weight of patients was 80.40±1.81 (78-83) kg. When patients are assessed in terms of substance use, 60% of patients smoked and 10% drank alcohol. The mean total number of medications used due to comorbid diseases was 1.8 (0-6). The mean ASA score for patients was 2.20±0.42. In terms of initial location, 6 patients had lesions in the scrotum (60%), 1 on the penis (10%) and 3 in the perineal region (30%). The mean duration until surgery was 8.71±4.95 (3-17) days, with mean number of surgeries after diagnosis 1.67±0.81 (1-3), and mean dressing duration 22.14±5.30 (15-30) days (Table 1). Pathology results for one patient identified squamous cell cancer (10%).

Conclusion: In spite of all developments, Fournier's gangrene is still an emergency situation associated with high levels of morbidity and mortality. In clinics experienced with this disease, it may be treated close to perfectly with high success rates and low complication rates. We believe the most important points for treatment are early diagnosis, effective

Key words: Fournier's gangrene, debridement, experience

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INTRODUCTION

Fournier's gangrene is a progressive necrotizing fasciitis tableau frequently involving the external genital organs and perineal region, that may spread to the abdomen, lower extremities, and chest, with high morbidity and mortality. This severe infectious disease comprises less than 1% of all anorectal sepsis cases (1,2). The disease was named for Jean-Alfred Fournier; however, it was first described in 1764 by Bauriene (3). Fournier first described it in the scrotum and used the term 'fulminating gangrene' of the penis and scrotum. The cause is not fully known. Most cases receive diagnosis when gangrene occurs. A study identified genitourinary causes in 24% of cases, anorectal causes in 24% and intraabdominal causes in 10%, but could not identify any underlying cause in 38% of cases (4). Whatever the cause, most cases have an infection focus identified beginning in the scrotal or anorectal region.

The most important feature of the disease is that it is a toxic tableau that may rapidly progress resulting in mortality. For this reason, rapid diagnosis and treatment carries vital importance (3). From the moment of diagnosis, hospitalization with intense support and treatment is required. In treatment, antibiotic use encompassing polymicrobial agents, debridement of necrotic tissue and wound care are critically important. This disease should be seen as an emergency and actions taken accordingly (5). Sufficient experience and knowledge of this topic has a very important place in treatment and preventing complications in this disease. Inexperienced clinics and individuals may lead to severe progression in this disease.

The aim of this study is to share our clinical experience of Fournier's gangrene and present our results.

METHODS

Study Design and Patients

Patient data were retrospectively obtained from patient records. Data from 10 patients attending Ordu University Education-Research Hospital Urology clinic with diagnosis of Fournier's gangrene from April 2017 to April 2021 were used. Cases developing after surgery, with compression wounds, and related to radiotherapy were excluded. Information like patient history, demographic features, comorbid diseases, physical examination findings and treatment outcomes were recorded.

Clinical Assessment

All patients were assessed with history and physical examination. Cases with progressive wounds with necrotic character observed in the scrotal or perineal region were assessed as Fournier's gangrene. All patients were admitted to hospital as emergency cases. The infectious diseases clinic was consulted. After the necessary preparations, patients were taken for emergency surgery. If necessary, cases were taken for surgery to perform more than one debridement. Wound care was performed twice per day. During this time, wound care was performed with oxygenated water, physiologic serum and rifocin. Postoperative success was accepted as control of the disease and cosmetically acceptable appearance.

Surgical Technique

Patients were informed in detail about treatment choices, outcomes and the need for repeated surgery. Care was taken to be sure that they understood the

process as they could not fully imagine the appearance that will develop postoperatively. According to our experience, at least one patient relative should be included in this process. Written consent was obtained from all patients. Surgical procedures were performed under anesthesia.

During surgery, aggressive excision (debridement) should be performed. Surgeons should be sure that white/necrotic tissue is fully resected until live, bleeding tissue is reached. It may be beneficial to preserve tissue with survival possibilities for later processes. At this point, no closed area should be left, it is important to open all cavities. During this process, it is necessary to avoid devascularization of normal tissues so as not to create new necrotic areas. Deep fascia should be opened to assess muscle status. Sterile dressings should be used without closing the wound. In our practice, wound care is performed with physiologic serum, oxygenated water and rifocin two times per day. We think keeping the wound moist eases wound healing and reduces pain.

If necrotic tissue is observed, debridement and fasciotomy should be repeated at 24-48-hour intervals until clinical healing. Performing this procedure should never be avoided in suspect situations. Removal of the testis should be on the agenda, if necessary, especially for people without fertility concerns. Problems may be experienced related to testis being inserted under the skin due to lack of scrotum, especially with severe debridement.

When the disease is under control, the patient should be discharged after necessary information for secondary closure. However, when patients require close monitoring at home, they are given numbers where they can reach us if necessary. Generally, 3 months are left before closure of the defect due to the debrided tissue (reconstruction). In necessary cases, a plastic surgeon is consulted.

Statistical analysis

Statistical assessment calculated mean values and standard deviation as this study was descriptive research. Parameters with normal distribution are given as mean ± SD, while parameters without normal distribution are given as median ± interquartile range (IQR). Analysis of data used the SPSS 20.0 program.

RESULTS

The study included outcomes for 10 patients. Mean age was identified as 71.50±9.09 (51-78) years. All of our patients were male, with no female patient among our cases. Mean body weight of patients was 80.40±1.81 (78-83) kg.

When patients are assessed in terms of substance use, 60% of patients smoked and 10% drank alcohol. The mean total number of medications used due to comorbid diseases was 1.8 (0-6). The mean ASA score for patients was 2.20±0.42. In terms of initial location, 6 patients had lesions in the scrotum (60%), 1 on the penis (10%) and 3 in the perineal region (30%). Pathology was not observed on rectal examination of any patient.

When laboratory parameters are investigated, WBC count 15.84±3.90 (9.2-21.3) mm3, Hgb 11.34±2.08 (9-15) g/dl, PLT 280.20±4.81.55 (158-360) 103 /µI, NLR 11.59±9.30 (1.61-23.46), and CRP 24.38±13,49 mg/L (8.5-2438) were identified (mean±SD). The mean duration until surgery was 8.71±4.95 (3-17) days, with mean number of surgeries after diagnosis 1.67±0.81 (1-3), and mean

dressing duration 22.14±5.30 (15-30) days (Table 1). Pathology results for one patient identified squamous cell cancer (10%). Comorbid diseases for our patients are shown in Table 2.

Table-1: Demographic Characteristics of the Patient

Patient Characteristics	
Age(years)	71.50±9.09 (51-78)[a]
Body weight (kg)	80.40±1.81 (78-83)[a]
Time to surgery (day)	8.71±4.95 (3-17)
Follow-up time (month)	13.19±9.11 (2-36)
Success n (%)	10 (100)
Patient satisfaction n (%)	9 (90)

a= mean ± SD, b= median ± IQR

Tablo 2. Co-morbidities in Patient

	Frequancy	**Percent (%)**
Diabetes Mellitus	6	60
Lung Disease	3	30
Hypertension	4	40
Heart Disease	3	30
Use of Anticoagulants	2	80
Neurological Disease	2	20

DISCUSSION

Fournier's gangrene is accepted as an emergency disease due to rapid spread and threat to life. Rapid and effective local and systemic treatment carry vital importance. The aim of this study was to share our experience related to patients followed and treated in our clinic for Fournier's gangrene and to present our results. The most important finding identified in this study is that close to perfect outcomes can be obtained as a result of follow-up and treatment for these patients in experienced centers. Additionally, most patients attend hospital in the very late stage.

As seen in our study, the disease frequently affects the male gender; however, it may be rarely observed in women and children. The disease commonly begins with fever, shivering, fatigue and local complaints, and rapidly worsens (6). Diagnosis may be easily missed in the patient group with difficulty expressing themselves. Delay of diagnosis makes progression to malignant tableau like bad odor, necrosis and crepitation easier at the lesion site. The process may progress with tachycardia, high fever, hypotension, disrupted general status and death (7). For this reason, care should be taken as this disease may be easily missed in patients who are addicts, live alone, have advanced age or cognitive problems. This situation should be remembered for patients attending with septic tableau, especially. In our observations, we identified that this disease is frequently missed and progresses more severely in elderly or addicted patients who cannot express themselves. Additionally, this patient group may be hospitalized more and be exposed more to the destructive effects of this disease. This disease may be easily ignored by people and branches without sufficient experience related to this disease especially. A patient attending our clinic recently received diagnosis at the end of 36 days. This patient was followed by an external center for urinary tract infection diagnosis and the lesion in the perineal area was not noticed during hospitalization. When he attended our clinic, perineal Fournier's gangrene was very complicated, and it took weeks for the patient to recover.

In fact, the presence of urogenital or anorectal infections that are not questioned is notable in many patient histories. Infection and gangrene have high risk in terms of rapid spread especially for patients with advanced age, diabetes mellitus, chronic diseases, immunosuppressive status, neurological diseases with general care problems, and substance

use. This also means increased morbidity and mortality (4,7,8,9,10). A study by Malik et al. reported that mortality was 17.8% in the patient group with intense diabetic disease especially (11). Mortality is severely increased in patients with uncontrolled diabetes. Mortality was not observed in our patients. As mentioned above, if this disease is not considered in differential diagnosis, diagnosis is frequently delayed, and this causes associated complications. In short, this disease has potentially destructive and mortal effects; and these effects are inversely correlated with early diagnosis and effective treatment. Diagnosis is very easy and specific (12,13). Diagnosis may be easily made due to pain, edema, increased temperature and tension in the perineal area and scrotum. Progression of the tableau rapidly disrupts circulation, and skin necrosis and bad odor develop (6,14). Additionally, crepitation is very important for identifying the presence of gas-producing bacteria. This is an important marker showing extension of the lesion into deep tissues or severity of the tableau (3).

Emergency approaches are important for this disease that may have very dramatic progression. Commonly hospitalization is required for systemic and surgical treatment. Inflammatory parameters like leukocytosis and CRP are frequently increased. In our results, WBC and CRP levels were identified to increase especially at time of first attendance. These values begin to fall with clinical amelioration. CRP monitoring especially provides very important information in terms of prognosis. CRP is the most important marker used for patient follow-up and prognosis. Additionally, radiological imaging like DUSG and CT may use used to identify subcutaneous gas and spread of the disease in necessary situations. However, routine use is not recommended.

If urinary tract infection is considered the source, urinary diversion may be performed. This is a very beneficial procedure for special situations like incontinence and urethral involvement. Stopping contact with urine and keeping the environment dry contributes to rapid amelioration. However, we do not have adequate data about performing it as a routine practice.

During surgery, the surgeon should be certain that effective debridement is performed. In these patients, polymicrobial agents comprising aerobic and anaerobic bacteria are commonly observed. Sometimes the lesion appearance may be misleading. We recommend culture and tissue biopsies for polymicrobial agents. This is important in terms of selection of appropriate antibiotics and identification of possible underlying malignant events. In our patient group, squamous cell cancer was identified in one patient. As seen in our results, these patients frequently require more than one surgery. Testicular necrosis develops very rarely because the blood circulation and venous drainage of the testis is different from the skin. Thus, orchiectomy is not required in many cases and orchiectomy was not performed for any of our cases. In cases with advanced age and no concerns about fertility, if there is advanced degree of scrotal tissue loss and the testis needs to be inserted under the skin, orchiectomy may be performed after discussions with these patients. Problems like cosmetic problems and pain may make the patient uncomfortable in some cases with the testis preserved by insertion under the skin. We experienced serious problems in some patients and in

one case orchiectomy was necessary. In our study, all patients had the disease controlled with mean 22-day dressing duration. When the literature is examined, the hospitalization duration is nearly 25-30 days (8). Nearly 3 months should be left before closure of the defects left after debridement.

Limitation

This study has some limitations. The first of these is the retrospective nature of the study. Another is the limited patient numbers and not knowing the degree of comorbid diseases. This data should be added to the results for a center. There is a need for prospectively planned multicenter studies including more patients.

CONCLUSIONS

In spite of all developments, Fournier's gangrene is still an emergency situation associated with high levels of morbidity and mortality. As the disease may sometimes be asymptomatic, it should be remembered for addicted people who cannot express themselves. Preventive precautions should be taken especially for risky cases. In addition to early diagnosis, supportive and effective treatment has vital importance for prognosis of the disease.

As seen in our study results, the disease may be treated close to perfectly with high success rates and low complication rates in experienced clinics. We think the most important points for treatment are early diagnosis, effective repeated debridement and the use of broad-spectrum antibiotics. Additionally, we believe it is necessary to create centers with adequate experience about this topic.

Ethics Committee Approval: Ethics committee approval was received for this study from the Clinical Research Ethics Committee of Ordu University (2020/05).

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Frequency of Paroxysmal Nocturnal Hemoglobinuria in Patients with Lymphoma

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Abstract

Objective: To investigate the frequency of paroxysmal nocturnal hemoglobinuria (PNH), an acquired clonal hematopoietic stem cell disease resulting in complement-mediated hemolysis, in patients with lymphoma by flow cytometry.

Methods: Fifty patients with lymphoma who were admitted to the hematology clinic, newly diagnosed and not yet treated were included in this study conducted in 2014. The presence of PNH clones was checked by FLAER flow cytometry method in peripheral blood samples. FLAER is a non-hemolytic fluorescently labeled inactive toxin aerolysin method that can detect up to 0.5% of PNH cells instead of bacterial toxin aerolysin, which binds to RBCs via the GPI anchor and initiates hemolysis for PNH screening or PNH clone detection. With this technique, PNH clones in all hematopoietic cell lines can be detected in an assay.

Results: PNH clone was observed over 10% in two patients, one male and the other female. However, no hemolysis was found in patients with PNH clones. The lymphoma subtypes of the patients with positive PNH clone were B-cell small-cell lymphocytic lymphoma in the male patient and primary splenic lymphoma in the female patient.

Conclusion: PNH or PNH-like disorders accompanying hematological malignancies, especially lymphomas, are not very common in the literature. There is a need to elucidate the relationship between hematological malignancies and PNH with the help of more advanced molecular techniques.

Key words: Paroxysmal nocturnal hemoglobinuria, PNH, lymphoma, cytometry, FLAER

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INTRODUCTION

Lymphoma is a group of malignant lymphoproliferative diseases arising from different lymphoid tissue cells, primarily B and T cells in the lymphatic system (1). Lymphoma is the most common form of hematological malignancies in developed countries. The classification, which was previously accepted as Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL) and changed several times, was lastly revised by the World Health Organization (WHO) in 2016 (2). More than 90 lymphoid neoplasms with different histopathology and heterogeneous behavior are divided into five main categories: "mature B-cell", "mature T and NK cell", "Hodgkin lymphoma", "posttransplant lymphoproliferative disorders" and "histiocytic and dendritic cell neoplasms".

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare acquired clonal hematopoietic stem cell (HSC) disease that can affect all three blood cell lines. The defect in PNH is a somatic mutation of the Xp22.1 gene, called pig-A, located on the short arm of the X chromosome. As a result of this mutation, the binding protein to the cell membrane is impaired and a chronic, uncontrolled complement activation and intravascular hemolysis process begins due to the defect in the cell membrane. Morbidity and mortality depend on cytopenia, thrombophilia and secondary transformations. A better standard of living and prognosis have been achieved with targeted agent therapy (eculizumab) that stops hemolysis (3).

It has been reported that PNH may accompany other hematological diseases (4). Many patient groups with PNH have a history of diagnosis of aplastic anemia (AA) or myelodysplastic syndrome (MDS). In addition, it can progress or transform into some diseases such as AA, leukemia as well as with other diseases (5).

In this study, PNH clone was examined in patients who applied to the Hematology clinic and were found to have lymphoma in their workups. It is aimed to determine the frequency of PNH, which may have similar findings and complications with lymphoma.

METHODS

Patient Selection

Patients who applied to department of Internal Medicine, Hematology clinic between March 2014 and June 2014 and were newly diagnosed with lymphoma were included in the study.

Exclusion criteria were pediatric age group, geriatric patients over the age of 80, those with severely impaired general condition, those who were excluded from the diagnosis of lymphoma during their follow-up, and those who did not want to be included in the study.

Patients were staged according to the Costwold staging classification. For clinical staging, patients' histories were taken, and physical examinations were performed. Blood count and biochemical results were taken into account in patient follow-ups. Again, radiological examinations for the diagnosis of lymphoma were examined.

Collection and Transport of Blood Samples

Since glycosylphosphatidylinositol (GPI) anchor differentiation in the bone marrow is at different stages, peripheral blood sampling was preferred to diagnose PNH by Fluorescein-labeled proaerolysin (FLAER) (6). The blood samples taken were sent to the laboratory of the department of Immunology, and

the samples were studied with the FLAER on the same day.

Experiment Method

PNH clones were studied by 4-color flow cytometry (FCM) with FLAER and analyzed with the FACSDiva Version 6.1.2 data program.

To detect GPI-AP expression:

• For neutrophils, FLAER (Alexa)/CD24 (PE)/CD15 (PerCP)/CD45 (PeCy7) antibody,

• For monocytes, FLAER (Alexa)/CD14 (PE)/CD64 (PerCP)/CD45 (PeCy7) antibody,

• For erythrocytes, CD235a (FITC)/CD59 (PE) antibody was used.

PNH clone values of 10% and above were considered positive for the diagnosis of PNH.

Statistical analysis

Numerical data are shown as mean and standard deviation.

RESULTS

Fifty newly diagnosed lymphoma patients who applied to department of Internal Medicine, Hematology clinic between March 2014 and June 2014 were included in the study.

The youngest case in the study was 24 years old, the oldest case was 76 years old, and the mean age of these cases was 55.66 (Table 1). Of the cases, 22 (44%) were female and 28 (56%) were male (Table 2).

The lymphoma subtypes and numbers of the cases were determined by their clinical records (Table 3), (Figure 1). Accordingly, 33 (64.70%) B-cell lymphomas, 6 (11.76%) T-cell lymphomas, 12 (23.52%) Hodgkin lymphomas, and 0 (0%) others were determined.

Table 1. Age information of the cases

n	Lowest Age	Highest Age	Average Age	Standard Deviation
50	24	76	55,66	15,74

Table 2. Gender information of the cases

Sex	n	Ratio (%)
Female	22	%44
Male	28	%56
Total	50	%100

Table 3. Lymphoma subtypes and their numbers

Lymphoma Type	N	Ratio (%)
B cell lymphoma	32 (13)	64
T cell lymphoma	6 (3)	12
Hodgkin lymphoma	12 (6)	24
Histiocytic and dendritic lymphoma	0	0
Posttransplant lymphoproliferative disorders	0	0

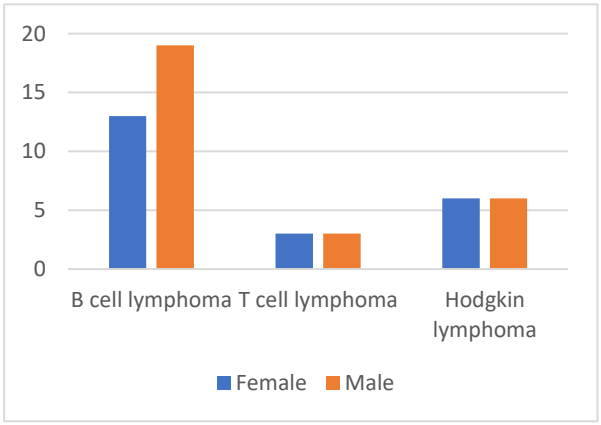

Figure 1. Distribution plot of lymphoma subtypes by gender

In FLAER flow cytometric analysis, PNH clone was observed as > 10% in 2 out of 50 cases, one male and one female (Table 4). The rate of patients with positive PNH clone was 4%. The FLAER results of two patients are shown in Figure 2 and 3. Hemolysis was not found in patients with positive PNH clone. The lymphoma subtypes of the patients with positive PNH clone were B-cell small-cell lymphocytic lymphoma in the male patient and primary splenic lymphoma in the female patient.

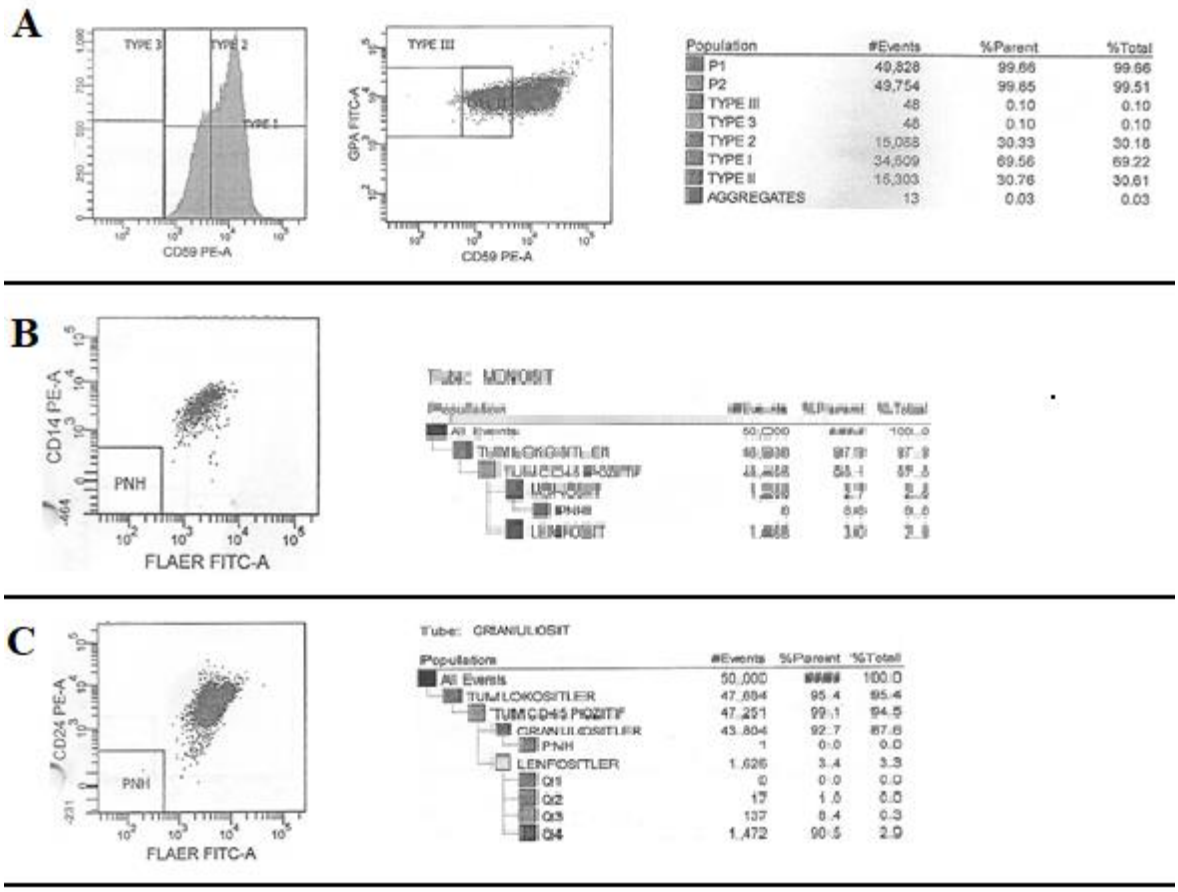

Figure 2. FLAER erythrocyte (A), monocyte (B) and granulocyte (C) results of the first patient (male) with PNH clone

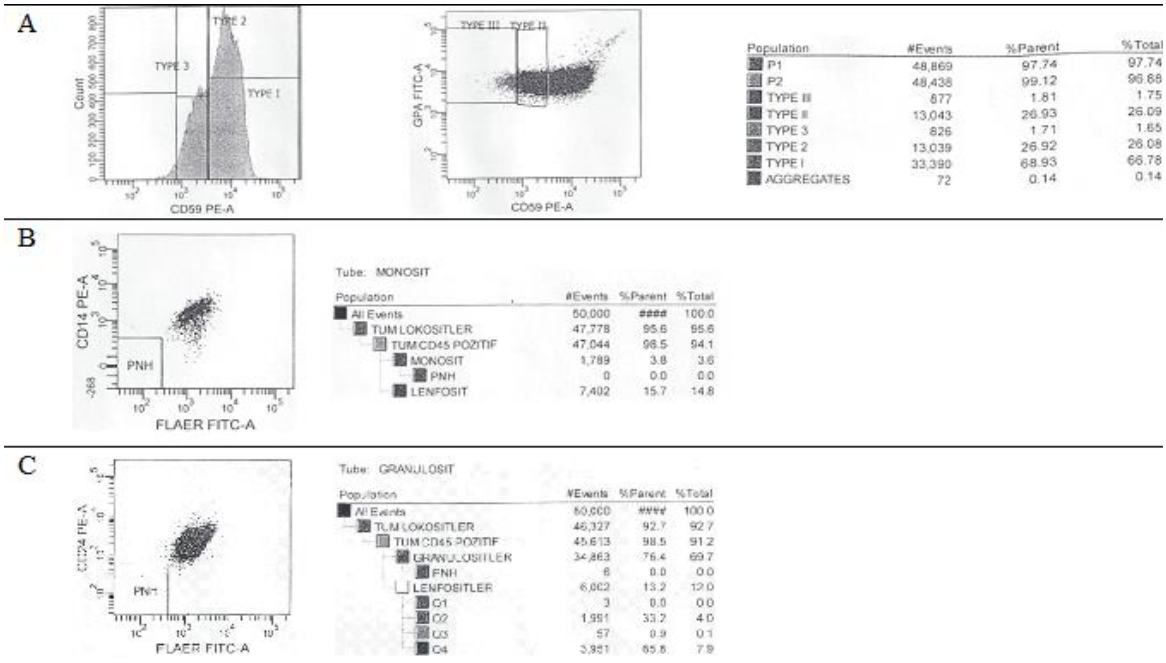

Figure 3. FLAER erythrocyte (A), monocyte (B) and granulocyte (C) results of the second patient (female) with PNH clone.

