




Determination of Antidepressant Drug Use Among Inpatients in Medical and Surgical Clinics

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ABSTRACT

Objective: This cross-sectional study was performed to determine antidepressant drug use among inpatients in medical and surgical clinics.

Methods: The study sample consisted of 478 inpatients from a state hospital, between December 1, 2015 and January 1, 2016. The information form was applied to the patients. Number and percentage distribution were used for data analysis.

Results: Of the 478 patients, 34.5% had visited a psychiatrist once in their lifetime, 13.6% were diagnosed with depression, and 13.8% did not know the diagnosis of mental disease; 32.2% were suggested medication by their doctor, 16.7% did not know the name of this medication, and 13.2% stated that the suggested drug was antidepressant. Moreover, 24.9% of the patients were known to use antidepressant at least once in their lifetime, and 16.3% were still using antidepressants. Among patients using antidepressants, 32% continued using this drug upon doctor's recommendation and 13.6% continued with the diagnosis of depression.

Conclusion: It might be concluded that one-fourth of the patients used antidepressant once in their lifetime; more than one-half of these patients were still using antidepressants, and most of them were using the drug upon doctor's recommendation without any knowledge about antidepressants.

Keywords: Antidepressant drug, nursing, patient

1. INTRODUCTION

According to the Economic Policy Research Foundation of Turkey, the rate of antidepressant use increased 65% in the last 5 years. The consumption was 20 million boxes in 2005 and increased over 34 million in 2010. Antidepressant consumption was 0.29 boxes per capita in 2005, but it increased to 0.45 in 2010 (1). According to the Intercontinental Marketing Service (IMS) data, the growth rate of the antidepressant sales was 160% in the last 9 years in Turkey (2). This increase might be a result of prescriptions by physicians other than psychiatrists and over the counter sales. Psychiatric consultation requested for the hospitalized patients in the departments of the internal medicine, surgery, and physiotherapy might also be responsible for the growth in the consumption of antidepressants. Recent studies have reported that there was an increase in the psychiatric consultations, and depression was one of the most common diagnoses during these consultations; consequently, the use of the antidepressant drugs was increased (3-5). The consultation was requested mostly by the departments of internal medicine, neurology, neurosurgery, physiotherapy and rehabilitation, and pulmonology.

Investigation of the studies focused on psychiatric consultation revealed that the most common diagnosis related to the

psychiatric diseases was depressive disorders, and the most commonly recommended drugs for the treatment of this disease were antidepressants (3-7). As the most common diagnosis among the hospitalized patients was depression, antidepressants were inevitably the most frequently used medications. Nevertheless, the frequent use of this drug group might be associated with certain problems. Several studies in the literature have demonstrated the emergence of extremely severe side effects related to antidepressants. The analysis of these studies showed following side effects encountered: dry mouth, constipation, weight gain, diarrhea, insomnia, yawning, urination problems, drowsiness, headache, and nausea (8, 9). Of the available studies, Ashton et al. (10) reported that patients prescribed treatment for depression reported "gained a lot of weight," "unable to have an orgasm," "lost interest in sex," "unable to have erection," and "tired during the day" (10).

In addition to these severe side effects, uncontrolled use and misuse of the antidepressive agents might cause life-threatening complications. Studies have shown that antidepressants were one of the most frequently encountered drugs in intoxication cases (11-13). Furthermore, according to the investigations, antidepressants were preferred for suicide

in 74.4% attempts (11). In light of these data, we believe that it becomes important to determine how patients access these drugs, whether there is a real need for their use, and who are prescribing them. Treatments administered by the physicians (except psychiatrists) were often insufficient regarding the appropriate and required dosage and the treatment duration. Consequently, the disease became often chronic with labor loss, and mortality increased due to emergence of the untreated disease (2). In light of this information, it should be emphasized that physicians should be more cautious during the diagnosis and prescription of the antidepressive agents. Additionally, it should be considered that nurses responsible for the execution of the physicians' orders also have a major responsibility for the implementation the treatment (14). It is also necessary that nurses inform patients about the side effects, what should be done if the side effects occur, importance of consistent compliance with the treatment, interactions with other substances, periodic tests, time of the onset of the action, and the importance of gradual discontinuation of the treatment (15). We believed that this study would be an important step in indicating the current condition related to antidepressant use and in determining the way for solving the detected problems. In this regard, our objective was to find out the antidepressant use among hospitalized patients in the clinics of internal medicine and surgery.

2. METHODS

2.1. Study Design

This study was a cross-sectional, descriptive survey design. Subjects In total, 478 hospitalized patients treated in the internal medicine and surgery clinics of the Giresun Prof. Dr. İlhan Özdemir Public hospital between December 1, 2015 and February 1, 2016 were included and consented voluntarily to participate in the study.

2.2. Materials

Investigators prepared an information form for the patients, which was in line with the relevant literature (2, 3, 9, 16-18). The information form contained 33 questions referring the demographic characteristics of the patients, such as the age, gender, and education status and other characteristics, such as visiting a psychiatrist, antidepressant use, and encountered side effects.

2.3. Process

Before the start of the study, approvals of the administration of the Giresun Prof. Dr. İlhan Özdemir Public hospital and the ethics committee of the General Secretary of the Giresun Prof. Dr. İlhan Özdemir Public Hospitals Union were obtained. The study was conducted according to the principles of the Helsinki Declaration. Furthermore, every

patient was informed about the objective of the study. It was explained that they could chose to discontinue from the study at anytime and this act would not affect their treatment. Written consent was also obtained. The enrolled patients (who met the inclusion and exclusion criteria of the study) were questioned within the first week of their hospitalization in their rooms while they were alone.

Inclusion criterias were age >18 years, treatment in the hospital, stay at hospital at least 1 week, no difficulty in communication. Exclusion criterias were stay at hospital <7 days, outpatient, unconscious patients.

2.4. Statistical Analysis

Statistical Package for Social Sciences (SPSS In.; Chicago, IL, USA) for Windows, version 16.0, was used for data entry and analysis. The analysis was conducted with numeric and percentage distribution.

3. RESULTS

Some of the characteristics of the patients are summarized in Table 1; 29.9% of the patients were in the age group of 41–60 years, 52.1% were females, 47.9% were primary school graduates, and 84.5% were not working. In addition, 45.8% of the patients were known to live in small towns, and 53.9% had an income equal to their expenditure (Table 1).

Table 1. Patient characteristics

		n	%
Age group	≤20 years	4	0.8
	21–40 years	49	10.3
	41–60 years	143	29.9
	61–80 years	186	38.9
	≥81 years	96	20.1
Gender	Female	249	52.1
	Male	229	47.9
Educational status	Illiterate	184	38.5
	Primary school	229	47.9
	Middle school	32	6.7
	High school and university	33	6.9
Working status	Working	74	15.5
	Not working	404	84.5
Marital status	Married	327	68.4
	Single	151	31.6
Living location	Village	219	45.8
	Town	137	28.7
	City	122	25.5
Income level	Income equal to expenditure	258	53.9
	Income less than expenditure	207	43.3
	Income more than expenditure	13	2.7

Table 2 shows that 34.5% of the patients visited a psychiatrist at least once, 13.6% were diagnosed with depression, 13.8% were not aware of the psychological diagnosis they received, 32.2% had a medication recommended by the physician, 16.7% did not know the name of the drug, and 13.2% had an antidepressant as the recommended drug.

Table 2. Patients’ characteristics related to visiting the psychiatrist and psychiatric drug use

		n	%
Visit to a psychiatrist	Visited	165	34.5
	Not visited	313	65.5
Psychiatrist visiting time	Not visited	313	65.5
	1–10 years	149	31.2
	≥11 years	16	3.3
Psychiatric disorder	I don’t have a disease	313	65.5
	I don’t know the diagnosis	66	13.8
	Major depression	65	13.6
	Schizophrenia	1	0.2
	Anxiety disorder	8	1.6
	Substance abuse	1	0.2
	Dementia	13	2.7
	Sleep disorder	10	2.1
	Bipolar affective disorder	1	0.2
Psychiatrist suggestion	Not visited	313	65.5
	Use of medication	154	32.2
	Hospitalization	1	0.2
	No suggestion	10	2.1
Type of medication	Not visited	313	65.5
	No medication	6	1.3
	I don’t know brand name of drug	80	16.7
	Antidepressant	63	13.2
	Anxiolytic	3	0.6
	Antipsychotic	9	1.9
	Sedative-hypnotic	4	0.8
Duration of drug use	Not visited	313	65.5
	Not use a drug	12	2.5
	1 year and ago	96	20.1
	2–10 years	49	10.3
	≥11 years	8	1.7

It was also observed that 24.9% of the patients used an antidepressant at least once in their lifetime, and 16.3% of the patients were using an antidepressant during the study. In addition, 32% of the patients were using an antidepressant agent, which was recommended by a psychiatrist and 13.6% were continuing to use this drug with a diagnosis of depression (Table 2).

Table 3 shows the side effects most commonly encountered by the patients who used an antidepressant at least once in their lifetime: dryness in the mouth (33.6%), weakness (29.4%), dysmnesia (29.4%), lightheadedness (27.7%), restlessness (26.1%), somnolence (26.1%), hot flash (22.7%), and dizziness (21%; Table 3).

Table 3. Adverse effects of antidepressant drugs (n=119)

Adverse effects	Present		Absent	
	n	%	n	%
Sweating	19	16	100	84
Dryness in the mouth	40	33.6	79	66.4
Hot flash	27	22.7	92	77.2
Lightheadedness	33	27.7	86	72.3
Flutter	22	18.5	97	81.5
Urinary retention	10	8.4	109	91.6
Loss of appetite	14	11.8	105	88.2
Constipation	10	8.4	109	91.6
Sleepiness	20	16.8	99	83.2
Weakness	35	29.4	84	70.6
Loss of weight	7	5.9	112	94.1
Loss of sexual desire	7	5.9	112	94.1
Restlessness	31	26.1	88	73.9
Increased appetite	15	12.6	104	87.4
Dysmnesia	35	29.4	84	70.6
Nausea	23	19.3	96	80.7
Increased weight	6	5	113	95
Thoughtfulness	23	19.3	96	80.7
Irritability	21	17.6	98	82.4
Somnolence	31	26.1	88	73.9
Defect of vision	13	10.9	106	89.1
Dizziness	25	21	94	79

Table 4 shows that two-thirds of the patients stated that the symptoms relieved partially, and only 47.1% of them expressed that they would use the drug along the duration recommended by the physician. Patients who did not use the drug declared the following reasons: fear of addiction (21.6%), belief that it will not solve their problems (13.7%), and fear of side effects (17.6%).

Table 4. Patient thoughts regarding antidepressant drug use

	n	%	
Did antidepressant drugs relieve the symptoms of the disease? (n=119)	Symptoms relieved completely	20	16.8
	Symptoms relieved partially	78	65.5
	Symptoms not relieved	21	17.6
How long do you plan to use antidepressant drugs? (n=119)	Duration recommended by the physician	56	47.1
	Duration symptoms relieved completely	11	9.2
	At least 6 months	1	0.8
	Discharged from the hospital	2	1.7
	I don’t think to use drug	27	22.7
	I don’t know	22	18.5
Reasons of not using antidepressant drugs after discharged (n=51)	Fear of addiction	11	21.6
	I think I’m not crazy	1	2.0
	Belief that it will not solve their problems	7	13.7
	Think that my disease relieved completely	15	29.4
	Fear of side effects	9	17.6
	I feel worse when use drugs	4	7.8
	Other	4	7.8
Who provided information about antidepressant drugs (n=119)	Doctors and nurses	113	95
	Pharmacist	6	5

Table 5 shows that 99.2% of the patients did not know the effects of the drugs, 100% did not know the time of the onset of the effect, 96.6% did not know the duration of the treatment, 97.5% did not know when to discontinue the drug, and 99.2% did not know the most important side effects which might emerge during the treatment. However, the patients wished to be informed regarding the effects of the drugs (20%), duration of the treatment (13.4%), possible risk of the drug (13.4%), drug's effects on the body (7.6%), methods of coping with the side effects (2.5%), and addiction potential of the drug (0.8%). Additionally, most of the patients requested this information, particularly from physicians and nurses (Table 4).

Table 5. Patients' knowledge related to level of antidepressant drugs (n=119)

	Know		Not know	
	n	%	n	%
Effects of antidepressant drugs	1	0.8	118	99.2
Time of the onset of the effect of the drugs	-	-	119	100
Duration of the treatment	4	3.4	115	96.6
Time of the discontinuing the drugs	3	2.5	116	97.5
Most important side effects of the drugs	1	0.8	118	99.2

4. DISCUSSION

The objective of our study was to determine the antidepressant use among patients hospitalized in the internal medicine and surgery clinics. In this context, we questioned the prescribing physicians, symptoms aimed to treat with the prescription, awareness about the side effects, the encountered side effects, duration of the treatment, and experienced benefits of the treatment.

One of the findings of our study was that 24.9% of the patients used an antidepressant agent at least once in their lifetime, and 16.3% of them were still using an antidepressant. Overall, 32% of the patients stated that they were using an antidepressant agent according to the recommendation of a psychiatrist.

The studies focused on this topic showed that the rate of the antidepressant use among the hospitalized patients was between 31.4% and 36.3% (4, 6). In a study conducted in Norway, this rate was 21.7% among 4,374 patients treated because of opioid addiction (19). It was reported that 10.5% of 928 patients who visited a psychiatrist used an antidepressant agent, and 73.6% of these patients received their prescription from a physician who was not a psychiatrist (20). In a study, it was determined that 15.6% of the 16,780 heart failure patients, who were not diagnosed with clinical depression, used antidepressants (21).

In another study, it was reported that 33% of 218 heart failure patients used an antidepressant, and 26% were not diagnosed with depression before the antidepressant use; the drug was prescribed by a second-step physician (16). The most commonly prescribed medication in medical and surgical patients was antidepressant. Also, doctors

not specialized in psychiatry were responsible for most prescriptions of antidepressant drugs (17). According to these findings, it might be suggested that the use of antidepressant agents was common abroad as well as in our country, and antidepressant treatment was initiated without prior diagnosis of depression in some patients and probably prescribed by a physician who was not a psychiatrist.

Another finding of our study was that the most common side effects encountered in the patients using an antidepressant at least once in their lifetime were dryness in the mouth, weakness, dysmnnesia, lightheadedness, irritability, somnolence, hot flash, and dizziness. In addition to these side effects, we observed that patients experienced side effects, which might negatively affect their quality of life and interindividual relations, such as decreased libido, palpitation, visual impairment, increase in panic symptoms, inattentiveness, irritability, and dizziness.

A research study has reported that the most common side effects, which were experienced by 811 depression patients using antidepressants, were dryness in the mouth, constipation, weight gain, insomnia and diarrhea (8). Another study has determined that 22% of the patients who had an antidepressant treatment did not comply with the treatment because of the problems, such as weight gain, sexual dysfunction, lack of sexual desire, and weakness (10). The most common side effects of the antidepressant treatments were also headache and nausea (9).

As seen in our study along with studies from abroad, patients often encounter anticholinergic side effects caused by the antidepressants. Moreover, there were other studies demonstrating that extrapyramidal symptoms, such as parkinsonism, acute dystonia, tardive dystonia, and dyskinesia, were seen during the antidepressant treatment (22-24).

The rate of the most common side effect in our study was 33%, although the rate of some side effects was up to 74% in the studies previously mentioned. As the patients experienced the side effects before the onset of the therapeutic effect and therefore experienced difficulty to comply with the treatment and discontinue the medication, they should be informed that the drug must be administered at tolerable doses; they should also be able to continue with the treatment after the onset of the side effects and be able to manage the side effects during treatment.

One of the most important outcomes of our study was that almost all of the patients had no information regarding the effect of the drug, duration of the effect, treatment duration, time of treatment discontinuation, and the most important side effects during the treatment. However, they expressed that they wanted to receive information about the effects of the drugs, duration of the treatment, about the potential harms of the drugs, effects to the body, management of the side effects, and the addictive potential of the drugs. These results might be related to the lack of briefing of the patients

by the physicians and nurses or to the lack of interest of the patients.

We accessed only one study conducted in Turkey, which would contribute significantly to this topic. Striking results were obtained by this descriptive study, which the researchers conducted by accessing 120 family physicians working in 6 different districts of Istanbul. Although 80.8% of the family physicians suggested that they had sufficient information and experience to diagnose depression, the investigators determined 47.5% of them were not sufficiently informed about the treatment of depression. In the same study, only 1.5% of the physicians were able to identify all of the depression symptoms, and 89.2% expressed that they needed regular training about the use of the antidepressants in the treatment (18).

In a study conducted abroad, 72.0% of 137 physicians, who were prescribing antidepressants, stated that they recommended the patients to use the drugs for least 6 months (25). In the same study, 401 patients were questioned about their treatment, and 34.0% of them stated that their physicians recommended them to use the medication for at least 6 months, and 56% stated that they did not get any explanation in this regard. In addition, patients who informed their physicians about the experienced side effects had a higher compliance rate than those who did not. These results showed that the patients should be trained regarding the effects, side effects, management of the side effects, and duration of the treatment to achieve a good compliance to the treatment period.

4.1. Study Limitations

All data were obtained from the patients hospitalized only in one hospital. All data were based on the personal declaration of the patients.

5. CONCLUSION

Similar to studies mentioned previously, our study showed that the patients were not adequately informed about the antidepressant use. The physicians and nurses should brief the patients. In this context, enhancement of the knowledge of the prescribing physicians and practicing nurses regarding the antidepressant agents might be useful.

These findings showed that informing the patients about the drug's effects, onset of the effect, duration of the treatment, time of treatment discontinuation, and the most important side effects and their management was essential for compliance to treatment and for benefitting from the drug therapy. It might be recommended that the knowledge level of the practicing nurses and physicians (except psychiatrists) about the antidepressant agents used by the patients should be evaluated, and if necessary, in-service training on the required information should be organized so that they are capable of fulfilling the information needs of the patients

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Assessment of Consumer Perceptions in Ankara (Turkey) Toward Herbal Medicinal Products: A Survey Analysis in the Etimesgut District

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ABSTRACT

Objective: In the current study, we analyzed a survey on herbal medicinal product (HMP) use among 250 Turkish participants to provide an insight into how consumers have been considering and using non-prescription herbal medicines.

Methods: A cross-sectional survey of 250 consumers (56% males and 44% females) who had visited pharmacies in 2011 in Etimesgut (Ankara) was conducted. The findings were comparatively interpreted through statistical analysis using independent variables, including gender, age, educational status, profession, monthly income, and habitation with the participant answers.

Results: The results indicated that the participants trusted a physician's recommendation to use HMPs. However, only 8.8% of the participants have found the pharmacists to be sufficient in directing toward HMP use. Besides, they have preferred traditional herbalists and the pharmacies at an equal rate for purchasing herbal medicines.

Conclusion: This is the first survey study performed by a pharmacy faculty in Turkey aiming to determine the aptitude of people toward HMPs. The necessity to consult the role of pharmacists in the rational use of HMPs has been highlighted through the survey results.

Keywords: Natural product, survey, pharmacist, consumer, health, physician

1. INTRODUCTION

Plants have been utilized for healing purposes since ancient times and their popularity is still maintained due to their health-promoting effect in the modern times. Although the access rate to conventional medicines is markedly high in many countries, herbal medicinal products (HMPs) are also in great demand worldwide for health care (1). Several studies have been conducted on plants for their possible therapeutic effects, whereas some of them have remained with unproven pharmacological activity. Since communication sources in the present day, such as social and visual media, and internet, possess a high influence on preferences of consumers in many ways, HMPs have been a popular subject for these sources in terms of marketing and sales (2). In fact, many consumers consider HMPs as "if herbal, no harm," whereas the perception of most of the physicians on these products is "if herbal, no efficacy." Moreover, manufacturers offer a wide range of therapeutic effects attributable to HMPs, and these purported benefits fascinate consumers to perceive this kind of natural preparations, particularly against obesity, memory impairment, and sexual dysfunction, which seem to be a safer alternative to conventional drugs. Nevertheless, consumers and even pharmacists and physicians are not aware of unwanted, adverse, or side effects or even

herb-drug interactions of HMPs in most of the cases, which generate a great risk to public health. Without any doubt, "natural/herbal" claim for any product does not guarantee at all it to be safe. Another concern with HMPs is quality control, efficacy, adulteration, and regulatory issues, which vary from country to country. Despite all these issues, consumers are still eager to use HMPs in a great demand as herbal therapeutics are rapidly becoming an inevitable part of mainstream health care. Consistently, large-scale survey studies in the USA revealed that individuals are demanding complementary and alternative medicine (CAM) therapies and use of HMPs with a growing interest (3, 4), while the quality is still the main issue for HMPs ranging from high to low due to intrinsic, extrinsic, and regulatory factors (5). In addition, another problem with HMPs is self-medication.

Several studies have examined the consumer tendency to HMPs use based on the criteria, such as gender, education, insurance, and social status. (6-9). However, only a few extremely small survey studies have revealed consumer inclination on HMPs in Turkey. There have been ongoing conflicts on the regulation and licensing issues of HMPs in Turkey between the Ministry of Health and Ministry of Food, Agriculture, and Animal Husbandry; eventually, efficacy, safety, quality control, licensing, and marketing guidelines

were regulated according to Legislation of Traditional Herbal Medicinal Products in 2010 as authorized by the Ministry of Health. In contrast, dietary supplements are still under the control of Ministry of Food, Agriculture, and Animal Husbandry in our country. Nevertheless, the great demand of HMPs in the country creates a massive market for consumers through internet, television, and radio sales, and health stores as well as pharmacies, which is rather hard to control due to a great product variety. Hence, in the current work, we aimed to undertake a survey analysis on HMP use among 250 Turkish participants to provide an insight into how consumers have been considering and using non-prescription herbal medicines. For this purpose, a questionnaire of 21 questions was applied to all participants and the answers were statistically evaluated.

2. METHODS

2.1. Study Design

The participants (250 persons) were from residents of Etimesgut suburb located at the west of Ankara (Turkey) (Fig. 1), who came over to the pharmacies in the area during the year of 2011. Participants were recruited according to the simple random sampling method. Since the population of Etimesgut was 414,739 in 2011 according to the data provided by Turkish Statistical Institution, the minimum sample unit was calculated as 245 persons based on $p=0.8$ and $q=0.2$ values at the confidence level of 95%. A verbal explanation about the nature of the survey was provided to the participants by the pharmacists and their verbal consent was obtained.

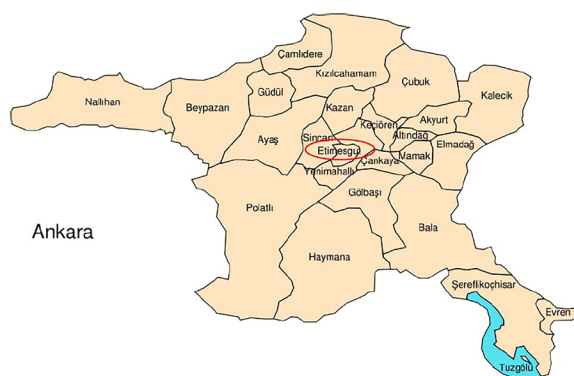


Figure 1. Location of Etimesgut district in Ankara province (Turkey)

2.2. Materials

This study was carried out in accordance with Helsinki Declaration of 1964, as revised in 2013 (Brazil). A questionnaire was designed to collect information on the inclination of participants toward HMPs. Each participant was provided with the questionnaire and requested to complete it independently without indicating the name.

The survey consisted of 21 questions covering all alternative responses. The first 6 questions were aimed to get general demographic information, including sex, age, education, residence, monthly income, and profession, while rest of the questions prepared in accordance with a Likert scale focused on measuring the tendency of the participants against HMPs. For the Likert responses, all responses with any degree of agreement were grouped as positive responses, and all responses with any degree of disagreement were grouped as negative responses.

2.3. Statistical analysis

The collected data were analyzed using Statistical Package for Social Sciences for Windows 20 (IBM Corp. Released 2011, Armonk, New York, USA). Non-parametric tests were used in the analyses. Besides, the Chi-Square test was employed to determine the presence of a possible correlation between independent variables (demographic factors) and participant responses.

3. RESULTS

A total of 250 participants were requested to complete the questionnaire, and all of them responded to the survey. The respondents consisted of 44% females and 56% males, with a varying degree of education: 38.0% with high school, 36.8% university graduate, 8% postgraduate, 16% of primary/secondary school degree, and 2% of illiterate (Table 1). The age of the participants mostly ranged 26–31 (31.2%), 19–25 (25.2%), and 32–40 (20.8%) years; 32.4% of the participants had a minimum monthly wage from +1 to 1000 Turkish Lira (TL). Most of the participants (38%) declared their professions as worker, while 20.8% of them were civil servants and 15.6% included merchant/shopkeepers (Table 1).