Anemia and thrombocytopenia were evident in the complete blood count (CBC) of the first patient with PNH, a male patient, while the CBC of the second female patient had only mild anemia and thrombocytosis (Table 5).

Table 4. Clone levels in erythrocytes of patients with positive PNH clone

PNH clone	First patient	Second patient
Type II	% 30,33	% 26,08
Type III	% 0,1	% 1,75
Total	% 30,61	% 28,8

Table 5. Complete blood count and some biochemical values of patients with PNH.

CBC and Biochemistry Values	1th Patient	2nd Patient
White blood cell (WBC) ($x10^3$/uL)	6,3	21,4
Hemoglobin (HGB) (g/dL)	8,97	11,3
Hematocrit (HCT) (%)	26,1	34,6
Thrombocyte (PLT) ($x10^3$/uL)	57,9	709
Creatinine (mg/dL)	0,78	0,67
Total Bilirubin (mg/dL)	1,8	0,2
Direct Bilirubin (mg/dL)	1,2	0,1
Lactate dehydrogenase (LDH) (U/L)	267	394
Uric acid (mg/dL)	3,7	5,8
C-reactive protein (CRP)	7,96	6,99

DISCUSSION

PNH clone can be seen with many hematological clonal diseases. In studies, the association of bone marrow, which is one of the organs of the hematopoietic system, and disease groups arising from it, and PNH or PNH-like disorder took place. On the other hand, there are a few studies coexistence of PNH and lymphoma, a disease of the lymphatic system, which is another organ of the hematopoietic system.

Unlike leukemic transformation in patients with PNH, PNH-like deficiencies of CD55 and CD59 have been reported in acute leukemias (7,8). Although rare, PNH-like cell defects have been detected in chronic myeloproliferative diseases, chronic myeloid leukemia (CML) and Philadelphia chromosome negative chronic myeloproliferative diseases (9–11).

Detection of PNH clones in myelodysplastic syndrome is better known and is more common than other hematological diseases (12–14). However, myelodysplastic findings in the bone marrow can also be observed in PNH patients. Therefore, the relationship between both diseases is mixed and controversial (14). The presence of PNH together with lymphoproliferative diseases is an extremely rare condition. There are case reports or presentations in which a few cases are collected in the literature (15–17). In different lymphoproliferative disease types, different rates of PNH clones can be detected in untreated patients, as well as in patients who have received some special treatments such as anti-CD52 antibody (CAMPATH-1H) (18,19). Fukuda et al. showed complete loss of CD55 (type III clone) in two of 10 patients with non-Hodgkin lymphoma, but not in any of the 6 patients with chronic lymphocytic leukemia (CLL) (20). Seya et al. reported that CD55 loss may occur in NHL patients rather than other hematological malignancies (21).

In the largest systematic study available in the literature, investigating the PNH clone in 195 patients with lymphoproliferative disease, most of whom had CLL, the double negative rate of CD55 and CD59 in erythrocytes was found to be 9.2%. Isolated CD55 and CD59 negativity rates were found to be 8.7% and 0.9%, respectively. CD59 expression appears to be

better preserved in these patients. Researchers stated that none of these patients had signs of hemolysis (13). The reason for the absence of hemolysis, unlike that seen in classical PNH, can be explained by the decreased expression of GPI-anchor proteins in a small population of red blood cells, which is not sufficient for hemolysis. It has also been suggested that CD55 deficiency alone is not sufficient for hemolysis (22).

Similarly, there were no signs of hemolysis in patients with positive PNH clones in our study. In the first patient (KD), whose PNH clone was detected by evaluating CD59 expression in erythrocytes, partial loss of CD59 (type II clone) was detected at a rate of 30.33%. A severe loss of CD59 (type III clone) was detected at a rate of 0.1%. In the second patient (DS), the type II clone rate was 27% and the type III clone rate was 1.8%. CD55 level was not evaluated in our study.

We found PNH-like disorder in 4% of all lymphoma patients. This is slightly lower than that found in previous studies of lymphoproliferative diseases (13,20).

The fact that only CD59 was investigated in our cases and the CD55 level was not measured suggests that some cases that may indicate low CD55 may have been overlooked.

Again, in the study of Meletis et al., CD55 and CD59 deficiency was observed at a higher rate in low-grade B-cell NHLs than in other NHL types (13). In our study, lymphomas of both patients were low grade but advanced.

In this prospective study, we used a relatively new flow-cytometric method, FLAER, to detect the PNH clone. In previous similar studies, CD55 and CD59 expression levels were used by conventional flow-cytometry, and Ham and acid sucrose lysis tests were used in previous studies and case reports.

Consistent with most case reports and studies in the literature, PNH clone was not detected in neutrophils and monocytes. The PNH-like disorder in our study concerned only erythrocytes.

PNH clone was detected in lymphocytes in two separate studies; GPI deficiency was detected in T cells in CLL patients who were administered anti-CD52 antibody (CAMPATH-1H). This abnormality is explained as anti-CD52 antibody binding to CD52, a GPI-dependent protein, may lead these cells to apoptosis, causing T lymphocytes with low GPI levels to gain clonal advantage and increase them. (18,19). Indeed, it has been shown that CD55 and CD59 expression are decreased in B and T lymphocytes after administration of CAMPATH-1H in in-vitro cultures (23).

Interestingly, PNH or PNH-like erythrocytes with CD55 and CD59 deficiency are more commonly detected in patients with CLL and low-grade NHL. In one study, the rate of erythrocytes with decreased CD55 and CD59 expression was found to be less than 10% in different lymphoproliferative disease groups. In PNH disease, the decrease in the expression of these proteins is usually greater. Therefore, it is understood that the PNH clone, which can be detected rarely in hematological diseases, does not indicate a true PNH disease. We can say that this is a PNH-like side finding that is not reflected in the clinic or a laboratory finding that may accompany it. The absence of clinical findings of PNH in patients with PNH clones in the study by Meletis et al. supports this thesis. (13). In the same study, CD55 and CD59

deficiency were also found in erythrocytes in patients with nodular sclerosing subtype in classical Hodgkin lymphoma.

Other hypotheses have also been proposed to explain the presence of the PNH phenotype in lymphoproliferative diseases and other clonal diseases. Somatic mutations developing in stem cells in lymphoproliferative diseases may also cause other somatic mutations. It is thought that the PNH clone is usually found in such low amounts that it cannot be detected in normal individuals. During the course of the lymphoproliferative disease, the PNH clone can reach a detectable level, perhaps by gaining a survival advantage through an immune mechanism.

In a study by Fukuda et al., CD55 expression level was found to be low in only 2 NHL patients out of 38 people with most lymphoproliferative diseases, including 6 patients with chronic myeloid leukemia. In the related study, the presence of CD55 expression was examined in mononuclear cells instead of erythrocytes. For this reason, it has been explained by researchers that there may be loss of CD55 in lymphoma cells (20). This finding is not consistent with the two cases in our study in which CD59 deficiency was detected only in erythrocytes. As reported in a case report, when unexpected cytopenia, thrombosis or hemolysis develops in a patient with lymphoma, it should be kept in mind that PNH disease or a PNH-like disorder may coexist. (16).

The disappearance of the PNH-like clone in erythrocytes after chemotherapy in one of the two cases in our study is also interesting in that it shows that this disorder occurs in association with lymphoma. A similar finding was not mentioned in other studies and case reports.

It is important to differentiate PNH disease from the PNH-like disorder found in other clonal diseases. Hemolysis did not occur in the increase of PNH clones in PNH-like disorder or with another hematological disease, as observed in other studies and the cases in our study. This can be interpreted as the absence of classical PNH findings, since the PNH clone is found at a very low level in these diseases.

The fact that the methods used in the studies and case reports are different, and the lack of studies with FLAER makes it difficult to compare our results with others. Further and standardized studies with the help of flow-cytometry and molecular techniques are necessary to elucidate the relationship between hematological malignancies and PNH and to develop new treatment methods.

CONCLUSION

PNH is a disease that characterized by episodes of hemolysis, thrombosis, and cytopenias associated with bone marrow failure.

In our study, we detected positive PNH clone in two (4%) of 50 patients. According to the literature, the presence of PNH clones in patients with lymphoma in our study is less frequent. No signs of hemolysis were observed in patients with positive PNH clones.

Although PNH or PNH-like disorder is not common in patients with lymphoma, it is a pathology that should be considered. It should be known that it can be seen without hemolysis and may accompany hematopoietic diseases. It should also be kept in mind that the PNH clone may appear later and may disappear spontaneously or after treatments (such as chemotherapy).

Performing PNH clone presence and frequency studies with a new technique, FLAER, and in larger patient groups will provide more accurate results and will allow better elucidation of the molecular and clinical association of lymphoma and PNH.

Ethics Committee Approval: Ethics committee approval was received for this study from Kocaeli University Clinical Research Ethics Committee. (Date: 03.18.2014; Decision no: 6/2)

Peer-review: Externally peer-reviewed.

Author Contributions: Concept: A H Design: AH, M A; Data Collection and Processing: M O, Analysis or Interpretatio, Writing: A T V. M O Critical review: A H

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The Change in Acute Ischemic Stroke Numbers in the Emergency Service During Early Phase of COVID -19 Pandemic

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Abstract

Objective: Although the actual relationship between COVID -19 and the incidence of stroke has not yet been clearly defined, various potential mechanisms such as hypercoagulation or viral infecton burden have been reported as risk factors that can increase the risk of stroke. However, various anecdotal reports have emphasized the falling rate of new ischemic stroke diagnoses during period of COVID-19. This study was conducted to estimate the change in the number of new stroke diagnoses and evaluate the approximate causes of such situations during the early period of the COVID-19 outbreak.

Methods: In this retrospective observational descriptive study, the patients were divided into two groups as January-February 2020 (Pre-COVID−19) and March-April 2020 (COVID-19 Period), based on when the first COVID-19 case was reported in Turkey in March 2020. Patients who were admitted to the emergency department (ED) between 01 January 2019 and 30 April 2019 and diagnosed with ischemic cerebrovascular disease were included as the control group to estimate the number of cases predicted for 2020. The data of the groups were retrospectively analyzed in terms of the number of stroke admissions and demographic features.

Results: Among the 274 patients diagnosed with acute ischemic stroke during the 4-month study period, 112 (40.9%) were detected during the COVID-19 period. Considering the linear relationship between the number of patients diagnosed with ischemic stroke in January-February 2019 and March-April 2019 in the control group of the study, this number was expected to be 163 in March-April 2020, since the number of patients with ischemic stroke diagnosed in January-February 2020 was 162. While it was determined that a 25.35% decrease had occurred in January-February 2020 compared to the January-February 2019, it was determined that a 48.9% decrease had occurred in March-April 2020 compared to the same period of the previous year.

Conclusion: This study showed that the number of patients admitted to the hospital with a diagnosis of ischemic stroke in the March-April 2020 decreased statistically significantly compared to the pre-pandemic period of the same year.

Key words: Coronavirus, COVID-19, epidemiology, incidence, ischemic stroke

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INTRODUCTION

Coronavirus 2019 (COVID-19), which causes severe respiratory diseases such as pneumonia and lung failure, was first reported in Wuhan, China in December 2019 (1). On January 7, 2020, the causative agent was identified as a new coronavirus (2019-nCoV) that had not been detected in humans before. A few months after the first report, SARS-CoV-2, which was aptly named due to its similarity to SARS-CoV spread worldwide, reached an epidemic level and was declared as a global health emergency by the World Health Organization (WHO) (2). Clinically, COVID-19 often causes respiratory problems. However, cases involving different systems such as cardiovascular, gastrointestinal, and nervous systems and the skin, have also been reported (3-7).

A stroke is a sudden focal neurological deficit that develops due to impaired blood flow in the corresponding region of the brain (8). Strokes are divided into two groups as hemorrhagic and ischemic, with most of them being ischemic. In an epidemiological study, various risk factors of stroke including diet, obesity, alcohol use, hypercoagulability, infection burden, hormone replacement therapy, physical inactivity, were determined as modifiable risks that depend on lifestyle and environmental factors. On the other hand, age, gender, race and family history of stroke were determined as unmodifiable risk factors (9). Although the true relationship between COVID-19 and the incidence of stroke has not yet been clearly defined, various potential mechanisms such as hypercoagulability (increase in D-dimer level), viral infection load, direct viral infection of the central nervous system or increased cytokine storm have been reported as risk factors that can increase the risk of stroke (6,10). On the other hand, some studies have emphasized that if modifiable risk factors are controlled, the incidence of stroke will decrease (11-14). Various authors have published the clear message that emerged from the results of the WHO survey regarding the decrease in the number of acute stroke admissions in many countries, including Chile, Colombia, Iran, Greece, England, Belgium and Italy (15). This was shared by global news portals and on scientific blogs (16). Despite previous epidemiological studies reporting that the COVID-19 infection itself is a risk factor for stroke, some anecdotal records and survey results determined a dramatic decrease in the incidence of ischemic stroke during the pandemic.

The aim of this study was to determine whether the incidence of ischemic stroke decreased during the COVID-19 pandemic.

METHODS

Study Design and Settings

Giresun University Training and Research Hospital is the only tertiary care hospital in the province where all acute ischemic stroke cases are diagnosed and treated. The hospital has maintained the hallmark of being the epicenter of diagnosis and treatment regarding acute stroke patients during the pandemic process.

During the study period, only COVID-19 patients did not apply to the hospital where the study was conducted. Non-COVID patients also applied to the hospital. This study was planned retrospectively and approved by the local institutional ethical board (Date: 18.02.2021 / Decision number: 13).

Data Collection

In this retrospective descriptive study, patients who visited the emergency department (ED) of Giresun University Training and Research Hospital between 01 January 2020 and 30 April 2020 and were diagnosed with ischemic stroke by brain diffusion MRI were included. The patients were divided into two groups as January-February 2020 (Pre-COVID−19) and March-April 2020 (COVID-19 Period), based on when the first COVID-19 case was reported in Turkey in March 2020. In order to predict the number of cases predicted for March-April 2020, patients who were admitted to the ED between 01 January 2019 and 30 April 2019 and diagnosed with ischemic cerebrovascular disease were included as the control group. Considering the relationship between the number of patients diagnosed with ischemic stroke in January-February 2019 and March-April 2019 in the control group of the study, the number of expected ischemic stroke cases in March-April 2020 may be estimated according to a change in the number of patients with ischemic stroke diagnosed in January-February 2020. Those under the age of 18, patients who had ischemic cerebrovascular disease while they were hospitalized in any clinical service, cases of ischemic stroke during an outpatient clinic admission, and cases of non-vascular diffusion restriction such as mass were excluded from the study. The demographic characteristics and brain diffusion MRI findings of the patients with ischemic cerebrovascular disease were recorded.

Statistical analysis

The statistical analysis was done using IBM SPSS V23. The Kolmogorov-Smirnov (K-S) test was used to determine whether the quantitative data showed a normal distribution. Mann-Whitney U test was used to compare the two groups in cases where the data did not show normal distribution. The qualitative data were compared using the Pearson Chi-Square test. Descriptive statistics were presented as median (minimum - maximum) and n (%). The statistical significance value was set at $p < 0.05$.

RESULTS

Among the 274 patients diagnosed with acute ischemic stroke in 2020, 112 (40.9%) were detected during the COVID-19 period. When compared to the control group, the number of patients diagnosed with acute ischemic stroke in March-April 2020 was expected to be 163. However, in the COVID −19 period only 112 patients were diagnosed. As a result, it was observed that there were fewer patients in the time interval corresponding to the COVID pandemic in 2020 compared to the same period of the previous year ($p<0.05$) (Table 1). In addition, the accumulated incidence of patients diagnosed with acute ischemic stroke between January and April 2020 decreased compared to the same periods of the previous year (Figure-1).

Table 1. Comparison of acute ischemic stroke numbers

	2019	2020	p
Jan-Feb*	217 (49.8)	162 (59.1)	**0.015**
Mar-Apr*	219 (50.2)	112 (40.9)	

* n (%)

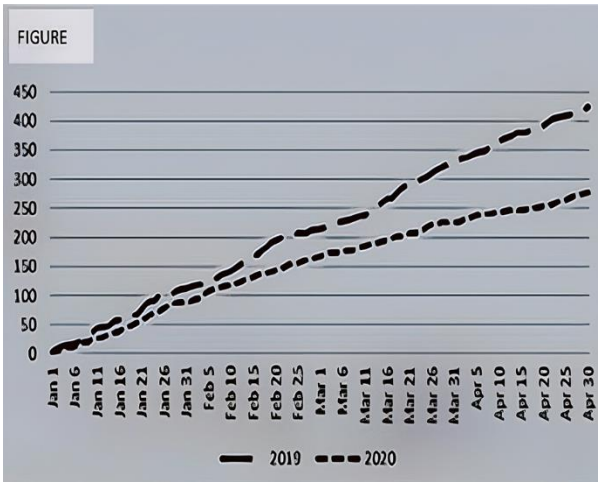

Figure-1. Accumulated incidence of acute ischemic stroke cases in January- April of 2019 and 2020

There was no significant difference in the age and gender distribution of patients diagnosed with ischemic stroke in 2019 or 2020 (p> 0.05) (Table 2). In addition to the main result of the study, there was no significant difference in brain diffusion MRI findings before and after the COVID pandemic, compared to March and April 2019. However, right hemisphere involvement and bilateral involvement decreased significantly in the COVID-19 period (p < 0.05).

Table 2. Basic characteristics of the patients and the main features of ischemia detected on brain MRI

	Jan-Feb 2019	Mar-Apr 2019	Jan-Feb 2020	Mar-Apr 2020	p***
Age*	80 (23-97)	76 (23-99)	80 (40-98)	78 (35-98)	0.125
Female**	111 (51.2)	109 (49.8)	78 (48.1)	61 (54.5)	0.419
Right Hemisphere**	115 (53)	151 (68.9)	93 (57.4)	63 (56.3)	0.022
Left Hemisphere**	149 (68.7)	126 (57.5)	91 (56.2)	61 (54.5)	0.594
Unilateral**	170 (78.3)	161 (73.5)	140 (86.4)	100 (89.3)	0.001
Bilateral**	47 (21.7)	58 (26.5)	22 (13.6)	12 (10.7)	

* median (min – max), ** n (%), ***comparison between Mar-Apr 2019 and Mar-Apr 2020

DISCUSSION

According to a report published by WHO (17), as of January 5, 2022, there have been over 293 million cases and approximately 5.5 million deaths since the start of the pandemic. Due to the rapid spreading of the pandemic, health systems have been significantly affected. Protective measures have been taken in many countries around the world, including Turkey, to prevent the spread of COVID-19, which has a high human-to-human contagion and infection rate. For example, in Turkey, full-fledged hospitals in provinces around the country have been determined as pandemic hospitals and patients suspected of having COVID-19 have been admitted to such hospitals. The rate of COVID-19 infections in the community has been tried to be controlled by imposing curfews, practicing social distancing, using of masks and implementing strict hygiene rules. In addition, the green zone admission in emergency services has been terminated, flexible working hours have been implemented and the number of polyclinics has been reduced. Elective surgeries have been delayed, and endovascular treatments have been cut down or stopped in many units.

According to a study in the literature, COVID-19 was reported to be an independent risk factor for ischemic stroke (18). In this regard, ischemic stroke rates that develop secondary to COVID-19 and other infections may have decreased due to controlling the infectiousness during the pandemic period. Some

studies have reported that mild symptoms due to small vessel occlusions cannot be noticed by patients or their relatives during COVID pandemic (19,20). In addition, it is thought that patient admissions to emergency services regarding mild complaints have decreased due to the fear of getting the coronavirus infection and therefore, ischemic stroke diagnoses are made late. In the present study we believe the fact that patients who have had a stroke may be hesitant to call 112 (emergency service call number in Turkey) or go to the hospital for fear of getting COVID-19 infection. So, we also believe that the patients without severe cortical findings (severe aphasia, vision loss, motor loss, etc.) have referred to ED less frequently. However, in a study conducted by Siegler et al., it was reported that the number of patients with large vessel occlusion (LVO) did not significantly change during the COVID-19 period compared to the pre-COVID-19 period. The authors determined a significant increase in the rates of ischemic strokes with large vessel occlusion during the pandemic period (21). In this respect, considering the severity of the disease and cortical findings, it is thought that such a generalization is invalid for ischemic strokes regarding large vessel involvement. Another factor that may contribute to lower stroke rates is the reduction in the use of MRI. However, due to the easy access to MRI within our hospital and the lesser use of it, at least for clinically significant infarctions, we do not believe this. Various studies have reported that the left hemisphere ischemic stroke is more common and often has worse outcomes than the right side (22,23). In our study, it was also determined that the rates of right-sided ischemic stroke detected during the COVID period decreased significantly. This can be explained by the decrease in the number of admissions regarding ischemic stroke, which causes less explicit symptoms on the right side, especially due to the fear of getting coronavirus infection from hospitals. Additional factors may be contributing for declining in the number of ischemic strokes rate during early phase of the pandemic. Restriction of patient admissions in neurology outpatient clinics may cause insufficient recognition of stroke in the community. Thus, the number of patients with acute ischemic stroke who were referred to the emergency department after being recognized in outpatient clinics may have decreased.