Table 1. Demographic data of the participants

Participants (n=250)		%
Gender	Male	56
	Female	44
Age, years	14 and below	1.2
	15-18	4.0
	19-25	25.2
	26-31	31.2
	32-40	20.8
	41-50	10.4
	51-60	6.0
61 and over	1.2	
Educational status	Illiterate	2.0
	Primary and secondary school	16.0
	High school	38.0
	University graduate	36.0
	Postgraduate	8.0
Residential area	City center	60.0
	County	38.4
	Suburb	1.2
	Village	0.4

Monthly income, TL	1– Minimum wage	22.0
	Minimum wage +1 TL – 1000 TL	32.4
	1001 TL – 1500 TL	27.2
	1501 TL – 3000 TL	15.2
	3001 TL – 6500 TL	1.2
	6500 TL and over	2.0
Profession	Doctor–engineer–lawyer	2.8
	Merchant–shopkeeper	15.6
	Teacher–academician	2.8
	Farmer	1.2
	Civil servant	20.8
	Housewife	4.8
	Student	10.0
	Worker	38.0
	Other	4.0

TL: Turkish Lira

The study had a response rate of 100.0%. The response of the participants to the question “which one (pharmacies or local herbal product sellers) do you prefer to purchase any herbal medicinal products from?” is given in Table 2 according to the independent parameters, including gender, age, educational status, residential area, monthly income, and profession. According to the data, 56.0% of the male participants and 44.0% of the female participants preferred to purchase HMPs from pharmacies, mostly in dried/fresh/powdered plant form rather than any pharmaceutical formulation. The data given in Table 2 were similar considering all parameters. Most of the participants chose to use HMPs as cosmetics or vitamins, while the use of HMPs against internal disorders was also quite common among the participants aged 51–60 (40%) years and residents in suburbs (33.0%; Table 3); the Chi-square results are presented in Table 4. Vitamin use was observed to be higher among the participants from the professional group of doctors–engineers–lawyers (42.9%). Among the groups of farmers (66.7%), workers (47.4%), and teacher–academicians (42.9%), use of HMPs in cosmetics form was highly popular. According to Table 5, 62.9% of the male and 60.9% of the female participants expressed to be influenced by their physicians in their choice of HMP use. Interestingly, pharmacists had an impact on only 7.1% of the male and 10.9% of the female participants, whereas they had no effect on the professional groups, such as doctors–engineers–lawyers, teacher–academicians, and farmers (0%). Although social and visual media are very effective in encouraging people for HMP use in advertorial and unconscious ways in Turkey, the media seemed to have a low effect on our participants. However, the highest proportion of the participants influenced by media (33.3%) as well as friends (33.3%) belonged to the participants living in suburbs. The chi-square results for Table 5 according to the parameters age, educational status, residential area, monthly income, and profession are presented in Table 6. Considering the total data represented in Table 7, 62.8% of the participants declared not using any herbal preparations for the health effect. In fact, 50% of them preferred to purchase HMPs from

pharmacy, although the effect of pharmacists appeared to be no or minimal on consumer behavior for HMP use. Traditional herbalists who have always played a significant role in the formation of Anatolian folk medicine were the choice of the other half (50%) of the participants as a place to purchase HMPs. Consistent with Table 2, only 21.6% of them preferred to buy these products in a pharmaceutical form. Following vitamins, HMPs have been popular for use against internal disorders (Table 2). The influence of physicians on consumer choice for HMP use was rather superior (62.0%) compared to pharmacists (8.8%; Table 5). From this viewpoint, the influence of traditional herbalists was close to that of pharmacists (8.4%).

Table 2. Data on preference of purchase places and type of HMPs by the participants

Independent parameters		Preference of purchase place of HMPs (%)		Preference of type of HMPs (%)	
		Pharmacy	Local herbal markets	Dried/fresh/powdered plant material	Pharmaceutical formulations (tablet, syrup, capsule, etc.)
Gender	Male	56.0	44.0	81.4	18.6
	Female	44.0	56.0	74.5	25.5
Age, years	14 and below	100.0	0.0	0.0	100.0
	15-18	70.0	30.0	80.0	20.0
	19-25	63.5	36.5	82.5	17.5
	26-31	44.9	55.1	82.1	17.9
	32-40	42.3	57.7	69.2	30.8
	41-50	34.6	65.4	88.5	11.5
	51-60	40.0	60.0	80.0	20.0
Educational status	61 and over	100.0	0.0	33.3	66.7
	Illiterate	100.0	0.0	80.0	20.0
	Primary and secondary school	60.0	40.0	75.0	25.0
	High school	51.6	48.4	80.0	20.0
	University graduate	42.2	57.8	78.9	21.1
Residential area	Postgraduate	45.0	55.0	75.0	25.0
	City center	50.7	49.3	79.3	20.7
	County	49.0	51.0	79.2	20.8
	Suburb	33.3	66.7	0.0	100.0
Monthly income, TL	Village	100.0	0.0	100.0	0.0
	1–minimum wage	58.2	41.8	76.4	23.6
	Minimum wage +1 TL – 1000 TL	53.1	46.9	82.7	17.3
	1001 TL – 1500 TL	42.6	57.4	77.9	22.1
	1501 TL – 3000 TL	50.0	50.0	71.1	28.9
	3001 TL – 6500 TL	0.0	100.0	66.7	33.3
Profession	6500 TL and over	40.0	60.0	100.0	0.0
	Doctor–engineer–lawyer	57.1	42.9	57.1	42.9
	Merchant–shopkeeper	59.0	41.0	82.1	17.9
	Teacher–academician	14.3	85.7	85.7	14.3
	Farmer	66.7	33.3	100.0	0.0
	Civil servant	40.4	59.6	75.0	25.0
	Housewife	41.7	58.3	75.0	25.0
	Student	68.0	32.0	80.0	20.0
	Worker	50.5	49.5	76.8	23.2
	Other	40.0	60.0	100.0	0.0

TL: Turkish Lira; HMP: Herbal medicinal product

Table 3. Data (%) on preferred uses of HMPs by the participants

Independent parameters		Cosmetics	Skeletal system	Obesity	Oncological disorders	Internal disorders	Vitamins	Asthma–Bronchitis	Other
Gender	Male	26.4	5.0	7.9	0.7	16.4	23.6	3.6	16.4
	Female	52.7	5.5	5.5	0.9	10.9	14.5	1.8	8.2
Age, years	14 and below	0.0	0.0	0.0	0.0	33.3	66.7	0.0	0.0
	15-18	40.0	0.0	20.0	0.0	10.0	30.0	0.0	0.0
	19-25	50.8	3.2	3.2	0.0	7.9	20.6	0.0	14.3
	26-31	39.7	6.4	7.7	2.6	12.8	20.5	2.6	7.7
	32-40	42.3	5.8	9.6	0.0	9.6	13.5	3.8	15.4
	41-50	19.2	7.7	3.8	0.0	23.1	23.1	3.8	19.2
	51-60	6.7	6.7	6.7	0.0	40.0	13.3	13.3	13.3
61 and over	0.0	0.0	0.0	0.0	33.3	0.0	0.0	66.7	
Educational status	Illiterate	40.0	0.0	0.0	0.0	40.0	0.0	0.0	20.0
	Primary and secondary school	30.0	2.5	7.5	0.0	17.5	25.0	12.5	5.0
	High school	35.8	5.3	8.4	2.1	14.7	15.8	1.1	16.8
	University graduate	44.4	6.7	5.6	0.0	12.2	16.7	1.1	13.3
	Postgraduate	35.0	5.0	5.0	0.0	5.0	45.0	0.0	5.0
Residential area	City center	39.3	4.0	6.7	0.7	10.0	23.3	1.3	14.7
	County	37.5	7.3	7.3	1.0	19.8	13.5	4.2	9.4
	Suburb	0.0	0.0	0.0	0.0	33.3	33.3	33.3	0.0
	Village	0.0	0.0	0.0	0.0	0.0	0.0	0.0	100.0
Monthly income, TL	1 –minimum wage	40.0	9.1	7.3	0.0	14.5	18.2	1.8	9.1
	Minimum wage +1 TL – 1000 TL	44.4	2.5	7.4	1.2	9.9	18.5	2.5	13.6
	1001 TL – 1500 TL	39.7	5.9	2.9	1.5	16.2	19.1	5.9	8.8
	1501 TL – 3000 TL	21.1	5.3	10.5	0.0	18.4	26.3	0.0	18.4
	3001 TL – 6500 TL	33.3	0.0	0.0	0.0	0.0	33.3	0.0	33.3
	6500 TL and over	20.0	0.0	20.0	0.0	20.0	0.0	0.0	40.0
Profession	Doctor–engineer–lawyer	14.3	0.0	0.0	0.0	14.3	42.9	0.0	28.6
	Merchant–shopkeeper	30.8	2.6	7.7	0.0	12.8	35.9	0.0	10.3
	Teacher–academician	42.9	14.3	0.0	0.0	28.6	14.3	0.0	0.0
	Farmer	66.7	33.3	0.0	0.0	0.0	0.0	0.0	0.0
	Civil servant	26.9	5.8	5.8	1.9	17.3	21.2	7.7	13.5
	Housewife	41.7	16.7	8.3	0.0	25.0	8.3	0.0	0.0
	Student	28.0	4.0	8.0	4.0	8.0	32.0	0.0	16.0
	Worker	47.4	4.2	7.4	0.0	13.7	10.5	3.2	13.7
	Other	60.0	0.0	10.0	0.0	0.0	10.0	0.0	20.0

TL: Turkish Lira; HMP: Herbal medicinal product

Table 4. Chi-square results for the responses obtained from Table 3 for gender, age, educational status, and profession

Gender	Value	Df	Asymp. Sig. (2-sided)
Pearson Chi-Square	19.638	7	.006
Likelihood Ratio	19.846	7	.006
Linear-by-Linear Association	17.269	1	.000
Number of Valid Cases	250		
Age			
Pearson Chi-Square	61.938	49	.102
Likelihood Ratio	61.736	49	.105
Linear-by-Linear Association	8.096	1	.004
Number of Valid Cases	250		
Educational status			
Pearson Chi-Square		28	.052
Likelihood Ratio	37.000	28	.119
Linear-by-Linear Association	1.206	1	.272
Number of Valid Cases	250		
Profession			
Pearson Chi-Square	58.096 ^a	56	.398
Likelihood Ratio	61.104	56	.298
Linear-by-Linear Association	4.480	1	.034
Number of Valid Cases	250		

Df: Degrees of freedom; Asymp. Sig: Asymptotic significance

4. DISCUSSION

The use of HMPs is increasing worldwide, whereas the adverse effects and drug-herb interactions are also well realized. However, physicians seem unaware of these interactions. Turkey is one of those countries with a stable demand for the use of HMPs. The physicians do not believe much in the curative effect of herbal remedies compared to other CAM therapies (10, 11). However, only in some countries, such as Germany, physicians are qualified or educated well about CAM and recommend and prescribe these remedies to their patients as well as apply it in their daily practice (12). Moreover, pharmacists may not be considered the ideal consultants in terms of use of HMPs and other CAM applications, which is consistent with our data. Although women have been reported to have a higher propensity toward the use of HMPs (6, 7, 13, 14), gender was not an indicator for the use in our study. According to the Harvard survey study performed by Eisenberg et al (3), the frequency of CAM usage was 44% in the USA with users aged 25–49 years, which is in accordance with our current data. Another survey study conducted with 231 patients residing in Sant'Andrea in Italy indicated that 35.5% of

the patients expressed to use herbal preparations, while 72% of them confessed not to be aware of their side or adverse effects as well as drug interactions (15).

Similar to our study, internal disorders were the most preferred disease group for using HMPs (38.1%) among the participants in Brazil (16), wherein 30% of them bought the plant materials from free markets. In our case, with the question “where do you prefer to buy HMPs?,” 44 (56%) of the males and 56 (44%) of the female responders reported to purchase from the local herbal markets and pharmacies, respectively, (Table 2). According to a report on herbal remedies sold in Palestine for breast cancer treatment (17), only 1.4% of the patients favored to buy the herbal remedies from pharmacies. In another study conducted in Kayseri, Turkey, a positive correlation was observed between the educational status and inclination of herbal remedy use among patients, while 39% of them reported to have reduced blood glucose levels after using self-medicated herbal remedies (18). However, our survey findings indicate that the participants mostly rely on the recommendation by their physicians to use any herbal remedies (Table 5). Moreover, we observed that the preference

Table 5. Data (%) on who influences the participants for purchase for HMPs

Independent parameters		Physician	Pharmacist	Local herbal markets	Internet	Media	Friend	Other
Gender	Male	62.9	7.1	7.1	7.1	5.7	7.9	2.1
	Female	60.9	10.9	10.0	7.3	4.5	6.4	0.0
Age, years	14 and below	66.7	33.3	0.0	0.0	0.0	0.0	0.0
	15-18	50.0	10.0	10.0	10.0	10.0	10.0	0.0
	19-25	69.8	7.9	1.6	6.3	4.8	7.9	1.6
	26-31	61.5	6.4	10.3	9.0	2.6	10.3	0.0
	32-40	59.6	13.5	11.5	5.8	5.8	1.9	1.9
	41-50	57.7	3.8	7.7	7.7	15.4	7.7	0.0
	51-60	53.3	13.3	13.3	6.7	0.0	6.7	6.7
61 and over	66.7	0.0	33.3	0.0	0.0	0.0	0.0	
Educational status	Illiterate	40.0	20.0	0.0	20.0	0.0	0.0	20.0
	Primary and secondary school	55.0	10.0	15.0	2.5	7.5	7.5	2.5
	High school	57.9	14.7	8.4	5.3	6.3	6.3	1.1
	University graduate	67.8	2.2	6.7	12.2	3.3	7.8	0.0
	Postgraduate	75.0	5.0	5.0	0.0	5.0	10.0	0.0
Residential area	City center	69.3	7.3	8.0	4.7	4.0	6.7	0.0
	County	52.1	11.5	9.4	11.5	6.2	7.3	2.1
	Suburb	33.3	0.0	0.0	0.0	33.3	33.3	0.0
	Village	0.0	0.0	0.0	0.0	0.0	0.0	100.0
Monthly income, TL	1 –minimum wage	63.6	7.3	14.5	5.5	5.5	1.8	1.8
	Minimum wage +1 TL – 1000 TL	61.7	11.1	6.2	8.6	2.5	9.9	0.0
	1001 TL – 1500 TL	64.7	8.8	5.9	4.4	5.9	10.3	0.0
	1501 TL – 3000 TL	60.5	7.9	7.9	10.5	7.9	2.6	2.6
	3001 TL – 6500 TL	0.0	0.0	33.3	33.3	0.0	33.3	0.0
	6500 TL and over	60.0	0.0	0.0	0.0	20.0	0.0	20.0
Profession	Doctor–engineer–lawyer	85.7	0.0	0.0	0.0	0.0	14.3	0.0
	Merchant–shopkeeper	59.0	5.1	12.8	10.3	5.1	5.1	2.6
	Teacher–academician	42.9	0.0	0.0	42.9	14.3	0.0	0.0
	Farmer	66.7	0.0	0.0	0.0	0.0	33.3	0.0
	Civil servant	55.8	13.5	11.5	1.9	3.8	13.5	0.0
	Housewife	58.3	25.0	8.3	8.3	0.0	0.0	0.0
	Student	56.0	12.0	8.0	8.0	8.0	8.0	0.0
	Worker	66.3	6.3	7.4	7.4	6.3	4.2	2.1
	Other	80.0	10.0	0.0	0.0	0.0	10.0	0.0

for pharmacists as herbal medicine consultant seems to be relatively low compared to physicians. In contrast, 72.71% of the female participants in an Italian survey study confessed not to consult with a health professional in case of using HMPs (19), which is contrary to our findings.

Several survey studies have pointed out the outcome that herbal medicines are usually used particularly by women with higher education (20-22), whereas some studies revealed no correlation between the educational status and HMP use (23, 24). Nevertheless, we have not obtained a clear finding from our own study. However, a correlation has been reported between HMP use and higher income (25, 26), which may lead to a conclusion that HMPs are affordable by people with higher income due to their generally high prices. Relevantly, it is also interesting to note that the Turkish individuals who participated in two separate multicentered international survey studies were observed to pay the highest price for HMPs, despite their relatively lower income among the countries that participated (27, 28).

Table 6. Chi-square results for the responses obtained from Table 5 between gender, age, educational status, and profession

Gender	Value	Df	Asymp. Sig. (2-sided)
Pearson Chi-Square	4.341 ^a	6	.631
Likelihood Ratio	5.451	6	.487
Linear-by-Linear Association	.484	1	.486
N of Valid Cases	250		
Age			
Pearson Chi-Square	31.837 ^a	42	.873
Likelihood Ratio	32.604	42	.851
Linear-by-Linear Association	.345	1	.557
N of Valid Cases	250		
Educational status			
Pearson Chi-Square	40.729 ^a	24	.018
Likelihood Ratio	33.793	24	.088
Linear-by-Linear Association	1.826	1	.177
N of Valid Cases	250		
Residential area			
Pearson Chi-Square	101.868 ^a	18	.000
Likelihood Ratio	26.865	18	.082
Linear-by-Linear Association	12.859	1	.000
N of Valid Cases	250		
Monthly income			
Pearson Chi-Square	44.092 ^a	30	.047
Likelihood Ratio	35.070	30	.240
Linear-by-Linear Association	2.505	1	.113
N of Valid Cases	250		
Profession			
Pearson Chi-Square	45.912 ^a	48	.559
Likelihood Ratio	45.693	48	.568
Linear-by-Linear Association	.878	1	.349
N of Valid Cases	250		

Df: Degrees of freedom, Asymp. Sig: Asymptotic significance

Social and visual media seem to play a great role in manipulating consumers in their preferences to use HMPs in Turkey. In particular, some celebrities or apparently experts on HMPs, highly recommend about how and which herbs or HMPs to use on television. Hence, we also attempted to determine how much the participants were influenced by these factors in media. In contrast to our expectations, only 5.2% of the participants reported to be affected by media, while the internet had an influence of HMP use on only 7.2% of them (Table 7), which was supported by a correlation between educational status and HMP use according to our statistical data.

Table 7. Total data on some attitudes of the participants

	Response	%
Have you ever used HMP for any health benefit?	Yes	37.2
	No	62.8
Which one do you prefer to purchase as HMP?	Pharmacy	50
	Local herbal markets	50
Which type of HMP do you prefer to use?	Dried/fresh/powdered herbal materials	78.4
	Pharmaceutical formulations (tablet, syrup, capsule, etc.)	21.6
Which type of health problems do you prefer to use HMP for?	Cosmetics	38.0
	Skeletal system	5.2
	Obesity	6.8
	Oncological	0.8
	Internal	14.0
	Vitamins	19.6
	Asthma-bronchitis	2.8
Other	12.8	
Which one influences your choice on use of HMPs?	Physicians	62.0
	Pharmacists	8.8
	Local herb market owners	8.4
	Internet	7.2
	Media	5.2
	Friends	7.2
Other	1.2	

HMP: Herbal medicinal product

5. CONCLUSION

In our survey study to define inclinations toward HMP use in Etimesgut district of Ankara conducted with 250 participants, the results were evaluated in comparison to independent variables of gender, age, educational status, profession, monthly income, and habitation. Since the residents of this district who undertook the survey are considered to possess relatively higher educational status in the province of Ankara, the results on HMP use seemed to be closer to the ideal. Briefly, the participants desire to consult with physicians rather than pharmacists to use any HMP; consequently, this data point out the fact that we need to emphasize a more active role of pharmacists in herbal drug use consultancy and improve Turkish physicians' knowledge on herbal medicines. Since it appears that the Turkish people

usually have a marked demand to use herbs for therapeutic purposes, HMPs of a good quality should be licensed to prevent health risks. To the best of our knowledge, this is the first survey study to establish inclinations of the Turkish people on HMP use conducted by a pharmacy faculty.

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The Examination of the Some Aspects of the Therapeutic Environment of Psychiatric Inpatient Clinics in Turkey

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ABSTRACT

Objective: The aim of the present study was to determine the current status of psychiatry clinics in Turkey in terms of therapeutic environment.

Methods: The present study was performed cross-sectionally and descriptively in 195 institutes comprising the psychiatry clinic in Turkey. A survey of 42 questions was used that included the characteristics of clinics obtained by reviewing the literature and listing specialist opinions. Data were collected via telephone between June 25, 2014 and July 15, 2015. Analysis of data was performed using the SPSS 18.0 software. Numbers and percentages were used as descriptive statistics with respect to hospitals.

Results: It was found that 63.1% of clinics had 6–10 nurses, 77.9% of them had 1–10 doctors, and 37.4% of them did not have a visit room, whereas 47.2% of them had an occupation room. It was discovered that 99% of clinic activities for patients were performed, 45.6% of them with occupational therapy were not performed, 16.9% of them with occupational therapy were performed, and 57.5% of them with regular sport activities were not performed. It was detected that psychoeducation was not performed in 66.2% of the clinics, whereas it was performed in 33.8% of them.

Conclusions: It was observed that when the results of the study were evaluated, there were deficiencies in physical configuration in our country and limited therapeutic activities.

Keywords: Therapeutic environment, Physical environment, Psychiatry clinic

1. INTRODUCTION

Physical environments of psychiatric clinics are important in the treatment of individuals with mental disorders. In some cases, individuals could be hospitalized after the diagnosis of mental disorder; the physiological and psychological needs of patients should be fulfilled in this stage to ensure their safety and physical comfort and to maintain daily life activities conveniently (1). Upon hospital admission, they are pulled away from their personal life and come to a strange environment where they encounter various hindrances that can lower their quality of life at some scale. In this case, these hindrances must be minimized as much as possible (2, 3). This necessity introduced the therapeutic environment concept as first described by Maxwell Jones in 1953 and explained its benefits (4). Today, the purpose of the psychiatric clinics is to assist patients to talk about the psychiatric problem that caused them to be hospitalized and to recover. Therefore, an ideal hospital environment must be one that provides an opportunity to individuals through social organizations, supportive characteristics, and community values to take advantage of their self-strength instead of putting the disease into prominence (5).

When therapeutic environment characteristics are taken into consideration, two constituent dimensions come to attention: physical characteristics and activities implemented in the clinic. As one of the prominent physical characteristics, the position of the clinic in the hospital comes to mind. The clinic must be positioned on the ground floor in a hospital or in another individual building so that patients must be provided an opportunity to take a walk and to have access to the garden conveniently. Moreover, providing environments in which individual or group therapies could be held in the clinic is important in terms of quality of treatment. Furthermore, there must be a department or room either inside or outside of the clinic to provide electroconvulsive therapy (ECT) opportunity (6). In determining the interior color of the clinic, light and soft tones must be preferred to support positive affections of individuals. For patients who exhibit aggressive behaviors and who need to be taken into a seclusion room for a certain period due to the risk of harming others and themselves in clinics, appropriate colors must be preferred to allow these individuals to be relaxed (7). Seclusion rooms must be sunny and available for aeration. These are considered as supportive precautions for comfort of patients (8). In addition, there must be some other

measures in patients' rooms for physical safety of patients (8). As physical safety precautions need to be taken for patients with risk of harming others or themselves, or of running away, windows must be secured with iron bars or they must have a lock system; window glasses should be shatter-proof and safety glass; curtains should be solid and inseparable from their apparatus; piercing, sharp, and inflammable objects should not be kept in rooms; mirrors should be made up of stainless steel, and medications should be kept in the special pharmacy rooms under double locks (9). As another characteristic of the therapeutic environment, sport, art and similar activities performed in the clinic, individual or group therapies, and meetings are significantly important. A hall in which individuals feel at home and in a family environment during their stay in the clinic, they can express themselves conveniently and which constitutes an atmosphere supporting communication with others, where dining room or occupation therapies could be handled is necessary, and this hall is required to be equipped with materials to provide individuals to perform various activities and hobbies (10). In the environment in which patients interact together, there could be TVs under surveillance of health professionals. These units must be assembled onto the wall for security precaution (11).

There are limited studies on determination of current status of therapeutic environments in Turkey. The single study that reports the physical structure of psychiatric clinics in Turkey was the master thesis conducted by Ergün (2005), which describes education status and population of mental health professionals in Turkey (12). Therefore, acquisition of therapeutic environment data concerning psychiatric clinics in Turkey would contribute into the evaluation of the current status. As it was prescribed in the psychiatric nursing practice standards issued by the Union of American Nursing, "creating and maintenance of therapeutical environment" is considered as one of the fundamental skills; and it constitutes a foundation for maintenance of nursing practices in clinic environment (5). In this regard, propounding therapeutic environment characteristics that constitute the roof of the psychiatric nursing practices is considered as a significant step in terms of determination and improvement of the present status. The purpose of the present study was to investigate therapeutic environments of psychiatric clinics in Turkey in terms of physical environment and activities and to make contribution to develop psychiatric clinics in Turkey regarding their therapeutic environments.

2. METHODS

2.1. Study design and aim

While the present study is cross-sectional, descriptive and quantitative in nature, it aimed to investigate therapeutic environments of psychiatric clinics in Turkey in terms of physical aspect.