Limitations

This study has some potential limitations that can be a reference for future studies. The study was designed as a single-center retrospective study and included a short period. Prospective, comprehensive, and long-term clinical studies can show the relationship between the COVID- 19 pandemic and the incidence of ischemic stroke more clearly. In this respect, the result of the present study has a local effect and could not be generalized. In addition, the study could not show the direct effect of ischemic stroke risk factors during the COVID -19 pandemic periods.

CONCLUSIONS

This study focused on the number of ischemic strokes in the pandemic period. In conclusion in this study, a significant decrease of acute ischemic stroke rates was determined in the first two months of the COVID-19 pandemic compared to the pre-pandemic period of same year. Theoretically, the reduced incidence of stroke suggests that the modifiable risk factors for stroke were under control. However,

comprehensive, and long-term controlled clinical studies are required to prove this relationship. On the other hand, in the present study we believe the fact that patients without severe cortical findings (severe aphasia, vision loss, motor loss, etc.) refer to ED less frequently due to the worry of getting an infection.

Ethics Committee Approval: This study was approved by the Ethical Committee of Giresun University, Giresun Province, Turkey. (Date: 18.02.2021 / Decision number: 13)

Peer-review: Externally peer-reviewed.

Author Contributions: Concept- A.V, I.A, M.E, Design- A.V, I.A, M.E, Materials- A.V, I.A, M.E, Data Collection and/or Processing- A.V, I.A, M.E, Literature Review- A.V, I.A, M.E.

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One Year Analysis of Hematological and Inflammatory Parameters to Predict the Severity of COVID-19 Infection in Pregnant Women

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Abstract

Objective: The study aims to demonstrate the usability of admission hematological parameters in the prognosis of COVID-19 infection in pregnant population and to introduce the cut-offs values of these parameters for pregnant women.

Methods: The cohort of this retrospective study consisted of 71 COVID-19 PCR positive pregnant women who were hospitalized in Ordu University Medical Faculty Training and Research Hospital between 1 May 2020 and 1 May 2021. The pregnant women were divided into two groups based on the severity of the disease.

Results: White blood cell count, neutrophil count and C-reactive protein (CRP) levels was significantly higher (p=0.000, p=0.000), whereas red blood cell count and lymphocyte count were significantly lower (p=0.002, p=0.002) in severe group. High NLR (neutrophil-to-lymphocyte ratio) (p=0.000), dNLR (derived neutrophil-to-lymphocyte ratio) (p=0.000), MLR (monocyte-to-lymphocyte ratio) (p=0.004), PLR (platelet-to-lymphocyte ratio) (p=0.008), NPR (neutrophil-to-platelet ratio) (p=0.005), NLRNPR (neutrophil-to-lymphocyte ratio/neutrophil-to-platelet ratio) (p=0.008) and SII (Systemic immune inflammation index) (p=0.000) were found in severe group.

Conclusion: This paper revealed that severe COVID-19 disease in pregnant women is mainly associated with hematological parameters. Among these parameters NLR, dNLR and SII have largest AUC in ROC, with cutoff values 5.3, 3.52 and 994.8 respectively. Further investigations regarding the use of hematologic tests as prognostic factor of COVID-19 disease severity in pregnant women are needed to assess the risk of serious disease, to predict the prognosis of COVID-19 and to reduce perinatal and maternal morbidity/mortality.

Key words: COVID-19, complete blood count, c-reactive protein, hematological parameters, pregnancy.

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INTRODUCTION

At the end of 2019, a novel corona virus named COVID-19 was identified in Wuhan city in Mainland China, which caused severe viral pneumonia and spread rapidly. Within three months, the disease was detected in more than 200 countries around the World and COVID-19 was therefore declared as a global pandemic by the World Health Organization (WHO) on the 11th of March 2020 (1). In Turkey, the first polymerase chain reaction (PCR) test positive COVID-19 case was reported on the same date as the declaration, and positive cases started increasing since March 2020. As of May 1, 2021, the total number of cases reached almost 5 million in Turkey (2).

The nucleic acid amplification tests that also known as PCR tests are commonly used to detect COVID-19 in nasopharyngeal and oropharyngeal secretions. Although these tests have high specificity, false negativity rates can increase up to 40% (3). In addition to PCR, CT and X-ray applications are recommended by official guidelines, many studies have revealed alterations in laboratory findings in COVID-19 patients. More than 30 parameters were studied during the pandemic process and various parameters were found to be associated with COVID-19 prognosis, severity, mortality and response to treatments in non-pregnant adult population. Hematological effects including neutrophilia, lymphopenia and thrombocytopenia; immunological effects and also inflammatory indicators including high CRP levels were examined in general population with COVID-19 (4). However, pregnancy have alterations in cell mediated immunity and cardiopulmonary adaptations; and this condition makes the pregnant vulnerable to infectious diseases (5). Also, lung infection with any infectious pathogens in pregnancy is an important mortality and morbidity factor for pregnant population (6).

Hitherto, most studies have described clinical characteristics of pregnant with COVID-19 infection including symptomatology, pregnancy outcomes, lung CT (computed tomography) findings, mother-infant transmissions, routine laboratory scans (7,8). In a large multinational cohort study, it is shown that pregnant women is related with low rate mortality but 11,1% rate of admission to intensive care unit which may increase diverse maternal and perinatal conditions (9). Therefore, blood count parameters and hematological derived inflammatory markers are feasible, accurate and applicable in all health institutions, to discriminate severe cases which would need further care. The hyper inflammation and endothelial damage appear to be the main pathologic mechanism underlying the worsening conditions with COVID-19 infection. Thereof, investigations were concentrated on infectious and inflammatory blood parameters which could predict the prognosis of the patients. Especially, NLR has been used to predict severity of oncological diseases, cardiovascular mortality and also as a prognostic marker in patients with the acute respiratory syndrome (10,11). Besides NLR, importance of PLR which is accepted as a marker of acute inflammation and tendency to thrombosis, has been described to predict the clinical deterioration of the COVID-19 patients (12). SII is also a ratio studied as a prognostic indicator in the sepsis and in the cancer patients and also the COVID-19 infection (13,14).

In our study, we aimed to demonstrate the usability of admission hematological parameters in the prognosis of COVID-19 infection in pregnant population and to introduce the cut-offs values of these parameters for pregnant women. The blood count is an inexpensive, fast, side-effect-free laboratory test that can be applied in any hospital and there is scarce of investigation related with these blood parameters and the indicators derived from peripheral blood parameters, in pregnant population.

METHODS

This single-center, retrospective, cohort study was conducted between May 1th, 2020, and May 1th, 2021, in Ordu University Training and Research Hospital which is a tertiary hospital in the Middle Black Sea Region of Turkey. The hospital has been designated as a corona virus pandemic hospital by the Ministry of Health, and the only hospital in Ordu Province which accepts pregnant women with COVID-19 infection. The present study protocol was approved by the ethics committee of the Ministry of Health Republic of Turkey with issue number 2020-05-11T19_06_54. The study was conducted in accordance with the principles outlined in the Declaration of Helsinki.

The study group consisted of 71 COVID-19 PCR test positive pregnant women that were hospitalized. The inclusion criteria in our study were COVID-19 pregnant women who were hospitalized in our hospital. Real-time reverse transcriptase polymerase chain reaction (RRT_PCR) tests were performed with Bio Speedy SARS CoV-2 detection kit (Bioeksen R&D Technologies, Istanbul, Turkey) that provided by the Ministry of Health of Turkey. Non-confirmed PCR negative cases, even if they were symptomatic or with a history of contact, were excluded from the study. Exclusion criteria in our study were pregnant women with comorbidities such as hypertension, diabetes, asthma, and morbid obesity. Medical records of pregnant women who were hospitalized during the study period were analyzed retrospectively. Clinical symptoms and other features (age, gestational week, length of hospital stay) were recorded.

The pregnant women were divided into two groups based on the severity of the disease. Thence, there was a non-severe group (consisting of 49 patients) and a severe group (consisting of 22 patients). Severe disease group which requiring oxygen therapy was characterized by dyspnea, shortness of breath, high respiratory rate (>30 breaths per minute), low oxygen saturation (<93% on room air and rest). The other pregnant women, who have been hospitalized and never required oxygen therapy or showed aforementioned symptoms, were described as non-severe group.

The initial triage protocol of inpatient COVID-19 patients includes blood sampling. A blood sample for complete blood count (CBC) was taken from all patients upon admission before any treatment began. CBCs were analyzed within 30 minutes by an automatic blood count device (Sysmex Corporation, ZN 1000i, Kobe, Japan). Simultaneously with CBC other blood sample was taken for measurement of C-reactive protein (CRP) levels by using a spectrophotometric chemical analysis device (Roche Diagnostics, Cobas E 501, California, USA). Demographic characteristics and clinical features of patients are represented in Table 1. Hematologic indices, hematologic ratios and CRP levels was

presented in Table 2. These hematological indices were calculated as NLR, which is the ratio between the count of neutrophils (×109cells/L) and the count of lymphocytes (×109 cells/L), dNLR is the ratio of neutrophils/(white blood cells- neutrophils), PLR is the ratio between the count of platelets (×1011 cells/L) and the count of lymphocytes (×109 cells/L) and the SII is defined as the counts of neutrophils (×109 cells/L) multiplied by the counts of platelets (×1011 cells/L) and divided by the count of lymphocytes (×109 cells/L), NPR is the ratio between the count of neutrophils (×109 cells/L) and the count of platelets (×1011 cells/L).

Statistical analysis

The study aims to demonstrate the usability of admission hematological parameters in the prognosis of COVID-19 infection in pregnant population and to introduce the cut-offs values of these parameters for pregnant women.

For analyzing the results of the study, IBM SPSS Statistics Package (Version 20 Armonk, NY: IBM Corp.) was used. Analyzes were carried out in a 95% (p=0.05) confidence interval. Descriptive statistical methods and correlation analyzes had been used in the study. Descriptive data derived from the study was presented as mean ± standard deviation or median. The normal distribution of numerical variables was studied with the Kolmogorov-Smirnov and the Shapiro-Wilks tests. The independent samples t-test was used when the numerical variables had a normal distribution, or the Mann-Whitney U test was used when the numerical variables did not have normal distribution.

The analysis of the receiver operating characteristic (ROC) curve was used to discover the optimal cut-off values of the levels of the peripheral blood parameters to predict the severity of patients in the study group. AUC was interpreted as excellent if 0.9-AUC-1, good if 0.8-AUC-0.9, moderate if 0.7-AUC-0.8, poor if 0.6-AUC-0.7, and failed if 0.5-AUC-0.6. Multivariate Cox regression analyses were used to evaluate the independent predictors of severity progression of disease.

RESULTS

Totally, 71 COVID-19 PCR test positive pregnant women in Ordu city were enrolled in this retrospective, cohort research. All of the patients included in the study were followed up and treated by hospitalization. Twenty-two of the patients (31%) were in the severe group that requiring oxygen therapy. Dyspnea, high respiratory rate (>30 breaths per minute) and low oxygen saturation (<93% on room air and rest) was observed in this group of patients. There were no fetal or maternal demise along the study period.

The mean age of the entire study cohort was 31.68+6.26 (19-48). And the mean gestational age of pregnant women was 27.72+9.33 weeks. In addition, the majority of patients were in the third trimester with the ratio of 62%, while the rate of first and second trimester pregnancies was 8.4% and 29.6%, respectively. There was no statistically significant difference between the groups in terms of neither age nor gestational week (p=0.193 and p=0.116). However, a significant difference was observed between the groups in terms of length of hospital stay (p=0.000). The hospitalization period of the patients in the severe group that required oxygen therapy was two times longer than the other group (9.45+2.4 vs. 4.9+2.1).

Thirty (42.25%) patients were asymptomatic. In symptomatic patients, headache (70.7%) was the most common symptom followed by fatigue (63.4%) and fever (56%). Dyspnea and shortness of breath was detected in 22 (53.6%) patients and these patients were in the severe group. Cough (48.7%) and diarrhea (31.7%) were the other symptoms. The demographic characteristics and clinical symptoms of patients were recorded and demonstrated in Table 1.

The data as the percentages above the normal reference range for the entire group was also examined. High CRP, lymphopenia, anemia, neutrophilia was found in 83%, 54.9%, 47.8% and 28.1% of patients, respectively. White blood cell count and neutrophil count was significantly higher, whereas red blood cell count and lymphocyte count were significantly lower in severe group. Besides, C-reactive protein was significantly higher in severe group that required oxygen therapy.

COVID-19 PCR positive pregnant women who required oxygen therapy presented significantly higher baseline values of NLR (neutrophil-to-lymphocyte ratio) (9.38 vs. 4.15, p=0.000), dNLR (derived neutrophil-to-lymphocyte ratio) (5.52 vs. 2.68, p=0.000), MLR (monocyte-to-lymphocyte ratio) (0.664 vs. 0.419, p=0.004), PLR (platelet-to-lymphocyte ratio) (208.9 vs. 153.1, p=0.008), NPR (neutrophil-to-platelet ratio) (0.049 vs. 0.033, p=0.005), NLRNPR (neutrophil-to-lymphocyte ratio/neutrophil-to-platelet ratio) (208.9 vs. 153.2, p=0.008) and SII (Systemic immune inflammation index = neutrophils multiplied by platelets and divided by lymphocytes) (1753.7 vs. 833.2, p=0.000). Hematologic indices, hematologic ratios and CRP levels was presented in Table 2.

ROC analysis evaluating COVID-19 severity revealed that optimal cut-off values for most laboratory parameter and blood count derived ratios were statistically significant. The largest AUC for dNLR was 0.921 with the cut-off value of 3.52 (sensitivity 86% and specificity 83%). The second largest AUC of 0.905 was observed in NLR with a cut-off value of 5.3 (sensitivity 81.8% and specificity 81.6%). The excellent AUC which was determined as 0.9-AUC-1, have been observed in NLR and dNLR; good AUC (0.8-AUC-0.9) have been observed in SII; moderate (0.7-AUC-0.8) have been observed in CRP, WBC, RBC, Hb, Hct, Neu, Lym, MLR, PLR, NPR, NLNPR; and the other AUC for blood count parameters have been determined as poor or failed. The sensitivity and specificity values of all laboratory parameters under the optimal cut-off values that statically significant were presented in Table 3.

Potential risk factors, including CRP, WBC, RBC, Hb, Hct, Neu, Lym, NLR, dNLR, MLR, PLR, NPR, SII, NLNPR were investigated using binary logistic regression analysis. In Table 4. MLR (monocyte lymphocyte ratio) (p=0.008, OR=8.63, confidence interval=1.746-42.681), dNLR (p=0.000, OR=3.794, confidence interval=2.016-7.138), NPR (p=0.014, OR=2.749, confidence interval=506.8-1.491) were seen as with the best predictive values for pregnant who may have worse clinical course.

Table 1: Demographic characteristics and clinical features of patients

	Severe Group (n=22)		Non-severe Group (n=49)		P value
	Mean+SD	*Number (Ratio)*	*Mean+SD*	*Number (Ratio)*	
Demografik features					
Age	30.23+5.9		32.33+6.3		0.193
Gestational week	30.32+6.1		26.55+10.3		0.116
Length of hospital stay	9.45+2.4		4.90+2.1		0.000*
Clinical symptoms **					
Fever		14/22 (63.6%)		9/49 (18.3%)	0.000*
Fatigue		11/22 (50%)		15/49 (30.6%)	0.097
Cough		12/22 (54.5%)		8/49 (16.3%)	0.002*
Headache		14/22 (63.6%)		15/49 (28.5%)	0.348
Diarrhea		4/22 (18.1%)		9/49 (18.3%)	0.632

*Statically significant
** Since the grouping was made according to the dyspnea symptom, it is not included in the table

Table 2. Hematologic indices, hematologic ratios and CRP levels

	Overall	Severe Group	Non-severe Group	P value
C-reactive protein (CRP) (mg/L)	23.12+27.19	43.43+38.24	14.03+12.79	0.000*
- >5	59 (83%)	21 (95.4%)	38 (77.5%)	
White Blood Cell Count (WBC) (K/mL)	8.46+3.48	10.50+4.06	7.54+2.76	0.001*
- >1.2	9 (12.6%)	5 (22.7%)	4 (8.1%)	
Red Blood Cell Count (RBC) (K/mL)	3.96+0.49	3.69+0.41	4.07+0.48	0.002*
- <4	44 (61.9%)	18 (81.8%)	26 (53%)	
Hemoglobin (Hb) (g/dL)	11.10+1.36	10.52+1.13	11.3+1.38	0.015*
- <11	34 (47.8%)	14 (63.6%)	20 (40.8)	
Hematocrit (Hct) (g/dL)	33.78+3.58	31.92+2.61	34.60+3.67	0.003*
- <33	34 (47.8%)	16 (72.7%)	18 (36.7%)	
Platelet (Plt) (K/mL)	198+77	196+70	200+80	0.852
Mean Corpuscular Volume (MCV) (fL)	85.69+6.52	86.80+6.43	85.19+6.56	0.342
Mean corpuscular hemoglobin (MCH) (g/dL)	28.19+2.95	28.63+3.05	27.98+2.91	0.397
Mean corpuscular hemoglobin concantration (MCHC) (g/dL)	32.84+1.39	32.93+1.58	32.79+1.30	0.701
Red Cell Distribution Width (RDW)(%)	44.50+5.88	43.25+3.46	45.05+6.64	0.234
Platelet Distribution Width (PDW) (%)	11.48+2.26	11.29+1.85	11.56+2.42	0.634
Platecrit (PCT) (%)	0.200+0.670	0.199+0.069	0.200+0.065	0.958
Mean Platelet Volume (MPV) (fL)	10.06+1.62	10.18+0.76	10.00+1.88	0.665
Neutrophil (Neu) (K/mL)	6.58+2.98	8.76+3.55	5.59+2.07	0.000*
- >8	20 (28.1%)	15 (68.1%)	5 (10.2%)	
Lymphocyte (Lym) (K/mL)	1.37+0.62	1.03+0.45	1.52+0.62	0.002*
- <1.5	39 (54.9%)	18 (81.8%)	21 (42.8%)	
Monocyte (Mono) (K/mL)	0.57+0.30	0.65+0.41	0.53+0.23	0.109
Eosinophil (Eos) (K/mL)	0.045+0.064	0.039+0.057	0.047+0.066	0.622
Basophil (Baso) (K/mL)	0.016+0.016	0.020+0.025	0.013+0.008	0.139
NLR (neutrophil-to-lymphocyte ratio)	5.78+3.64	9.38+3.88	4.15+2.01	0.000*
dNLR (derived neutrophil-to-lymphocyte ratio)	3.57+2.05	5.52+2.34	2.68+1.09	0.000*
MLR (monocyte-to-lymphocyte ratio)	0.495+0.336	0.664+0.353	0.419+0.302	0.004*
PLR (platelet-to-lymphocyte ratio)	170.4+82	208.9+74	153.1+81	0.008*
NPR (neutrophil-to-platelet ratio)	0.038+0.023	0.049+0.026	0.033+0.020	0.005*
MPVPR (mean platelet volum-to-platelet ratio)	0.062+0.032	0.058+0.020	0.064+0.044	0.597
LYM*PLT (lymphocyteXplatelet)	286.0+203	221.1+177	315.1+209	0.072
RDWPR (red cell distribution width-to-platelet ratio)	0.270+0.142	0.000+0.00	0.102+0.30	0.124
NLRNPR (NLR/NPR)	170.4+82	208.9+74	153.2+81	0.008*
SII (systemic immune inflammation index)	1118.4+747	1753.7+782	833.2+528	0.000*

*Statically significant

Table 3. The sensitivity and specificity values of all laboratory parameters under the optimal cut-off values

	AUC	cutoff	*P*	Confidence interval	Sensitivity %	Specificity %
CRP	0.786	15.15	0.000	0.67-0.903	68	67
WBC	0.746	8.63	0.001	0.610-0.882	72.7	73.5
RBC	0.732	3.88	0.002	0.601-0.863	68.2	69.4
Hb	0.704	10.85	0.006	0.571-0.837	63.6	63.3
Hct	0.731	32.8	0.002	0.609-0.854	68	65
Neu	0.794	6.51	0.000	0.666-0.923	77	75
Lym	0.723	1.185	0.003	0.599-0.846	77	67
NLR	0.905	5.3	0.000	0.836-0.975	81.8	81.6
dNLR	0.921	3.52	0.000	0.856-0.987	86	83
MLR	0.743	0.415	0.001	0.622-0.864	77.3	73.5
PLR	0.734	170.7	0.002	0.611-0.856	77.3	71.4
NPR	0.748	0.0355	0.001	0.627-0.869	72.7	75.5
SII	0.857	994.821	0.000	0.766-0.948	86.4	75.5
NLNPR	0.733	172.5	0.002	0.611-0.856	72.7	71.4

Table 4. The Odds ratio and confidence intervals of all laboratory parameters

	P	OR (Odds ratio)	(CI) Confidence Interval
CRP	0.000	1.066	1.011-1.023
WBC	0.004	1.343	1.100-1.638
RBC	0.002	0.135	0.034-0.538
Hb	0.02	0.605	.396-.925
Hct	0.006	0.778	0.650-0.931
Neu	0.001	1.63	1.238-2.152
Lym	0.004	0.195	0.065-0.586
NLR	0.002	1.853	1.395-2.462
dNLR	0.000	3.794	2.016-7.138
MLR	0.008	8.63	1.746-42.681
PLR	0.01	1.009	1.002-1.015
NPR	0.014	2.749	506.8-1.491
SII	0.000	1.002	1.001-1.003
NLNPR	0.012	1.009	1.002-1.015

DISCUSSION

As the COVID-19 pandemic is gradually increasing, early classification of the pregnant patients at high risk of progression to a severe disease is important both to differentiate the clinically important group and also to consider an aggressive intervention and hospitalization. Considering the limited healthcare capacity, early prediction of COVID-19 disease severity should be considered as the main point in combating the pandemic. Only in this way, regardless of the development level of the countries, intensive care unit occupancy rates can be kept at a reasonable level by predicting serious patients in the early period.

In systematic reviews and meta-analysis, alterations in various laboratory parameters have been investigated and linked to COVID-19 severity. Among the other laboratory findings, the most striking test is undoubtedly the CBC. Because CBC is on the one hand a fairly inexpensive, routine and effective test, and on the other hand it is applicable even in peripheral hospitals. And most of studies have

reported that CBC test is valuable in predicting the prognosis of COVID-19, especially in countries with low socioeconomics with limited healthcare opportunities (15-17). Nevertheless, there is inadequate data about blood parameters of pregnant women having COVID-19 disease.