2.2. Study sample

The population of the study was composed of 270 hospitals with inpatient clinic in Turkey. In the present study, sampling selection was not preferred; instead, whole population was tried to be accessed. However, 75 of these target hospitals were not included in the study because of various reasons, such as difficulty in research permission, refusal of clinic psychologists and nurses to fill in forms voluntarily, or avoiding giving official answer and ignoring correspondence both in written and on the phone. In total, 195 (72.2%) hospitals were included in sampling of the study.

2.3. Measurement

In the present study, a survey form developed by researchers through review of the relevant literature and consulting experts was utilized. Pilot application of the prepared survey form was conducted in five psychiatric clinics of hospitals excluded from the scope of the sampling by lot. As a result of the pilot application, certain amendments were made on the survey form, and finally it comprised 42 questions. The survey form includes questions regarding position of the clinic at the hospital, whether there is private garden, characteristics of windows, colors of the wall, patient rooms, examination room, the ECT room, visit room, separate dining room, treatment room, occupation or activity room and other questions investigating physical structure; number of physicians, psychiatrists, nurse and janitor at the clinic, and activities held in the clinic. The survey form was answered by authorized personnel at the psychiatric clinics, such as physicians, psychiatrics, or the nurse in charge.

2.4. Data collection

The study data were collected in the period between June 25, 2014 and July 15, 2015 via telephone interviewing. Before data collection period, potential respondents in clinics were informed about the process, and authorized correspondents at clinics were called at the time determined jointly once again to conduct the interview over the phone. During the interview process, which took 25 min on average, answers declared by respondents were recorded into the form.

2.6. Ethical consideration

For the implementation of the study, the necessary permission was requested from the ethical board of human researches at the university (2013.255.IRB3.144). The necessary institutional permission was taken from the Ministry of Health at the first instance, then from the General Secretariat of Public Hospitals located at each city and from university hospital administrations through individual petitions submitted to individual administrations.

2.5. Data analysis

Collected data were analyzed through the SPSS 18.0 software. In assessment of descriptive data concerning hospitals, the number, mean, min-max, and percentage were utilized.

3.RESULTS

In terms of distribution of psychiatric clinics in Turkey, while 62.6% were under roof of the Union of Public Hospitals, 23.1% under university hospitals, 8.2% under training and research hospitals, 4.1% under mental, neurological diseases hospitals, and 2.1% under private hospitals.

Table 1. Number of mental health professionals in inpatient clinics (n=195).

Profession	n	%
No. of nurses		
1–5	36	18.5
6–10	123	63.1
11–15	26	13.3
16 and over	10	5.1
No. of doctors		
1–10	152	77.9
11–20	30	15.4
21–30	8	4.1
31 and over	5	2.6
No. of specialists		
Not	31	15.9
1–5	143	73.3
6–10	16	8.2
11 and over	5	2.6
No. of psychologists		
Not	14	7.2
1–5	174	89.2
6 and over	7	3.6
No. of servants		
1–5	147	75.4
6–10	40	20.5
11 and over	8	4.1

In terms of professional employed by the clinics, across the clinics taken within the scope of the study, 63.1% were employing 6–10 nurses; 77.9% were employing 1–10 psychiatrist; 15.9% were not employing any specialists as shown in Table 1. Additionally, it was observed that 89.2% of clinics were employing 1–5 psychiatrics; that the proportion of the ones that do not have any psychiatrics was 7.2%; and 75.4% of clinics were employing 1–5 servants (Table 1).

Table 2 shows the characteristics of rooms within the building structure of psychiatric clinics. It could be observed that 37.4% of clinics have no any interview room; 44.1% have no occupation room, and 51.3% have no dining hall. In terms of number of patient rooms, it was determined that 41.0% of clinics have 1–5 beds capacity; 32.8% have 6–10 beds capacity.

Table 2. Characteristics of rooms in inpatient clinics (n=195).

Rooms	n	%
No. of interview room		
0	73	37.4
1	87	44.6
2	17	8.7
3 and over	18	7.3
No. of occupation room		
0	86	44.1
1	92	47.2
2	15	7.7
3	2	1.0
No. of patient rooms		
1–5	80	41.0
6–10	64	32.8
11–15	28	14.4
16 and over	23	11.8
Features of patient rooms		
1 patient 1 room	9	4.6
2 patients 1 room	120	62.5
3 patients 1 room	43	22.1
4 patients 1 room	15	7.7
5 patients 1 room	3	1.5
6 patients 1 room	1	.5
7 patients 1 room	1	.5
10 patients 1 room	1	.5
Smoking room		
Yes	105	53.8
No	90	46.2
Features of lock for treatment room		
Single lock	84	43.1
Double lock	110	56.4
Pyxis (fingerprint reading system)	1	.5
ECT room		
Yes	32	16.4
No	145	74.4
Operating room	18	9.2

*ECT=electroconvulsive therapy.

Whereas one was shared by 2 patients in 62.5% of clinics; 4.6% of clinics have single rooms for patients. It was also determined that 56.4% of psychiatric clinics were equipped with double locks; 43.1% were with single lock.

With respect to positions of psychiatric clinics within hospital, rate of the clinics in an independent building within the body of the hospital was determined as 8.2%. Whereas the rate of the clinics located at the ground floor was 20.5%, the ones located at the 1st floor were determined as 16.4%. It was determined that mostly cream and white colors were preferred on the interior walls of psychiatric clinics with 43.6% and 12.3%, respectively.

Table 3. Therapeutic activities for patients in inpatients clinics (n=195).

Activities	n	%
Group meeting		
Not done	78	40.0
1–2 times in a month	12	6.2
Twice in a week	23	11.8
Ones in a week	42	21.5
Everyday	40	20.5
Occupation therapies		
Not done	89	45.6
Paint, make jewelry, handcrafted activity	57	29.2
Music, TV, games etc.	13	6.7
Paint, play games, chess	3	1.5
All planned activities; cinema, reading book, paint etc.	33	16.9
Controlling clinics for stab		
Nor done	6	3.1
Ones in a week	3	1.5
Twice in a week	5	2.6
Three times in a week	12	6.2
Every day	169	86.7
Sport activities		
Not done	112	57.5
Table tennis	9	4.6
Activities with sport equipment in garden	74	37.9
Activities		
Activity of sweet day cooking		
Yes	54	27.7
No	130	66.7
Rarely	11	5.6
Kermess		
Not done	143	73.3
Ones in a year	32	16.4
Rarely	12	6.2
A few times in a year	8	4.1
Individual therapy		
Not done	21	10.8
By doctors	161	82.6
By psychologists	10	5.1
By nurses	2	1.0
By doctors, psychologists, nurses	1	.5
Group therapy		
Not done	142	72.8
By doctors and psychologists	40	20.5
By doctors	9	4.6

It was reported that some activities were being performed for patients in 99% of clinics. While there was no regular group meeting in the 40% of clinics included in the research, the proportion of the clinic that organizes daily group meeting was determined as 20.5%. It was determined that 45.6% of clinics were not holding occupational therapy; 3.1% were not maintaining control of clinic for stab; 57.5% were not performing regular sport activities; 66.7% were not performing sweet day cooking activities; and 73.3% were not

organizing kermess activities. It was determined that while individual therapies are held in 89.2% of psychiatric clinics, 82.6% of these therapies are conducted by psychologists. Additionally, it could be observed from the table that no any group therapy was held for patients by 72.8% of the psychiatric clinics included in the study (Table 3).

While no any stab and sharp materials were found near patients in the 85.1% of the clinics included in the study, they were determined in 14.9% of clinics. In terms of type of the stab and sharp objects found in rooms, 10.8% were tools, 2.6% was glass cup, and 1.5% was knife.

Additionally, it was determined that while 63.1% investigated clinics, patients were able to carry lighter or match with them; in 36.9% of clinics, patients were not allowed to do so.

Regarding the lock mechanism of the windows used in psychiatric clinic included in the study, whereas windows of 72.8% of clinics were not lockable; 27.2% were lockable. According to the characteristics of windows, it was observed that 29.2% of clinics had iron bars, glasses were frangible, and 20% had both iron bar and safety glass.

4. DISCUSSION

Therapeutic environment is one of the essential factors, which allow inpatients at the psychiatric clinic to take advantage of the process (13). In our contemporary world, there are numbers of psychiatric clinic that spend effort to conform to certain standards in terms of therapeutic environment and establish their professional staff (14-16). Research findings are important in terms of investigation of psychiatric clinics in Turkey from the view of therapeutic environment characteristics and of determining and fixing deficiencies.

Holistic consideration of psychiatric issues and multifactorial approach in treatment field brought provision of certain services by various professions jointly in the agenda (17). Member staffs are responsible for maintaining therapeutic environment. Person who spend longest time period with patients are psychiatric nurses. In other words, nurses are the professionals who spend the most effective time with patients in clinic, who ensures patients to participate in various activities through therapeutic communication methods effectively, and who sometimes play therapist and sometimes ruler of the environment (13). In Turkey, although the number of physicians, psychologists and nurses in psychiatric clinics is considered adequate, it was determined that distribution of their population was not homogenous. Significant member staff at psychiatric clinics is psychiatrics. Although they take position in both clinic and diagnosis and treatment processes at policlinics, and take effective position in personal and group therapies, it was determined that some clinics (15.9%) do not employ specialist psychiatrist. When it is considered that there is an absolute need to employ psychiatrics at the inpatient treatment unites, it is possible claim that this is one of the issues that needs to be resolved certainly.

In an environment organized according to the therapeutic purpose, it is important to have sufficient free spaces, personal and group therapy rooms, socialization areas, occupational therapy areas and adequate number of specially designed rooms in which necessary privacy could be provided (13). It was revealed that there is no individual therapy (visit) room in some of psychiatric clinics (37.4%) in Turkey. Since personal therapies are considered beneficent for patients in gaining new skills to handle their problems and allow their self-esteem to improve; thus, they contribute into the treatment. Accordingly, the relevant finding of our study regarding insufficient private room is rather adverse situation (16,18). In majority of clinics (82.6%), individual therapies are conducted by clinical psychologists. Very rare, nurses and psychiatrists are responsible for this process. If proportion of group therapies is taken into consideration, it could be considered that this rate is lower than individual therapies. In majority of clinics, it is encountered that group therapy is not used as a treatment method and it is not practiced by nurses in therapeutic environment; and these deficiencies are required to be improved.

Almost half of the clinics in Turkey (44.1%) lack occupation room as well. This situation illustrates a pessimistic picture which could degrade efficiency of treatment. Nurses are directly responsible for occupation activities. Nurses need an adequate and efficient area to implement these activities. Single or double accommodation opportunities in patient rooms at the psychiatric clinics are appropriate since personal spaces of persons could be violated in crowded environments (19). When patient rooms at the psychiatric clinics are taken into consideration, it was observed that majority of clinics (62.5%) were providing one room to two patients; the rest of the clinics were offering one room to three patients. This finding suggests that each patient could gain sufficient area for their personal privacy, safety and comfort. This research finding could be considered as a positive result.

It was determined that there is no dining hall in almost half of evaluated clinics (51.3%); and that patients have their meals in their rooms. While this opportunity is provided within a separate room located in clinic; the number of clinic with an independent dining hall is rather limited (12.3%). It was revealed that part of these dining halls (24.6%) was designed and furnished in the form of living room. Of the fundamental characteristics of therapeutic environment, comfort and safety are crucial. Having a separate dining hall furnished with comfortable couches in which patients could have their meals comfortably, communicate with other patients, and have a chance to express themselves is an inseparable part of modern psychiatry (20).

The ECT rooms in psychiatric clinics in Turkey are mostly avoided (74.4%). The ECT is widely recognized effective treatment method in treatment of number of psychiatric disorder in both Turkey and the world. However, the generally adopted approach in this treatment method is building of this room in surgery room standards (21). According to the research findings, small portion of the clinics (9.2%)

implement the ECT practices in clinics; majority of clinics prefer surgery room conditions. Again, there are rooms in few clinics (16.4%) where the ECT practices are conducted.

In terms of keeping medications safe, it is necessary to have a specific room in clinics where treatments are prepared and medications are kept safe under double lock system and to put nurses in charge about these rooms. More than half of the psychiatric clinics in Turkey have double lock system; but, some clinics maintain single lock system. Direct and convenient access of patients to medications is certainly not appropriate in terms of therapeutic environment (13). There is need for a room in clinics, where treatments are prepared and medications are kept under double lock. More than half of clinics (66.2%) conform to this condition. However, simultaneous utilization from nurse rooms in one-third of clinics as treatment room is considered as an adverse situation since nurse rooms are only appropriate for interaction with patients and they should not be used for any other purposes (22).

There are risks in clinics associated with patients in terms of harming others and themselves time to time. In such cases, it is necessary to have specific room for patients where they could be isolated for a while. In this process, nurses need to make explanations within the certain professional framework approaches. It was determined that there is no such a seclusion room in majority of clinics (66.7%). This situation suggests that one of the therapeutic elements of psychiatric clinics is missing.

In psychiatric clinics, it will be appropriate to eliminate smoking in terms of maintaining healthy therapeutic environment and protecting individuals' health. However, it was emphasized in studies on therapeutic environment that patients with smoking habit need to be allowed to smoke. However, solution must be introduced for them by eliminating passive smoker risk of remaining patients (22). In this regard, there should be reserved rooms in the clinics for smoking. Smoking rooms exist in more than half of the psychiatric clinics in Turkey. However, lack of such room in other half of the clinics across Turkey indicates that there is still a problem requiring attention.

Psychiatric clinics should not be positioned higher floors of hospitals in order to fulfill safety needs. They must be positioned on the ground floor and have separate entry than main gates of hospitals. In fact, the appreciated form is that it is structured in a separate building with individual garden and activity field (23). Position of clinic in a separate building could allow protection of privacy of inpatients in a psychiatric clinic and prevent them to be judged by others. According to findings, it was observed that clinics were positioned on the 1st and 12th floors, not appropriate to qualities of therapeutic environment.

It should be paid attention to the wall colors of the psychiatric clinics which could affect affections of patients directly. What is meant at this point is that wall color should not have either positive or negative simulative influence on patients. In this

regard, white and cream colors must be the tones preferred mostly. Especially, since white implies cleanliness of health area; and it creates transparency and spacious perception, they might be considered in wall color designations (24). Although they were few, it was determined with some clinics that some stimulant colors were applied.

Regarding physical safety characteristics in therapeutic environment, it was indicated that glass materials (glass cups, vase, salt and pepper holders) and other sharp tools (knife and jack-knife) should be avoided and dismissed from the environment (13). In order to fulfill security need in clinics, patients should be free from inflammable objects such as match and lighter. It was determined that majority of clinics do not allow patients to possess these materials; however, 14.9% of clinics allow these materials.

In treatment understanding of psychiatric clinics, sport, art and similar occupation activities and personal, group therapies and meetings constitute significant portion. In almost all clinics, such activities are implemented. When content of these activities are evaluated, some differences among clinics could be recognized. There is no sport activity in majority of clinics. Majority of rest of the clinics were offering opportunity to perform sport activities in their garden, interior sports such as table tennis or fitness are preferred in few clinics. When psychiatric clinics are taken into consideration in Turkey, it was seen that only very few of them has independent garden; in majority of them, hospitals have their own gardens. In terms of therapeutic environment, it is crucial that nurses conduct sport activities for patients (25).

It was also determined that sweet day cooking activity was not held in majority of clinics (66.7%). These activities are important because they allow patients to undertake responsibilities adequate to their individual capacities, to prepare daily life, to provide them opportunity to express them during activity in a safe environment and to distract them from symptoms of their disease by joining social activities (13).

In the present research, inability to include all psychiatric clinics into the sampling group constitutes a limitation for the purposes. Although relevant permissions were taken about the research, exclusion of 75 psychiatric clinics from the study in the data collection process because of various reasons such as refusing participation into study, closure of clinic due to assignment of physician to another position or temporary suspension of service is the limitation of the research.

5.CONCLUSION

According to study results, it could be observed that there are deficiencies in physical structuring of psychiatric services in Turkey; and that therapeutic activities are implemented in limited scope. In terms of shortening hospitalization periods of patients, psychiatric nurses play significant role in therapeutic environment. Therefore, it is necessary that

mental and psychiatric nurses need to implement caring activities by conforming to the principles of the therapeutic environment. It could be suggested that mental and psychiatric nurses who are responsible for establishment, maintenance and control of therapeutic environments could raise awareness about therapeutic practices; and could take initiatives about making regulations on the determined deficiencies.

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Determining Homophobic Attitudes of Nursing Students in Turkey and the Factors Affecting Them

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ABSTRACT

Objective: The investigation of homophobic attitudes of nursing students is an important issue as it may result in homosexual individuals' refraining from health services. The study was carried out to determine the homophobic approaches of nursing students and factors affecting them.

Methods: In this descriptive study (n:295), the data were collected using a personal information form developed by the researchers and a homophobic scale developed by Hudson and Rickett, which is called as Hudson and Rickett Homophobic Scale (HRHS). Frequency and percentage calculations, sample T-test, one-way Anova analysis and Tukey HSD test were also used for the statistical analysis.

Results: In the light of the findings of the research, it was revealed that 87.8 % of the students had no homosexual friends, and 71.9 % said their family would not approve a homosexual friend. 98.6% of the students has had no experience of caring a homosexual patient yet. 74.6% of them reported that their attitudes towards a patient would not change when the patient was homosexual; however, the mean HRHS score (91.83±23.83) indicates the opposite. In addition, mothers' having a higher education level, taking sexual health courses, having a homosexual friend, and the approval of the family were the effective parameters in reducing homophobic attitudes ($p<0.05$).

Conclusion: In the study, nursing students have a negative attitude towards homosexuality. Homophobic attitudes are one of the factors affecting the health care of homosexual individuals. It is therefore important to plan initiatives to reduce negative attitudes.

Keywords: Homophobia, attitude, LGBTI, nursing students, health care

1. INTRODUCTION

Homosexuality is defined as an emotional and sexual attraction to members of the same sex (1). Homophobia, on the other hand, is defined as negative feelings, attitudes, and/or behaviors towards people who have different sexual orientations or identities other than heterosexuality such as female homosexuals, male homosexuals, bisexuals and transsexuals (2). In other words, homophobia is the feelings of rage and abhorrence against these individuals and their sexual desires and practices, and also behaviors and feelings including fear, hatred, physical and verbal abuse towards them, who are internationally recognized with the abbreviation "LGBTI" (Lesbian-Gay-Bisexual-Transsexual-Intersex) (3). Today, individuals with an orientation other than heterosexuality face homophobic attitudes in many communities; they are generally shown less respect and perceived as sick or abnormal and they are usually discriminated (4,5). This leads homosexuals to encounter attitudes and behaviors such as fear, anxiety, rage, and anger in many areas of life (6). One of the areas where these negative attitudes and behaviors are faced is health services (7). When health staff notice their patients' sexual

orientation is lesbian or gay, they are likely to give negative and unfriendly reactions to them (8). It is reported that homophobia has a high rate among physicians, dentists, and nurses (9-11). However, it is health care professionals who should be aware of negative judgments and attitudes of society against homosexual individuals. They should be concerned of the problems these individuals are likely to experience and know that they are from vulnerable groups; otherwise, the attitudes of health care professionals can adversely affect these individuals in benefiting from health services or prevent them from receiving health services (8).

Nurses are among the health professionals that spend the most time and keep in touch with individuals receiving services in the health system. Their negative attitudes towards homosexual individuals can negatively affect the quality of the care they provide these individuals. As a result of this, it might not be possible for these individuals to receive the personal and comprehensive care which they need and deserve (12,13). Recently, patient-centered care and attention to the needs of LGBTI patients has been an important issue in health services, but nurses do not have the necessary education concerning the care for these patients. Thus, their negative attitudes and

behaviors can be explained with this lack of education (14). In addition, it is reported in the literature that nurses and other health care specialists need education on sexual orientations and homophobia (15-17). It should be noted that the attitudes of health professionals can be shaped during their education. Thus, investigating the behaviors of the students studying at the departments related to health sciences towards homosexuals is a key aspect. This situation can be improved by the inclusion of classes about sexuality and homosexuality at faculties where nurses receive the basics of their education. Therefore, examining the nursing students' attitudes can be helpful in attaining this. There are several studies in the literature regarding the behaviour of the students of health sciences against homosexuality. Campo-Arias et al. (2010) investigated homophobia among nursing students and found that homophobia is quite frequent (12). The statement "homosexuality is a psychological disorder that requires therapy" in the study of Kan and his colleagues was agreed by more than 25% of the medical students and more than 15% claimed that they would hold back from any physical contact as they see the risk of infecting them with diseases such as AIDS (18). Similarly, medical students from Colombia were reported to have a high sexual prejudice towards homosexual individuals with a 22.9% rate (19). Another study by Wilson et al. (2014) investigated the personal factors behind homophobia and found that the students of health sciences who are reported to be very religious and who lack the familiarity with religious aspects about sex have less positive attitudes against LGBTI individuals (20). These results indicate the importance of personal factors to develop a curriculum for LGBTI patient care. It is recommended that institutions educating health professionals should determine the students' homophobic attitudes, raise awareness about sexual orientations, and give comprehensive education on sexual health. However, there is limited research on this issue in Turkey. Therefore, the focus of this research is to examine the extent of homophobia among prospective nursing students.

Nursing training represents a very good opportunity to approach the problem and decrease sexual prejudice in future nurses. In order to prevent the sufferings of such individuals in the health system, current education should be improved and the awareness regarding homosexuals' health and sexual orientations should be enhanced through sexual education at faculties and academies. For this reason, this study investigates the homophobic approaches of nursing students and the factors behind them to provide an insight into nursing education.

2. METHODS

2.1. Research Questions

Research questions of the current study are:

- Do nursing students have homophobic attitudes?
- What are the factors affecting the homophobic attitudes of nursing students?

2.2. Study Design

As a descriptive research design, the study was carried out on nursing students in Turkey. It should be noted that "homosexuality" is used as an umbrella term to define male and female homosexuals in this study.

2.3. Participants

The study was conducted in the nursing departments of two state universities in Ankara, the capital of Turkey. Many young people prefer this city for university education. The reason for the inclusion of these two universities was that they were both state universities with similar programs. All of the volunteer students (n=324) matching the inclusion criteria were taken into sampling coverage. Inclusion criteria were as follows: the candidate should be 18 or over and registered as a second year student. Although they meet the inclusion criteria, 29 students did not accept to participate in the study during the data collection process. The questionnaires were given to 324 students but 295 students participated as mentioned above (response rate 91%).

2.4. Measures

The data were collected via two instruments; a personal information form developed by the researchers and Hudson and Rickett Homophobic Scale (HRHS).

2.5. Personal Information Form

This form consisted of two parts. The first part included 9 questions about such informative characteristics as age, family type, the mother and father's education level, etc., and the second part consisted of questions investigating their attitudes such as "having a gay friend", "having looked at a homosexual patient".

Hudson and Rickett Homophobia Scale (HRHS); it was developed by Hudson and Ricketts (1980) to measure attitudes towards homosexual individuals (21). The Cronbach Alpha value of the original scale was calculated as 0.90. (21). The scale is a Likert-type of scale graded from 1 to 6 and has 25 items. The Turkish adaptation of the scale and its validity and reliability study was conducted by Sakallı and Uğurlu (2001) (22). During the Turkish adaptation of the scale, one of the original items was excluded from the scale as it was thought to be inappropriate for our country's conditions, and eventually a 24-item form of the scale was obtained (22). The Cronbach Alpha value of the Turkish form of the scale was found as 0.94 (20). It was determined to be 0.91 in our study. The participants were asked to rate the items in the scale with a value ranging between 1 (strongly disagree) and 6 (strongly disagree). The total score was found by reversing the items 5, 6, 8, 10, 11, 13, 17, 18, 23 and 24 in the scale. Finally, the higher the score from the scale, the higher the rate of homophobia level (22).

2.6. Pilot Study

The pilot study was conducted with 32 nursing students, 10 % of the total sampling, to determine the comprehensibility and usability of the Personal Information Form. The pilot study was carried out at a university in Ankara that is different from the two universities, in which we carried out our study. Then the data collection process was launched following the necessary amendments.

2.7. Implementation of the Study

The data of the study were collected in the spring term of 2014-2015 academic year after the classes were completely finished. Prior to the data collection process, the students were informed about the purpose of the study, and the volunteers were included in the sampling. The students themselves filled in the data collection forms. The forms had no items intending to reveal students' identity. It took about 15-20 minutes to fill in the forms.

2.8. Limitations

Only one of the universities had elective "Sexual Health" lesson in the spring semester of the second year. We chose second grade nursing students to determine the effect of this course on homophobic attitudes. In addition determining students' homophobic attitudes on the second grade could provide an opportunity to make plans to eliminate their negative behaviors towards homosexuals in the future. These reasons, second grade nursing students were included in this research and this is the limitation of the study.

2.9. Statistical analysis

The data of the study were evaluated using a statistical software package at computer medium. All the analyses in the study were performed based on 95% confidence level. First type error level in the study was 5%. In the analysis of the data, the following analyses were used: frequency, percentage, independent sample T-test, one-way ANOVA, and Tukey HSD test to determine the groups creating the difference as a result of this analysis

3. RESULTS

The results of the data collected in this study were divided into three parts in line with the measures. Firstly, the demographic information and secondly the opinions on homosexuality obtained through the personal information form will be presented. Finally, the results about the attitudes towards homosexuals obtained from the scale will be given.

3.1. Demographic Results

Mean age of the students participating in the study was 20.17 ± 1.50 . 84.4% of the students had nuclear family structure, 63.7% stated that they had equal income and

expenses. The longest inhabited settlement of 47.1% of the students was province whereas that of 35.9% was Central Anatolian Region. The mothers of 68.7% of the students and the fathers of 56.8% of them had elementary school or lower education. The fathers of 71.2% of the students and the mothers of 18.3% were employed. Only 36.9% of the participants took sexual health course. The sexual health course was given theoretically in 2 hours a week fashion for 14 weeks. Within the scope of this course, topics such as sexuality concept, sexual rights, identity, orientation and development according to life cycles, sexual health problems and safe sexual behaviors were given theoretically.

3.2. Opinions on Homosexuality

The participants' opinions were gathered with eight questions. Five questions were asked to find out their personal opinions on homosexuality and three questions were asked to learn how their opinions would be as candidate nurses. Starting with the first group of questions, it was seen that 87.8% of the students stated they did not have a homosexual friend to date. 71.9% of the participants stated that their family would not approve their having a homosexual friend. The participants replied the sub question which asks the reasons why families disapproved having a homosexual friend as "it does not fit my family structure" (34.1%), "my family does not consider homosexuality appropriate for social, cultural and moral values (28.1%). Some of them found it inappropriate in terms of religious grounds (11.9%), and some stated that it was due to ignorance and prejudices (9.6%). The participants (24.7%) said they would end their friendship if they learned that their friend was homosexual. When they were asked if their attitude would change if the same happened with a colleague, 29.2% of the students said they would not like it. The last question in this group was about getting a kind of service from a homosexual individual and their answers were "I would not like it" (22.4%).

The second group of the questions was related to the participants' opinions as candidate nurses. 98.6% of the students stated that they had not given care to a homosexual patient so far. 74.6% said their attitude towards the patient would not change if the patient said that s/he was homosexual. 14.2% stated that they were hesitant about how they would behave in that case. The last question asked if the homosexual individuals should receive health care separately or not and 86.4% of the participants agreed with this statement. The reasons for this statement were "in order to prevent homosexual individuals from feeling uncomfortable" (46.2%) and the other one "in order to prevent the other people from feeling uncomfortable because of homosexual individuals" (26.9%).

3.3. Attitudes towards homosexuals according to HRHS

Item of the HRHS were given in Table 1. The mean HRHS score was found as 91.83 ± 23.83 . When some of the characteristics of the students were examined based on their HRHS scores,

the mean HRHS score of the students whose mothers were university graduates was 79.07 ± 27.68 . The mean HRHS score of the students whose mothers were university graduates was statistically and significantly lower than the ones whose mothers were elementary school graduates or lower and high school graduates (94.23 ± 22.51 and 88.96 ± 25.12 , respectively; $p < 0.05$) (Table 2). As the mother's education level increased, the score obtained from the scale decreased. It was determined that the mean HRHS score of those who

had a homosexual friend was significantly lower than those who did not (72.27 ± 22.88 and 94.55 ± 22.70 , respectively), and the mean score of those who stated their family would not approve a homosexual friend () was also significantly lower than that of those who said they would (77.20 ± 20.45 and 97.56 ± 22.02 , respectively; $p < 0.001$). The mean HRHS score for students taking sexual health course was significantly lower than that of the ones who did not take the course (88.24 ± 23.21 and 93.94 ± 24.00 , respectively; $p < 0.01$).

Table 1. Items of Hudson and Ricketts Homophobia Scale

Items	Strongly disagree		Moderately disagree		Slightly disagree		Slightly agree		Moderately agree		Strongly agree	
	n	%	n	%	n	%	n	%	n	%	n	%
1. I would feel nervous being in a group of homosexuals.	65	22	31	10.5	35	11.9	76	25.8	47	15.9	41	13.9
2. If a member of my sex made a sexual advance toward me I would feel angry.	21	7.1	23	7.8	30	10.2	50	16.9	59	20.0	112	38
3. I would feel disappointed if I learned that my child was homosexual.	18	6.1	16	5.4	25	8.5	60	20.3	60	20.3	116	39.3
4. I would be upset if I learned that my brother or sister was homosexual.	15	5.1	15	5.1	21	7.1	58	19.7	60	20.3	126	42.7
5. I would enjoy attending social functions at which homosexuals were present	104	35.3	57	19.3	45	15.3	43	14.6	28	9.5	18	6.1
6. I would feel comfortable if I learned that my daughter's teacher was a lesbian.	86	29.2	58	19.7	34	11.5	44	14.9	32	10.8	41	13.9
7. If a member of my sex made an advance toward me, I would be offended.	25	8.5	28	9.5	25	8.5	38	12.9	61	20.7	118	40.0
8. I would feel at ease talking with a homosexual person at a party.	53	18.0	33	11.2	30	10.2	70	23.7	54	18.3	55	18.6
9. I would feel uncomfortable knowing that my son's male teacher was homosexual.	31	10.5	34	11.5	27	9.2	55	18.6	53	18.0	95	32.2
10. I would feel comfortable working closely with a male homosexual.	44	14.9	24	8.1	31	10.5	64	21.7	67	22.7	65	22.0
11. I would feel comfortable if a member of my sex made an advance toward me.	129	43.7	50	16.9	39	13.2	30	10.2	24	8.1	23	7.8
12. I would feel that I had failed as a parent if I learned that my child was gay.	76	25.8	36	12.2	39	13.2	61	20.7	39	13.2	44	14.9
13. I would be comfortable if I found myself attracted to a member of my sex.	131	44.4	39	13.2	25	8.5	37	12.5	33	11.2	30	10.2
14. If I saw two men holding hands in public, I would feel disgusted.	50	16.9	37	12.5	43	14.6	62	21.0	38	12.9	65	22.0
15. I would disturb me to find out that my doctor was homosexual.	71	24.1	45	15.3	40	13.6	50	16.9	31	10.5	58	19.7
16. I would feel uncomfortable if I learned that my boss was homosexual.	77	26.1	40	13.6	43	14.6	52	17.6	33	11.2	50	16.9
17. If a member of my sex made an advance toward me, I would feel flattered.	189	64.1	31	10.5	30	10.2	21	7.1	10	3.4	14	4.7
18. I would feel comfortable working closely with a female homosexual.	67	22.7	43	14.6	42	14.2	54	18.3	42	14.2	47	15.9
19. I would feel uncomfortable if I learned that my spouse or partner was attracted to members of his or her sex.	13	4.4	22	7.5	17	5.8	33	11.2	39	13.2	171	58.0
20. I would feel uncomfortable if I learned that my neighbor was a homosexual.	67	22.7	35	11.9	41	13.9	58	19.7	37	12.5	57	19.3
21. I would feel uncomfortable being seen in a gay bar.	34	11.5	27	9.2	27	9.2	59	20.0	48	16.3	100	33.9
22. I would feel comfortable knowing that my clergyman was a homosexual.	35	11.9	28	9.5	28	9.5	38	12.9	41	13.9	125	42.4
23. I would feel comfortable if I learned that my best friend of my sex was homosexual.	79	26.8	41	13.9	36	12.2	50	16.9	34	11.5	55	18.6
24. I would feel comfortable knowing that I was attractive to members of my sex.	108	36.6	48	16.3	32	10.8	45	15.3	26	8.8	36	12.2

Table 2. The range of mean scores of Hudson and Ricketts Homophobia Scale according to some characteristics of the students (n: 295)

Identifying characteristics	n	Mean HRHS \pm S.D	Statistical Analysis
Place of Settlement			
Province	139	90.83 \pm 22.78	p>0.05
County	104	93.23 \pm 25.41	F=0,300
Town/Village	52	91.73 \pm 23.66	
The longest inhabited region			
Western Anatolia	62	88.61 \pm 24.43	p>0.05
Southern Anatolia	71	92.16 \pm 23.95	F=0.577
Central Anatolia	106	94.16 \pm 24.18	
Northern Anatolia	45	90.77 \pm 22.92	
Eastern Anatolia	11	89.81 \pm 21.47	
Family Type			
Nuclear Family	249	90.69 \pm 24.04	p>0.05
Extended Family	38	97.57 \pm 22.98	F=0.151
SingleParents Family	8	100.25 \pm 16.89	
Perceived Income Status			
Income is less than expenses	76	90.68 \pm 25.28	p>0.05
Income and expenses are equal	188	93.48 \pm 21.75	F=1.948
Income is more than expenses	31	84.67 \pm 30.80	
Mother's Employment Status			
Work	46		p>0.05
Not work	241	92.43 \pm 23.70	F=0,616
Retired	8	92.25 \pm 26.17	
Father's Employment Status			
Work	210	92.27 \pm 24.96	p>0.05
Not work	16	93.87 \pm 14.80	F=0.287
Retired	69	90.04 \pm 22.80	
Mother's Education			
Elementary school or lower (a)	187	94.23 \pm 22.51	p<0.05
High School (b)	94	88.96 \pm 25.12	F=3.702
University (c)	14	79.07 \pm 27.68	(a-c, b-c)*
Father's Education			
Elementary school or lower	126	94.44 \pm 22.16	p>0.05
High School	129	88.86 \pm 25.02	F=1.838
University	40	93.22 \pm 24.51	
Sexual Health Course			
Took sexual health course	109	88.24 \pm 23.21	p<0.05
Did not take sexual health course	186	93.94 \pm 24.00	t=-1,990
Having a homosexual friend			
Yes	36	72.27 \pm 22.88	p<0.001
No	259	94.55 \pm 22.70	t=-5.510
Family attitude towards having a homosexual friend			
Approves	83	77.20 \pm 20.45	p<0.001
Doesn't approve	212	97.56 \pm 22.02	t=-7.135
Attitude towards a homosexual patient when giving care			
More thoughtful (a)	30	92.93 \pm 25.49	p<0.001
Makes no difference in terms of attitudes and behaviors (b)	220	88.74 \pm 23.44	F=9.170
Unsure about how to behave (c)	42	104.04 \pm 18.10	(a-d, b-c, b-d)*
Wouldn't like to give care to such a patient (d)	3	136.66 \pm 2.30	

*Inter group differences

When students were asked how they would behave if they had to give care to a homosexual patient, it was determined that the mean HRHS score of the students who said it would make no difference (88.74 ± 23.44) was lower than that of the other students, and that the mean HRHS score of those who stated they would not give care to such a patient was the highest (136.66 ± 2.30). It was found based on HRHS scale scores that there was a significant difference between the groups in terms of attitudes and behaviors in the case of giving care to a homosexual patient. It was determined in the analyses that differences were between the students who stated they would behave more thoughtfully (92.93 ± 25.49) and those who would not give care to such a patient (136.66 ± 2.30), and between students who stated there would be no difference in their attitudes and behaviors (88.74 ± 23.44) and who were indecisive (104.04 ± 18.10) and who said they would not like to give care to such a patient (136.66 ± 2.30) ($p < 0.001$). On the other hand, there was not a significant difference between mean HRHS score and family type, place of settlement, the longest inhabited region, the father's education level and the parents' employment status ($p > 0.005$).

4. DISCUSSION

Homophobic attitudes and behaviors towards individuals whose sexual orientation is not heterosexual are common all over the world. In this study, which was conducted to identify if the nursing students have homophobic attitudes and if so it is also aimed to find out the factors affecting them, the majority of the students stated that they did not have a homosexual friend, and that their families would not approve a homosexual friend. Students articulated that their families would not approve such a friendship as they would not find it appropriate for their family structure, and social, ethical and religious values. It is known that cultural values, family, prejudice, religion and lack of knowledge are among the factors affecting the attitudes towards homosexual individuals (23,24). It is reported in the literature that religious values affect attitudes and behaviors towards homosexuals and negative stereotypes and homophobia existed more in male dominant societies (25,26). Turkey is a Muslim country which is generally male dominant, and where sexuality is taboo and sexual health subjects are not sufficiently included in the formal education curriculum, and which has teachings that do not ratify homosexuality. The reason why the majority of students do not have homosexual friends might be due to their families' homophobic attitudes, cultural, moral and religious values of the environment they live in. In addition, due to all these reasons, it may be possible for these students to have homosexual friends, but they are not aware of their homosexual identity as these individuals might hide their sexual orientations in order not to be excluded from the society they live in.

In the investigation of homophobic attitudes of the prospective nursing students, HRHS was utilized and it was found that the participants are highly homophobic considering the score 91 in the 24-144 score interval. The

factors affecting this result were also analyzed in this study and a significant difference between the mother's education level and homophobic attitudes of the students was found. The homophobic behaviors of the students whose mothers' education level was high was significantly lower than those of others. However, the father's education level was not found to be effective in homophobic attitudes. In Turkish family structure, the mother is usually the parent who is mostly responsible for taking care of the child. It is reported in the literature that as the education level of individuals increase, their negative attitudes towards homosexual men and women decrease (27-29). Thus, it can be concluded that when the education level of the mother is high, this contributes to the development of both mother and the child's health and intellectual level positively and makes it easy to accept some differences as mothers are the ones who spend the most time with the children.

Acceptance is the key to shape an individual's attitudes and behaviors. Saraç (2015) determined that the attitudes of individuals towards homosexuals who had a homosexual friend were more positive than those who did not (25). In a study conducted by Cirakoğlu (2006), it was determined that university students who had homosexual friends exhibited more positive attitudes towards homosexuals (30). Şah (2012) found that individuals who had homosexual, bisexual, or transsexual friends were more positive to these people than those who did not (31). Anderssen (2002) obtained findings that the attitudes of people who had positive social relations with homosexuals would develop more positively in time. In line with the literature, although it is limited to a small population of the participants, those who had homosexual friends seemed to have more positive attitudes when compared to others (32).

One of the reasons why individuals had negative attitudes and behaviors towards homosexuals was lack of information. It is emphasized in the literature that nurses and other health professionals lacked information about homosexuality and sexual orientations, and therefore it is necessary that health care professionals should be informed about these issues during their education (3,15-17). It was determined in a study carried out by Akhan and Ünsal-Barlas (2013) that health care professionals lacked information that homosexuals were not abnormal or sick, yet that they had different health needs compared to heterosexuals. In this study, it was found that those who took sexual health course had lower homophobic attitudes than those who did not take it (33). It was therefore stated in this study that health professionals needed a comprehensive sexual health education to reduce homophobic attitudes of nursing students. As for the participants' opinions as candidate nurses, significantly lower homophobic scores were found for students who stated that there would be no change in their attitudes than that of students who were hesitant about how to behave and who would not give care to such a patient at all. The score was also significantly lower for the students who stated they would be more thoughtful than the score of the students who would not give care to such a patient. These results suggest that the attitudes towards

homosexuals can affect behaviors in professional roles. It is emphasized in the literature that negative attitudes of nurses towards homosexuals can influence care services and applications (4,8) and it is recommended that students should be supported in terms of respectful approaches towards sexual orientations in nursing education (4,34). In addition, Klotzbaugh and Spencer (2014) states that as the negative attitudes of nurses towards LGBTI decreased, these individuals felt better in defending themselves (35). As it is widely known, homosexuals cannot live a life that is worthy of human dignity and cannot get services in many areas of life due to various reasons such as social values, disapproval and marginalization. Nursing is one of the most common health services that homosexuals may need to receive; therefore, the attitudes and behaviors of nurses and the related education of nursing students are of great importance.

5. CONCLUSION

This study showed that nursing students have homophobic attitudes towards homosexuals and taking sexual health course, education level of mother, having a homosexual friend, and approval of family for having a homosexual friend were found to be the factors affecting this result.

In line with these findings, it is recommended that sexual health courses should be included in the curriculum of nursing schools, social responsibility projects should be carried out that particularly involve mothers, and non-governmental organizations serving within the scope of this issue should be cooperated. Besides, it can also be suggested that some activities to increase interactions between nursing students and LGBTIs such as panels, symposiums etc. be held.

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Perceived Stigmatization Levels of Patients with Tuberculosis Applying to Tuberculosis Dispensaries in Istanbul

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ABSTRACT

Objective: In Turkey, tuberculosis (TB) is considered to be one of the formerly known social diseases. Similar researches exist for AIDS in many countries. There are very few publications about the tuberculosis stigma in our country at international level. This study aimed to assess tuberculosis-related stigma levels and associated factors in patients with tuberculosis applying to tuberculosis dispensaries.

Methods: This descriptive study was conducted in two different tuberculosis dispensaries at Istanbul. We used the stigmatization scale for patients with tuberculosis to assess and compare stigma levels of our study population. Nonparametric statistical tests were used for comparison of stigma scores.

Results: In our study population, stigmatization because of tuberculosis was found to be related to low income, pulmonary involvement, occupation, and nonexistence of a relative with tuberculosis in the close environment.

Conclusion: Combating the causes of stigmatization can assist patients in accessing their healthcare provider. Patients would be more likely to abide by the treatment schedule, thus reducing tuberculosis resistance in the community and decreasing its spread.

Keywords: Dispensary, Istanbul, stigma, tuberculosis, Turkey

1. INTRODUCTION

Tuberculosis (TB) is a chronic, necrotizing infectious disease caused by Mycobacterium species and is transmitted to humans from other humans. According to the World Health Organization's 2016 report, the TB frequency was found to be 18 in 100,000 in Turkey (1). In addition to high morbidity and mortality rates, social effects of the disease such as absences from work and other social activities because of airborne transmission of the organism in active TB cases exist (2, 3).

In Turkey, TB is considered to be one of the formerly known social diseases. After Robert Koch described the tuberculosis bacilli, the illness gained a bad reputation, known as "ince hastalık," (i.e., "fragiles' disease") in Turkish. In Turkey, TB earned this social reputation with the belief that fragile people acquired it mostly because of deep sorrow. Even physicians would not actually tell a patient with TB, with the medical diagnostic name as "verem" (i.e., "tuberculosis"). Instead, the physician would express the diagnosis as "Ciğerlerinde duman var," i.e., "I detected smoke in your lungs." In addition, people required consolation to accept high mortality, with some even preferring death rather than the stigmatization of having "ince hastalık." The disease was so highly stigmatized that many scenarios regarding patients with TB appeared in movies and films (4-6).

In social sciences, stigmatization is a label that negatively affects a person's social identity and is defined as physical or behavioral characteristics that lead to the rejection of a person by the society. It presents in two forms: felt and internalized stigma (7). The experience of actual rejection, on the basis of that patients are not socially accepted, is called internalized stigmatization (7, 8). The embarrassing feeling of the patient himself because of having a stigmatized illness and the fear of being exposed is called felt stigmatization (1, 9).

There are several studies in the local language that describe the social dimensions of TB (10-12). Patients with TB are isolated from the society, depending on their own causes, and also by causes that originate from the society. Many patients are excluded and stigmatized by the society because of TB infection owing to long treatment durations and lack of knowledge regarding TB, together with fear and prejudice (13). Friends of patients with TB may stay away from them, and patients may be forced to separately eat and sleep at home. Besides this, patients often isolate themselves with the fear that they will infect or be humiliated by others (14).

Stigmatization delays diagnosis, aborts treatment, results in depression, and diminishes self-esteem (2, 15). All these conditions can lead to the development of drug resistance and increase treatment cost (16, 17).

Investigating the stigmatization levels and accompanying conditions in TB-diagnosed patients may contribute to reducing stigma and indirectly increase treatment success, reduce costs, and increase the quality of life. We aimed to investigate the stigmatization status and associated factors of patients with TB in a group within the Turkish population.

2. METHODS

2.1. Settings and study population

This descriptive study was conducted in two different TB dispensaries in Istanbul between January and March 2015.

In Turkey, TB dispensaries are established to diagnose and treat patients with TB and establish prophylactic measures for their families. The first TB dispensary was established in Istanbul in 1923 and new dispensaries started to be opened nationwide (18). Directly observed treatment short course (DOTS) is used for TB treatment in our country (19). Medication is given free of charge to patients at dispensaries. The DOTS application strategy in Turkey is as follows. Patients who are nearby will visit the dispensary themselves and take their medication, whereas those who are far away from the dispensary are expected to visit the nearest health facility (health center, pharmacy, hospital, etc.) and take their medication there (20). Special training is given on DOTS therapy to particular health personnel (20).

Istanbul is the most crowded city in Turkey, and has immigrants from all over Turkey and even from other countries. Ethnically and socioeconomically, Istanbul shows a similar structure to Turkey as a whole (21). The city is divided into two main regions by the Bosphorus, one on the Anatolian side and the other on the European side.

The study population comprised 217 patients who applied to two TB dispensaries. There are 27 dispensaries in Istanbul. While choosing the two dispensaries sampling was not used. One dispensary on each side of the Istanbul Bosphorus gave us permission for collecting data, and thus, was included in our study. Patients with TB infection who completed their treatment and patients with active TB were included. No sample selection was made; attempts were made to contact the entire study population between January and March 2015. Among 217 patients, 203 patients were reached; 186 of these patients agreed to participate in the study.

2.2. Data collection and Ethics

Data collection was conducted using a face-to-face questionnaire. The stigmatization scale for patients with tuberculosis (SSPT) was used as a data collection tool along with the questions regarding sociodemographic characteristics. SSPT was developed by Sert (2010) (22). SSPT measures how stigmatized the patient perceives himself/herself. The Cronbach alpha coefficient of the scale is 0.91. The scale had a total of 33 Likert-type questions that aims at measuring the perceived stigmatization level of patients with TB. Some questions (2, 4, 17-19, 22, 23, 25-28, 30 and 31) are scored in reverse. Scale is scored as "4" if participant absolutely participates that phrase, "3" if participating, "2" if not participating, "1" if absolutely not participating. As the perceived stigmatization level increases,

the scale score is expected to increase. There are four subscales: stigmatization, self-perception, family–friend relationship, and internalized stigmatization. The highest score that could be obtained was 132, and the lowest score was 33.

Ethics approval for our study was granted by a local Ethical Committee. All procedures performed in this study that involved human participants were according to the ethical standards of the institutional and national research committee and the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Written informed consent was also provided from all the participants.

2.3. Statistical analysis

Kolmogorov Smirnov test was used for assessing normality assumption and found $p < 0.001$. Gaussian distributions could not be obtained therefore, the Mann–Whitney U and Kruskal–Wallis tests were used for analyzing data. The Chi-square test was used for analyzing categorical data. The α error level for statistical significance was set at 5%. Analyses were performed with IBM SPSS software version 20.

3. RESULTS

The study was completed with 186 patients, of which 76 were women and 110 were men. The sociodemographic characteristics of the participants is shown in Table 1. When questioned, 26.9% of patients declared that they had low income, while no respondents indicated that they had high income. Nearly half of the participants (40.3%) declared that they had no work. This was followed by the most frequently stated working status as being a permanent worker (26.3%) (Table 1).

Table 1. Sociodemographic characteristics of participants

	n	%
Sex		
Female	76	40.9
Male	110	59.1
Marital status		
Married	110	59.1
Single/Other	76	40.9
Education level (Graduated last school)		
Illiterate	11	5.9
Below high school	98	52.7
High school and above	77	41.4
Living place		
Urban	155	83.3
Rural	31	16.7
Declared income level		
Low	50	26.9
Middle	136	73.1
Working status		
Own business/employer	21	11.3
Permanent worker	49	26.3
Officer	23	12.4
Casual employee/temporary worker	18	9.7
Not working	75	40.3

When the participants' results from the TB treatment were examined, it was observed that approximately half of the participants were healed. The proportion of individuals with complicated TB (chronic TB or TB with multiple drug resistance) was 3.8%. Approximately three quarters of the participants were found to have pulmonary TB involvement. The proportions of individuals who had TB in their family or relatives who had TB within the previous year along with other descriptive data regarding patients are shown in Table 2.

Table 2. Descriptive data of participants with respect to tuberculosis

	n	%
Treatment status		
Still undergoing treatment	51	27.4
Complicated TB	7	3.8
Healed TB	91	48.9
Other	37	19.9
Location of TB involvement		
Pulmonary	141	75.9
Extrapulmonary	45	24.2
There is someone living in the same house having TB in the family/neighborhood—at the time of study		
	12	6.5
There is someone living in another house with TB in the family/neighborhood—at the time of study		
	3	1.6
There is someone living in the same house with TB in the family/neighborhood—previous year		
	12	6.5
There is someone living in another house with TB in the family / neighborhood—previous year		
	8	4.3

All subscale and total scale scores were found to be higher in participants with low perceived income levels ($p<0.001$ for felt stigma subscale score, $p<0.001$ for other subscale and total scale scores) and in participants with pulmonary TB involvement ($p<0.001$ for all). When stigma was examined according to the TB treatment status, all subscale and scale total scores were found to be lower in participants whose treatment was completed (felt stigma $p<0.001$, self perception $p:0.030$, family friendship relationship $p:0.003$, internalized stigma $p:0.007$, total stigma $p:0.001$). According to the employment status, total scale and family friend relationship subscale scores were found higher in employees working as temporary workers than those with other employments ($p:0.014$ for all) (Table 3).