In meta-analysis, it was reported that, neutrophilia, lymphopenia and hence neutrophil lymphocyte ratio correlates with severe COVID-19 disease in adults (18-20). Also in a multi-center study, it is shown that lymphopenia; reduced lymphocyte to leukocyte ratio and increased neutrophil to lymphocyte ratio is indicating pregnant women with acute respiratory syndrome having COVID-19 disease (21). Lymphopenia is not just specific to COVID-19. It has also been seen in other viral causes of pneumonia, especially mostly investigated in influenza cases (22). In our study, in line with the literature, high neutrophil and low lymphocyte counts were found in severe group pregnant patients who needed oxygen therapy. Neutrophilia upon admission was related with 1.6 times risk of getting severe COVID-19 infection in pregnancy.

Beyond the proven knowledge related with neutrophilia and lymphopenia in COVID-19 patients both adults and pregnant ones in terms of disease severity, the ratios of hematological parameters such NLR, PLR, SII and NPR came into prominence to predict COVID-19 disease severity (21,23). NLR and PLR actually have been used to evaluate extension of inflammatory conditions. NLR, especially, is used to decide severity in oncological patients, as an indicator of endothelial dysfunction and an important indicator of cardiovascular and ARDS mortality. PLR have been used as an indicator in acute inflammation and prothrombotic states and as a reflector of cytokine release in COVID-19 infected patients; because platelets not only play a role in homeostasis, also they act in inflammation and host defense (24-29). Until to date, there is no consensus on optimal cut-off value for NLR nor PLR. Cutoff values of 3.3 to 5.9 have been used to predict severity with COVID-19 infection (30-32); while 7.9 to 11.8 cutoff values were used to predict mortality (33,34). This wide range of cutoff values shows us the variability of NLR according to race, gender and specific diseases and condition. So, it must be clearly stated in specific groups like pregnant women with COVID-19 infection.

In a study taking the value of NLR>5, having a NLR bigger than 5 is suggesting getting severe disease with COVID-19 infection (22). In another study, it is suggested that having NLR cutoff as 3.3 to show disease progression from mild to severe in adult group (25). In pregnant with COVID-19 infection, NLR is found to be significantly higher than normal pregnant population (35), also in a multi-center study comparing ARDS having COVID-19 pregnant ones with non-ARDS COVID-19 infection ones, significantly difference have been found when NLR>7.5 was studied as cut-off between two groups (21). Also, it is determined in our results that NLR with a cut-off value of 5.3 (sensitivity 81.8% and specificity 81.6%) was a valuable marker to predict severe course in pregnant patients. Also, PLR in our results were statistically significantly high in severe group (p=0.008); but its AUC was 0.734 and OR was 1.009. However, dNLR which is commonly used in cancer patients to predict mortality and chemotherapy response (36); also, is studied in critically ill COVID-

19 infected patients to predict mortality and severity (37). There are no optimal values or cutoffs for dNLR in pregnant women with COVID-19 infection. In our study, dNLR was found to be significantly high in severe group (p=0.000) and when looked for ROC curve, dNLR showed high AUC (0.921) with a cutoff value of 3.52; with sensitivity 86% and specificity 83% and OR was 3.7 for dNLR in pregnant women. When SII is investigated in our pregnant population, which is an index showing instable inflammatory response, SII was higher in severe group (p=0.000), and AUC in ROC was significantly high for defining cutoff value. There is no study revealing these all-inflammatory indices in pregnant population, but in studies in adult COVID-19 infection, SII is found to be significant (38).

Neutrophils, the main component of the WBC count, are responsible for the production of pro-inflammatory mediators. According to the current knowledge about inflammation, the overproduction of pro-inflammatory mediators that also named cytokine storm has been associated with critical illness. In addition, studies investigating the pathogenesis of COVID-19 revealed that neutrophils can cause organ damage secondary to direct infiltration or coagulopathy (19,23). In our study, it was noted that pregnant women with high WBC levels on admission had developed severe disease, while normal WBC level was found to be a protective factor.

In a study which is comparing the hematological parameters and perinatal outcomes in pregnant women with COVID-19 disease in terms of adverse perinatal outcomes, MLR was found as a supportive diagnostic marker (35). In our study, also, MLR (p=0.008, OR=8.63, confidence interval=1.746-42.681) is found to be a good predictor for severe course in pregnant COVID-19 infected patients when logistic regression was used.

Pregnant women with COVID-19 infection which were enrolled in this study were in first, second and third trimesters. Despite there was no statistical difference between severe and non-severe COVID-19 infected pregnant women, in terms of gestational week, it would be better to investigate trimester specific severity of the hematological parameters. Another limitation is the retrospective design and unfortunately small sample size.

The strength of our study is, to the best of our knowledge, this is the first study comparing large scale of hematological parameters and their derivations in pregnant population. Being a single center study and evaluation of the patients by the same team overall period are other advantages of the study.

CONCLUSIONS

There is scarce information related with pregnancy COVID-19 infection especially clinical course and hematological parameters, despite 16 months have passed with COVID-19 pandemics. The aim of this study was to investigate which hematological parameters are associated with severe COVID-19 disease in pregnant and openly reveal all inflammatory indices which can be easily obtained with a baseline blood count.

This paper revealed that severe COVID-19 disease in pregnant women is mainly associated with leukocytosis, neutrophilia and increased NLR, dNLR, MLR, PLR, NPR, SII and NLNPR. Among these parameters NLR, dNLR and SII have largest AUC in

ROC, with cutoff values 5.3, 3.52 and 994.8 respectively.

Although these markers have been investigated in general population, there is limited number of studies in the literature that conducted among pregnant population. Further investigations regarding the use of hematologic tests as prognostic factor of COVID-19 disease severity in pregnant women are needed to assess the risk of serious disease, to predict the prognosis of COVID-19 and to reduce perinatal and maternal morbidity / mortality.

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One Year Analysis of Hematological and Inflammatory Parameters to Predict the Severity of COVID-19 Infection in Pregnant Women

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Abstract

Objective: The study aims to demonstrate the usability of admission hematological parameters in the prognosis of COVID-19 infection in pregnant population and to introduce the cut-offs values of these parameters for pregnant women.

Methods: The cohort of this retrospective study consisted of 71 COVID-19 PCR positive pregnant women who were hospitalized in Ordu University Medical Faculty Training and Research Hospital between 1 May 2020 and 1 May 2021. The pregnant women were divided into two groups based on the severity of the disease.

Results: White blood cell count, neutrophil count and C-reactive protein (CRP) levels was significantly higher (p=0.000, p=0.000), whereas red blood cell count and lymphocyte count were significantly lower (p=0.002, p=0.002) in severe group. High NLR (neutrophil-to-lymphocyte ratio) (p=0.000), dNLR (derived neutrophil-to-lymphocyte ratio)(p=0.000), MLR (monocyte-to-lymphocyte ratio)(p=0.004), PLR (platelet-to-lymphocyte ratio)(p=0.008), NPR (neutrophil-to-platelet ratio)(p=0.005), NLRNPR (neutrophil-to-lymphocyte ratio/neutrophil-to-platelet ratio)(p=0.008) and SII (Systemic immune inflammation index)(p=0.000) were found in severe group.

Conclusion: This paper revealed that severe COVID-19 disease in pregnant women is mainly associated with hematological parameters. Among these parameters NLR, dNLR and SII have largest AUC in ROC, with cutoff values 5.3, 3.52 and 994.8 respectively. Further investigations regarding the use of hematologic tests as prognostic factor of COVID-19 disease severity in pregnant women are needed to assess the risk of serious disease, to predict the prognosis of COVID-19 and to reduce perinatal and maternal morbidity/mortality.

Key words: COVID-19, complete blood count, c-reactive protein, hematological parameters, pregnancy.

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INTRODUCTION

At the end of 2019, a novel corona virus named COVID-19 was identified in Wuhan city in Mainland China, which caused severe viral pneumonia and spread rapidly. Within three months, the disease was detected in more than 200 countries around the World and COVID-19 was therefore declared as a global pandemic by the World Health Organization (WHO) on the 11th of March 2020 (1). In Turkey, the first polymerase chain reaction (PCR) test positive COVID-19 case was reported on the same date as the declaration, and positive cases started increasing since March 2020. As of May 1, 2021, the total number of cases reached almost 5 million in Turkey (2).

The nucleic acid amplification tests that also known as PCR tests are commonly used to detect COVID-19 in nasopharyngeal and oropharyngeal secretions. Although these tests have high specificity, false negativity rates can increase up to 40% (3). In addition to PCR, CT and X-ray applications are recommended by official guidelines, many studies have revealed alterations in laboratory findings in COVID-19 patients. More than 30 parameters were studied during the pandemic process and various parameters were found to be associated with COVID-19 prognosis, severity, mortality and response to treatments in non-pregnant adult population. Hematological effects including neutrophilia, lymphopenia and thrombocytopenia; immunological effects and also inflammatory indicators including high CRP levels were examined in general population with COVID-19 (4). However, pregnancy have alterations in cell mediated immunity and cardiopulmonary adaptations; and this condition makes the pregnant vulnerable to infectious diseases (5). Also, lung infection with any infectious pathogens in pregnancy is an important mortality and morbidity factor for pregnant population (6).

Hitherto, most studies have described clinical characteristics of pregnant with COVID-19 infection including symptomatology, pregnancy outcomes, lung CT (computed tomography) findings, mother-infant transmissions, routine laboratory scans (7,8). In a large multinational cohort study, it is shown that pregnant women is related with low rate mortality but 11,1% rate of admission to intensive care unit which may increase diverse maternal and perinatal conditions (9). Therefore, blood count parameters and hematological derived inflammatory markers are feasible, accurate and applicable in all health institutions, to discriminate severe cases which would need further care. The hyper inflammation and endothelial damage appear to be the main pathologic mechanism underlying the worsening conditions with COVID-19 infection. Thereof, investigations were concentrated on infectious and inflammatory blood parameters which could predict the prognosis of the patients. Especially, NLR has been used to predict severity of oncological diseases, cardiovascular mortality and also as a prognostic marker in patients with the acute respiratory syndrome (10,11). Besides NLR, importance of PLR which is accepted as a marker of acute inflammation and tendency to thrombosis, has been described to predict the clinical deterioration of the COVID-19 patients (12). SII is also a ratio studied as a prognostic indicator in the sepsis and in the cancer patients and also the COVID-19 infection (13,14).

In our study, we aimed to demonstrate the usability of admission hematological parameters in the prognosis of COVID-19 infection in pregnant population and to introduce the cut-offs values of these parameters for pregnant women. The blood count is an inexpensive, fast, side-effect-free laboratory test that can be applied in any hospital and there is scarce of investigation related with these blood parameters and the indicators derived from peripheral blood parameters, in pregnant population.

METHODS

This single-center, retrospective, cohort study was conducted between May 1th, 2020, and May 1th, 2021, in Ordu University Training and Research Hospital which is a tertiary hospital in the Middle Black Sea Region of Turkey. The hospital has been designated as a corona virus pandemic hospital by the Ministry of Health, and the only hospital in Ordu Province which accepts pregnant women with COVID-19 infection. The present study protocol was approved by the ethics committee of the Ministry of Health Republic of Turkey with issue number 2020-05-11T19_06_54. The study was conducted in accordance with the principles outlined in the Declaration of Helsinki.

The study group consisted of 71 COVID-19 PCR test positive pregnant women that were hospitalized. The inclusion criteria in our study were COVID-19 pregnant women who were hospitalized in our hospital. Real-time reverse transcriptase polymerase chain reaction (RRT_PCR) tests were performed with Bio Speedy SARS CoV-2 detection kit (Bioeksen R&D Technologies, Istanbul, Turkey) that provided by the Ministry of Health of Turkey. Non-confirmed PCR negative cases, even if they were symptomatic or with a history of contact, were excluded from the study. Exclusion criteria in our study were pregnant women with comorbidities such as hypertension, diabetes, asthma, and morbid obesity. Medical records of pregnant women who were hospitalized during the study period were analyzed retrospectively. Clinical symptoms and other features (age, gestational week, length of hospital stay) were recorded.

The pregnant women were divided into two groups based on the severity of the disease. Thence, there was a non-severe group (consisting of 49 patients) and a severe group (consisting of 22 patients). Severe disease group which requiring oxygen therapy was characterized by dyspnea, shortness of breath, high respiratory rate (>30 breaths per minute), low oxygen saturation (<93% on room air and rest). The other pregnant women, who have been hospitalized and never required oxygen therapy or showed aforementioned symptoms, were described as non-severe group.

The initial triage protocol of inpatient COVID-19 patients includes blood sampling. A blood sample for complete blood count (CBC) was taken from all patients upon admission before any treatment began. CBCs were analyzed within 30 minutes by an automatic blood count device (Sysmex Corporation, ZN 1000i, Kobe, Japan). Simultaneously with CBC other blood sample was taken for measurement of C-reactive protein (CRP) levels by using a spectrophotometric chemical analysis device (Roche Diagnostics, Cobas E 501, California, USA). Demographic characteristics and clinical features of patients are represented in Table 1. Hematologic indices, hematologic ratios and CRP levels was

presented in Table 2. These hematological indices were calculated as NLR, which is the ratio between the count of neutrophils (×109cells/L) and the count of lymphocytes (×109 cells/L), dNLR is the ratio of neutrophils/(white blood cells- neutrophils), PLR is the ratio between the count of platelets (×1011 cells/L) and the count of lymphocytes (×109 cells/L) and the SII is defined as the counts of neutrophils (×109 cells/L) multiplied by the counts of platelets (×1011 cells/L) and divided by the count of lymphocytes (×109 cells/L), NPR is the ratio between the count of neutrophils (×109 cells/L) and the count of platelets (×1011 cells/L).

Statistical analysis

The study aims to demonstrate the usability of admission hematological parameters in the prognosis of COVID-19 infection in pregnant population and to introduce the cut-offs values of these parameters for pregnant women.

For analyzing the results of the study, IBM SPSS Statistics Package (Version 20 Armonk, NY: IBM Corp.) was used. Analyzes were carried out in a 95% (p=0.05) confidence interval. Descriptive statistical methods and correlation analyzes had been used in the study. Descriptive data derived from the study was presented as mean ± standard deviation or median. The normal distribution of numerical variables was studied with the Kolmogorov-Smirnov and the Shapiro-Wilks tests. The independent samples t-test was used when the numerical variables had a normal distribution, or the Mann-Whitney U test was used when the numerical variables did not have normal distribution.

The analysis of the receiver operating characteristic (ROC) curve was used to discover the optimal cut-off values of the levels of the peripheral blood parameters to predict the severity of patients in the study group. AUC was interpreted as excellent if 0.9-AUC-1, good if 0.8-AUC-0.9, moderate if 0.7-AUC-0.8, poor if 0.6-AUC-0.7, and failed if 0.5-AUC-0.6. Multivariate Cox regression analyses were used to evaluate the independent predictors of severity progression of disease.

RESULTS

Totally, 71 COVID-19 PCR test positive pregnant women in Ordu city were enrolled in this retrospective, cohort research. All of the patients included in the study were followed up and treated by hospitalization. Twenty-two of the patients (31%) were in the severe group that requiring oxygen therapy. Dyspnea, high respiratory rate (>30 breaths per minute) and low oxygen saturation (<93% on room air and rest) was observed in this group of patients. There were no fetal or maternal demise along the study period.

The mean age of the entire study cohort was 31.68+6.26 (19-48). And the mean gestational age of pregnant women was 27.72+9.33 weeks. In addition, the majority of patients were in the third trimester with the ratio of 62%, while the rate of first and second trimester pregnancies was 8.4% and 29.6%, respectively. There was no statistically significant difference between the groups in terms of neither age nor gestational week (p=0.193 and p=0.116). However, a significant difference was observed between the groups in terms of length of hospital stay (p=0.000). The hospitalization period of the patients in the severe group that required oxygen therapy was two times longer than the other group (9.45+2.4 vs. 4.9+2.1).

Thirty (42.25%) patients were asymptomatic. In symptomatic patients, headache (70.7%) was the most common symptom followed by fatigue (63.4%) and fever (56%). Dyspnea and shortness of breath was detected in 22 (53.6%) patients and these patients were in the severe group. Cough (48.7%) and diarrhea (31.7%) were the other symptoms. The demographic characteristics and clinical symptoms of patients were recorded and demonstrated in Table 1.

The data as the percentages above the normal reference range for the entire group was also examined. High CRP, lymphopenia, anemia, neutrophilia was found in 83%, 54.9%, 47.8% and 28.1% of patients, respectively. White blood cell count and neutrophil count was significantly higher, whereas red blood cell count and lymphocyte count were significantly lower in severe group. Besides, C-reactive protein was significantly higher in severe group that required oxygen therapy.

COVID-19 PCR positive pregnant women who required oxygen therapy presented significantly higher baseline values of NLR (neutrophil-to-lymphocyte ratio) (9.38 vs. 4.15, p=0.000), dNLR (derived neutrophil-to-lymphocyte ratio) (5.52 vs. 2.68, p=0.000), MLR (monocyte-to-lymphocyte ratio) (0.664 vs. 0.419, p=0.004), PLR (platelet-to-lymphocyte ratio) (208.9 vs. 153.1, p=0.008), NPR (neutrophil-to-platelet ratio) (0.049 vs. 0.033, p=0.005), NLRNPR (neutrophil-to-lymphocyte ratio/neutrophil-to-platelet ratio) (208.9 vs. 153.2, p=0.008) and SII (Systemic immune inflammation index = neutrophils multiplied by platelets and divided by lymphocytes) (1753.7 vs. 833.2, p=0.000). Hematologic indices, hematologic ratios and CRP levels was presented in Table 2.

ROC analysis evaluating COVID-19 severity revealed that optimal cut-off values for most laboratory parameter and blood count derived ratios were statistically significant. The largest AUC for dNLR was 0.921 with the cut-off value of 3.52 (sensitivity 86% and specificity 83%). The second largest AUC of 0.905 was observed in NLR with a cut-off value of 5.3 (sensitivity 81.8% and specificity 81.6%). The excellent AUC which was determined as 0.9-AUC-1, have been observed in NLR and dNLR; good AUC (0.8-AUC-0.9) have been observed in SII; moderate (0.7-AUC-0.8) have been observed in CRP, WBC, RBC, Hb, Hct, Neu, Lym, MLR, PLR, NPR, NLNPR; and the other AUC for blood count parameters have been determined as poor or failed. The sensitivity and specificity values of all laboratory parameters under the optimal cut-off values that statically significant were presented in Table 3.

Potential risk factors, including CRP, WBC, RBC, Hb, Hct, Neu, Lym, NLR, dNLR, MLR, PLR, NPR, SII, NLNPR were investigated using binary logistic regression analysis. In Table 4. MLR (monocyte lymphocyte ratio) (p=0.008, OR=8.63, confidence interval=1.746-42.681), dNLR (p=0.000, OR=3.794, confidence interval=2.016-7.138), NPR (p=0.014, OR=2.749, confidence interval=506.8-1.491) were seen as with the best predictive values for pregnant who may have worse clinical course.

Table 1: Demographic characteristics and clinical features of patients

	Severe Group (n=22)		Non-severe Group (n=49)		P value
	Mean+SD	*Number (Ratio)*	*Mean+SD*	*Number (Ratio)*	
Demografik features					
Age	30.23+5.9		32.33+6.3		0.193
Gestational week	30.32+6.1		26.55+10.3		0.116
Length of hospital stay	9.45+2.4		4.90+2.1		0.000*
Clinical symptoms **					
Fever		14/22 (63.6%)		9/49 (18.3%)	0.000*
Fatigue		11/22 (50%)		15/49 (30.6%)	0.097
Cough		12/22 (54.5%)		8/49 (16.3%)	0.002*
Headache		14/22 (63.6%)		15/49 (28.5%)	0.348
Diarrhea		4/22 (18.1%)		9/49 (18.3%)	0.632

*Statically significant
** Since the grouping was made according to the dyspnea symptom, it is not included in the table

Table 2. Hematologic indices, hematologic ratios and CRP levels

	Overall	Severe Group	Non-severe Group	P value
C-reactive protein (CRP) (mg/L)	23.12+27.19	43.43+38.24	14.03+12.79	0.000*
- >5	59 (83%)	21 (95.4%)	38 (77.5%)	
White Blood Cell Count (WBC) (K/mL)	8.46+3.48	10.50+4.06	7.54+2.76	0.001*
- >1.2	9 (12.6%)	5 (22.7%)	4 (8.1%)	
Red Blood Cell Count (RBC) (K/mL)	3.96+0.49	3.69+0.41	4.07+0.48	0.002*
- <4	44 (61.9%)	18 (81.8%)	26 (53%)	
Hemoglobin (Hb) (g/dL)	11.10+1.36	10.52+1.13	11.3+1.38	0.015*
- <11	34 (47.8%)	14 (63.6%)	20 (40.8)	
Hematocrit (Hct) (g/dL)	33.78+3.58	31.92+2.61	34.60+3.67	0.003*
- <33	34 (47.8%)	16 (72.7%)	18 (36.7%)	
Platelet (Plt) (K/mL)	198+77	196+70	200+80	0.852
Mean Corpuscular Volume (MCV) (fL)	85.69+6.52	86.80+6.43	85.19+6.56	0.342
Mean corpuscular hemoglobin (MCH) (g/dL)	28.19+2.95	28.63+3.05	27.98+2.91	0.397
Mean corpuscular hemoglobin concantration (MCHC) (g/dL)	32.84+1.39	32.93+1.58	32.79+1.30	0.701
Red Cell Distribution Width (RDW)(%)	44.50+5.88	43.25+3.46	45.05+6.64	0.234
Platelet Distribution Width (PDW) (%)	11.48+2.26	11.29+1.85	11.56+2.42	0.634
Platecrit (PCT) (%)	0.200+0.670	0.199+0.069	0.200+0.065	0.958
Mean Platelet Volume (MPV) (fL)	10.06+1.62	10.18+0.76	10.00+1.88	0.665
Neutrophil (Neu) (K/mL)	6.58+2.98	8.76+3.55	5.59+2.07	0.000*
- >8	20 (28.1%)	15 (68.1%)	5 (10.2%)	
Lymphocyte (Lym) (K/mL)	1.37+0.62	1.03+0.45	1.52+0.62	0.002*
- <1.5	39 (54.9%)	18 (81.8%)	21 (42.8%)	
Monocyte (Mono) (K/mL)	0.57+0.30	0.65+0.41	0.53+0.23	0.109
Eosinophil (Eos) (K/mL)	0.045+0.064	0.039+0.057	0.047+0.066	0.622
Basophil (Baso) (K/mL)	0.016+0.016	0.020+0.025	0.013+0.008	0.139
NLR (neutrophil-to-lymphocyte ratio)	5.78+3.64	9.38+3.88	4.15+2.01	0.000*
dNLR (derived neutrophil-to-lymphocyte ratio)	3.57+2.05	5.52+2.34	2.68+1.09	0.000*
MLR (monocyte-to-lymphocyte ratio)	0.495+0.336	0.664+0.353	0.419+0.302	0.004*
PLR (platelet-to-lymphocyte ratio)	170.4+82	208.9+74	153.1+81	0.008*
NPR (neutrophil-to-platelet ratio)	0.038+0.023	0.049+0.026	0.033+0.020	0.005*
MPVPR (mean platelet volum-to-platelet ratio)	0.062+0.032	0.058+0.020	0.064+0.044	0.597
LYM*PLT (lymphocyteXplatelet)	286.0+203	221.1+177	315.1+209	0.072
RDWPR (red cell distribution width-to-platelet ratio)	0.270+0.142	0.000+0.00	0.102+0.30	0.124
NLRNPR (NLR/NPR)	170.4+82	208.9+74	153.2+81	0.008*
SII (systemic immune inflammation index)	1118.4+747	1753.7+782	833.2+528	0.000*

*Statically significant

Table 3. The sensitivity and specificity values of all laboratory parameters under the optimal cut-off values

	AUC	cutoff	*P*	Confidence interval	Sensitivity %	Specificity %
CRP	0.786	15.15	0.000	0.67-0.903	68	67
WBC	0.746	8.63	0.001	0.610-0.882	72.7	73.5
RBC	0.732	3.88	0.002	0.601-0.863	68.2	69.4
Hb	0.704	10.85	0.006	0.571-0.837	63.6	63.3
Hct	0.731	32.8	0.002	0.609-0.854	68	65
Neu	0.794	6.51	0.000	0.666-0.923	77	75
Lym	0.723	1.185	0.003	0.599-0.846	77	67
NLR	0.905	5.3	0.000	0.836-0.975	81.8	81.6
dNLR	0.921	3.52	0.000	0.856-0.987	86	83
MLR	0.743	0.415	0.001	0.622-0.864	77.3	73.5
PLR	0.734	170.7	0.002	0.611-0.856	77.3	71.4
NPR	0.748	0.0355	0.001	0.627-0.869	72.7	75.5
SII	0.857	994.821	0.000	0.766-0.948	86.4	75.5
NLNPR	0.733	172.5	0.002	0.611-0.856	72.7	71.4

Table 4. The Odds ratio and confidence intervals of all laboratory parameters

	P	OR (Odds ratio)	(CI) Confidence Interval
CRP	0.000	1.066	1.011-1.023
WBC	0.004	1.343	1.100-1.638
RBC	0.002	0.135	0.034-0.538
Hb	0.02	0.605	.396-.925
Hct	0.006	0.778	0.650-0.931
Neu	0.001	1.63	1.238-2.152
Lym	0.004	0.195	0.065-0.586
NLR	0.002	1.853	1.395-2.462
dNLR	0.000	3.794	2.016-7.138
MLR	0.008	8.63	1.746-42.681
PLR	0.01	1.009	1.002-1.015
NPR	0.014	2.749	506.8-1.491
SII	0.000	1.002	1.001-1.003
NLNPR	0.012	1.009	1.002-1.015

DISCUSSION

As the COVID-19 pandemic is gradually increasing, early classification of the pregnant patients at high risk of progression to a severe disease is important both to differentiate the clinically important group and also to consider an aggressive intervention and hospitalization. Considering the limited healthcare capacity, early prediction of COVID-19 disease severity should be considered as the main point in combating the pandemic. Only in this way, regardless of the development level of the countries, intensive care unit occupancy rates can be kept at a reasonable level by predicting serious patients in the early period.

In systematic reviews and meta-analysis, alterations in various laboratory parameters have been investigated and linked to COVID-19 severity. Among the other laboratory findings, the most striking test is undoubtedly the CBC. Because CBC is on the one hand a fairly inexpensive, routine and effective test, and on the other hand it is applicable even in peripheral hospitals. And most of studies have

reported that CBC test is valuable in predicting the prognosis of COVID-19, especially in countries with low socioeconomics with limited healthcare opportunities (15-17). Nevertheless, there is inadequate data about blood parameters of pregnant women having COVID-19 disease.

In meta-analysis, it was reported that, neutrophilia, lymphopenia and hence neutrophil lymphocyte ratio correlates with severe COVID-19 disease in adults (18-20). Also in a multi-center study, it is shown that lymphopenia; reduced lymphocyte to leukocyte ratio and increased neutrophil to lymphocyte ratio is indicating pregnant women with acute respiratory syndrome having COVID-19 disease (21). Lymphopenia is not just specific to COVID-19. It has also been seen in other viral causes of pneumonia, especially mostly investigated in influenza cases (22). In our study, in line with the literature, high neutrophil and low lymphocyte counts were found in severe group pregnant patients who needed oxygen therapy. Neutrophilia upon admission was related with 1.6 times risk of getting severe COVID-19 infection in pregnancy.

Beyond the proven knowledge related with neutrophilia and lymphopenia in COVID-19 patients both adults and pregnant ones in terms of disease severity, the ratios of hematological parameters such NLR, PLR, SII and NPR came into prominence to predict COVID-19 disease severity (21,23). NLR and PLR actually have been used to evaluate extension of inflammatory conditions. NLR, especially, is used to decide severity in oncological patients, as an indicator of endothelial dysfunction and an important indicator of cardiovascular and ARDS mortality. PLR have been used as an indicator in acute inflammation and prothrombotic states and as a reflector of cytokine release in COVID-19 infected patients; because platelets not only play a role in homeostasis, also they act in inflammation and host defense (24-29). Until to date, there is no consensus on optimal cut-off value for NLR nor PLR. Cutoff values of 3.3 to 5.9 have been used to predict severity with COVID-19 infection (30-32); while 7.9 to 11.8 cutoff values were used to predict mortality (33,34). This wide range of cutoff values shows us the variability of NLR according to race, gender and specific diseases and condition. So, it must be clearly stated in specific groups like pregnant women with COVID-19 infection.

In a study taking the value of NLR>5, having a NLR bigger than 5 is suggesting getting severe disease with COVID-19 infection (22). In another study, it is suggested that having NLR cutoff as 3.3 to show disease progression from mild to severe in adult group (25). In pregnant with COVID-19 infection, NLR is found to be significantly higher than normal pregnant population (35), also in a multi-center study comparing ARDS having COVID-19 pregnant ones with non-ARDS COVID-19 infection ones, significantly difference have been found when NLR>7.5 was studied as cut-off between two groups (21). Also, it is determined in our results that NLR with a cut-off value of 5.3 (sensitivity 81.8% and specificity 81.6%) was a valuable marker to predict severe course in pregnant patients. Also, PLR in our results were statistically significantly high in severe group (p=0.008); but its AUC was 0.734 and OR was 1.009. However, dNLR which is commonly used in cancer patients to predict mortality and chemotherapy response (36); also, is studied in critically ill COVID-

19 infected patients to predict mortality and severity (37). There are no optimal values or cutoffs for dNLR in pregnant women with COVID-19 infection. In our study, dNLR was found to be significantly high in severe group (p=0.000) and when looked for ROC curve, dNLR showed high AUC (0.921) with a cutoff value of 3.52; with sensitivity 86% and specificity 83% and OR was 3.7 for dNLR in pregnant women. When SII is investigated in our pregnant population, which is an index showing instable inflammatory response, SII was higher in severe group (p=0.000), and AUC in ROC was significantly high for defining cutoff value. There is no study revealing these all-inflammatory indices in pregnant population, but in studies in adult COVID-19 infection, SII is found to be significant (38).

Neutrophils, the main component of the WBC count, are responsible for the production of pro-inflammatory mediators. According to the current knowledge about inflammation, the overproduction of pro-inflammatory mediators that also named cytokine storm has been associated with critical illness. In addition, studies investigating the pathogenesis of COVID-19 revealed that neutrophils can cause organ damage secondary to direct infiltration or coagulopathy (19,23). In our study, it was noted that pregnant women with high WBC levels on admission had developed severe disease, while normal WBC level was found to be a protective factor.

In a study which is comparing the hematological parameters and perinatal outcomes in pregnant women with COVID-19 disease in terms of adverse perinatal outcomes, MLR was found as a supportive diagnostic marker (35). In our study, also, MLR (p=0.008, OR=8.63, confidence interval=1.746-42.681) is found to be a good predictor for severe course in pregnant COVID-19 infected patients when logistic regression was used.

Pregnant women with COVID-19 infection which were enrolled in this study were in first, second and third trimesters. Despite there was no statistical difference between severe and non-severe COVID-19 infected pregnant women, in terms of gestational week, it would be better to investigate trimester specific severity of the hematological parameters. Another limitation is the retrospective design and unfortunately small sample size.

The strength of our study is, to the best of our knowledge, this is the first study comparing large scale of hematological parameters and their derivations in pregnant population. Being a single center study and evaluation of the patients by the same team overall period are other advantages of the study.

CONCLUSIONS

There is scarce information related with pregnancy COVID-19 infection especially clinical course and hematological parameters, despite 16 months have passed with COVID-19 pandemics. The aim of this study was to investigate which hematological parameters are associated with severe COVID-19 disease in pregnant and openly reveal all inflammatory indices which can be easily obtained with a baseline blood count.

This paper revealed that severe COVID-19 disease in pregnant women is mainly associated with leukocytosis, neutrophilia and increased NLR, dNLR, MLR, PLR, NPR, SII and NLNPR. Among these parameters NLR, dNLR and SII have largest AUC in

ROC, with cutoff values 5.3, 3.52 and 994.8 respectively.

Although these markers have been investigated in general population, there is limited number of studies in the literature that conducted among pregnant population. Further investigations regarding the use of hematologic tests as prognostic factor of COVID-19 disease severity in pregnant women are needed to assess the risk of serious disease, to predict the prognosis of COVID-19 and to reduce perinatal and maternal morbidity / mortality.

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Surgical Nurses' Pain Related Knowledge, Attitude and Clinical Decision Making Skills

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Abstract

Objective: To examine the knowledge, behavior, and clinical decision-making abilities of surgical nurses.

Methods: The research was conducted in 95 surgical nurses working in a state and a university hospital. Data were collected using A Personal Information Form, the Pain Questionnaire, and the Clinical Decision Making Questionnaire in February 2018-July 2020. Data analysis was performed with SPSS 25 and legal permissions were obtained.

Results: The statement "In cases where the necessary information about the surgery to be performed is not given, the severity of postoperative pain increases with increasing anxiety" received the highest number of correct answers (88.4%), while the statement "Opioids should not be given to patients with a substance abuse history because these patients are at high risk for recurrent addiction" received the least number of correct answers (7.4%). It was determined that 57.9% of the nurses observed the patient's behaviors to describe pain severity, and 76.8% of them used a pain scale in pain assessment. Of the nurses, 93.7% stated that the most commonly used pain relievers in their clinics were non-opioid drugs.

Conclusion: It is noteworthy that the surgical nurses in this study had inaccurate/incomplete information about the use of pain scales and placebo, drug/opioid side effects, and non-pharmacological interventions. Furthermore, it was found that nurses experienced ethical dilemmas due to the risk of respiratory depression. Therefore, it is recommended to review the knowledge/practices related to pain management during nursing education/in-service training in order to increase the quality of pain management in surgical nurses.

Key words: Behaviour, clinical decision making, knowledge, pain, surgical nurse.

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INTRODUCTION

Pain is a subjective condition that everyone often experiences in their lives (1). The International Association for the Study of Pain defines pain as "an unpleasant emotional state and behavioral pattern associated with the past experiences of people, originating from any part of the body with actual or potential tissue damage" (2). Surgical interventions are significant pain reasons. Pain is the most common problem that the patients experience in the postoperative period. It is reported that 73 million patients are operated in the USA every year, and 80% of them experience acute postoperative pain and approximately 20% experience severe pain. A study conducted in Turkey found that the incidence of postoperative pain was 77.3%. The same study determined that 39.7% of the patients experienced pain at a disturbing level (3).

Mediators released locally, humorally and neurally from the wound due to the surgical incision are known to be effective on the beginning and continuation of pain (4). Factors such as the severity, location, duration of the surgical intervention, anesthesia type, subjective nature of pain, and the importance the patient attributed to pain and treatment affect the incidence of pain. Pain is a threat for the organism regardless of its reason, and the organism provides a stress response against this situation (2). If pain which is addressed as a stressor in this situation prolongs, the organism develops a physiopathological response against pain. Atelectasis, hypoxemia, high blood pressure, tachycardia, increasing oxygen consumption, decreasing stomach and bowel motilities, urine retention, increased blood sugar, tendency to infection, retardation on wound healing, immobility, fear, anxiety and sleep deprivation are among the physiopathological responses developed against pain (2,5,6).

It is important to decide on and apply nonpharmacological interventions, and to evaluate the patient's responses and the applications' effectiveness in addition to analgesic application to reduce or eliminate the postoperative pain. Nurses have an important role in this process (5,6). The fact that the nurses are together with the patient longer than other health staff, that they guide the patient in terms of coping with pain and that they monitor the results of the applications and use their empathy skills requires them to have an active role on pain control (7,8). However, nurses have lack of knowledge on the pain signs and symptoms, diagnosing the pain intensity, and pharmacological and nonpharmacological pain treatment methods (5,8). It should be remembered that effective pain management requires accurate knowledge and positive attitudes as well as clinical decision making skills regarding pain (9).

There is a number of studies on determining the pain related knowledge level of surgical nurses in the literature (5,6,10). However, there are no studies on determining the clinical decision making skills of surgical nurses regarding pain. Accordingly, this study was carried out to determine the pain related knowledge, attitude and clinical decision making skills of nurses who work at surgery clinics.

METHODS

Aim and Design

This descriptive study was carried out to investigate the surgical nurses' pain related

knowledge, attitude and clinical decision making skills.

Setting

The study was conducted at the surgery clinics of a state hospital and a university hospital between February 2018 and July 2020. In the clinics where the study was conducted, only pain intensity is routinely evaluated. There are numbered pain scales in the observation forms of the nurses, and they were asked to record the pain intensity on this form.

Sample

The population of the study included 112 nurses who worked at the surgery clinics of the mentioned hospitals. No sampling method was used and the whole universe was tried to be reached in the study. The sample of the study included 95 nurses who agreed to participate in the study. The participation rate of the nurses was 85%.

Data collection tools

A Personal Information Form, the Pain Related Knowledge and Attitude Questionnaire and the Clinical Decision Making Survey were used as the data collection tools. Personal Information Form has seven questions about age, sex, education level, institution worked at, clinic worked at, years of working and total years of working at the surgery clinic. The Pain Related Knowledge and Attitude Questionnaire was formed after a literature review, and it has 20 statements (9 are true and 11 are false) (11,12). The Clinical Decision Making Survey has 14 questions and determines the pain related clinical decision making skills of the nurses. It was developed by Ferrell et al., and its Turkish validity and reliability study was conducted by Özer et al. (11,13). The survey does not have a scoring system.

Data collection

Data were collected with the face-to-face interview method in the clinics where the nurses worked between March 2019 and May 2019. The researcher introduced the data collection tools to the nurses, asked them to fill these forms when they are available, and collected the forms within 2-3 days. It takes 15-20 minutes to answer the questions.

Statistical analysis

The study data were analyzed by Statistical Package of Social Science (SPSS) 25.0 software. Descriptive statistical methods (frequency, percentage, mean, and standard deviation) were used to evaluate the date.

RESULTS

The descriptive characteristics of the nurses who participated in the study are shown in Table 1.

Of the nurses, 47.4% were aged between 28 and 37, 66.3% were female, 77.9% were high school graduates, and 54.7% worked at the university hospital. Almost half of the nurses served at the general surgery clinic, 69.5% were working for six or more years, and 43.2% were working at the surgery clinic for six or more years.

The true-false ratios of the nurses on the knowledge and attitude questions are presented in Table 2.

Table 1. Descriptive Characteristics of the Nurses (n=95)

Descriptive characteristics	n	%
Age		
18-27	20	21.1
28-37	45	47.4
38-47	24	25.3
48-57	6	6.3

Sex		
Female	63	66.3
Male	32	33.7
Education level		
High school	5	5.3
Associate degree	8	8.4
Undergraduate	74	77.9
Postgraduate and higher education	8	8.4
Institution worked at		
University hospital	52	54.7
State hospital	43	45.3
Clinic worked at		
General surgery	44	46.3
Orthopedics	15	15.8
Organ transplantation	11	11.6
Urology	8	8.4
Otolaryngology	6	6.3
Neurosurgery	5	5.3
Cardiovascular surgery	4	4.2
Thoracic surgery	2	2.1
Years of working		
5 years and less	29	30.5
6 years and more	66	69.5
Years of working in the surgical clinic	54	56.8
5 years and less	41	43.2
6 years and more		

The statement that "In cases when the necessary information regarding the operation to be performed is not provided, postoperative pain intensity increases with increasing anxiety" had the highest number of correct answers (88.4%) while the statement that "Opioids should be given to the patients with substance abuse history because these patients are at high risk for recurrent addiction" had the lowest number of correct answers (7.4%) (Table 2).

Considering the nurses' answers on the clinical decision making survey, 57.9% stated that they observe the patient's behaviors when defining the pain intensity, and 76.8% stated that they use pain scale in pain evaluation. Of them, 93.7% stated that nonopioid drugs are the most commonly used pain reliever drugs in the clinics. When they were asked what they pay attention while giving the drugs ordered as if needed, 78.9% stated that they give the drugs as ordered. Of them, 94.7% recorded their diagnoses regarding pain, and all of them recorded on the nurse observation form. The study found that the cold application was the most commonly used nonpharmacological intervention to relieve pain in clinics where the study is conducted at the rate of 58.9%. Of the nurses, 97.9% contacted the doctor regarding pain and 70.5% reported the changes on pain during this contact. The problem that the nurses encountered the most in pain relief was insufficient drug ordering at the rate of 20%, and of the nurses, 64.2% had to decide on describing the pain intensity, and the most common ethical dilemma faced in pain relief was concern about respiratory depression at the rate of 32.6%. Of the nurses, 71.6% stated that they need information about diagnosing pain (Table 3a and b).

Table 2. Nurses' Pain Related Knowledge and Attitudes (n=95)

	Pain related knowledge and attitudes	True		False		True answers %
		n	%	n	%	
1.	In cases when the necessary information regarding the operation to be performed is not provided, postoperative pain intensity increases with increasing anxiety (T)	84	88.4	11	11.6	88.4
2.	The most reliable indicator in pain evaluation is the patient's own pain expression (T)	78	82.1	17	17.9	82.1
3.	Early mobilization decreases due to pain and risk of thromboembolic complications increases (T)	78	82.1	17	17.9	82.1
4.	Respiratory depression rarely emerges on the patients who have been receiving opioid for a long time (months) (T)	66	69.5	29	30.5	69.5
5.	Pain intensity should be evaluated by the healthcare professionals instead of the patient (F)	34	35.8	61	64.2	64.2
6.	Pain that cannot be eliminated in surgical patients increases mortality and morbidity (T)	58	61.1	37	38.9	61.1
7.	Nurses should trust the parents regarding pain intensity in children younger than 11 (F)	43	45.3	52	54.7	54.7
8.	Only analgesic agent should be used on a patient in pain instead of combined drug groups (e.g. Opioid+ NSAİDs) (F)	53	55.8	42	44.2	44.2
9.	The patient should be encouraged to withstand pain as long as possible before applying a pain relief method (F)	54	56.8	41	43.2	43.2
10.	The patient should be advised to use nonpharmacological techniques alone and not in combination with pain medications (F)	56	58.9	39	41.1	41.1
11.	If the patient's attention can be directed to another way, this means that the patient does not have a high intensity of pain, as stated (F)	56	58.9	39	41.1	41.1
12.	The patient can sleep even with moderate or severe pain (T)	33	34.7	62	65.3	34.7
13.	Nonpharmacological interventions (e.g. hot application, music) are quite effective on moderate pain, but not as effective on severe pain (F)	69	72.6	26	27.4	27.4
14.	Using the pain scale increases the rate of analgesics protocols (T)	25	26.3	70	73.7	26.3
15.	Aspirin and other NSAİDs are not effective analgesics for chronic pain due to metastases (F)	75	78.9	20	21.1	21.1
16.	The addiction rate of opioids is very low (T)	18	18.9	77	81.1	18.9
17.	Hot and cold application should be made only to the painful area to be effective (F)	79	83.2	16	16.8	16.8
18.	If the patient is relieved with placebo, pain is not real (F)	79	83.2	16	16.8	16.8
19.	The rate of opioids causing respiratory depression is very low (T)	13	13.7	82	86.3	13.7
20.	Opioids should be given to the patients with substance abuse history because these patients are at high risk for recurrent addiction (F)	88	92.6	7	7.4	7.4

NSAİDs; Non-steroid anti-inflammatory drugs.

Table 3a. *Nurses' Pain Related Clinical Decision-Making Statuses (n=95)*

Nurses' pain related clinical decision-making statuses	n	%
Observation criteria for defining pain intensity*		
I observe the patient's behaviors	55	57.9
I ask the patient how much pain he/she has	46	48.4
I review the information on the doctor's notes	19	20.0
I evaluate the information that I receive from other nurses verbally	19	20.0
Using pain scale		
Yes	73	76.8
No	22	23.2
Most commonly used pain reliever drugs		
Nonopioids	89	93.7
Opioids	6	6.3
Conditions to be considered while giving drugs that are ordered if needed		
I give the drug as ordered	75	78.9
I give the drug less often than ordered	15	15.8
I give another drug than analgesics for pain (Antiemetic, sedative etc.)	5	5.3
Recording the diagnostics regarding pain		
Yes	90	94.7
No	5	5.3
Where pain diagnostics are recorded		
Nurse observation	95	100
Nonpharmacological interventions ordered in the clinic		
Cold application	56	58.9
Not ordered	31	32.6
Hot application	16	16.8
Physiotherapy	6	6.3
TENS	2	2.1
Other	9	9.5
Contacting the doctor regarding pain		
Yes	93	97.9
No	2	2.1
Matters that are discussed with the doctor*		
I report the changes regarding pain	67	70.5
I discuss the need for increasing drug dosage	32	33.7
I discuss the side effects of the drugs (e.g. nausea)	27	28.4
I discuss the need for changing the drug or the drug delivery method	24	25.3
Encountering an obstacle/issue in pain relief		
No	48	50.5
Yes	47	49.5

Table 3b. *Nurses' Pain Related Clinical Decision-Making Statuses (n=95)*

Obstacles/issues encountered in pain relief		
Insufficient drug ordering	19	20.0
Knowledge of the patient and family	18	18.9
Patient cooperation on taking drugs	11	11.6
Time	10	10.5
Cooperation with the doctor	7	7.4
Nurses' knowledge	5	5.3
Doctors' knowledge	4	4.2
Situations where the nurses need to decide regarding pain*		
Describing the pain intensity of the patient	61	64.2
Drugs to be given to the patient	37	38.9
Describing the patient's pain	31	32.6
Timing of the drugs to be given to the patient	30	31.6
Ethical dilemma that is placed first in pain relief		
Concern about respiratory depression	31	32.6
Concern/problem about drug overdose	27	28.4
Feeling that the patient's pain is not sufficiently relived	13	13.7
Concern/problem about giving a small amount of drug	10	10.5
Concern about addiction	6	6.3
Knowing and not accepting that the patient has pain	5	5.3
Suspecting that the pain is real	3	3.2
Information needed in pain management as first		
Pain diagnosis	68	71.6
Pharmacological management of pain	11	11.6
Technical matters such as analgesia pumps	8	8.4
Pain management in specific populations	4	4.2
Nonpharmacological (drug free) intervention	3	3.2
Psychosocial matters regarding pain	1	1.1

TENS; Transcutaneous Electrical Nerve Stimulation
** More than one answers were given.*

DISCUSSION

Although the improvements on surgical techniques, anesthesia, pharmacology and pain control, the pain prevalence among the surgical patients is high (2,14). An effective pain management may prevent postoperative complications, but applications regarding this matter is not sufficient (15). The quality of pain management is based on the knowledge, attitude and clinical decision making skills of the health staff. The nurses who ensure the coordination between the doctor and patient, and who closely monitor the patient's pain and comfort have a significant role in this process (11). Accordingly, this study was carried out to determine the pain related knowledge, attitude and clinical decision making skills of nurses who work at surgery clinics.