Felt stigma subscale, self-perception subscale, and total scale scores were found to be higher in patients with close relatives having TB at the time of the study ($p:0.004$, $p:0.012$ and $p:0.006$, respectively). Scale scores were found to be similar in participants with a relative in the household having TB ($p>0.05$ for all). In addition, scale scores were similar for patients with an acquaintance with TB within the previous year (Table 3).

Additional results of SSPT for the patients are shown in Table 3. There were no statistically significant differences between the stigmatization scores according to sex, marital status, education level, and location of residence. These data were not presented in the table form ($p > 0.05$).

Table 3. Distribution of stigma scale scores according to participant characteristics

	Felt stigma subscale score		Self-perception subscale score		Family-friend relationship subscale score		Internalized stigma subscale score		Total stigma scale score	
	Median	(Range)	Median	(Range)	Median	(Range)	Median	(Range)	Median	(Range)
Declared income level										
Low	34	(21–44)	18	(10–27)	14	(8–20)	19	(9–26)	90	(60–114)
Middle	30	(21–44)	14	(7–25)	12	(6–20)	16	(9–27)	77	(57–115)
p value ^a	0.001*		<0.001*		0.001*		<0.001*		<0.001*	
Working status										
Own business/employer	33	(23–44)	16	(7–25)	13	(6–19)	17	(10–27)	78	(59–107)
Permanent worker	31	(21–44)	15	(9–27)	12	(7–20)	16	(9–25)	77	(57–115)
Officer	35	(22–42)	14	(12–22)	13	(8–20)	19	(13–26)	83	(63–109)
Casual employee/temporary worker	32	(24–42)	19	(12–23)	15	(11–20)	20	(13–25)	91	(73–114)
Not working	30	(21–43)	15	(7–23)	12	(6–20)	16	(9–26)	77	(60–114)
p value ^b	0.366		0.053		0.014*		0.051		0.014*	
Location of TB involvement										
Pulmonary	33	(21–44)	16	(7–27)	13	(6–20)	18	(9–27)	84	(58–115)
Extrapulmonary	25	(21–41)	14	(7–20)	12	(7–19)	14	(10–20)	66	(57–104)
p value ^a	<0.001*		<0.001*		<0.001*		<0.001*		<0.001*	
Treatment status										
Still receiving treatment	31	(23–42)	16	(9–21)	13	(6–19)	17	(9–25)	79	(58–115)
Complicated TB	33	(26–43)	16	(12–23)	15	(12–19)	18	(13–25)	89	(71–114)
Healed TB	26	(21–44)	14	(7–27)	12	(7–20)	15	(10–27)	70	(57–114)
Other	37	(24–43)	17	(7–23)	13	(6–20)	20	(9–25)	87	(62–110)
p value ^b	<0.001*		0.030*		0.003*		0.007*		0.001*	
There is someone living in the same house with TB in the family / neighborhood—at the time of study										
Yes	24	(22–35)	14	(12–17)	12	(10–15)	14	(13–18)	67	(63–89)
No	32	(21–44)	16	(7–27)	13	(6–20)	17	(9–27)	81	(57–115)
p value ^a	0.004*		0.012*		0.091		0.051		0.006*	

^a Mann–Whitney U test, ^b Kruskal–Wallis test, * Statistically significant

4. DISCUSSION

TB is not only an infectious disease but also a public health problem that has physical, social, and psychological dimensions. Patients may be exposed to stigmatization for reasons such as long treatment duration and incorrect beliefs from the previous period of modern therapy. Stigmatization is an additional psychological burden on patients (23, 24).

In our study, there was no significant difference in terms of stigma levels between sexes; these results are different from those reported in the literature. Suleiman et al (25) also indicated that there was no difference in TB stigma according to sex. In another study in Bangladesh, higher mean index values for stigma were reported in women than in men, possibly because of cultural factors and the situation of women in the society (26).

Stigmatization levels were found to be higher in individuals who reported low income, possibly because of the direct effect of the income on stigma, as well as the coexistence of the low income education levels (27). However, no significant difference was found between the scale scores according to educational level. Coreil et al (28) stated that the felt stigma was influenced by economic level and many other factors. Moreover, the stigma level was higher in individuals with low income. Chowdhury et al (29) also reported that stigma levels were higher in individuals with low income. Soomro et al (30) reported that tuberculous stigma was more clearly experienced by patients with low incomes who had lost their jobs and had financial distress. Attitudes of societies to low-income individuals may also be a contributing factor to stigmatization. The low income level and the coexistence of carrying an infectious disease may have caused the stigma to be felt at a higher level in these patients.

In our study, patients with pulmonary TB were stigmatized at a higher level than those with extrapulmonary TB. Tuberculosis with other visceral involvement may be felt to be less stigmatizing than pulmonary tuberculosis because of the lower incidence of infectivity and greater acceptability as an ordinary disease. Also in extrapulmonary TB, findings are less noticeable than pulmonary TB; this may also reduce stigmatization levels. Park et al (31) showed that patients with extrapulmonary TB were more compatible with drug treatment in their studies, suggesting that extrapulmonary TB is not observed as a stigmatizing condition but as an ordinary disease by patients. Chowdhury et al (29) also found that stigma in patients with pulmonary TB was higher than those with extrapulmonary TB.

We also found that the presence of another person with TB in the same house at the time of study was found to reduce stigmatization. An explanation for this could be that the patients with a relative in the same situation in the immediate vicinity normalizes the psychological dimension of the disease (32) Also while family-friend relationships (family-friend relationships subscores) were significantly affected by all other variables (like income level, working status or location

of TB involvement etc.), this relationship was maintained in patients who have a relative with TB. This is a finding that supports patients who have similar diseases in their vicinity and find tuberculosis more acceptable. Wieland et al (33) also reported that stigmatization in patients with TB caused concealment, embarrassment, fear, and isolation. Even if a disease is stigmatizing, it may be more easily accepted by patients in the presence of an acquaintance having the illness and living in close vicinity of the patient.

Total stigma levels were found to be higher in temporary workers than in those in other occupational groups. In addition, family friendships were also more affected in this group. Temporary workers often work collectively and in crowded groups at their workplaces. Therefore, they are more likely to be stigmatized by their societies because of the disease symptoms. Ozturk and Hisar (24) revealed that stigma scores were found to be higher in employees working at their jobs than civil servants and housewives. The reason for the different results between previous studies may be that employees such as temporary workers were not involved in the study groups of the mentioned research. However, in our study, the stigma levels were higher in temporary workers than those who had no work.

The limitations of the study include the fact that multivariate analyses could not be performed because of data characteristics and the independent effects of factors that affect stigma could not be investigated. Another limitation is that the results of our study could not be generalized to all TB patients who admitted to dispensaries since study conducted at only two dispensaries.

5. CONCLUSION

TB stigmatization was found to be related to low income, pulmonary involvement, occupation, and nonexistence of a relative with TB in the close environment. Combating the causes of stigmatization can assist patients in accessing their healthcare provider and encouraging compliance of the treatment schedule, thereby reducing TB resistance in the community and decreasing its spread. Furthermore, individuals will seek medical care earlier and receive better treatment with fewer complications. Qualitative studies are recommended to examine the causes of stigmatization in patients with TB more deeply.

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The Comparison of Effects of Applications of Compound 48/80 and Mast Cell Mediator Suspension on Inflammation in Rats: A Methodological Study for Acute Inflammatory Pain

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ABSTRACT

Objective: Inflammation underlies the pathological basis of most diseases. Substance-P is a key mediator that participates in various inflammatory processes and painful conditions. Mast cells (MCs) have a key role in inflammatory processes via mediators released from their granules. The experimental models for the investigation of pathogenesis and treatment of inflammatory diseases represent merely certain characteristics of inflammatory cases, therefore, more comprehensive models are required. We aimed to compare effects of administrations of the compound-48/80 and mast cell mediator suspension (MCMS) obtained from peritoneal MCs on the inflammation in rats.

Methods: Rats were divided into five groups (n=6): Intraperitoneally, Control group received 0.2 ml saline; C-48/80 group received 2 mg/kg compound-48/80; MCMS group received 0.2 ml MCMS; Cr+C-48/80 group received 10 mg/kg cromolyn plus compound-48/80; Cr+MCMS group received cromolyn plus MCMS. Potent inflammatory markers, plasma substance-P levels, and number and degranulation of dural MCs were measured. Data were analyzed using one-way ANOVA followed by Dunnett's post hoc test.

Results: Compound-48/80 increased plasma substance-P levels ($p<0.05$) and dural MC-degranulation ($p<0.001$). Likewise, MCMS increased substance-P levels and dural MC-degranulation ($p<0.001$) as well as number of dural MCs ($p<0.01$). MC stabilizer cromolyn inhibited increases in the parameters induced by compound-48/80 and MCMS ($p<0.01$ and $p<0.05$, respectively).

Conclusion: MCMS administration had greater impact to increase the plasma substance-P levels and number and degranulation of dural MCs than that of the compound-48/80 administration. The results demonstrate the potent inflammatory effect of MCMS treatment over the compound-48/80 administration. Administration of MCMS could be a useful tool to study inflammatory conditions.

Keywords: Inflammatory pain, mast cell degranulation, substance-P, compound-48/80.

1. INTRODUCTION

Inflammation is a complex biological response of tissues to endogen or exogen detrimental stimuli. Acute inflammation is induced by various stimuli including chemical mediators generated by damaged host cells, infections, chemical agents, tissue injuries, and immune reactions. Inflammation is characterized by pain, swelling, and leukocyte infiltration in the site of injury (1). Mast cells (MCs) are tissue resident inflammatory cells participating in immune responses during inflammatory reactions (2). Normally activation of MCs is useful to establish homeostasis of body systems, but their over activation can chronically induce inflammatory responses such as in the case of asthma and arthritis (3). MCs participate in the inflammatory processes by releasing various pro-nociceptive, vasoactive and pro-inflammatory mediators from their granules through a process called degranulation (4). MC-derived mediators such as serotonin, prostaglandin, histamine, tryptase, tumor necrosis factor-alpha (TNF- α), and interleukin (IL)-1 β are able to trigger and enhance inflammatory reactions (5). Increments in the number and degranulation of MCs

in their resident environment contribute to hyperalgesia in various rodent models of pain (6,7). It was previously reported that chronic inflammatory processes following pathological stimuli can be restrained by application of mast cell stabilizing agents such as ketotifen and cromolyn (8,9).

Substance P (SP) is a neuropeptide consisting of 11 amino acids and is produced by neurons and cells of the immune system such as MCs, macrophages, and dendritic cells. It exerts its effects by binding to the neurokinin-1 receptor (NK-1R) (10). SP is a crucial mediator of inflammation, and plays a key role in the generation and maintenance of inflammation. It is involved in the pathophysiology of various inflammatory diseases such as rheumatoid arthritis and joint inflammation (11, 12). SP participates in the inflammatory processes by inducing the release of proinflammatory cytokines such as IL-1, IL-2 and TNF- α from various cells (13). Inhibition of substance P activity by using NK-1 receptor antagonists or via gene deletion produces potent anti-inflammatory analgesic effects (14) and reduces edema formation in humans (15). Increased number and enhanced degranulation of MCs, and increased

SP levels accompanying hyperalgesia have been involved in various pathologies associated with pain (7).

Animal models of inflammatory pain are important tools to investigate pain mechanisms and analgesic effects of potential drugs for the treatment of inflammatory diseases. Various inflammatory substances including inflammatory cytokines, formalin, lipopolysaccharide and Freund's adjuvant have been used to construct animal models of inflammatory pain via application of these substances to cutaneous tissues, joints and muscles (16). Yet, none of these models mimic all the characteristics of inflammatory pains, however, they represent certain points of inflammatory pain conditions. Herein, we have compared effects of intraperitoneal administrations of the basic secretagogue agent compound 48/80 which is used to produce hyperalgesia and inflammation associated with the degranulation of mast cells as well as mast cell mediator suspension obtained from peritoneal MCs on the inflammation in rats.

2. METHODS

2.1. Experimental Animals

Thirty male Wistar rats weighing 170-200 g were used in present study. The rats received a standard pellet diet and water *ad libitum* and were housed in their cages with a 12 hour light/dark cycle at 22 ± 2 °C. All experimental applications were approved by Animal Experiments Local Ethics Committee of Abant İzzet Baysal University (licence number 2017/23).

2.2. Reagents

Compound 48/80, cromolyn sodium salt, toluidine blue, phosphate-buffered saline (PBS) and paraformaldehyde (PAF) were purchased from Sigma-Aldrich, (Schnellendorf, Germany). Substance-P ELISA kit was purchased from ELABscience (Wuhan, P.R. China).

2.3. Experimental groups and treatments

Thirty rats were randomly divided into five groups with six rats in each group. Intraperitoneal administration were performed as follows; rats in control group (n=6) were administered with 0.2 ml normal saline; rats in C-48/80 group (n=6) were administered with mast cell degranulating agent 2 mg/kg compound 48/80 (17); rats in mast cell mediator suspension (MCMS) group (n=6) were administered with 0.2 ml autologous mast cell mediator suspension (1.5×10^5 /ml cells); 30 min prior to the administration of compound 48/80, rats in Cromolyn+C-48/80 group (n=6) were treated with mast cell stabilizer agent with an amount of 10 mg/kg cromolyn sodium (8); 30 min prior to the administration of 0.2 ml autologous mast cell mediator suspension, rats in Cromolyn+MCMS group (n=6) were treated with 10 mg/kg cromolyn sodium.

2.4. Isolation of peritoneal mast cells from rats

Peritoneal mast cells were obtained from rats using peritoneal saline washing method as previously described (18). Rats were

anesthetized with ketamine (90 mg/kg, i.p.). Peritoneal lavage was carried out by injecting 10 ml normal saline containing heparin (5 U/ml) into peritoneal cavity. Abdominal massage was gently applied to the rats for 4 min. Then, 6 ml of peritoneal mast cell rich fluid was collected with a 10 ml syringe from the peritoneal cavity. The fluid was then centrifuged at 32 g for 2 min at room temperature. Precipitated peritoneal mast cells were mingled in 1 ml PBS and counted using a thoma chamber. To obtain mast cell mediator suspension, peritoneal mast cells in PBS were treated with compound-48/80 (10 µg/ml) for 15 min at 37 °C (17). Isolation of peritoneal mast cells were carried out to all rats to standardize experimental groups, but only rats in the MCMS and Cromolyn+MCMS groups were exposed to injections of 0.2 ml autologous mast cell mediator suspension (1.5×10^5 /ml cells). Intact and compound 48/80-induced degranulated peritoneal mast cells are shown in Figures 1A and 1B.

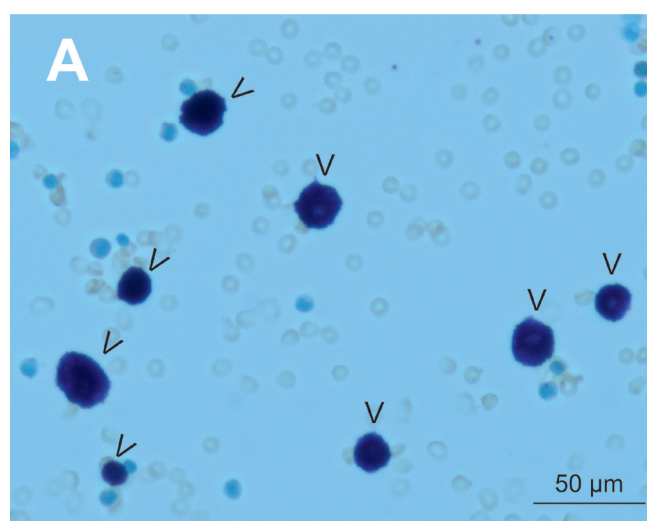


Figure 1A. Intact peritoneal mast cells before compound 48/80 treatment *in vitro*. X40 magnification. Open arrowheads show intact mast cells (staining, toluidine blue).

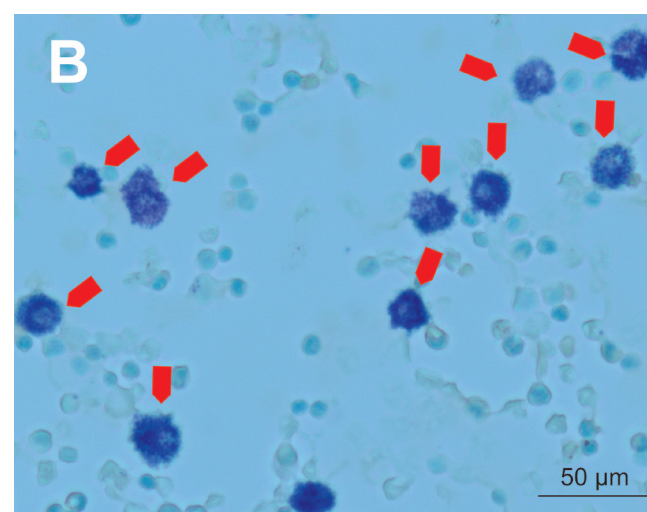


Figure 1B. Degranulated peritoneal mast cells after compound 48/80 treatment *in vitro*. X40 magnification. Red solid arrowheads show degranulated mast cells (staining, toluidine blue).

2.5. Blood sample collection from animals

Two and a half hours after administration of drugs or autologous mast cell mediator suspension all rats were anesthetized with ketamine (90 mg/kg, i.p.). Blood was collected intracardially and coagulated at room temperature for 30 min. The blood samples were centrifuged at 3000 rpm, at 4 °C for 15 min. The supernatants were stored at – 20 °C until assayed for substance-P immunoreactivity.

2.6. Dura mater preparations and toluidine blue staining for dural mast cells

After blood sample collection, all rats were instantly perfused intracardially with 100 ml phosphate-buffered saline (PBS; 0.1 M, pH 7.4) and PBS followed by 200 ml 4% paraformaldehyde. After perfusion process, whole-mount preparations of cranial dura mater were prepared on the glass slides as described previously (19). Briefly, the head was separated from the body, the skulls were opened carefully, and the dura maters were removed. The dura maters were postfixed in 4% paraformaldehyde solution overnight. Then, the dura maters were stained with toluidine blue staining (pH: 2.5) to observe mast cells in dura mater. Mast cells were counted in five objective areas including the main branches of the middle meningeal artery in both sides of dura mater, and categorized with regards to granulation or degranulation under a light microscope (Olympus CX21) by a blinded observer. The granulation term refers to the intact mast cells, on the contrary degranulation term expresses mast cells at the activated state that release various mediators such as histamine, prostaglandin, IL-1 β from their cytoplasmic granules to outside the cell. The percent of degranulated mast cells in each dura mater was calculated as follows: [(number of degranulated mast cells)/ (number of total mast cells)] X 100%. Number of total mast cells and the percent of degranulated mast cells were calculated, and their microscopic images were taken with a camera (Nikon DS-Fi1, Nikon, Japan) which was attached to the microscope (Nikon Eclipse 80i, Nikon, Japan).

2.7. Measurement of substance-P levels in plasma

Substance-P content of plasma was measured using ELISA method with detection kits. The Substance-P detection limit is approximately 46.88 pg/ml. The protocol was carried out in reference to the manufacturer's instructions and in duplicates. Briefly, 50 μ L of substance-P standard or plasma samples were added to each well. Immediately after, 50 μ L of biotinylated detection Ab was added to each well and the plates were incubated at 37 °C for 45 min. Followed by removal of liquid from each well 100 μ L of HRP conjugate were added and the 96-well plates were incubated for 30 min at 37 °C. After the incubation, the wells were rinsed for 5 times with the wash buffer. Then 90 μ L of substrate reagent was added to each well, finally, the plate was incubated for 15 min at 37 °C. After the incubation, 50 μ L of stop solution was added to each well quickly. Then, optical density was measured at 450 nm using a microplate reader (Epoch BioTek Instruments, Inc. Highland Park, Winooski, VT, USA). Optical density curve was constituted by using standards with defined substance-P concentrations.

2.8. Statistical analysis

The data were stated as mean \pm standard error of mean. Statistical analysis was performed using SPSS for Windows (version 17.0, SPSS Inc., Chicago, IL, USA). Statistical differences were determined using one-way analysis of variance test (ANOVA) followed by Dunnett's post hoc test. $p < 0.05$ was considered as statistically significant.

3. RESULTS

To activate mast cell degranulation, we used basic secretagogue agent compound 48/80, which leads to systemic mast cell degranulation through the body when administered intraperitoneally. Therefore intraperitoneal administration of compound 48/80 (2 mg/kg) induced massive degranulation of mast cells in the dura mater compared to controls (from $6.7 \pm 0.4\%$ to $45.6 \pm 3.5\%$, $p = 0.0002$, Figs. 2A, 2B and 3A).

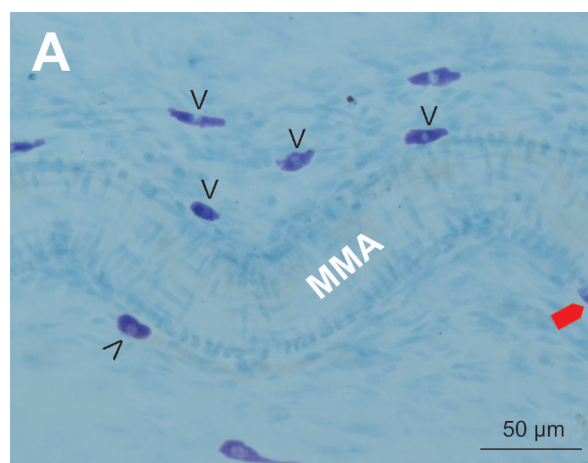


Figure 2A. Normally intact mast cells in the dura mater in control group. X20 magnification. While open arrowheads show intact mast cells, red solid arrowheads show degranulated mast cells (staining, toluidine blue). MMA: middle meningeal artery.

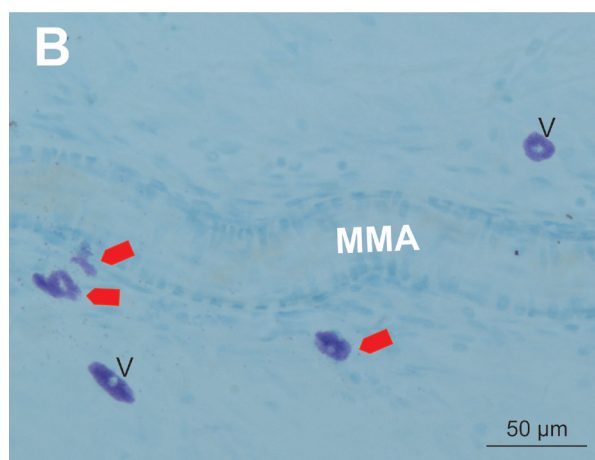


Figure 2B. Compound 48/80-induced degranulation of mast cells in the dura mater in compound 48/80 treatment group. X20 magnification. While open arrowheads show intact mast cells, red solid arrowheads show degranulated mast cells (staining, toluidine blue). MMA: middle meningeal artery.

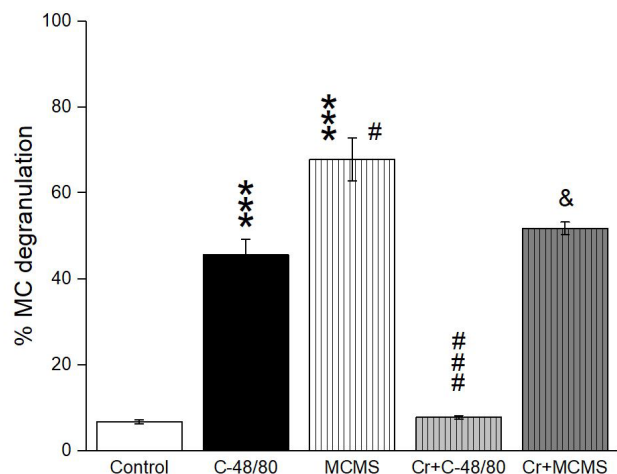


Figure 3A. While compound 48/80 and mast cell mediator suspension increased the percent of degranulated mast cells, these increments were inhibited by cromolyn, respectively. Mast cell mediator suspension further increased dural mast cell degranulation to compound 48/80. (** $P < 0.001$, * versus control group; # $P < 0.05$ and ### $P < 0.001$, # versus compound 48/80 group; & $P < 0.05$, & versus mast cell mediator suspension group). MC: mast cell, C-48/80: compound 48/80, MCMS: mast cell mediator suspension, Cr: cromolyn.