The statement that "In cases when the necessary information regarding the operation to be performed is not provided, postoperative pain intensity increases with increasing anxiety" was answered correctly by

88.4% of the nurses in this study. The literature states that preoperative anxiety is effective on the postoperative pain, and education provided in the preoperative period decreases anxiety. The fact that most nurses have accurate information on this matter will have positive effects on postoperative pain management (16).

According to the study results, 82.1% of the nurses stated that the most reliable indicator on pain evaluation is the patient's own pain statement. Two separate studies conducted with surgical nurses have similar results (5,17). It is pleasing that the nurses consider the patient's own statement as the most reliable indicator on pain evaluation.

The statement that "Early mobilization decreases due to pain and risk of thromboembolic complications increases" was answered correctly by 82.1% of the nurses. It is emphasized in the literature that movement restrictions occur in the postoperative period due to pain, and that the nurses should provide effective pain management to prevent complication that may develop due to immobility (9,18). The fact that most of the nurses in this study had high level of awareness about this matter will be beneficial for eliminating pain and pain-induced complications.

The statement that "Respiratory depression rarely emerges on the patients who have been receiving opioid for a long time (months)" was answered correctly by 69.5% of the nurses. In the study by Shogurat, majority of the surgical nurses also answered the same question correctly (5). In the study by Bouri, 61.8% of the orthopedic nurses answered this question incorrectly (19). Lack of knowledge and inaccurate beliefs on opioids are important problems in pain management (20).

In this study, 64.2% of the nurses reported that the statement that "Pain intensity should be evaluated by the healthcare professionals instead of the patient" is false. On the contrary, a similar question was answered incorrectly at the rate of 64.6% in another study (17). Undoubtedly, it is very important that nurses believe patients' pain statements and allow the patient to evaluate pain for effective pain management (21). The fact that a considerable part of the nurses reported that the pain intensity should be evaluated by healthcare professionals in this study is engrossing.

It is stated in the literature that using pharmacological methods along with nonpharmacological methods is more effective on the management of severe pain (12). Only 27.4% of the nurses correctly answered the statement that "Nonpharmacological methods are quite effective on moderate pain, but not as effective on severe pain." In another study, the same statement was answered correctly by 7% of the participants. This indicates that nonpharmacological approaches are not sufficiently involved in nursing education and in-service training.

The statement that "using the pain scale increases the rate of analgesics protocols" was answered correctly by 26.3% of the nurses. However, one of the possible reasons for insufficient pain management is not using the pain scale (22). This result shows that the nurses who participated in the study were not sufficiently aware of the importance of using the pain scale.

It is reported in the literature that the nurses are still unable decide on using opioids (23). Similarly, the statement that "the addiction rate of opioids is very low" was stated as true by only 18.9% of the

nurses in this study (21,24). This result indicates that a pain that can be eliminated with opioids cannot be eliminated due to the nurses' fear of addiction. The statement that "If the patient is relieved with placebo, pain is not real" was answered correctly by a very small number of participants. It can be observed that a significant part of the nurses has false information about this matter in similar study (5,25). However, it is stated in the literature that the majority of patients with a diagnosable physical pain cause may be relieved when given a placebo (26).

It is important observe pain-related behaviors such as contraction, clenching, pulling the aching organ or area away from the stimulus in the evaluation of pain which is a subjective symptom (25). This study determined that 57.9% of the nurses observed the patient's behaviors when diagnosing the pain intensity. Another study on this matter also found a similar result. Undoubtedly, observing the patient's behaviors will have a positive effect on the postoperative pain management.

Using pain measurement tools is an integral part the postoperative pain management (17). This study found that 76.8% of the nurses used the pain scale. While 64.8% of the nurses used the pain scale in another study, (27) this rate was 18.7% in the study by Özer et al. (11).

In the pharmacological management of pain, the nurses have a bigger role than just applying the drug. This responsibility is much higher especially in "analgesic if needed" requests that are still dominantly written in surgical fields (28) When the conditions to be considered while giving drugs that are ordered if needed are examined, the study found that 15.8% of the nurses gave the drugs less often than ordered. Similarly, another study found that 17.5% of the emergency nurses gave the drugs less often than ordered (12). In the management of pain, which is an expected problem in surgical patients, it is wrong to wait for the patient to experience pain before applying "analgesic if needed" (28). This result indicates that the nurses do not have sufficient knowledge about this matter.

The American Pain Association determined the importance of recording the pain to improve the pain treatment (12). This study found that 94.7% of the nurses recorded the pain and all of them recorded it on the nurse observation form. Similarly, Özer et al. determined that 71.5% of the nurses recorded the pain statement in their study (11). These results are pleasing for the improvement of the pain treatment. It indicates that the surgical nurses are aware about recording the pain.

Another important matter for pain management to be of desired quality is undoubtedly a good team approach. This study found that 97.9% of the nurses contacted the doctor regarding the pain. Additionally, 70.5% of the nurses reported the changes on the pain level to the doctor. There are similar results in the literature (11,12). This is a pleasing result for the postoperative pain management.

The study found that the nurses are in an ethical dilemma due to their concerns about respiratory depression induced by pain relief. Özer et al. revealed that the most common ethical dilemma faced by the nurses was "concerning about respiratory depression" (11). Another study revealed that the most common ethical dilemma faced by the nurses was "concern/problem about drug overdose" (12). These results indicate that the nurses have lacking/incorrect

information about opioids. This will negatively affect the clinical decisions of the surgical nurses about pain management.

CONCLUSIONS

It is remarkable that the surgical nurses who participated in this study have incorrect/lacking knowledge on using pain scale, placebo, side effects of drugs/opioids and nonpharmacological interventions. Additionally, it was found that the nurses face an ethical dilemma due to the risk of respiratory depression. The study found that most nurses used the pain scale for pain evaluation, almost all of them recorded diagnoses regarding the pain, and that insufficient drug ordering was the most commonly encountered problem in pain relief, and the most common ethical dilemma faced in pain relief was concern about respiratory depression. The results of this study indicate that hospital education programmes about pain assessment and management for surgical nurses need to be a high priority. It can be suggested that more emphasis should be given to the subject of "pain" during nursing education, and that the "pain management" course should be included in the curriculum. Advanced future studies conducted with larger sample groups will provide results that are more definitive.

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"Perceived job stress and COVID- 19 pandemic related stress predictors among Nurses working in Saudi Arabia"

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Abstract

Objective: As the coronavirus disease 2019 (COVID-19) pandemic hastens the global health care systems which take the lead to great psychological stress on health care professionals especially nurses with COVID-19 illness patient care. This study focused on perceived job stress and covid-19 pandemic related job stress predictors among nurses working in ministry of health hospitals and health centers in Muhayil Aseer town, Saudi Arabia during the first wave of COVID-19 pandemic.

Methods: An analytical cross-sectional study addressed to examine the prevalent perceived job stress and covid-19 related perceived job stress predictors among nurses. A web-based google form english questionnaire was designed in sections aimed at collecting socio demographic and job variables, including the Perceived Stress Scale (PSS) and the Covid-19 pandemic related job stress predictors questionnaire. The data were collected using convenient sampling technique.

Results: 164 nurses have participated in this study among them, the overall nurses 97.57 % had experienced job stress during peak time of Corona virus spread and of them more than half (59.76 %) of the (98) nurses had moderate level of job stress and the mean PSS score 21.8 that represents moderate stress level. In multivariate regression analysis model, the perceived safety risk (LR= 95.53, χ^2 (6) = 27.91, P=.000), perceived worry (LR= 97.23, $\chi^2(6)$ = 29.60, P=.000) and perceived work difficulty (LR= 100.92, $\chi^2(6)$ = 33.29, P=.000) were found as significant predictors of perceived job stress during Covid-19 pandemic.

Conclusion: This study revealed that job stress is a common prevailing problem among nurses and the COVID-19 pandemic related job stress predictors were perceived safety risk and perceived worry about health while covid-19 exposure and perceived work difficulty as overworked during pandemic. Although efforts were enhanced to support their psychological well-being, more attention should be paid to the mental health of nursing staffs. The study recommends that strong strategy improvements need to be held in the health care institutions to reduce nurses' stress and enable them to combat the ongoing and future occurrences of pandemic effectively.

Keywords: Nurses' job stress, job Stress predictors, COVID-19 Pandemic, Perceived stress

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INTRODUCTION

World Health Organization (WHO) states that COVID-19 is an infectious disease caused by a newly discovered coronavirus (7). Worldwide, the highly contagious respiratory infection caused by the coronavirus 2 (SARS-CoV-2) has caused not only an economic crisis, but an increase in mortality and morbidity, and emotional distress among people. Globally the fatality rate and the consequences of COVID-19 have led to fears, worries, and anxiety.

A dramatic impact wrought by this occurrence on all aspects of our lives by new normalcy style (9). The coronavirus disease 2019 (COVID-19) pandemic has also strained the health system. The FDA has taken numerous actions to help increase supplies of medical equipment needed to fight COVID-19 and protect healthcare workers. The measures were undertaken to manage Healthcare Personnel with SARS-CoV-2 Infection or Exposure to SARS-CoV-2 in terms of handling Confirmed Coronavirus Disease (COVID-19) Patients. (11)

In the outbreak period, among health professionals, especially frontline nurses, faced great challenges and endured higher risks of psychological problems such as depression, anxiety, and insomnia (4). They are being exposed for several working hours per day to COVID infected patients, face several issues that lead to physical/psychological disturbance (1).

Stress is a normal human reaction that happens to everyone resulting in physical, emotional, and intellectual responses whereas Job stress is the harmful physical and emotional responses that occur when the requirements of the job do not match the capabilities, resources, or needs of the worker (24, 25). The global COVID-19 pandemic has created new causes of job-related stress (8). In this light of magnitude, this present study sought to explore perceived job stress level among nurses during the COVID-19 outbreak in Saudi Arabia.

This study aimed to explore perceived job stress level and stress predictors related to COVID-19 pandemic among nurses during the outbreak in Saudi Arabia.

METHODS

Study Design:

An analytical cross-sectional study was conducted in December 2020 during the COVID-19 outbreak first wave in Saudi Arabia. An ethical approval was granted only from the Institutional research committee at College of Applied medical Sciences, Muhayil Aseer, Saudi Arabia.

Sample population:

This study included both male and female nurses who were currently working in ministry of Health hospitals and health centers at Muhayil town area, Saudi Arabia at the time of the study. The participants excluded those who were on long vacation during outbreak.

Sample Recruitment:

The sample size was calculated using Raosoft software (9). The required sample size was estimated at the 95- confidence level with an estimated 50% response distribution and a margin of error of ±5%. The recommended minimum sample size is 169. An online google survey form was sent to all nurses who

were working in Ministry of Health Hospitals and Health Centers at Muhayil town, Saudi Arabia during the first wave of COVID-19 pandemic.

Data collection

Nurses were invited to participate via cell phone text messages. The messages explained the study objectives, the purpose of the study and guided the Nurses to complete the electronic english version questionnaire link. Convenience sampling technique was adopted to collect responses, only 164 working nurses responded.

Description of tool

The The online survey questionnaire was comprised of four parts:

(a) Socio-demographic data of the nurses, such as age, gender, nationality, marital status, and history of chronic diseases.

(b) Work-related characteristics, such as job title, qualification, working unit, working shift system, and working experience in years.

(c) The perceived stress scale (PSS) is a 10-items tool used to measure a Nurse's perception of stress over the past month. The PSS (4) is a validated, reliable (Cronbach's alpha 0.85), easy-to-use, and popular stress questionnaire. A Likert-type 5-point scale was used to capture responses in the PSS (never-0, almost never-1, sometimes-2, fairly often-3, and very often-4). The total sum score of PSS can range from 0 to 40 where the stress levels are 0 considered as No Stress, 1-13: low stress, 14-26: moderate and 27-40: high stress.

d) To assess the Nurse's perceived Job stress predictors, Covid pandemic related Perceived job stressor variables of 4 items questionnaire developed by researchers. The internal consistency of the tool reliability was tested using Cronbach's alpha (α= 0.699) and Inter item correlation mean (0.37) (Optimal mean inter-item correlation values range from .2 to .4 as recommended by Briggs & Cheek 1986). This questionnaire (table 4) includes work related perceived worry about health while exposure with covid positive patients, perceived the safety risk of Covid-19 infection with tested positive, perceived fear regard to covid fatality and Perceived work difficulty during covid pandemic. All the statement responses such as "Always/Little/Not at all" were considered as predictive factors of perceived job stress among Nurses.

Statistical analysis

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) version 16.0 software for windows (SPSS Inc., September 13, 2007). The percentages and frequencies were calculated for all nominal variables for the different items of the PSS-10 and Nurses' perceived job stress Predictor questionnaire-4. Also, we calculated the mean, median, and standard deviation ranges of the total score of the PSS-10. The significance of association of job characteristics with perceived stress score was analysed using in contingency tables by Pearson's chi-square test (categorical variables). To explore COVID-19 pandemic -related predictors associated with perceived job stress, multinominal logistic regression analysis was performed using the main effects method (17). In this regression model, the PSS score stress level was used as a dependent variable, while categorical variables were as perceived fear, perceived worry, and perceived safety risk and perceived work difficulty were measured as

predictive factors. Results are considered significant for P-values below 0.05 (P < 0.05).

RESULTS

Socio demographic Characteristics of Enrolled Nurses

Demographic characteristics of nurses who filled the online questionnaire are reported in Table 1. Most participants were almost equally distributed between <25 -40 years age categories, with only few 3 nurses (1.8%) aged more than 50 years old; 132 (80.5%) study subjects were female nurses. More than a half of our sample was married (54.9%) the majority (73.8%) 121 nurses were belonging to Saudi nationality. However, none of the sociodemographic characteristics of the nurses were associated with their perceived job stress levels.

In Table 2 stated that less than half of the nurses (81) 49.3% were working in a COVID-19 Unit, the majority 73.3% (22) nurses were holding a job position as head nurse reported moderate level of stress. The following job characteristics associated with their perceived job stress that are working unit (p=0.007) and nurses 'qualification (p=0.022), also the years of working experience (p=0.035) at 0.05 significance level respectively. Regarding the history of chronic health problems among studied nurses, the predominant one was lower back pain (32.3%) and then migraine headache (14.7%) depicted in figure 1.

Nurses' perceived job Stress predictors during Covid-19 pandemic

Figure 4 shows that most of the Nurses 67 (40.9%) were reported little perceived safety risk, and only 81(49.4%) of nurses were addressed that not at all perceived worry about health due to exposure with positive patients, and many of the nurses 67 (40.9%) experienced work difficult during COVID– 19, then 62 (37.8%) nurses perceived fear concerning Covid fatality during Pandemic peak in Saudi Arabia.

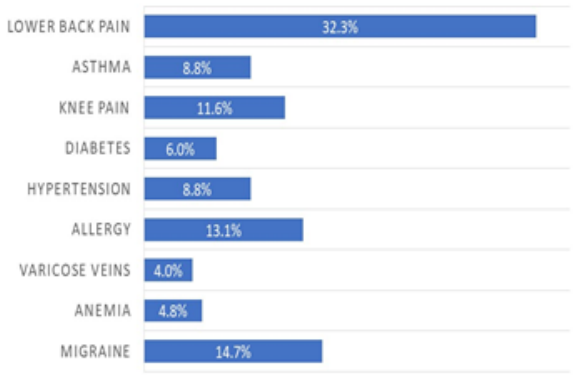

Figure 1. History of Chronic Health Problems Among Nurses

Nurses' perceived job Stress during Covid-19 pandemic

The descriptive statistics revealed that the Standard deviation (SD) 8.308 and overall mean Perceived job stress score was 21.8 on a 0-40 range PSS scale that depicts moderate stress level during pandemic period (Figure 2). The large (97.57 %) number of the nurses experienced job stress during peak time of Corona virus spread and more than half (59.76 %) of the 98 nurses had moderate level of job stress, 45 nurses had (27.44%) High stress, and 17 had (10.37%) low stress (Figure: 3).

Figure 2. Mean score of perceived stress related to Covid-19 pandemic

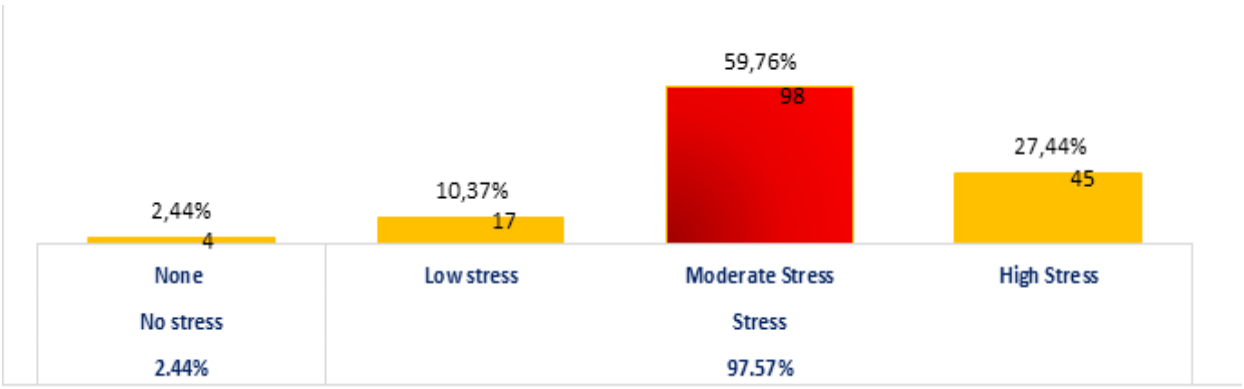

Figure 3. Nurse's Covid-19 pandemic related perceived job stress level

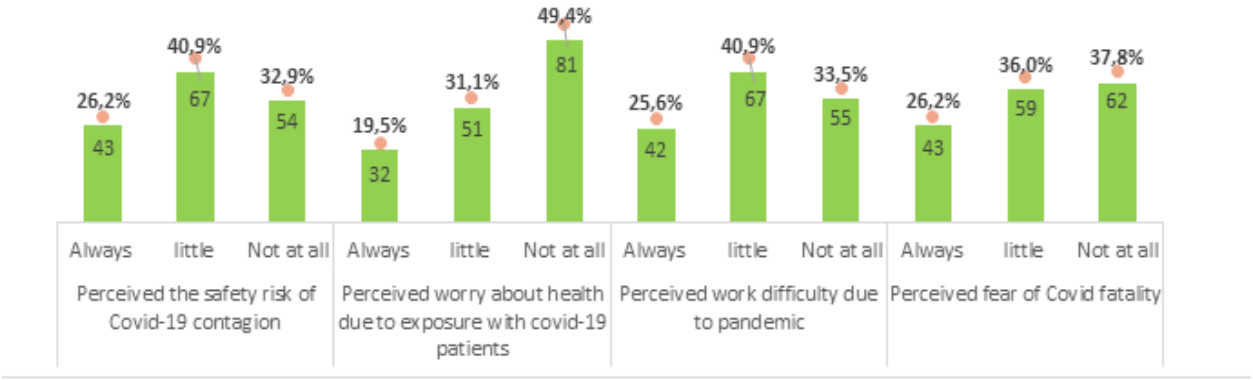

Figure 4. Nurses' perceived job stressors related to Covid-19 pandemic

Table: 1 Socio demographic Characteristics of Nurses (N=164)

	Perceived job Stress Level		
	Frequency (n) %	Chi square $_{df}$	P value
Gender			
Male Nurses	(32) 19.5 %	3.686_{3}	.297
Female Nurses	(132) 80.5%		
Age			
<25 – 30 years	(79) 48.2)	12.874_{9}	.168
31- 40 years	(74) 45.1%		
41-50 years	(8) 4.9 %		
>50 years	(3) 1.8%		
Nationality			
Saudi	(121) 73.8%	19.538_{12}	.076
Philippine	(22) 13.4%		
Indian	(14) 8.5%		
Egyptian	(2) 1.2%		
other nationality	(5) 3.0%		
Marital status			
Married	(90) 54.9 %	16.634_{9}	.055
Single	(69) 42.1%		
Separated	(3) 1.8%		
widowed	(2) 1.2%		

Table:2 Nurses' job Characteristics and perceived Job stress level

Job Characteristics	None	Low	Moderate	High	Chi-square $_{df}$	P- value
1. Nursing Qualification	4.1 % (2)	18.4% (9)	63.3% (31)	114.3% (7)	9.638_3	0.022
Diploma						
Bachelor	1% (2)	7.0% (8)	58.3% (67)	33.0% (38)		
2. Working Unit	2.4% (4)	6.1% (10)	32.9% (54)	9.1% (15)		
Non Covid unit					10.527_3	0.007
Covid Unit	.0% (0)	4.3% (7)	26.8% (44)	18.3% (30)		
3. Working Shift	.6% (1)	6.7% (11)	28.0% (46)	15.9% (26)	3.831_3	0.280
Rotated shift						
Same shift	1.8% (3)	3.7% (6)	31.7% (52)	11.6% (19)		
4. Working Experience	.0% (0)	2.4% (4)	9.8% (16)	5.5% (9)	16.725_9	0.053
Fresher < 1 year						
1- 10 years	.0% (0)	3.0% (5)	31.7% (52)	15.9% (26)		
11-20 years	2.4% (4)	4.9% (8)	16.5% (27)	6.1% (10)		
>20 years	.0% (0)	.0% (0)	1.8% (3)	.0% (0)		
5. Job Position	.0% (0)	.0% (0)	6.1% (10)	3.0% (5)	11.187_{12}	0.513
Nurse Intern						
Staff nurse	1.8% (3)	8.5% (14)	27.4% (45)	15.2% (25)		
Head Nurse	.6% (1)	.6% (1)	13.4% (22)	3.7% (6)		
Nurse Specialist	.0% (0)	.6% (1)	7.3% (12)	3.7% (6)		
Nurse Supervisor	.0% (0)	.6% (1)	5.5% (9)	1.8% (3)		
6. Work related exposure to Covid- 19 patients care	2.4% (4)	6.1% (10)	34.8% (57)	20.7% (34)	6.507_3	0.089
Yes						
No	.0% (0)	4.3% (7)	25.0% (41)	6.7% (11)		
7. Nurses who Tested Covid -19 Positive	.6% (1)	4.3% (7)	23.3% (38)	12.9% (21)	1.153_3	0.764
Yes						
No	1.8% (3)	6.1% (10)	36.2% (59)	14.7% (24)		

Table 3 – Multinominal Logistic Regression model parameter Estimates: Covid -19 pandemic related Nurses' perceived Job stressors

Stress Category		Low stress					Moderate stress					High stress				
Perceived Stressors		B	Std. Error	P value	Exp(B)	95% CI	B	Std. Error	P value	Exp(B)	95% CI	B	Std. Error	P value	Exp(B)	95% CI
1.Perceived safety risk	Not at all	.970	2940.76	1.00	2.637	.000-.[b]	.737	1808.	1.000	2.090	.000 -[b]	-17.281	2965.	.995	3.125E-8	.000-[b]
	Little	15.735	2318.71	.995	6.817E6	.000-.[b]	17.66	.565	.000	4.68E7	1.549E7-1.417E8	15.591	.000	.995.	5.904E6	59037.1-5903.10
	Always	0[c]	.	.	.		0[c]	.	.	.	.	0[c]	.	.	.	.
2.Perceived worry	Not at all	-.436	3291.51	1.00	.646	.000 -.[b]	-19.26	2863	.995	4.31E-9	.00-[b]	-36.806	4056	.993	1.036E-16	.000 -[b]
	Little	16.482	4467.302	.997	1.439E7	.00 -.[b]	-1.25	4162	1.000	.286	.00-[b]	-2.91	4162.	.999	.054	.000 -[b]
	Always	0[c]	.	.	.		0[c]	.	.	.	.	0[c]	.	.	.	.
3.Perceived work difficulty	Not at all	15.588	2699.92	.995	5.885E6	.000-.[b]	-1.588	1690	.999	.204	.00-[b]	-4.318	1690.	.998	.013	.000 -[b]
	Little	13.872	2551.05	.996	1.058E6	.00 -[b]	15.379	.574	.000	4.77E6	154830-1.472E7	13.826	.000	.	1.010E6	104.52 104.52
	Always	0[c]	.	.	.	.	0[c]	.	.	.	.	0[c]	.	.	.	.