Moreover, intraperitoneal administration of compound 48/80 also increased plasma substance-P levels compared to controls (from 121.6 ± 5.1 pg/ml to 154.5 ± 4.3 pg/ml, $p = 0.01$, Fig. 4), but it did not change total mast cell numbers in the dura mater compared to controls (from 358 ± 20 to 360 ± 10 , $p = 0.87$, Fig. 3B).

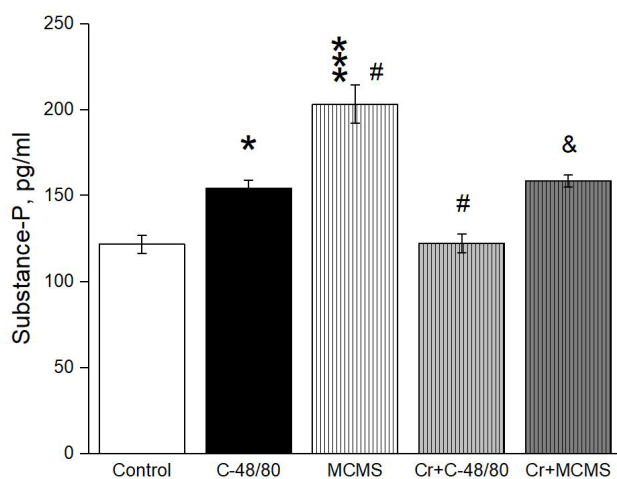


Figure 4. While compound 48/80 and mast cell mediator suspension increased the plasma substance-P levels, these increments were inhibited by cromolyn, respectively. Mast cell mediator suspension further increased the plasma substance-P levels to compound 48/80. (* $P < 0.05$ and *** $P < 0.001$, * versus control group; # $P < 0.05$, # versus compound 48/80 group; & $P < 0.05$, & versus mast cell mediator suspension group). C-48/80:

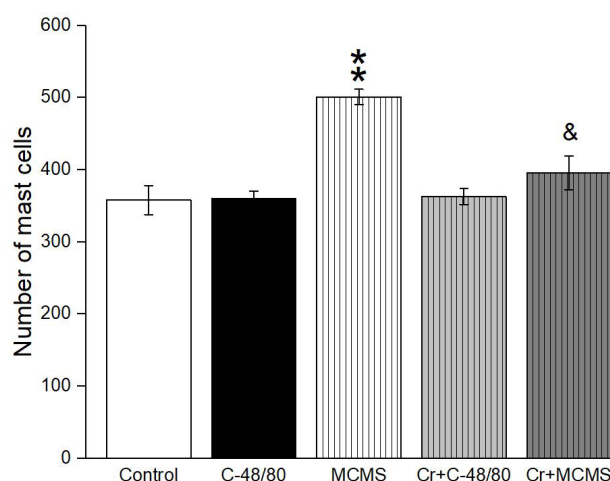


Figure 3B. While mast cell mediator suspension increased the number of mast cells in the dura mater, compound 48/80 did not change it. Cromolyn decreased the increments in the number of mast cells in the dura mater induced by mast cell mediator suspension. (** $P < 0.01$, * versus control group; & $P < 0.05$, & versus mast cell mediator suspension group).

To verify these effects of compound 48/80, we tested whether cromolyn sodium, a mast cell stabilizer, would prevent the actions induced by compound 48/80. When cromolyn was administered with compound 48/80 together, it blocked the effects of compound 48/80. Therefore cromolyn (10 mg/kg) prevented degranulation of mast cells in dura mater ($45.6 \pm 3.5\%$ in C-48/80 group versus $7.7 \pm 0.4\%$ in Cromolyn+C-48/80 group, $p = 0.0003$, Figs. 2C and 3A), and also it inhibited the increases in plasma substance-P levels induced by compound 48/80 (154.5 ± 4.3 pg/ml in C-48/80 group versus 122.3 ± 5.4 pg/ml in Cromolyn+C-48/80 group, $p = 0.007$, Fig. 4).

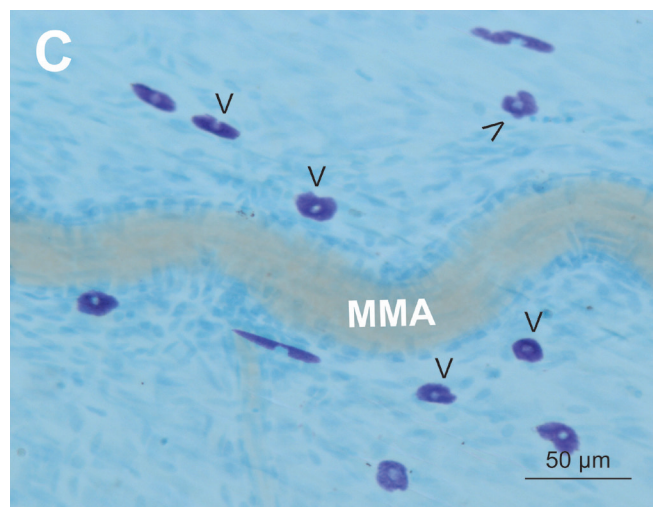


Figure 2C. Inhibition of mast cell degranulation in the dura mater by cromolyn in cromolyn plus compound 48/80 group. X20 magnification. Open arrowheads show intact mast cells (staining, toluidine blue). MMA: middle meningeal artery.

On the other hand, to compare effects of compound 48/80 and autologous mast cell mediator suspension, we first isolated peritoneal mast cells (Fig. 1A) and degranulated them by treating compound 48/80 (10 $\mu\text{g}/\text{ml}$) in vitro (Fig. 1B). Then, autologous mast cell mediator suspension was administered to the rats, immediately. Autologous mast cell mediator suspension administration significantly increased both the percent of degranulated mast cells (from $6.7\pm 0.4\%$ to $67.7\pm 4.9\%$, $p=0.0001$, Figs. 2D and Fig. 3A) and total mast cell numbers (from 358 ± 20 to 501 ± 10 , $p=0.002$, Fig. 3B) in the dura mater. It also increased plasma substance-P levels (from 121.6 ± 5.1 pg/ml to 203.1 ± 11.1 pg/ml, $p=0.0001$, Fig. 4) compared to control. Interestingly, the triggering effect of mast cell mediator suspension administration on the degranulation of mast cells in the dura mater ($45.6\pm 3.5\%$ in C-48/80 group versus $67.7\pm 4.9\%$ in MCMS group, $p=0.047$, Figs. 2B, 2D and 3A) and plasma substance-P levels (154.5 ± 4.3 pg/ml in C-48/80 group versus 203.1 ± 11.1 pg/ml in MCMS group, $p=0.015$, Fig. 4) was stronger than that of the compound 48/80. To clarify possible mechanism of these strong actions of mast cell mediator suspension, we tested whether cromolyn would inhibit the effects induced by mast cell mediator suspension. The results showed that cromolyn significantly attenuated both the percent of degranulated mast cells ($67.7\pm 4.9\%$ in MCMS group versus $51.7\pm 1.4\%$ in Cromolyn+MCMS group, $p=0.045$, Figs. 2D, 2E, and 3A) and total mast cell numbers (501 ± 10 in MCMS group versus 396 ± 23 in Cromolyn+MCMS group, $p=0.012$, Fig. 3B) in the dura mater. It also reduced autologous mast cell mediator suspension administration induced plasma substance-P levels (203.1 ± 11.1 pg/ml in MCMS group versus 158.5 ± 3.5 pg/ml in Cromolyn+DM group, $p=0.006$, Fig. 4).

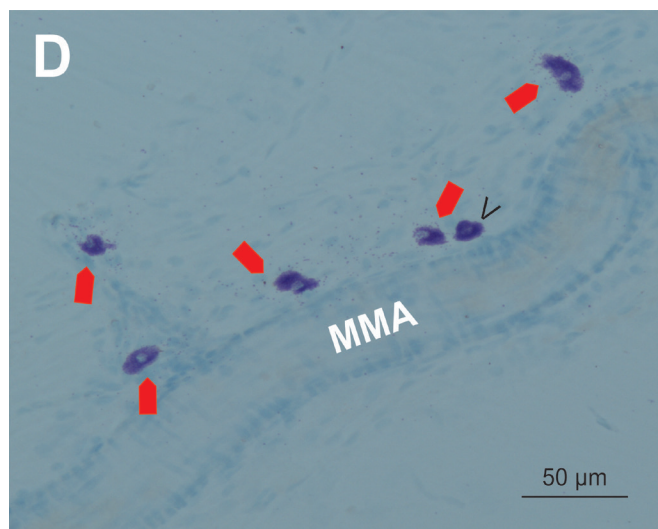


Figure 2D. Mast cell mediator suspension-induced massive degranulation of mast cells in the dura mater in peritoneal mast cell mediator suspension treatment group. X20 magnification. While open arrowheads show intact mast cells, red solid arrowheads show degranulated mast cells (staining, toluidine blue). MMA: middle meningeal artery.

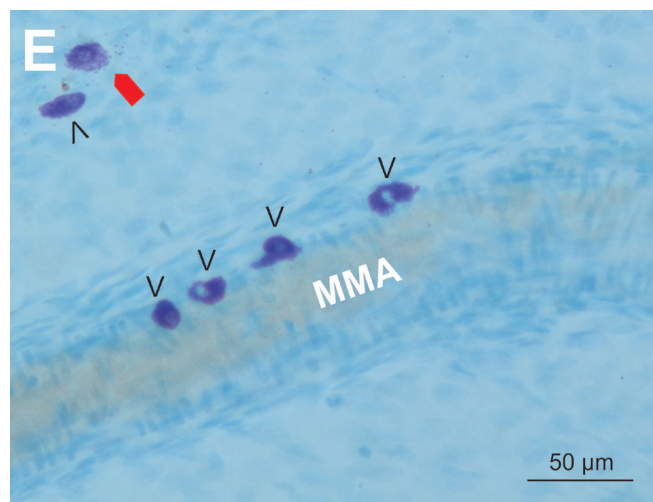


Figure 2E. Inhibition of mast cell degranulation in the dura mater by cromolyn in cromolyn plus mast cell mediator suspension group. X20 magnification. While open arrowheads show intact mast cells, red solid arrowheads show degranulated mast cells (staining, toluidine blue). MMA: middle meningeal artery.

4. DISCUSSION

The mast cell degranulator compound 48/80 is a synthetic secretagogue agent and widely used for non-IgE dependent activation of mast cells. Compound 48/80 treatment stimulates inflammatory responses in a variety of animal models such as systemic anaphylaxis (20), central nervous system inflammation (21), dural neurogenic inflammation and activation of trigeminal neurons in migraine (22), mast cell-mediated hyperalgesia (23), allergic inflammation and neuropathic pain (24). But in these models, compound 48/80 treatment leads to systemic mast cell degranulation throughout all body. Such applications make it difficult to focus on a specific disease in animal models of acute and chronic inflammation. The local application of compound 48/80 can solve the problem at the least in the tissues containing mast cells. In relation to this, we have recently shown that topical application of compound 48/80 to meninges evoked potently nociceptive firing in meningeal trigeminal nerve fibers in ex-vivo rat meningeal preparations through mast cell degranulation (22). But it is hard to see a specific or local effect of compound 48/80 treatment during in vivo applications because compound 48/80 diffuses almost all tissues of the body when it is injected. Therefore, in the present study, we used MC mediator suspension obtained from peritoneal mast cells degranulated by compound 48/80 for the first time to develop a model with both local and systemic effect for inflammatory diseases.

MC mediator suspension treatment exhibited more powerful effects than the effect of compound 48/80 on the plasma SP levels and number as well as degranulation of mast cells in the dura mater which are the most important markers of inflammation and acute inflammatory pain. In the present study, we chose plasma SP levels, and number

and degranulation states of mast cells in the dura mater to evaluate inflammation and inflammatory pain because of these parameters are accepted as valuable markers in most inflammatory diseases (3,7, 12, 25, 26).

It is known that mast cells and SP contribute a plethora of proinflammatory effects (12, 25). It was reported that SP levels and NK-1R expression were increased in the rectum and colon of patients with inflammatory bowel disease and in the synovial fluid and serum of patients with rheumatoid arthritis (27, 28). Moreover, SP leads to release of inflammatory mediators such as cytokines, serotonin, histamine, TNF- α , oxygen radicals and arachidonic acid derivatives from mast cells through receptor-independent mechanism. In a clinical study, a positive correlation has been shown between the plasma levels of SP and intensity of chronic pain in patients with osteoarthritis and rheumatoid arthritis (12). In the present study, we showed that intraperitoneal administration of compound 48/80 raised the plasma levels of SP, which is a critical marker of inflammation and inflammatory pain. However, mast cell stabilizers are also very important agents to control the plasma levels of SP in certain inflammatory diseases. It was reported that pretreatment with the mast cell stabilizer cromolyn decreased plasma levels of SP, CGRP and tryptase in transgenic sickle mice (29). Likewise, in the current study, pretreatment with the mast cell stabilizer cromolyn significantly diminished plasma levels of SP induced by compound 48/80 or mast cell mediator suspension. Inhibition of mast cell activation can be a considerable tool to prevent subsequent chronic inflammatory conditions such as asthma, headache, allergic and rheumatic disorders. For example, some mast cell stabilizers including ketotifen and cromolyn have been successfully used in the treatment of various allergic disorders (9). Moreover, reduction of mast cell numbers and/or inhibition of mast cell degranulation in their resident environment are also very important in the treatment of inflammatory diseases.

In the current study, cromolyn inhibited mast cell degranulation in the dura mater evoked by compound 48/80 or mast cell mediator suspension. Moreover, cromolyn decreased also mast cell mediator suspension-induced increments in the number of mast cells in the dura mater. Our findings are in accordance with the literature reporting the effects of the number and degranulation of mast cells in the inflammatory diseases (6, 7, 26). Previously published studies in the literature reported that there is an increase in the number and degranulation of mast cells in inflammatory pain conditions (6, 7, 26). The cranial dura mater is densely innervated by trigeminal afferent nerve fibers, and contains numerous mast cells.

Chemical or mechanical irritation of the dura mater causes release of vasoactive and proinflammatory neuropeptides such as SP and CGRP from trigeminal nerve terminals innervating the dura mater (4, 30, 31). Released SP and CGRP leads to plasma protein extravasation, vasodilatation of meningeal blood vessels and dural mast cell degranulation

which constitute triple trivet of dural neurogenic inflammation underlying migraine pain (5). Moreover degranulated mast cells in the dura mater release vasoactive, nociceptive and proinflammatory mediators such as SP, CGRP, serotonin, prostaglandins, histamine and a plethora of cytokines (2) which, in turn, further strengthen dural neurogenic inflammation and pain. On this basis, researchers developed an animal model of migraine through applying an inflammatory cocktail to dura mater to induce local inflammation at the dura mater (32, 33). This inflammatory cocktail known as inflammatory soup comprises a combination of serotonin, bradykinin, histamine, and prostaglandin PGE₂. Mast cells are known to contain these mediators. Such animal models to study inflammatory pain and hyperalgesia cannot mimic all characteristics of inflammatory pains due to the presence of only mast cell derived limited mediators such as serotonin, bradykinin, histamine, and prostaglandin PGE₂. Therefore, in the current study, we suggest a more realistic model including application of MC derived mediators to study mechanisms, pathophysiology and treatment of local or systemic inflammatory diseases. Moreover this new method has a number of advantages compared to existing methods. These are i) mast cell mediator suspension contain all mediators in the cytoplasmic granules of mast cells, ii) mediators used in the study are not synthetic, iii) the mediator suspension is autologous, iv) the mediator suspension also contains cytokines that are responsible for a broad spectrum of inflammatory responses, v) the mediator suspension can be applied intraperitoneally to induce systemic inflammatory conditions, or topically to constitute site-specific inflammatory diseases, vi) it can also be injected to cutaneous tissues, joints and muscles to establish local inflammatory diseases, vii) mast cell stabilizer cromolyn can be used as positive control to compare efficacy of new therapeutic agents for the treatment of inflammatory diseases.

5. CONCLUSION

Our results showed that administration of mast cell mediator suspension exhibited more potent inflammatory effects than compound 48/80 treatment, in terms of the increments in the plasma SP levels and the number and degranulation of dural MCs. Therefore intraperitoneal administration of mast cell mediator suspension could be a useful tool to investigate mechanisms of inflammatory conditions that are particularly associated with the degranulation of MCs.

However, our study has several limitations. These limitations are i) other inflammatory markers including, IL-1 β , bradykinin, TNF- α in peripheral blood should be studied following autologous mast cell mediator suspension administration, ii) in addition to pain and inflammatory markers in the plasma, behavioral tests such as von Frey and hot plate as indicator for the pain should also be performed to evaluate mast cell mediator suspension-induced inflammatory pain, iii) dose adjustment of autologous mast cell mediator suspension

administration should be studied in rats, mice and rabbits, and iv) further studies supporting our results are required.

Conflict of Interest: All authors declare no conflict of interest.





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The Prevalence of Paranasal Sinus Anatomic Variations on Cone Beam Computed Tomography Scan Images of Turkish Population

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ABSTRACT

Objectives: The paranasal sinuses include anatomic structures at the maxillofacial region that matters great importance for the surgeons working in the maxillofacial area. The imaging of anatomic variations of the paranasal sinuses is fundamental to evaluate the predisposing factors for the pathologic changes of paranasal sinuses. The aim of this study is to investigate the prevalence of anatomic variations of the paranasal sinuses by retrospective assessment of cone beam computed tomography (CBCT) images.

Methods: The paranasal sinus CBCT images of 300 adult patients who were referred to Marmara University, Faculty of Dentistry, Department of Oral Diagnosis and Radiology were evaluated retrospectively. The paranasal sinus variations and their prevalence were recorded.

Results: The prevalence of concha bullosa superior was 7,7%, and concha bullosa media was 54,7%. The prevalence of infraorbital ethmoid cell was 15,3%, agger nasi cell was 52,7% and onodi cell was 52.7%. There was no significant differences prevalence of this anatomic variations between males and females or between different age groups.

Conclusions: CBCT is a convenient radiographic examination to evaluate the paranasal sinus anatomic variations. Dental surgeons must be aware of such anatomic variations of the paranasal sinuses.

Keywords: CBCT, paranasal sinuses , anatomic variations

1. INTRODUCTION

The sinonasal cavities, presented by the ostiomeatal complex and paranasal sinuses, are the vital parts of the upper respiratory tract (1). Ostiomeatal complex is a functional unit which is a limited anatomical region consisting of: middle turbinate, uncinate process, bulla ethmoidalis as bony structures; frontal recess, ethmoidal infundibulum, middle meatus as air spaces; and anterior ethmoidal, maxillary and frontal sinuses as ostia. Furthermore, the paranasal sinuses include anatomic structures at the maxillofacial region that matters great importance for the surgeons working in the maxillofacial area (2).

Surgical approaches on the paranasal sinuses are among the most frequent operations in otorhinolaryngology and functional endoscopic sinus surgery (FESS) has become one of the commonest surgical procedures performed by otolaryngologists (3-6). The keystone of FESS is the capacity to treat even comparatively minor changes exactly, which obstruct mucociliary clearance of the frontal, ethmoid and maxillary sinuses in osteomeatal complex (6).

All the surgical interventions in this area require comprehensive information of anatomy and potential

anatomical variations. These variations with an impact on surgical reliability occur frequently and is essential particularly to investigate as a piece of preoperative evaluation (7). During FESS, the thorough elimination of these variations is necessary to ensure adequate opening of the sinuses and thus provide for physiological drainage and ventilation. The incomplete removal of variations in the sinuses is one of the most prevalent causes of FESS failure (7).

Anatomic variations, such as, concha bullosa, ethmoidal bulla hypertrophic, agger nasi cell and infraorbital ethmoid cell are common and evaluated in routine computed tomography (CT) images (8). CT is the gold standard modality for imaging the complex and variable anatomy of the paranasal sinuses for pre-operative recognition and especially in the assessment of causes for surgical failure (9,10). Multiplanar CT imaging achieves and greatly improves the understanding of the paranasal sinuses by standard axial or coronal CT images of the sinus with addition of sagittal reconstructions (11,12).

Cone beam computed tomography (CBCT), a more recent technological development, provides detailed anatomical information of mineralized maxillofacial tissues as three-dimensional images with minimal distortion. CBCT has been recommended as a perfect, relatively inexpensive instrument

for the assessment of these anatomical structures with lightly more radiation according to the panoramic radiograph and much fewer according to CT scan (13-15).

The aim of this retrospective study is to investigate the prevalence of anatomic variations of the paranasal sinus region using CBCT in a group of Turkish patients.

2. METHODS

2.1. Patient Data

Subjects for this retrospective study consist of all 300 patients who visited Marmara University, Faculty of Dentistry, Department of Oral Diagnosis and Radiology() and CBCT images of these patients between 2016-2017 were retrieved from the PACS system. CBCT imaging was performed with Planmeca Promax 3D Mid (Planmeca Oy, Helsinki, Finland) and assessment of CBCT was performed directly on monitor screen (Monitor 23 inch Acer 1920x1080 pixel HP Reconstruction PC). The purpose of CBCT scans were for impacted third molar surgery, orthodontic purposes, dental implant treatment and Le Fort I osteotomy. Patients with systemic diseases influencing growth and development, history of trauma and/or surgery involving the maxillofacial region, developmental anomalies/pathologies affecting the maxillofacial region, sinusitis, sinonasal polyposis, sinus malignancy, fibrous lesions, and previous sinus surgery were excluded from the study. The written informed consent was signed by the patients before CBCT scans. The study was carried out according to the recommendations of the Helsinki declaration and the study protocol was approved by the Local Committee of Research and Ethics of Marmara University, Faculty of Medicine (Protocol No: 09.2017.009).

2.2. Image interpretation

Two oral and maxillofacial radiologist (GU, ANYS) evaluated and interpreted anatomic variations; concha bullosa, agger nasi cell, infraorbital ethmoid cell and onodi cell. Before starting the radiographic examination in the study, the examiners were calibrated to recognize and agree on paranasal sinus anatomy and variations. For such purpose, a series of 50 CBCT were used (not included in this study) were examined. As part of the calibration phase, the examiners were given also explanations about radiographic and CBCT imaging.

The variations were identified on the left and right side separately. The recognition of these variations were made according to literature that were already described by means of multi-planar CT images (3).

Agger nasi cells (ANCs); are the most anterior ethmoid single cell, swelling along lateral nasal wall anterior to middle turbinate vertical attachment and are best viewed on coronal and sagittal planes. In the coronal plane, their position is inferior to the frontal sinus and anterior to the middle turbinate (16) (Figure 1).

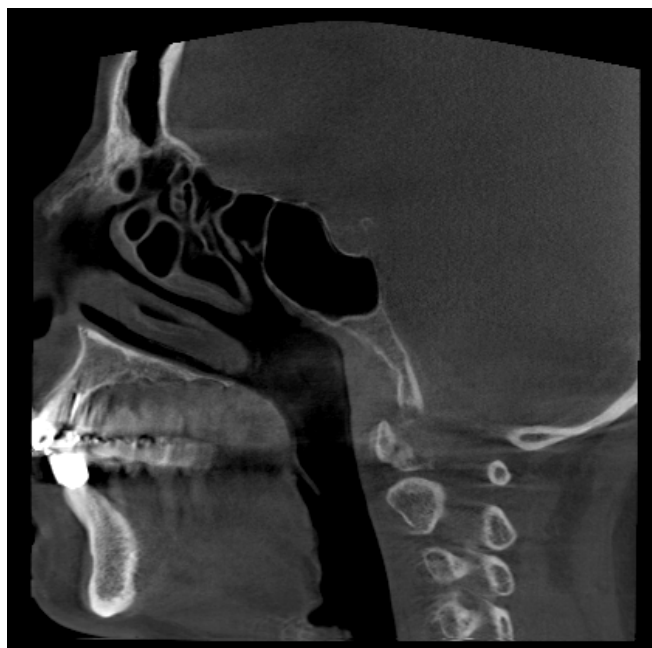


Figure 1. Sagittal view of agger nasi cell

Concha bullosa is described as occurrence of an air space within the lamina recurvata, free hanging portion of the turbinate. This space can be very small or can reach a pretty big size (Figure 2). Concha bullosa may be seen on the middle turbinate and, less often, on the inferior and superior ones. Concha bullosa can be identified in coronal CT scan images plainly (17,18).



Figure 2. Bilateral concha bullosa medium on coronal section

Infraorbital ethmoid cells are described as air cells situated below the ethmoid bulla along the roof of the maxillary sinus and the most inferior portion of the lamina papyracea, including air cells located within the ethmoid infundibulum

(Figure 3) (19). The existence of infraorbital ethmoid cells has been associated with various symptoms and diseases, including sinusitis, headaches, and mucoceles (19-21).

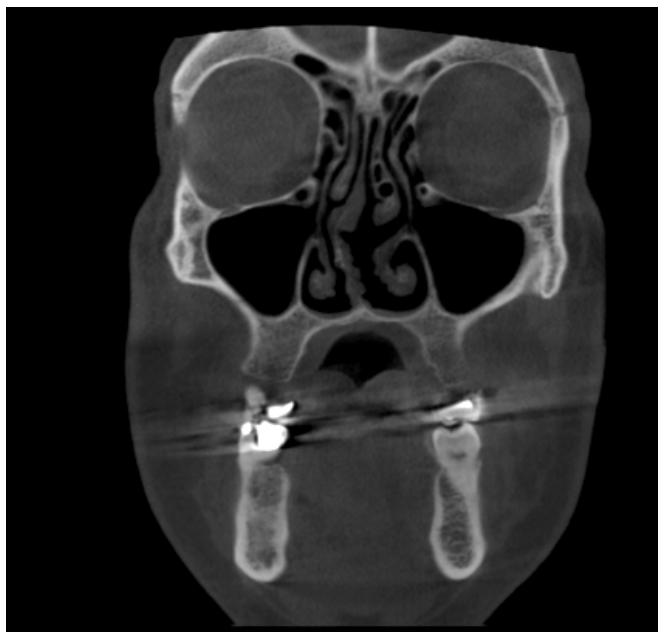


Figure 3 . Coronal view of bilateral infraorbital ethmoid cell

The Onodi cell is a posterior ethmoid cell which pneumatized far laterally and to some degree superiorly to the sphenoid sinus and is closely associated with the optic nerve (Figure 4) (18). Chmielik and Chmielik (22) suggested all multiplanar reconstructions of the CT examinations should be analyzed in the preoperative sinus CT evaluation, to identify and characterize Onodi cells, recommending axial and sagittal planes preferable in their study.

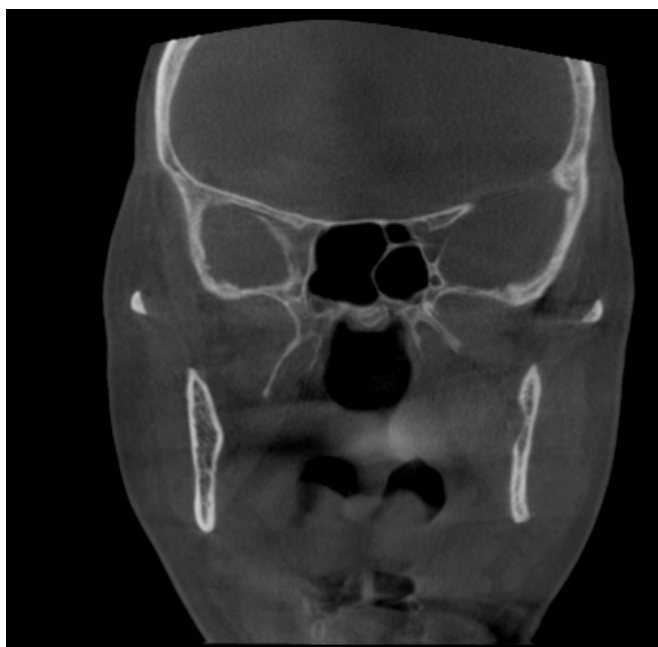


Figure 4. Onodi cell on coronal CBCT section

2.3. Statistical analysis

The data were analysed with IBM Statistical Package for Social Sciences (SPSS) for Windows 15.0 (SPSS Inc, Chicago, IL). Descriptive statistical methods (mean, SD, and frequency) were used for evaluation of the data. Chi-square test was used to compare qualitative data. Values of $p < 0.05$ were interpreted as significant.

3. RESULTS

A total of 300 patients met the inclusion criteria aged between 18 and 85 with 134 (44,7%) male and 166 (55,3%) female. The mean age is 47.13 ± 14.75 years. Of the 300 patients, 21 of the patients (7%) were between 18-24 years, 46 (15,3%) between the ages of 25-34, 68 (22,7%) between the ages of 35-44, 62 (20,7%) are between the ages of 45-54 and 103 (34,3%) are above the age of 55 (Table 1).

Table 1. Distribution of age and gender

		n	%
Age	18-24	21	7,0
	25-34	46	15,3
	35-44	68	22,7
	45-54	62	20,7
	Above 55	103	34,3
Gender	Male	134	44,7
	Female	166	55,3

While concha bullosa superior was not seen in 92,3% of the cases, bilateral, right and left concha bullosa superior was present in 2%, 2,3% and 3,3 respectively. Concha bullosa media was absent in 45,3%. They were present bilaterally in 22,3%, unilaterally right side in 14,7% and unilaterally left side in 17,7%. Concha bullosa inferior was not observed in any cases (Table 2).

Table 2. Paranasal Sinus Anatomical Variations

		n	%
Concha Bullosa Superior	Absent	277	92,3
	Bilateral	6	2,0
	Right	7	2,3
	Left	10	3,3
Concha Bullosa Media	Absent	136	45,3
	Bilateral	67	22,3
	Right	44	14,7
	Left	53	17,7
Concha Bullosa Inferior	Absent	300	100,0
Infraorbital ethmoid cells	Absent	254	84,7
	Bilateral	15	5,0
	Right	14	4,7
	Left	17	5,7
Agger Nasi Cell	Absent	142	47,3
	Bilateral	108	36,0
	Right	20	6,7
	Left	30	10,0
Onodi Cells	Absent	142	47,3
	Present	158	52,7

In 84,7% of the cases, no infraorbital ethmoid cells were observed, 5 % of the cases were bilateral, 4,7% were on the right side and 5,7% were on the left side. In 47,3% of the cases, agger nasi cells were absent; in 36% bilateral, in 6,7% on the right side and in 10% on the left side agger nasi cell were present. In 47,3% of the cases, no onodi cells were observed while in 52,7% of the cases onodi cells were present (Table 2).

There was no statistically significant difference between the incidence rates of concha bullosa superior and concha bullosa media, infraorbital ethmoid cells, agger nasi, onodi cells according to age groups ($p > 0.05$) (Table 3).

There was no statistically significant difference between the incidence rates of concha bullosa superior and concha bullosa media, infraorbital ethmoid cells, agger nasi, onodi cells according to gender ($p > 0.05$) (Table 4).

Table 3. Assessment of paranasal sinus anatomic variations according to age groups

		Age					p
		18-24	25-34	35-44	45-54	55+	
		n (%)	n (%)	n (%)	n (%)	n (%)	
Concha Bullosa Superior	Absent	18 (85,7%)	43 (93,5%)	65 (95,6%)	58 (93,5%)	93 (90,3%)	0,058
	Bilateral	0 (0%)	0 (0%)	2 (2,9%)	3 (4,8%)	1 (1%)	
	Right	0 (0%)	1 (2,2%)	1 (1,5%)	0 (0%)	5 (4,9%)	
	Left	3 (14,3%)	2 (4,3%)	0 (0%)	1 (1,6%)	4 (3,9%)	
Concha Bullosa Media	Absent	9 (42,9%)	25 (54,3%)	30 (44,1%)	26 (41,9%)	46 (44,7%)	0,310
	Bilateral	6 (28,6%)	4 (8,7%)	11 (16,2%)	20 (32,3%)	26 (25,2%)	
	Right	2 (9,5%)	6 (13%)	13 (19,1%)	9 (14,5%)	14 (13,6%)	
	Left	4 (19%)	11 (23,9%)	14 (20,6%)	7 (11,3%)	17 (16,5%)	
Infraorbital ethmoid cells	Absent	18 (85,7%)	38 (82,6%)	59 (86,8%)	49 (79%)	90 (87,4%)	0,509
	Bilateral	2 (9,5%)	4 (8,7%)	4 (5,9%)	2 (3,2%)	3 (2,9%)	
	Right	0 (0%)	1 (2,2%)	3 (4,4%)	4 (6,5%)	6 (5,8%)	
	Left	1 (4,8%)	3 (6,5%)	2 (2,9%)	7 (11,3%)	4 (3,9%)	
Agger Nasi Cell	Absent	12 (57,1%)	15 (32,6%)	31 (45,6%)	29 (46,8%)	55 (53,4%)	0,644
	Bilateral	5 (23,8%)	21 (45,7%)	28 (41,2%)	23 (37,1%)	31 (30,1%)	
	Right	1 (4,8%)	5 (10,9%)	4 (5,9%)	3 (4,8%)	7 (6,8%)	
	Left	3 (14,3%)	5 (10,9%)	5 (7,4%)	7 (11,3%)	10 (9,7%)	
Onodi Cells	Absent	9 (42,9%)	23 (50%)	26 (38,2%)	33 (53,2%)	51 (49,5%)	0,460
	Present	12 (57,1%)	23 (50%)	42 (61,8%)	29 (46,8%)	52 (50,5%)	

Table 4. Assessment of paranasal sinus anatomic variations according to gender

		Gender		p
		Male	Female	
		n (%)	n (%)	
Concha Bullosa Superior	Absent	120 (89,6%)	157 (94,6%)	0,428
	Bilateral	4 (3%)	2 (1,2%)	
	Right	4 (3%)	3 (1,8%)	
	Left	6 (4,5%)	4 (2,4%)	
Concha Bullosa Media	Absent	67 (50%)	69 (41,6%)	0,298
	Bilateral	29 (21,6%)	38 (22,9%)	
	Right	20 (14,9%)	24 (14,5%)	
	Left	18 (13,4%)	35 (21,1%)	
Infraorbital ethmoid cells	Absent	109 (81,3%)	145 (87,3%)	0,498
	Bilateral	9 (6,7%)	6 (3,6%)	
	Right	7 (5,2%)	7 (4,2%)	
	Left	9 (6,7%)	8 (4,8%)	
Agger Nasi Cell	Absent	68 (50,7%)	74 (44,6%)	0,180
	Bilateral	40 (29,9%)	68 (41%)	
	Right	9 (6,7%)	11 (6,6%)	
	Left	17 (12,7%)	13 (7,8%)	
Onodi Cells	Absent	65 (48,5%)	77 (46,4%)	0,714
	Present	69 (51,5%)	89 (53,6%)	

4. DISCUSSION

CT is defined as the gold standard in evaluating anatomic variations in paranasal sinuses also with preoperative anatomical evaluations, pathologies and bone integrity as it supplies adequate spatial resolution and generated data can be used for computer-assisted endoscopic sinus surgery (23-25). On the other hand, it is generally known that CT is liable for the majority of the medical radiation doses in the populations of modern societies. Recently, the use of CBCT in the evaluation of paranasal sinus anatomy has been studied and published (26-29), CBCT generates three-dimensional data on the maxillofacial area, and is progressively being used in numerous dental specialties as well as otorhinolaryngology. Although CT is important and primary choice for evaluating the paranasal sinuses, CBCT may definitely take on the same role in the planning of endoscopic surgery of the paranasal sinuses, making it possible to obtain high-resolution axial, coronal, and sagittal sections (26). Considering above mentioned arguments, we evaluated CBCT images for analyzing anatomic variations of paranasal sinuses.

Wormold (30) suggested that agger nasi cells are the key to figure out the anatomy of frontal recess at paranasal sinus area. In this study, the prevalence of agger nasi cells was 52,6%. The prevalence of agger nasi cells is remarkably variable, ranging in different studies. Sagar et al (31) has found the prevalence in 94 % of their cases respectively. Han et al (32) reviewed 202 CT scans and found that the agger nasi cells were present in 94,1% of Chinese patients. On the other hand, Talaiepour et al (33) evaluated 143 patients and agger nasi cells were found in 56,7% of the cases. Also; there are some other studies lower percentages in their respective studies (34-36). Angélico et al (37) stated that the reason for the discrepancy found in results, was the technique used for evaluation. They reported that researchers used only the CT scan with thicker axial and coronal slices larger than 3mm and found lower agger nasi cell percentages. The sagittal reconstructions, with thinner slices provided better examination of nasal structures and expanded the point of view in the understanding of the complex anatomy, allowing to evaluate the extent of structures of paranasal sinuses. In CBCT systems, image data can be usually demonstrated on a monitor simultaneously showing a segmented 'volume rendered' image as the fourth window in addition to axial, coronal and sagittal planes, which makes the evaluation of paranasal sinuses easy (38).

One of the most common variations of the sinonasal region is pneumatization of the concha – concha bullosa. This variation is most frequently seen in the middle concha followed by the superior concha. In this study, the prevalence of concha bullosa middle was 54,7% while concha bullosa superior was 7,7% with no concha bullosa inferior. Turna et al (39) has found that the most prevalent pneumatized concha was the middle concha (57.2%) with the least prevalent inferior concha by 1%. Aramani et al (40) reviewed 54 CT scans and found that the concha bullosa were present in 53.7%

patients. In our study, the prevalence of concha bullosa was consistent with these studies.

In 1756, infraorbital ethmoid cells were first presented by Albrecht Von Haller and were named as "haller cells". On the other hand the nomenclature for these cells has been replaced with infraorbital ethmoid cells, as they originate from the anterior ethmoid cells and are located in the medial orbital floor (19). The prevalence of infraorbital ethmoid cells presented in different studies includes a wide content between 5,5% and 45,9% (41). Fadda et al (42) found the incidence of infraorbital ethmoid cells as 22,8% on CT scans. Gocmen et al (43) reviewed 300 CBCT scans and from the 300 scans, 2,7% were showed infraorbital ethmoid cell on the right, 9,3% on the left and 7,3% bilaterally. In our study, while in 84,7% of the cases, no infraorbital ethmoid cells were observed, 4,7% of the cases were on the right side, 5,7% were on the left side and 5% were bilateral. The results of our study are in agreement with these studies.

Although conventional radiographic examinations are used frequently and as the first step examination in practical application, they do not allow for the obvious imaging of ethmoid and sphenoid sinuses. When these are compared by CT, rates of pseudo positive and pseudo negative findings are known to be very high (44). The reported prevalence of the onodi cell is higher in clinic-anatomic studies (42%-60%) than the radiologic ones (8%-24%). This discrepancy may relate to the angle of computed tomography acquisition or the complexity of imaging interpretation (45). In 47,3% of our cases, no onodi cells were observed while in 52.7% of the cases onodi cells were present compatible with the study presented by Senturk et al (46).

5. CONCLUSION

The findings of this study point out that CBCT can be used in the analysis of paranasal sinuses. The current study attempted to search numerous paranasal sinus variations and their prevalence. Such morphometric data may provide vital information to otolaryngologists and dental surgeons in preoperative analysis of surgeries associated with paranasal area and may facilitate accurate identification of the anatomy of the paranasal sinus region.

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Group B Streptococci Induce Interleukin 8 Production in Human Cervical Epithelial Cell Cultures: The Role of Capsule Polysaccharide

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ABSTRACT

Objective: Group B streptococci (GBS) are the major cause of pneumonia, sepsis, and meningitis in neonates and adults. Epithelial invasion and early cytokine response of female genital tract considered to be important in the pathogenesis of GBS infection. In this study, we studied the IL-8 induction in cervical epithelial cells in response to stimulus with encapsulated (COH1) and unencapsulated (COH1-13) strains of group B streptococci.

Methods: Human cervical epithelial cancer cell (HeLa) cultures were stimulated with different concentrations (10^6 CFU/ml and 10^8 CFU/ml) of two GBS strains. *E.coli* LPS was used as positive control and at specified time points (4, 8 and 24 hour) cell culture supernatant samples were collected. IL-8 level in samples was quantified by using ELISA assay.

Results: Both GBS strains caused an equal IL-8 response in HeLa cells in a time-dependent manner. In addition, cytokine levels triggered by different bacterial concentrations were similar and comparable with LPS.

Conclusion: Our study showed that GBS induce proinflammatory IL-8 levels in cervix epithelial cells. This induction seems to be independent from capsule polysaccharides and suggesting that other bacterial components are involved in IL-8 stimulation.

Keywords: Streptococcus Group B, bacterial capsule, epithelial cells, IL-8

1. INTRODUCTION

Group B Streptococci (GBS) or *Streptococcus agalactiae* are among the members of the microbiota residing in the human gastrointestinal, respiratory and genitourinary systems (1). This pathogen is an important cause of pneumonia, sepsis, and meningitis of newborns and also associated with invasive infections in pregnancy, immunocompromised people and elderly population (2).

Since the GBS infections in babies as well as in mothers in the postnatal period express high morbidity and mortality, GBS colonization in female genital tract attract remarkable scientific interest. There are numerous studies investigating the colonization rates of this pathogen in child-bearing age. Vaginal and/or rectal carriage rates of GBS vary between 15-35% in pregnant women globally (3). GBS colonization rates were found between 1-16% in Turkey based studies and differences in detection rates mainly related with methodological approaches (4). Several strategies are suggested to eradicate the pathogen in antenatal period to prevent the neonatal infections.

GBS produce several virulence factors that contribute the bacterial invasiveness and defense. A group of GBS virulence factors are well defined such as fibrinogen-binding proteins,

β -hemolysin/cytolysin, and polysaccharide capsule which have a distinct role in host cell adhesion, cellular invasion and immune evasion, respectively (5).

Most of the clinical GBS isolates carry a polysaccharide capsule demonstrating unique structure with sialic acid residues. Sialic acid renders the bacterial cell wall to mimic the mammalian cell surface expressing the glycans from the same family. So, the host immune system can not recognize the encapsulated GBS as an invader (6). Several studies are used the encapsulated and unencapsulated GBS strains to investigate the effects of capsule production on the pathogenesis of GBS infection (7).

Colonization of the female genital tract is the first step of GBS related diseases. After bacterial adhesion to epithelium; there are several pathways triggering the host immune response and the production of the bacterial virulence factors (8). From the host sight, PAMPs (Pathogen-Associated Molecular Patterns) from pathogenic bacteria interact with PRRs (Pattern Recognition Receptors) on the host cell to induce the production of proinflammatory cytokines such as Tumor Necrosis Factor-alpha (TNF-alpha), interleukin-1 β (IL-1 β), IL-6 and IL-8 as a triggering step of inflammation-infection cascade (9).

IL-8 is a member of CXC or alpha-chemokine family and secreted from monocytes, macrophages, and also from several non-immunological cells like fibroblasts, endothelial and epithelial cells (10). IL-8 has powerful chemoattractant capacity for neutrophils and some T lymphocyte subsets, and induces neutrophil activation and degranulation (11).

In this study, we focused on GBS interaction with cervix epithelial cells and investigated the effects of capsule production and the inoculum size on IL-8 response of epithelial cells.

2. METHODS

2.1. Bacterial strains

We used two GBS strains in this study, encapsulated one (COH1) and unencapsulated isogenic mutant of parent strain (COH1-13). COH1-13 strain was derived by transposon insertion mutagenesis (7). These strains were kindly provided by Dr. C.E. Rubens (University of Washington, Seattle, WA, USA).

2.2. Cell culture

The HeLa cell line was derived from cervical cancer cells and has been used for cytotoxicity and cytokine release experiments. Cells were cultured in minimal essential medium (MEM) (Sigma-Aldrich, St. Louis, MO, USA) supplemented with 10% heat-inactivated fetal calf serum (FCS) (Gibco, Invitrogen, Carlsbad, CA, USA), 2 mM L-glutamine (Invitrogen) and 1% antibiotic and antimycotic solution (Invitrogen) at 37°C with 5% CO₂. Cell viability was determined by 0.4% trypan blue staining and counting Thoma chamber. Before stimulation experiments, HeLa cells suspended in 0.5 mL of culture medium with 10% fetal calf serum were seeded into 6-well culture plates (Greiner Bio-One, Kremsmuenster, Austria) and incubated for 2 days at 37°C with 5% CO₂ to obtain monolayers. Nonadherent cells were removed by washing with MEM twice.

2.3. Bacterial inoculum preparation

COH1 and COH1-13 strains were grown in 20 mL fresh Todd-Hewitt broth (Oxoid, London, England) at 37°C overnight. Bacterial cultures were washed twice with sterile phosphate – buffered saline (PBS, pH 7.4) and suspended in PBS at cell density of 3.0x10⁹ CFU/mL by using spectrometry at 600 nm wavelength. Bacteria were heat killed by incubating the organisms at 56°C for 1 h, and samples subcultured on blood agar plates and incubated at 37°C for 48 h to ensure the killing process. Aliquots were stored at – 70°C for later use in the experiments.

2.4. Epithelial cell stimulation

HeLa cell monolayers were stimulated with heat killed COH1 and COH1-13 GBS strains at 10⁶ CFU/mL and 10⁸ CFU/mL cell densities. HeLa cells with medium alone served as negative control. Purified *Escherichia coli* 055:B5 LPS (Sigma-Aldrich, St. Louis, MO, USA) at 100 ng/mL final concentration was

added to wells as positive control. Culture supernatants were collected from study and control wells at selected incubation periods (4, 8, and 24 h), centrifuged, and stored at –20°C until IL-8 determination assay.

2.5. Determination of IL 8 levels

IL-8 levels secreted into the culture supernatants were detected with a commercial enzyme-linked immunosorbent assay (ELISA) kit (Quantikine ELISA, R&D Systems, Minneapolis, MN, USA) by following the manufacturer's instructions. This kit had 7.5 pg/mL sensitivity and assay range between 31.2-2000 pg/mL for human interleukin-8. All measurements were performed in duplicate.

2.6. Statistical analysis

IL-8 values are expressed as mean ± standard deviation of values. Differences between groups were analyzed with Microsoft Excel 2013 software (Microsoft, Redmond, WA, USA) for significance by using Student's unpaired t test (two-tailed P value). P value of 0.05 was considered to indicate statistical significance.

3. RESULTS

3.1. HeLa cells are stimulated by GBS to secrete IL-8

The induction of IL-8 production by cervix epithelial cells (HeLa) was evaluated after stimulation with heat-killed (56°C for 30 min) GBS strains. There was no difference in IL-8 production by HeLa cells exposed to the encapsulated (COH1, 10⁸ CFU/mL) or the isogenic unencapsulated mutant strain (COH1-13, 10⁸ CFU/mL) (mean IL-8 levels at 24 h, 440.9 vs 473.3 pg/mL, respectively; P>0.05). Cell culture supernatant from medium alone was used as negative control, and purified *E. coli* LPS (100 ng/mL) was used as positive control. Both strains were yielded responses similar to LPS in inducing IL-8 secretion (mean 364.7 pg/mL; P>0.05) and caused significantly higher cytokine production compared to negative control (72.9 pg/mL; P<0.05) (Figure 1).

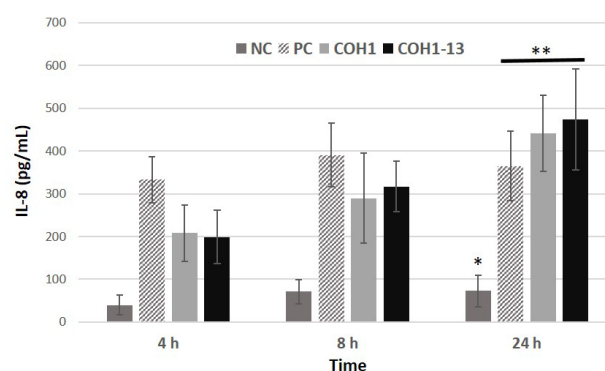


Figure 1. IL-8 production measured by ELISA in the supernatant of HeLa cells incubated with heat killed encapsulated (COH1) or unencapsulated (COH1-13) GBS (10⁸ cfu/mL). Media alone (unstimulated) was used as negative control (NC) and LPS from *E. coli* served as positive control (PC). Data are duplicate assays for each experiment (*: P<0.05; **: P>0.05).

3.2. Time course of epithelial cell IL-8 production in response to GBS

For the determination of the changes in IL-8 secretion after GBS stimulation, HeLa cells were incubated for up to 24 h with both GBS strains. The IL-8 level was significantly increased within 4 h (mean 223.2 pg/mL with COH1 and 222.8 pg/mL with COH1-13), and its concentration increased steadily over time. At 24 h, the mean IL-8 level was 4.4 and 5.0 fold greater than negative control for COH1 and COH1-13 strains, respectively (Figure 2).

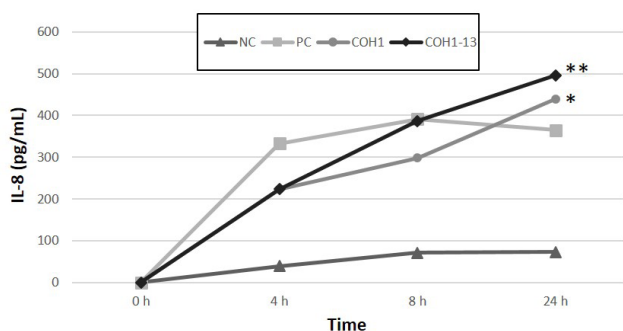


Figure 2. Time curves of IL-8 responses by HeLa cells after stimulation with encapsulated (COH1) or unencapsulated (COH1-13) GBS and with LPS (100 ng/mL) from *E. coli*. Media alone (unstimulated) was used as negative control (NC) and LPS from *E. coli* served as positive control (PC). Data are duplicate assays for each experiment (*: 4.4 fold increase versus NC; **: 5.0 fold increase versus NC).