Reference Category: No stress

Table 4 : COVID-19 Pandemic related job stress predictors Questionnaire

Items	Responses
1. Have you been perceived the safety risk of Covid-19 contagion?	Always, Little, Not at all
2. Have you felt worried about your health while exposure with covid positive patients?	Always, Little, Not at all
3. Have you felt difficulties as over worked to handle the patients during pandemic?	Always, Little, Not at all
4. Have you felt fear of covid fatality while providing nursing care for patients?	Always, Little, Not at all

Multinominal Logistic Regression Model of Nurse's job stress predictors related Covid-19 pandemic

Finally, the analysis plan considered a major effect method via using the multivariate logistic regression analysis. Table 3 displays the findings from the analysis model. Based on the model fitness LR test p value .000, the model containing the full set of predictors represents a significant improvement in fit (Likelihood Ratio χ^2 (24) = 188.578, P=.000). Pearson value is an additional chi-square goodness of fit test (χ^2 (132) = 32.531, p=1.000) for this model, when non-significant, that provides further evidence of a well-fitting model. Based on McFadden's, the full model containing our predictors represents a 58.2% improvement in fit. The overall classification accuracy for the model predicting category membership on the Dependent Variable (Job stress level). was 78.0%. In this model, the likelihood ratio and chi-square tests of the each (Independent Variables) predictors shown that a direct effect of perceived safety risk (LR= 95.53, χ^2 (6) = 27.91, P=.000), perceived worry (LR= 97.23, χ^2(6) = 29.60, P=.000) and perceived work difficulty during Covid-19 pandemic (LR= 100.92, χ^2(6) = 33.29, P=.000) were estimated as significant predictors of covid -19 pandemic related perceived job stress among nurses working in Saudi Arabia.

The Model parameter Estimates presented in the table 3. It shows that Nurses who perceived little safety risk of Covid-19 contagion were significantly predicted to have a moderate stress 17.66 times more than No stress category stress (Beta = 17.66, P value= .000). Secondly Nurses who perceived little work difficulty as over worked to handle the patients during pandemic Covid-19 were also significantly predicted to have a moderate stress 15.37 times more than No stress category stress (Beta = 15.37, P value= .000) respectively.

DISCUSSION

It is important to investigate perceived job stress level among health care providers during

COVID-19 pandemic. Especially nurses, are in frontline battle during this pandemic that cause emotional exhaustion which may lead to burnout gradually (13). We investigated in this study, the percentage of nursing staffs who were under stress and their job stress predictors related to Covid-19 pandemic.

Nurses job stress level and Sociodemographic Characteristics Association

Regarding sociodemographic characteristics of Nurses, we found that none were associated with their significantly associated with their job stress. Our study results are in line with some studies, that there was no relationship between the mean of perceived job stress of nurses and their gender stated in Alyahya.et.al, Farraji.et,al (2, 10). However, unlike our present study results, Romano.et.al and Shin et.al. (18, 23) reported that gender was significantly associated with nurses' stress. In our study, nurses' age group was not statistically significant. This is also

similar with these findings of Alyahya.et.al., Farraji.et,al and Romano et al., studies (2,10,18).

It is inferred that socio demographic characteristics may not have considerable impact on job stress concerning covid- 19 pandemic among nurses

Nurses job stress level and Job Characteristics Association

In our study, we investigated that some of the following job characteristics are significantly associated with Nurses' job stress level such as Nursing Qualification (P=0.035*) Working Experience (P=0.035*) and nursing Unit: Covid unit and non-covid unit (P=0.007*). It is evident that job stress is much related to particularly their working experience, level of qualification and working unit. It is apparent that working unit plays a greater role in causing job stress among nursing during outbreak.

The findings of this study have been shown to be consistent with the study undertaken by Bellanti et.al Shin et.al (3, 23) where Participants working in the Covid unit and ICU had a significantly higher than the other departments while those working in the General Ward.

In this current study, we found that significant association between the nurses' perceived job stress and their work experience (26).

Concerning the health problems experienced by the nurses, the very common problems were lower back pain (32.3%) and then migraine headache at the rate of (14.7%). Nurses are at a higher risk and six times higher prevalence to have lower back pain and back injury (5). These health problems could be from prolong standing and physical exhaustion during patient care. The other predominant health problem found in our results was headache, perhaps it might be due to keen concentration in clinical challenges related to their work. According to Atlanta-based Headache Center of Peachtree Neurological Clinic, headache usually stress-related; Still, headaches may indicate another underlying health issue. Our study results are almost parallel with study done by Kilic.et.al and Sabra.et.al (15, 19).

Nurses perceived job Stress during Covid-19 pandemic

The mean value of perceived job stress score was 21.8 on a 0-40 range PSS scale that depicts moderate stress. The overall nurses (97.57%) had experienced job stress during pandemic, of them (59.76 %) had moderate stress, and (27.44%) had high stress and then only (10.37%) experienced low stress respectively. It is evident that almost certainly all the nurses are facing job stress. The other recent study results that the Nurses stress level was moderate to high (10, 21).

COVID-19 related job stress predictors among Nurses

It is not surprising that nurses reported significantly higher mean score of perceived job stress. The literature has shown that, compared to other professionals, healthcare providers, especially nurses, have a higher risk of developing emotional distress like depression, anxiety, and burnout due to work-related stress (12). There are stress factors that appeared to increase the risk of developing job stress like perceived safety risk of covid-19 contagion, perceived worry about health while exposure covid-19 patients and perceived work difficulty as over worked to handle the covid-19 patients.

The recent studies conducted on nurses showed that predictors of job stress in the professional environment include the perceived fear of contracting

COVID-19, a decrease in the level of safety while conducting emergency medical procedures and nurses who tested positive to corona virus (14,16, 28). Of note, in our research only 3 significant job stress predictors related to Covid-19 revealed among nurses.

Limitations

This study limited only on nurses working in the government hospitals located in Muhayil town area, Aseer province of Saudi Arabia. And the second limitation was that only subjective health problems and job stress mentioned by nurses themselves were evaluated. Thirdly, the completion of job stress predictors model needs to be added with few more Covid-19 pandemic related factors. Un fortunately the sample size was less than recommended size just with 164 nurses only.

CONCLUSION

The substantial study findings reflected that job stress was perceived by almost all the nurses (97.57%) during pandemic and the job stress mean score was 21.8 which represents moderate level of perceived stress. The significant job stress predictors related to Covid-19 were "perceived safety risk, perceived worry about health while exposure and perceived work difficulty as over worked to handle the covid-19 patients". Therefore, this study recommends that the nurses need to be prepared well by strong strategy improvements for reducing the nurses' stress to pursue their efforts in more meaningful experience during pandemic (22, 27). A Longitudinal research studies need to be conducted to follow up on nurses' stress and develop evidence-based interventions.

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Ethics Committee Approval: An ethical approval was granted only from the Institutional research committee at College of Applied medical Sciences, Muhayil Aseer, Saudi Arabia. This study was performed on nurses working in different hospitals in Muhayil Asir Town, Saudi Arabia. Informed consent obtained by the nurses only. Ethical committee of King Khalid University was not required.

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"Perceived job stress and COVID- 19 pandemic related stress predictors among Nurses working in Saudi Arabia"

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Abstract

Objective: As the coronavirus disease 2019 (COVID-19) pandemic hastens the global health care systems which take the lead to great psychological stress on health care professionals especially nurses with COVID-19 illness patient care. This study focused on perceived job stress and covid-19 pandemic related job stress predictors among nurses working in ministry of health hospitals and health centers in Muhayil Aseer town, Saudi Arabia during the first wave of COVID-19 pandemic.

Material and Methods: An analytical cross-sectional study addressed to examine the prevalent perceived job stress and covid-19 related perceived job stress predictors among nurses. A web-based google form english questionnaire was designed in sections aimed at collecting socio demographic and job variables, including the Perceived Stress Scale (PSS) and the Covid-19 pandemic related job stress predictors questionnaire. The data were collected using convenient sampling technique.

Results: 164 nurses have participated in this study among them, the overall nurses 97.57 % had experienced job stress during peak time of Corona virus spread and of them more than half (59.76 %) of the (98) nurses had moderate level of job stress and the mean PSS score 21.8 that represents moderate stress level. In multivariate regression analysis model, the perceived safety risk (LR= 95.53, χ^2 (6) = 27.91, P=.000), perceived worry (LR= 97.23, $\chi^2(6)$ = 29.60, P=.000) and perceived work difficulty (LR= 100.92, $\chi^2(6)$ = 33.29, P=.000) were found as significant predictors of perceived job stress during Covid-19 pandemic.

Conclusion: This study revealed that job stress is a common prevailing problem among nurses and the COVID-19 pandemic related job stress predictors were perceived safety risk and perceived worry about health while covid-19 exposure and perceived work difficulty as overworked during pandemic. Although efforts were enhanced to support their psychological well-being, more attention should be paid to the mental health of nursing staffs. The study recommends that strong strategy improvements need to be held in the health care institutions to reduce nurses' stress and enable them to combat the ongoing and future occurrences of pandemic effectively.

Keywords: Nurses' job stress, job Stress predictors, COVID-19 Pandemic, Perceived stress

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INTRODUCTION

World Health Organization (WHO) states that COVID-19 is an infectious disease caused by a newly discovered coronavirus (7). Worldwide, the highly contagious respiratory infection caused by the coronavirus 2 (SARS-CoV-2) has caused not only an economic crisis, but an increase in mortality and morbidity, and emotional distress among people. Globally the fatality rate and the consequences of COVID-19 have led to fears, worries, and anxiety.

A dramatic impact wrought by this occurrence on all aspects of our lives by new normalcy style (9). The coronavirus disease 2019 (COVID-19) pandemic has also strained the health system. The FDA has taken numerous actions to help increase supplies of medical equipment needed to fight COVID-19 and protect healthcare workers. The measures were undertaken to manage Healthcare Personnel with SARS-CoV-2 Infection or Exposure to SARS-CoV-2 in terms of handling Confirmed Coronavirus Disease (COVID-19) Patients. (11)

In the outbreak period, among health professionals, especially frontline nurses, faced great challenges and endured higher risks of psychological problems such as depression, anxiety, and insomnia (4). They are being exposed for several working hours per day to COVID infected patients, face several issues that lead to physical/psychological disturbance (1).

Stress is a normal human reaction that happens to everyone resulting in physical, emotional, and intellectual responses whereas Job stress is the harmful physical and emotional responses that occur when the requirements of the job do not match the capabilities, resources, or needs of the worker (24, 25). The global COVID-19 pandemic has created new causes of job-related stress (8). In this light of magnitude, this present study sought to explore perceived job stress level among nurses during the COVID-19 outbreak in Saudi Arabia.

This study aimed to explore perceived job stress level and stress predictors related to COVID-19 pandemic among nurses during the outbreak in Saudi Arabia.

METHODS

Study Design:

An analytical cross-sectional study was conducted in December 2020 during the COVID-19 outbreak first wave in Saudi Arabia. An ethical approval was granted only from the Institutional research committee at College of Applied medical Sciences, Muhayil Aseer, Saudi Arabia.

Sample population:

This study included both male and female nurses who were currently working in ministry of Health hospitals and health centers at Muhayil town area, Saudi Arabia at the time of the study. The participants excluded those who were on long vacation during outbreak.

Sample Recruitment:

The sample size was calculated using Raosoft software (9). The required sample size was estimated at the 95- confidence level with an estimated 50% response distribution and a margin of error of ±5%. The recommended minimum sample size is 169. An online google survey form was sent to all nurses who

were working in Ministry of Health Hospitals and Health Centers at Muhayil town, Saudi Arabia during the first wave of COVID-19 pandemic.

Data collection

Nurses were invited to participate via cell phone text messages. The messages explained the study objectives, the purpose of the study and guided the Nurses to complete the electronic english version questionnaire link. Convenience sampling technique was adopted to collect responses, only 164 working nurses responded.

Description of tool

The The online survey questionnaire was comprised of four parts:

(a) Socio-demographic data of the nurses, such as age, gender, nationality, marital status, and history of chronic diseases.

(b) Work-related characteristics, such as job title, qualification, working unit, working shift system, and working experience in years.

(c) The perceived stress scale (PSS) is a 10-items tool used to measure a Nurse's perception of stress over the past month. The PSS (4) is a validated, reliable (Cronbach's alpha 0.85), easy-to-use, and popular stress questionnaire. A Likert-type 5-point scale was used to capture responses in the PSS (never-0, almost never-1, sometimes-2, fairly often-3, and very often-4). The total sum score of PSS can range from 0 to 40 where the stress levels are 0 considered as No Stress, 1-13: low stress, 14-26: moderate and 27-40: high stress.

d) To assess the Nurse's perceived Job stress predictors, Covid pandemic related Perceived job stressor variables of 4 items questionnaire developed by researchers. The internal consistency of the tool reliability was tested using Cronbach's alpha (α= 0.699) and Inter item correlation mean (0.37) (Optimal mean inter-item correlation values range from .2 to .4 as recommended by Briggs & Cheek 1986). This questionnaire (table 4) includes work related perceived worry about health while exposure with covid positive patients, perceived the safety risk of Covid-19 infection with tested positive, perceived fear regard to covid fatality and Perceived work difficulty during covid pandemic. All the statement responses such as "Always/Little/Not at all" were considered as predictive factors of perceived job stress among Nurses.

Statistical analysis

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) version 16.0 software for windows (SPSS Inc., September 13, 2007). The percentages and frequencies were calculated for all nominal variables for the different items of the PSS-10 and Nurses' perceived job stress Predictor questionnaire-4. Also, we calculated the mean, median, and standard deviation ranges of the total score of the PSS-10. The significance of association of job characteristics with perceived stress score was analysed using in contingency tables by Pearson's chi-square test (categorical variables). To explore COVID-19 pandemic -related predictors associated with perceived job stress, multinominal logistic regression analysis was performed using the main effects method (17). In this regression model, the PSS score stress level was used as a dependent variable, while categorical variables were as perceived fear, perceived worry, and perceived safety risk and perceived work difficulty were measured as

predictive factors. Results are considered significant for P-values below 0.05 (P < 0.05).

RESULTS

Socio demographic Characteristics of Enrolled Nurses

Demographic characteristics of nurses who filled the online questionnaire are reported in Table 1. Most participants were almost equally distributed between <25 -40 years age categories, with only few 3 nurses (1.8%) aged more than 50 years old; 132 (80.5%) study subjects were female nurses. More than a half of our sample was married (54.9%) the majority (73.8%) 121 nurses were belonging to Saudi nationality. However, none of the sociodemographic characteristics of the nurses were associated with their perceived job stress levels.

In Table 2 stated that less than half of the nurses (81) 49.3% were working in a COVID-19 Unit, the majority 73.3% (22) nurses were holding a job position as head nurse reported moderate level of stress. The following job characteristics associated with their perceived job stress that are working unit (p=0.007) and nurses 'qualification (p=0.022), also the years of working experience (p=0.035) at 0.05 significance level respectively. Regarding the history of chronic health problems among studied nurses, the predominant one was lower back pain (32.3%) and then migraine headache (14.7%) depicted in figure 1.

Nurses' perceived job Stress predictors during Covid-19 pandemic

Figure 4 shows that most of the Nurses 67 (40.9%) were reported little perceived safety risk, and only 81(49.4%) of nurses were addressed that not at all perceived worry about health due to exposure with positive patients, and many of the nurses 67 (40.9%) experienced work difficult during COVID– 19, then 62 (37.8%) nurses perceived fear concerning Covid fatality during Pandemic peak in Saudi Arabia.

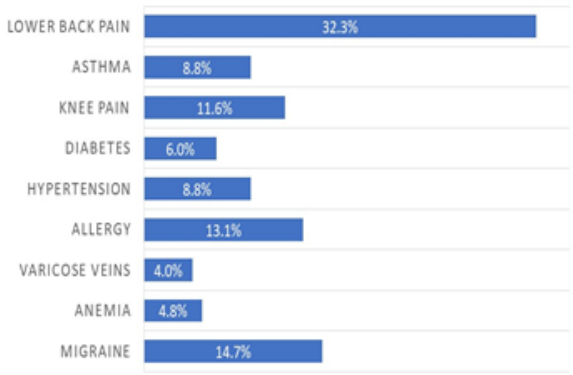

Figure 1. History of Chronic Health Problems Among Nurses

Nurses' perceived job Stress during Covid-19 pandemic

The descriptive statistics revealed that the Standard deviation (SD) 8.308 and overall mean Perceived job stress score was 21.8 on a 0-40 range PSS scale that depicts moderate stress level during pandemic period (Figure 2). The large (97.57 %) number of the nurses experienced job stress during peak time of Corona virus spread and more than half (59.76 %) of the 98 nurses had moderate level of job stress, 45 nurses had (27.44%) High stress, and 17 had (10.37%) low stress (Figure: 3).

Figure 2. Mean score of perceived stress related to Covid-19 pandemic

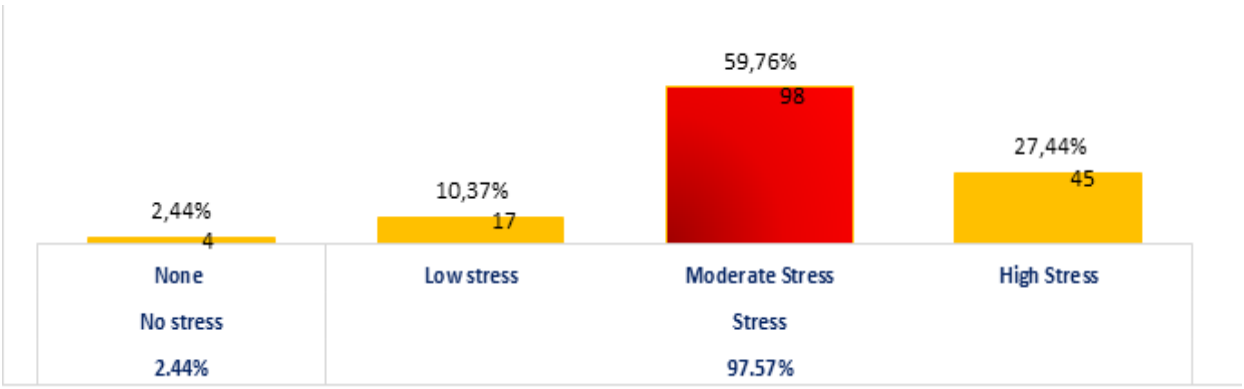

Figure 3. Nurse's Covid-19 pandemic related perceived job stress level

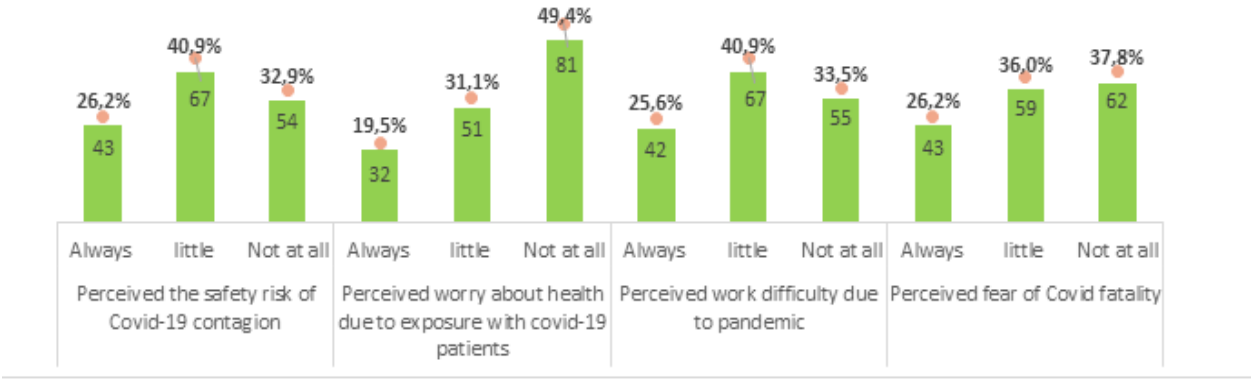

Figure 4. Nurses' perceived job stressors related to Covid-19 pandemic

Table: 1 Socio demographic Characteristics of Nurses (N=164)

	Perceived job Stress Level		
	Frequency (n) %	Chi square $_{df}$	P value
Gender			
Male Nurses	(32) 19.5 %	3.686_{3}	.297
Female Nurses	(132) 80.5%		
Age			
<25 – 30 years	(79) 48.2)	12.874_{9}	.168
31- 40 years	(74) 45.1%		
41-50 years	(8) 4.9 %		
>50 years	(3) 1.8%		
Nationality			
Saudi	(121) 73.8%	19.538_{12}	.076
Philippine	(22) 13.4%		
Indian	(14) 8.5%		
Egyptian	(2) 1.2%		
other nationality	(5) 3.0%		
Marital status			
Married	(90) 54.9 %	16.634_{9}	.055
Single	(69) 42.1%		
Separated	(3) 1.8%		
widowed	(2) 1.2%		

Table:2 Nurses' job Characteristics and perceived Job stress level

Job Characteristics	None	Low	Moderate	High	Chi-square $_{df}$	P- value
1. Nursing Qualification	4.1 % (2)	18.4% (9)	63.3% (31)	114.3% (7)	9.638_3	0.022
Diploma						
Bachelor	1% (2)	7.0% (8)	58.3% (67)	33.0% (38)		
2. Working Unit	2.4% (4)	6.1% (10)	32.9% (54)	9.1% (15)		
Non Covid unit					10.527_3	0.007
Covid Unit	.0% (0)	4.3% (7)	26.8% (44)	18.3% (30)		
3. Working Shift	.6% (1)	6.7% (11)	28.0% (46)	15.9% (26)	3.831_3	0.280
Rotated shift						
Same shift	1.8% (3)	3.7% (6)	31.7% (52)	11.6% (19)		
4. Working Experience	.0% (0)	2.4% (4)	9.8% (16)	5.5% (9)	16.725_9	0.053
Fresher < 1 year						
1- 10 years	.0% (0)	3.0% (5)	31.7% (52)	15.9% (26)		
11-20 years	2.4% (4)	4.9% (8)	16.5% (27)	6.1% (10)		
>20 years	.0% (0)	.0% (0)	1.8% (3)	.0% (0)		
5. Job Position	.0% (0)	.0% (0)	6.1% (10)	3.0% (5)	11.187_{12}	0.513
Nurse Intern						
Staff nurse	1.8% (3)	8.5% (14)	27.4% (45)	15.2% (25)		
Head Nurse	.6% (1)	.6% (1)	13.4% (22)	3.7% (6)		
Nurse Specialist	.0% (0)	.6% (1)	7.3% (12)	3.7% (6)		
Nurse Supervisor	.0% (0)	.6% (1)	5.5% (9)	1.8% (3)		
6. Work related exposure to Covid- 19 patients care	2.4% (4)	6.1% (10)	34.8% (57)	20.7% (34)	6.507_3	0.089
Yes						
No	.0% (0)	4.3% (7)	25.0% (41)	6.7% (11)		
7. Nurses who Tested Covid -19 Positive	.6% (1)	4.3% (7)	23.3% (38)	12.9% (21)	1.153_3	0.764
Yes						
No	1.8% (3)	6.1% (10)	36.2% (59)	14.7% (24)		

Table 3 – Multinominal Logistic Regression model parameter Estimates: Covid -19 pandemic related Nurses' perceived Job stressors

Stress Category		Low stress					Moderate stress					High stress				
Perceived Stressors		B	Std. Error	P value	Exp(B)	95% CI	B	Std. Error	P value	Exp(B)	95% CI	B	Std. Error	P value	Exp(B)	95% CI
1.Perceived safety risk	Not at all	.970	2940.76	1.00	2.637	.000-.[b]	.737	1808.	1.000	2.090	.000 -[b]	-17.281	2965.	.995	3.125E-8	.000-[b]
	Little	15.735	2318.71	.995	6.817E6	.000-.[b]	17.66	.565	.000	4.68E7	1.549E7-1.417E8	15.591	.000	.995.	5.904E6	59037.1-5903.10
	Always	0[c]	.	.	.		0[c]	.	.	.	.	0[c]	.	.	.	.
2.Perceived worry	Not at all	-.436	3291.51	1.00	.646	.000 -.[b]	-19.26	2863	.995	4.31E-9	.00-[b]	-36.806	4056	.993	1.036E-16	.000 -[b]
	Little	16.482	4467.302	.997	1.439E7	.00 -.[b]	-1.25	4162	1.000	.286	.00-[b]	-2.91	4162.	.999	.054	.000 -[b]
	Always	0[c]	.	.	.		0[c]	.	.	.	.	0[c]	.	.	.	.
3.Perceived work difficulty	Not at all	15.588	2699.92	.995	5.885E6	.000-.[b]	-1.588	1690	.999	.204	.00-[b]	-4.318	1690.	.998	.013	.000 -[b]
	Little	13.872	2551.05	.996	1.058E6	.00 -[b]	15.379	.574	.000	4.77E6	154830-1.472E7	13.826	.000	.	1.010E6	104.52 104.52
	Always	0[c]	.	.	.	.	0[c]	.	.	.	.	0[c]	.	.	.	.

Reference Category: No stress

Table 4 : COVID-19 Pandemic related job stress predictors Questionnaire

Items	Responses
1. Have you been perceived the safety risk of Covid-19 contagion?	Always, Little, Not at all
2. Have you felt worried about your health while exposure with covid positive patients?	Always, Little, Not at all
3. Have you felt difficulties as over worked to handle the patients during pandemic?	Always, Little, Not at all
4. Have you felt fear of covid fatality while providing nursing care for patients?	Always, Little, Not at all

Multinominal Logistic Regression Model of Nurse's job stress predictors related Covid-19 pandemic

Finally, the analysis plan considered a major effect method via using the multivariate logistic regression analysis. Table 3 displays the findings from the analysis model. Based on the model fitness LR test p value .000, the model containing the full set of predictors represents a significant improvement in fit (Likelihood Ratio χ^2 (24) = 188.578, P=.000). Pearson value is an additional chi-square goodness of fit test (χ^2 (132) = 32.531, p=1.000) for this model, when non-significant, that provides further evidence of a well-fitting model. Based on McFadden's, the full model containing our predictors represents a 58.2% improvement in fit. The overall classification accuracy for the model predicting category membership on the Dependent Variable (Job stress level). was 78.0%. In this model, the likelihood ratio and chi-square tests of the each (Independent Variables) predictors shown that a direct effect of perceived safety risk (LR= 95.53, χ^2 (6) = 27.91, P=.000), perceived worry (LR= 97.23, χ^2(6) = 29.60, P=.000) and perceived work difficulty during Covid-19 pandemic (LR= 100.92, χ^2(6) = 33.29, P=.000) were estimated as significant predictors of covid -19 pandemic related perceived job stress among nurses working in Saudi Arabia.

The Model parameter Estimates presented in the table 3. It shows that Nurses who perceived little safety risk of Covid-19 contagion were significantly predicted to have a moderate stress 17.66 times more than No stress category stress (Beta = 17.66, P value= .000). Secondly Nurses who perceived little work difficulty as over worked to handle the patients during pandemic Covid-19 were also significantly predicted to have a moderate stress 15.37 times more than No stress category stress (Beta = 15.37, P value= .000) respectively.

DISCUSSION

It is important to investigate perceived job stress level among health care providers during

COVID-19 pandemic. Especially nurses, are in frontline battle during this pandemic that cause emotional exhaustion which may lead to burnout gradually (13). We investigated in this study, the percentage of nursing staffs who were under stress and their job stress predictors related to Covid-19 pandemic.

Nurses job stress level and Sociodemographic Characteristics Association

Regarding sociodemographic characteristics of Nurses, we found that none were associated with their significantly associated with their job stress. Our study results are in line with some studies, that there was no relationship between the mean of perceived job stress of nurses and their gender stated in Alyahya.et.al, Farraji.et,al (2, 10). However, unlike our present study results, Romano.et.al and Shin et.al. (18, 23) reported that gender was significantly associated with nurses' stress. In our study, nurses' age group was not statistically significant. This is also

similar with these findings of Alyahya.et.al., Farraji.et,al and Romano et al., studies (2,10,18).

It is inferred that socio demographic characteristics may not have considerable impact on job stress concerning covid- 19 pandemic among nurses

Nurses job stress level and Job Characteristics Association

In our study, we investigated that some of the following job characteristics are significantly associated with Nurses' job stress level such as Nursing Qualification (P=0.035*) Working Experience (P=0.035*) and nursing Unit: Covid unit and non-covid unit (P=0.007*). It is evident that job stress is much related to particularly their working experience, level of qualification and working unit. It is apparent that working unit plays a greater role in causing job stress among nursing during outbreak.

The findings of this study have been shown to be consistent with the study undertaken by Bellanti et.al Shin et.al (3, 23) where Participants working in the Covid unit and ICU had a significantly higher than the other departments while those working in the General Ward.

In this current study, we found that significant association between the nurses' perceived job stress and their work experience (26).

Concerning the health problems experienced by the nurses, the very common problems were lower back pain (32.3%) and then migraine headache at the rate of (14.7%). Nurses are at a higher risk and six times higher prevalence to have lower back pain and back injury (5). These health problems could be from prolong standing and physical exhaustion during patient care. The other predominant health problem found in our results was headache, perhaps it might be due to keen concentration in clinical challenges related to their work. According to Atlanta-based Headache Center of Peachtree Neurological Clinic, headache usually stress-related; Still, headaches may indicate another underlying health issue. Our study results are almost parallel with study done by Kilic.et.al and Sabra.et.al (15, 19).

Nurses perceived job Stress during Covid-19 pandemic

The mean value of perceived job stress score was 21.8 on a 0-40 range PSS scale that depicts moderate stress. The overall nurses (97.57%) had experienced job stress during pandemic, of them (59.76 %) had moderate stress, and (27.44%) had high stress and then only (10.37%) experienced low stress respectively. It is evident that almost certainly all the nurses are facing job stress. The other recent study results that the Nurses stress level was moderate to high (10, 21).

COVID-19 related job stress predictors among Nurses

It is not surprising that nurses reported significantly higher mean score of perceived job stress. The literature has shown that, compared to other professionals, healthcare providers, especially nurses, have a higher risk of developing emotional distress like depression, anxiety, and burnout due to work-related stress (12). There are stress factors that appeared to increase the risk of developing job stress like perceived safety risk of covid-19 contagion, perceived worry about health while exposure covid-19 patients and perceived work difficulty as over worked to handle the covid-19 patients.

The recent studies conducted on nurses showed that predictors of job stress in the professional environment include the perceived fear of contracting

COVID-19, a decrease in the level of safety while conducting emergency medical procedures and nurses who tested positive to corona virus (14,16, 28). Of note, in our research only 3 significant job stress predictors related to Covid-19 revealed among nurses.

Limitations

This study limited only on nurses working in the government hospitals located in Muhayil town area, Aseer province of Saudi Arabia. And the second limitation was that only subjective health problems and job stress mentioned by nurses themselves were evaluated. Thirdly, the completion of job stress predictors model needs to be added with few more Covid-19 pandemic related factors. Un fortunately the sample size was less than recommended size just with 164 nurses only.

CONCLUSION

The substantial study findings reflected that job stress was perceived by almost all the nurses (97.57%) during pandemic and the job stress mean score was 21.8 which represents moderate level of perceived stress. The significant job stress predictors related to Covid-19 were "perceived safety risk, perceived worry about health while exposure and perceived work difficulty as over worked to handle the covid-19 patients". Therefore, this study recommends that the nurses need to be prepared well by strong strategy improvements for reducing the nurses' stress to pursue their efforts in more meaningful experience during pandemic (22, 27). A Longitudinal research studies need to be conducted to follow up on nurses' stress and develop evidence-based interventions.

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Laboratory Parameters and Clinical Courses in Covid-19 Prognosis: Case Reports

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Abstract

Coronavirus disease 2019 (COVID-19) has spread rapidly around the world since the outbreak in Wuhan, Hubei Province, China in 2019. COVID-19 is an infection caused by the novel coronavirus SARS-CoV-2.

In case 1, there were low white blood cells. In case 2, mild lung involvement was observed on his chest computed tomography. In case 3, high levels of ferritin and procalcitonin in blood parameters were found remarkably. During the COVID-19 pandemic, symptoms and laboratory parameters differ from person to person. Timely diagnosis, isolation and initiation of necessary treatments are necessary to significantly reduce the risk of disease transmission. Several biomarkers have been identified that could potentially assist risk classification models to predict severe and deadly COVID-19.

Keywords: SARS-Cov-2, hematologic parameters, prognosis, COVID-19

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INTRODUCTION

Virus infection with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) can be asymptomatic or causes mild to severe symptomatic disease (1,2).

There is an incubation period of 1 to 14 days in the pathogenesis of COVID-19 (3-5).

COVID-19 symptoms include fatigue, mild chills, fever, sore throat, shortness of breath, dry cough, severe respiratory distress, and pulmonary

pneumonia (6,7). Especially in patients with severe disease, fatigue, myalgia or arthralgia, hepatic and renal dysfunction, leukopenia, thrombocytopenia, lymphocytopenia, and high inflammatory biomarkers, as well as respiratory failure, have been identified. Clinical studies have reported elevated liver enzymes in COVID-19 patients (8,9).

CT imaging changes are common in COVID-19 patients. Covid-19 involves bilateral multilobular subsegmental consolidation of the lungs in the early stages followed by multiple mottling and ground-glass opacity (10).

Hypersensitive troponin and higher levels of aspartate aminotransferase and a long with lymphopenia, leukopenia, thrombocytopenia and RNAaemia, were observed in the blood laboratory profile of COVID-19 patients (1,11,12).

CASE-1

I am 41-year-old female. I have a history of severe atypical pneumonia about 1.5 years ago.

On November 10, 2020, I felt the first symptom of Covid-19 as fatigue in the evening in Ordu.

On November 11, 2020, I felt tiredness, weakness, mild chills. The real-time reverse transcriptase-polymerase chain reaction (RT-PCR) for SARS-CoV-2, performed by taking nasal and pharyngeal swabs was found to be positive. No lung involvement was observed in my chest X-rays, except for my previous lung sequelae (Figure 1).

Regarding hematologic parameters hematocrit and haemoglobin were normal, White blood cells (WBC) were detected low (WBC:2.70×109/UL, normal range 4.49-12.6×109 /UL), CRP washigh, (CRP: 6.3 mg/L, normal range 0-5 mg/L), aspartate aminotransferase (AST): 18 U/L (normal range 0-32 U/L), alanine aminotransferase (ALT): 9 U/L (normal range 0-33 U/L), ferritin was within normal limits.

I completed my treatment with favipiravir and anticoagulant drugs. When viewed 10 days after the initiation of treatment (on November 22, 2020), my ALT and AST values increased, AST: 59 U/L (normal range 0-32 U/L), ALT: 91 U/L (normal range 0-33 U/L), CRP was detected as 0.3mg / L (within normal range). On November 28, 2020, my hematological parameters are completely normalized (AST: 16 U/L, ALT: 29 U/L and others)

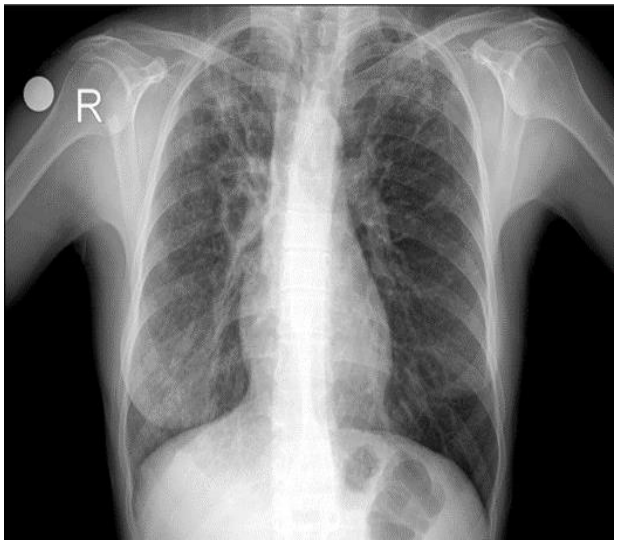

Figure 1. Image of previous lung sequelae

CASE-2

75-year-old my father, who has Parkinson's disease, showed symptoms simultaneously with me. On November 11, 2020, my father had complaints of weakness, tiredness and mild cough. RT-PCR test of my father who went to the hospital for testing was positive. His chest computed tomograpy (CT) showed mild bilateral ground-glass opacities associated with COVID-19 (Figure 2).

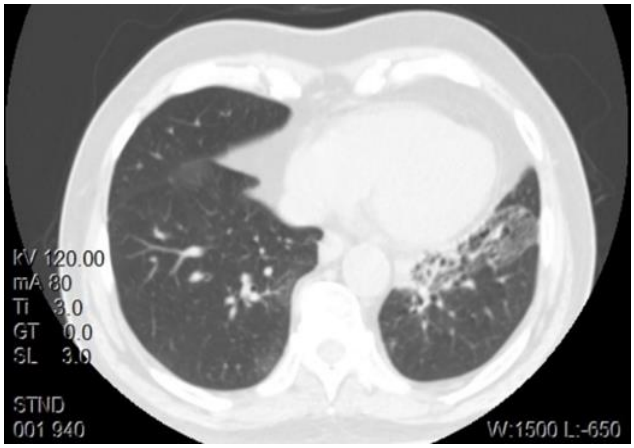

Figure 2. Mild bilateral ground-glass opacities

Despite his chronic illness, my father survived Covid-19 under home surveillance. My father was given only favipiravir and anticoagulant drugs. Fortunately, another problem was not observed.

CASE-3

On November 12, 2020, the PCR test was positive in my husband, a 45-year-old healthy man. My husband's chest CT showed mild bilateral ground-glass opacities associated with COVID-19 (Figure 3).

Figure 3. Mild bilateral ground-glass opacities

At first, only ferritin was detected abnormally in blood parameters. Ferritin:587µg/L (normal range 30-400 µg/). He was given the same medication (favipiravir and anticoagulant drugs). Despite the high ferritin level, my husband initially had no symptoms. On November 17, 2020, ferritin was 747 µg/L, erythrocyte sedimentation rate (ESR):29 (normal range 0-20), CRP was 0.7 mg/L (within normal limit), ALT:28 U/L, AST:23 U/L (within normal limits).

On November 20, 2020, ferritin and CRP were too high, (ferritin:1402 µg/L, CRP: 73mg/L), ALT:97 U/L (normal range 0-33 U/L), AST:47 U/L (normal range 0-32 U/L).

On November 23, 2020, ferritin and CRP were too high, (ferritin:1517 µg/L, CRP: 107.3mg/L), ALT:80 U/L (high), AST:39 U/L (high), WBC:11.44x109/UL, PLT (platelet):130x103/UL (normal range,150-450 x103/UL).

Meanwhile, symptoms such as fever, mild chill, excessive sweating, myalgia, weakness, fatigue appeared. Temperature: 38.3 °C (100.9 °F). Leukocyte was found to be quite high in urine analysis, leukocyte>204.55 (normal range, 1-4) HPF, erythrocyte:2 (normal range, 1-4) HPF. Infection detected in urine and antibiotic treatment was given (as Ciprofloxacin 500mg).

On November 25, 2020, ferritin:1188 µg/L, CRP: 108mg/L, ALT:45 U/L, AST:20 U/L. Prokalsitonin:0.495ng/mL (normal range, 0-0.046 ng/mL).

In urine, leukocyte:38 (1-4) HPF, erythrocyte:6 (1-4) HPF determined. There was a significant decrease in leukocyte in urine. The next day, symptoms began to regress.

On November 28, 2020, ferritin:1055 µg/L, CRP: 24.7mg/L, ALT:52 U/L, AST:35 U/L. In urine, leukocyte:2 (1-4) HPF, erythrocyte:<1.14 (1-4) HPF determined.

On December 06, 2020, ferritin:1011 µg/L, CRP: 20mg/L, ALT:45 U/L, AST:20 U/L. WBC:6.33x103/UL, PLT:283x103/UL. In urine, leukocyte<1.14 (1-4) HPF, erythrocyte:<1.14 (1-4) HPF determined.

On December 10, 2020, ferritin:919 µg/L, CRP: 0.5mg/L, ALT:43 U/L, AST:20 U/L.

On December 17, 2020, ferritin:747 µg/L, CRP: 0.5mg/L, ALT:28 U/L, AST:23 U/L, ESR:29 (normal range, 0-20).

DISCUSSION

Despite my (case 1) severe atypical pneumonia sequelaes, my Covid-19 symptoms were mild. No lung involvement was observed in my chest X ray except for my previous lung sequelae.

Regarding hematologic parameters: hematocrit, haemoglobin, platelet count, D-dimer were normal. White blood cells (WBC) were detected low (WBC:2.70× 109 /L), (normal range: 4.49-12.6 /UL), CRP were detected high level, (CRP: 6.3 mg/L), (normal range: 0-5 mg/L). While WBC is generally expected to increase, WBC was found to be in a decreased value in my hematologic parameters.

Although my father with Parkinson's disease (case 2) had lung involvement, Covid-19 symptoms were mild. Mild cough, weakness and myalgia that started on the 3rd day after possible contact continued for about 2 days.

CT imaging changes are common in Covid-19 patients (10). Although mild lung involvement was found in case 2 and 3, no progress to severe pneumonia was observed.

According to Gutiérrez et al. Lymphopenia (<1000 cells / mL), neutrophilia (> 10,000 cells / mL), high C-reactive protein (> 10 mg / dl), elevated LDH (> 350 IU / L), D-dimer (> 1 mg / ml), increases in hepatic transaminases, troponin and ferritin were determined as prognostic markers (13).

In case 3, a progressive increase in ferritin was detected after PCR positivity. When ferritin peaked in my husband's blood, his clinical symptoms peaked too.

Case 3 had a partial increase in procalcitonin level, procalcitonin: 0.495ng / mL (normal range: 0-0.046 ng / mL). This increase was supportive of the urinary tract infection detected as secondary infection with Covid-19.

According to literature findings, the presence of SARS-CoV-2 has rarely been shown in urine swabs of COVID-19 patients (8-14). The development of urinary tract infection in our COVID-19 patient (case 3) may be considered as a possible complication of COVID-19. Observing a significant increase in WBCs in severe Covid-19 may indicate a worsening clinical course. According to the literature (13), while the decreases are observed in lymphocytes, monocytes and eosinophils, the increase in WBC sappears to be triggered by high neutrophils. Regarding immunological biomarkers, significantly increases were detected for serum ferritin and IL-6 in non-survivors compared to survivors. Therefore, it is recommended that both parameters be used to understand prognosis during hospitalization in COVID-19 patients.

These elevations, together with high CRP, indicate the development of a systemic inflammatory response syndrome, a severe form of the disease (15).

In hospitalized people with respiratory distress, clinicians should consider the WBC count, platelet count, lymphocyte count, serum ferritin level and IL-

6 as potential signs of progression to critical illness. Since procalcitonin is considered to be a marker of secondary bacterial infection commonly observed in non-survivors, it should be measured regularly (16,17).

Clinical symptoms were longer and more severe in case 3, therefore ferritin, CRP, ESR, procalcitonin were useful in clinical surveillance. Laboratory blood parameters differed in case 1 and case 3. Detailed blood tests were not performed for case 2, who was in a different city.

CONCLUSION

During the COVID-19 pandemic, symptoms and laboratory tests differ from person to person. Timely diagnosis, isolation and initiation of necessary treatments are necessary to significantly reduce the risk of disease transmission. Several biomarkers have been identified that could potentially assist risk classification models to predict severe and deadly COVID-19.

As a result, it is thought that it will be useful to examine the WBC count, platelet count, lymphocyte count, serum ferritin level and IL-6 as markers for potential progression to critical disease in Covid-19 patients with respiratory distress.

Ethics Committee Approval: Approval was received for this study from the patient.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept: MAC. Design: MAC., Literature Search: MAC. Data Collection and Processing: MAC. Analysis and/or Interpretation: MAC., Writing: MAC.

Conflict of Interest: No conflict of interest was declared by the author.

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