3.3. Bacterial concentration independent IL-8 release

Both tested bacterial cell densities (10^6 and 10^8 CFU/mL) were equivalent in inducing IL-8 production for both GBS strains used in this study (mean 478 pg/mL and 457 pg/mL; $P > 0.05$). These data suggest that bacterial factors capable of causing IL-8 secretion are sufficient in both concentrations and were similar with that of LPS (100 ng/mL) (Figure 3).

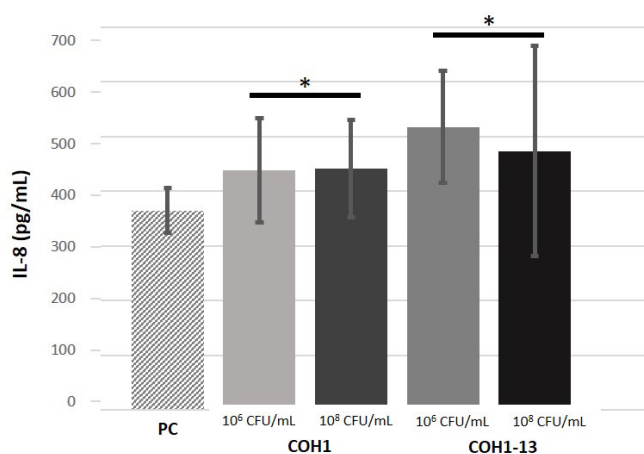


Figure 3. Dose-response effects of different concentrations (10^6 CFU/mL and 10^8 CFU/mL) of GBS strains on IL-8 secretion by HeLa cells. IL-8 was measured after 24 h of incubation at 37°C by ELISA assay (*: $P > 0.05$).

4. DISCUSSION

In this study, we demonstrated heat-killed Group B streptococci induced IL-8 secretion in human cervical epithelial cells *in vitro*. In addition, presence of bacterial capsule was not affected the induced IL-8 production (Figure 1). Furthermore, bacterial inoculum size was not related with the secreted IL-8 level from epithelial cells.

In general, capsule formation is considered a major virulence factor of GBS. The importance of the capsular polysaccharides in GBS virulence is maintained by the effect of protective type-specific anti-capsule antibodies and by the capability of encapsulated GBS to inhibit complement related opsonization, phagocytosis, and intracellular killing by human peripheral blood polymorphonuclear leukocytes (12). However, GBS with polysaccharide capsule (COH1) could induce IL-8 secretion in similar levels with the non-encapsulated isogenic strain (COH1-13). Concordant with our results, other studies have found similar findings for production of proinflammatory cytokines IL-6 and TNF- α from human monocytes using the same encapsulated and unencapsulated GBS strains used in our study (13, 14).

GBS induced cytokine release searching studies were also investigated the role of certain bacterial components, including capsular polysaccharide in triggering the cytokine response. Vallejo et al. studied the effects of whole cell GBS and also purified capsular polysaccharide, lipoteichoic acid and peptidoglycan isolated from of GBS cell wall, and group B polysaccharide on TNF- α release from neonatal monocytes. Their findings were highlighted significant TNF- α release with the induction by the group B polysaccharide or peptidoglycan. Additionally, they suggested any of the GBS components might have a synergistic role in the induction of cytokine release during infectious process (15).

Early cytokine responses have important roles in the host response to infection that is targeted for eradicating bacteria from the invaded body sites. IL-8 is a member of the chemokine family containing cytokines those have primary roles in attracting and activating immune effector cells such as neutrophils and macrophages. It plays a significant role in recruiting leukocytes at sites of acute inflammation (10). In this context, there is an increased level of IL-8 along with other proinflammatory cytokines such as TNF- α , IL-1 and IL-6 in the acute phase of GBS infection (16). On the other hand, there are some limitations of our study, since differentiated epithelial cells can show changed or unexpressed physiological cellular functions, extrapolation of the study results to physiological state may be limited. Over and above, our study does not allow us to establish the relationship between the IL-8 production and the responsible GBS components. Future studies aimed at defining the role of cellular factors of GBS in IL-8 response of epithelial cells would thus be of interest.

5. CONCLUSION

Our data suggest that GBS induced IL-8 release by cervical epithelial cells may be the initial trigger for the acute inflammatory reaction after bacterial invasion of mucosal tissue. Additionally, IL-8 production is not required that alive bacterial cells adhere or invade cervical epithelial cells. Moreover, the two strains of GBS examined here are also able to induce IL-8 by what appears to be a similar mechanism rather than capsule formation.

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The Relationship Between Patient Reported Dysphagia Symptom Severity and Swallowing Related Quality of Life in Patients with Neurological Disorders

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ABSTRACT

Objective: The aim of this study was to determine the relationship between patient reported dysphagia symptom severity and swallowing related quality of life (SRQOL) in patients with neurological disorders.

Methods: Patients with a diagnosis of neurological disorders who aged between 25 to 60 years were included. The dysphagia symptom severity was assessed with the Turkish Eating Assessment Tool (T-EAT-10). SRQOL was assessed by the Turkish version of the Swallow Quality of Life Questionnaire (T-SWAL-QOL).

Results: Eighty-four patients with neurological disorder were included. The mean T-EAT-10 score was 19.59 ± 11.16 (min = 0, max = 40), and the mean total score of T-SWAL-QOL was 50.63 ± 23.52 (min = 0, max = 90). A negative, good, statistically significant correlation between T-EAT-10 and total T-SWAL-QOL was found ($p < 0.05$).

Conclusion: Higher patient reported dysphagia symptom severity is associated with lower scores of SRQOL. Therefore, appropriate management strategies which also focus on patient reported symptoms may be necessary to minimize negative SRQOL issues of patients with neurogenic dysphagia.

Key words: Deglutition, deglutition disorders, neurogenic dysphagia, quality of life

1. INTRODUCTION

Neurological disorders cause a high prevalence of oropharyngeal dysphagia which has significant complications including malnutrition, dehydration, and recurrent pneumonia (1,2). Dysphagia also affects general health and wellbeing of patients due to several reasons. First, difficulty in swallowing causes inability to eat and drink. Second, risk of coughing, choking, and vomiting due to swallowing difficulty may cause increased anxiety and decreased self-esteem (3). Third, mealtimes may become stressful and mealtime pleasure may decrease due to dysphagia (4,5).

Swallowing related quality of life (SRQOL) assessments have been used as outcome measures of the effect of diseases and/or treatments (6). Quality of life of patients with neurogenic dysphagia has been investigated in several studies (7-11). One study concluded that SRQOL is associated with degree of swallowing impairment which is based on the penetration aspiration severity of the patients with amyotrophic lateral sclerosis (10). This study shows only one aspect related to swallowing disorders and therefore the relationship with more comprehensive aspect of swallowing disorders in addition to airway safety would also be investigated.

Patient reported outcome measures become very important because they are directly obtained from the patient without any interpretation. These outcomes are found to be related to disease and treatment effects (12) and allow clinicians to implement patient feedback into clinical practice (13). Therefore, patient reported information regarding their symptoms (i.e, type, frequency, severity of symptoms), perceptions and treatment effects should be essential for high quality clinical care (14). Patient reported outcome measures in dysphagia rehabilitation are also critical to understand different aspects of swallowing disorders including physiological as well as psychosocial aspects (15). It was reported that patient reported dysphagia symptom severity help to identify patients with oropharyngeal dysphagia and are sensitive to differences in dysphagia severity level (16-19). Therefore, patient reported dysphagia symptom severity would provide a comprehensive aspect of swallowing impairment. The aim of the current investigation was to determine the relationship between patient reported dysphagia symptom severity and SRQOL in patients with neurological disorders. We hypothesized that SRQOL would decrease in patients who perceived higher dysphagia symptom severity.

2. METHODS

Patients with a diagnosis of neurological disorders who were referred for the first time due to complaints about swallowing function, aged between 25 to 60 years, and being cognitively normal according to the Mini Mental State Examination (20) were included. Patients with neurological disorders who were clinically unstable, had abnormal cognitive function, and had no dysphagia symptoms were excluded from the study. This prospective study was approved by the Non-interventional Clinical Researches Ethics Board. The written and signed approval form was obtained from the patients.

Descriptive information including age, gender, height, weight, diagnosis and type of feeding was noted. The dysphagia symptom severity was assessed by the Turkish Eating Assessment Tool (T-EAT-10) (17). The T-EAT-10 has sufficient internal consistency, test-retest reliability, and criterion validity. It can be used to predict risk of aspiration in patients with neurological disorders, thereby help to identify and refer patients with dysphagia for further evaluation (21). Patients filled the T-EAT-10, and if they need any guidance in terms of meaning of the questions or scoring system, a physical therapist who specialized in dysphagia research helped. It has 10 questions and every question is scored on a 5-point scale between 0 to 4. The score 0 means 'no problem', and the score 4 indicates 'severe problem'. The scores of the 10 questions are summed to obtain a total score. A score of three or more from the instrument indicates being at risk of swallowing disorders (16). Patients with a T-EAT-10 score more than 15 were 2.4 times more likely to have airway aspiration (21). The administration of the T-EAT-10 takes less than 2 minutes.

SRQOL of the patients were questioned by the Turkish version of the Swallow Quality of Life Questionnaire (T-SWAL-QOL) (22). It is a 44-item questionnaire, and the completion of the instrument takes 20-30 minutes. T-SWAL-QOL has 10 subscales related to generic and SRQOL. The subscales related to generic quality of life include fatigue and sleep. The subscales related to SRQOL are burden, eating duration, eating desire, food selection, communication, fear, mental health and social functioning. There are two types of questions in the instrument. Patients are asked to define the frequency of a situation in some questions. The rest of questions focus on the degree of agreement of the items. Both frequency and evaluation questions are in the form of a 5 point Likert scale. All subscales range from 0 to 100, the lower the score, the worse SRQOL. It was reported that global scores in SWAL-QOL is approximately 65-80 (10).

All patients completed the instruments in a quiet room.

Statistical analysis

The IBM-SPSS for Windows version 20 was used to perform statistical analysis. Number/percent for qualitative data

and mean, standard deviation, minimum and maximum for quantitative data were used for descriptive statistics. The non-parametric Spearman correlation coefficient was used to assess correlation between quantitative variables. Correlation coefficients between 0.05-0.30 show low correlation; where, 0.30-0.40 show low to moderate correlation, 0.40-0.60 show moderate correlation, 0.60-0.70 show good correlation, 0.70-0.75 show strong correlation, and 0.75-1.00 show excellent correlation (23). The Mann-Whitney U test was used to compare the patients according to the type of feeding. A p-value of less than 0.05 was considered as statistically significant.

3. RESULTS

Eighty-four patients with neurological disorder were included, of which 57.1% were female. The mean age, height and weight of the patients were 48.14 ± 9.03 years (min = 25, max = 60), 162.56 ± 9.85 cm (min = 145, max = 190), and 68.16 ± 12.82 kg (min = 45, max = 98), respectively. A percentage of 71.4 of the patients (n = 60) were stroke patients, 15.5% (n = 13) were patients with Parkinson's disease, and 13.1% (n = 11) were patients with Multiple sclerosis. A percentage of 58.3 of the patients (n = 49) were fed orally and 41.7% of them fed non-orally (n = 35).

The mean T-EAT-10 score was 19.59 ± 11.16 (min = 0, max = 40), and the mean total score of T-SWAL-QOL was 50.63 ± 23.52 (min = 0, max = 90). The mean scores of the T-SWAL-QOL are shown in Table 1.

Table 1. The mean T-EAT-10 and T-SWAL-QOL scores

	X	SD	min-max
T-EAT-10	19.59	11.16	0-40
Total T-SWAL-QOL	50.63	23.52	0-90
Burden	40.09	31.79	0-100
Food selection	64.79	30.86	0-100
Eating duration	64.76	32.23	0-100
Eating desire	54.29	28.31	0-100
Fear	55.96	33.71	0-100
Sleep	45.84	30.99	0-100
Fatigue	43.04	31.17	0-100
Communication	51.85	33.43	0-100
Mental health	51.33	37.17	0-100
Social functioning	41.39	34.22	0-100

A negative, good, statistically significant correlation between T-EAT-10 and total T-SWAL-QOL was detected ($p < 0.001$, $r = -0.69$). The correlations between T-EAT-10 and the subscales of T-SWAL-QOL are displayed in Table 2. Worse scores in T-SWAL-QOL were associated with worse scores in T-EAT-10.

Table 2. The correlation T-EAT-10 and T-SWAL-QOL scores

	T-EAT-10	
	r	p
T-SWAL-QOL total	-0.69 ****	p<0.001
Burden	-0.39***	p<0.001
Food selection	-0.56***	p<0.001
Eating duration	-0.28*	0.01
Eating desire	-0.58***	p<0.001
Fear	-0.57***	p<0.001
Sleep	-0.49***	p<0.001
Fatigue	-0.37**	0.001
Communication	-0.34**	0.002
Mental health	-0.67****	p<0.001
Social functioning	-0.59***	p<0.001

* low correlation, ** low to moderate correlation, *** moderate correlation, **** strong correlation

A significant difference was found between patients according to the type of feeding in terms of the T-EAT-10 and T-SWAL-QOL ($p = 0.01$) (Table 3).

Table 3. The T-EAT-10 and T-SWAL-QOL scores of patients according to the type of feeding

	Patients who fed orally		Patients who fed non-orally		p
	X (SD)	min-max	X (SD)	min-max	
T-EAT-10	16.77 (9.70)	0–36	23.54 (11.96)	16.77 (9.70)	0.01
T-SWAL-QOL	55.85 (20.9)	13-90.7	43.32 (25.27)	55.85 (20.9)	0.01

4. DISCUSSION

In this study, we observed a relationship between patient reported dysphagia symptom severity and SRQOL. As hypothesized, the more patient reported dysphagia symptom severity, the worse the patient reported SRQOL.

Dysphagia is a common consequence of several neurologic diseases including stroke, multiple sclerosis, motor neuron disease, Parkinson's disease and myopathy due to sensorimotor impairment of the oral, pharyngeal and esophageal phases of swallowing (24-26). According to our study results, SRQOL is significantly reduced in patients with neurogenic dysphagia and the most affected subscales were burden, social functioning, fatigue and sleep. Literature defining SRQOL of patients with neurogenic dysphagia also points out that fatigue, eating duration, burden, and sleep were the mostly affected domains (10,11,26). A study investigating the social and psychological burden of dysphagia reported that approximately one third of the patients avoided eating with other people indicating decreased socialization (27) as our study results. Therefore, timely and efficient swallowing evaluation become important to identify symptoms and plan appropriate dysphagia rehabilitation program in patients with neurogenic dysphagia for reducing these swallowing related consequences.

SRQOL was associated with patient reported dysphagia symptom severity. Greater degree of dysphagia symptom severity was found to be associated with lower scores of SRQOL, and lower degree of dysphagia symptom severity was associated with better SRQOL. In addition, patients who fed orally (better swallowing function) had better SRQOL than patients who fed nonorally (worse swallowing function). Patient reported dysphagia symptom severity determined by the T-EAT-10 provides a global perspective related to patients' swallowing impairment. In a previous study conducted with Amyotrophic Lateral Sclerosis showed the relationship between SRQOL and degree of airway safety which is one aspect of swallowing impairment (10). Our study results could be complementary to this study result. As well as airway safety which can be considered as an objective measure of pharyngeal phase swallowing impairment, perceived dysphagia symptoms from patients' point of view are also associated with the amount of affected SRQOL. Therefore, patient reported dysphagia symptom severity can not only provide information regarding disease severity but also can help document the effect on the patients' quality of life.

This current study provides information regarding the relationship between patient reported dysphagia symptom severity and SRQOL. As the main outcome measures of this study are both patient reported, an objective swallowing evaluation will also be added to support current findings.

5. CONCLUSION

In conclusion, patient reported dysphagia symptom severity was found to be associated with SRQOL. The results of this study highlight that appropriate management strategies which also focus on patient reported symptoms may be necessary to minimize negative SRQOL issues of patients with neurogenic dysphagia.

Conflict of Interest: The authors declare that they have no conflict of interest.

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Effects of Childhood Abuse on Major Depressive Disorder

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ABSTRACT

Objective: Childhood trauma is a significant risk factor for major depressive disorder, which has a multifactorial etiology. We investigated the effects of childhood trauma, especially physical and sexual abuse, on depression later in adult life.

Methods: The study included 87 patients with depression and 87 healthy volunteers. Participants were asked to fill out the Childhood Trauma Questionnaire (CTQ) and Hamilton Rating Scale for Depression and Anxiety. We have used the three childhood trauma pattern groups by their CTQ scores. The first group consisted participants who did not report any childhood abuse. The second group comprised participants who had experienced emotional abuse and emotional or physical neglect. The third group included participants who reported physical and sexual abuse.

Results: Approximately half of pattern groups 1 and 2 consisted of healthy controls. However, all of the participants who were in pattern group 3 had major depressive disorder. Anxiety and depression levels both had positive correlations with emotional, physical, and sexual abuse. There was a statistically significant difference between pattern groups 2 and 3 in all of the five categories of CTQ.

Conclusion: In our study, we found that incidences of physical and sexual abuse increase the risk of depression. Furthermore, they indicate an increased risk for a relationship that consists of emotional neglect and abuse, which is an independent risk factor for major depressive disorder. Therefore, we should not only focus on the individual traumas on childhood trauma cases but also consider if there is a defective pattern of relationship.

Keywords: Trauma, Major depressive disorder, Anxiety disorder, Sexual abuse, Physical abuse

1. INTRODUCTION

According to the World Health Organization (WHO), major depressive disorder is the second most debilitating disease (1). Epidemiological studies in Turkey show that approximately 80% of the population suffers from major depressive disorder (2). Moreover, only a quarter of those patients receive adequate treatment (2). Childhood trauma is a significant risk factor for major depressive disorder, which has a multifactorial etiology (3).

Trauma is a deeply distressing or disturbing experience. Even if it caused clinical consequences or not, every individual who ever existed experienced trauma at some point in their life. However, childhood trauma is dissimilar to the ones experienced in older ages (4,5). The naive and helpless nature of minors makes them more susceptible, but it is not the only contrast they have with adults.

In adult life, conditions, such as acute stress disorder, post-traumatic stress disorder, and major depressive disorder, are associated with stress and trauma (6). Most of the time, these psychopathologies are limited to traumatic incidences. Psychopathology usually disappears when the experience is resolved (6). However, it is a very different story if it occurs

during childhood. Trauma during the early years of life also impairs neurodevelopmental and psychological progress (7,8). Moreover, it is debated to be the cause of personality disorders (9).

In the 1983 International Conference on Psychological Abuse of Children and Youth, abuse and neglect were investigated and thoroughly debated (10). Various classifications for abuse and neglect of children were brought forward since then. Emotional abuse, emotional neglect, physical abuse, physical neglect, and sexual abuse are the broad but distinct classifications of childhood abuse and neglect, which also are the five main categories in the Childhood Trauma Questionnaire (CTQ) (10–12).

According to WHO, child abuse means to harm a child's health, impair their sense of trust and responsibility, and compromise the process of their maturation. A child getting hurt physically in any other way than an accident is physical abuse (13). The frequency of physical maltreatment varies a lot with culture, and it is hard to collect precise data on the subject. Slapping and smacking are common discipline methods, especially in Eastern cultures. For example, in the United States, the rate of occurrence of physical abuse varies widely between 4% and 85%, and in Eastern countries, such

as Egypt or India, it is estimated to be between a quarter and three quarters (14). Moreover, the rates do not only vary with culture but also vary with socioeconomic status as well. Studies established that the risk of experiencing child abuse is higher than double in lower socioeconomic families (15).

Just like other kinds of abuses, most of the childhood experiences of sexual violence are caused by close relatives (16). This situation is one of the reasons why childhood sexual abuse is under-reported. In Turkey, less than a sixth of the sexual abuse cases are being reported (16). It makes it harder to detect the victim, criminally charge the perpetrator, and, in some cases, causes the sexual abuse to prolong if a case goes unreported. It has been reported that 9% to 18% of the pre-adolescent population in Turkey have experienced sexual injury (17). Even though the frequency of physical molestation is higher in the lower socioeconomic community, the rates of sexual abuse remain mostly the same (15).

On the other hand, neglect is a term used for not providing the sufficient necessities of a child, such as a shelter, education, healthcare, and compassion, by their parents or their legal guardians (7). As opposed to abuse, the definition of neglect has fuzzy edges. Actions, and in some cases inactions, which can be considered emotional neglect, vary with cultural and social norms (10).

According to a systematic review, childhood abuse and neglect cause an increase in psychiatric disorders, drug uses, suicide attempts, and risky sexual behaviors (18). However, the aftermath of childhood trauma is not limited to mental illnesses, and conditions, such as cardiovascular diseases, cancer, and autoimmune diseases, have been also associated with childhood trauma (19).

In the present study, we investigated the effects of childhood trauma on depression later in adult life in a Turkish population. Our hypothesis was that children who experienced childhood trauma, primarily physical and sexual abuse, are more susceptible to depression.

2. METHODS

2.1. Subjects

This was a case-control study design. The study group included 87 patients with major depressive disorder. All patients with major depressive disorder who were admitted to the outpatient clinic of Psychiatry Balikesir University between September 2015 and August 2016, who were receiving such diagnosis for the first time in their lives, who were not taking any psychotropic medication, and who have agreed to participate were enrolled in our study. The control group comprised 87 healthy volunteers who were matched in age and gender with the study group. Healthy controls were selected among the people who work in our institution and their relatives. All participants were examined and assessed according to the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) Axis I disorders (SCID-1) by psychiatrists in our

outpatient service. Study group participants were selected among patients who were diagnosed with major depressive disorder according to DSM-IV. Control group participants were not diagnosed with any psychiatric diseases after the SCID-1 assessment.

Participants of the study were examined by a physician, and their written medical history in our hospital and self-report medical history were investigated. Participants in both the study and the control groups were excluded if they had a medical history of delirium, dementia, psychotic disorders, bipolar disorder, or any other psychiatric disorders; mental retardation; and infectious disorders or with any other chronic diseases. Patients with depressive disorder or healthy volunteers who were pregnant were not admitted to the study. SCID-1 was applied to all our participants by psychiatrists in our outpatient service, and major depressive disorder was diagnosed in the participants in the study group after SCID-1 was applied.

Participants were asked to fill out sociodemographic data forms, and an informative consent form was given. CTQ, Hamilton Rating Scale for Depression (HAM-D), and Hamilton Rating Scale for Anxiety (HAM-A) were all applied to the participants by our clinic's psychologist. The local ethics committee approved the study. Informed consent was obtained from all the participants in the study.

2.2. CTQ

CTQ evaluates emotional abuse, emotional neglect, physical abuse, physical neglect, and sexual abuse that a participant has experienced during childhood years. The questionnaire is composed of 28 Likert-type items providing an assessment between 1 and 5; 1, never and 5, usually. Each of the five classifications, emotional abuse, emotional neglect, physical abuse, physical neglect, and sexual abuse, have five items assigned to their category; therefore, the least score a group can obtain is 5 (11,12).

In the validity and reliability study of the Turkish version of CTQ, any score >5 is suggested to be considered as positive for physical and sexual abuse categories. The same study indicates that 8 should be the cut-off score for emotional and physical neglect and 13 for emotional neglect (11).

On the other hand, these five different categories of childhood trauma usually are not in isolation from each other, and cases of solitary traumas are sparse. We cannot comprehend the cumulative effect of abuse and neglect if we investigate trauma as the sum of isolated incidents but a pattern of relationship between the abuser and the child (6).

Therefore, we have used the three childhood trauma pattern groups suggested by Schilling et al. (19). The first group consisted of participants with no childhood abuse (emotional abuse ≤ 7 , emotional neglect ≤ 12 , physical abuse = 5, physical neglect ≤ 7 , and sexual abuse = 5; all the criteria mentioned above have to be met for a participant to enroll into this group). The second group consisted of participants who

have experienced noteworthy emotional abuse, emotional neglect, and/or physical neglect. However, the participants in the second group encountered mild to no physical and sexual abuse ($5 < \text{physical abuse} < 10$ and $5 < \text{sexual abuse} < 8$, both of these criteria have to be met; one or more of the following criteria have to be met for emotional abuse > 7 , emotional neglect > 12 , and physical neglect > 7). The third group consisted of participants who have experienced significant physical and sexual abuse (sexual abuse ≥ 8 and physical abuse ≥ 10 , any of the two criteria have to be met).

2.3. Anxiety and depression scales

The Turkish versions of HAM-D and HAM-A were used to assess depression and anxiety levels of the participants at the time of the study. They are reliable and clinically valid rating scales that are widely used in practice (20-22) HAM-D and HAM-A are not suitable for diagnosing anxiety or depression; they are used for assessing the participant’s mood related to anxious and depressive feelings (20-22) Therefore, no cut-off score was set, and outcomes of HAM-A and HAM-D were used numerically for statistical analysis.

2.4. Sociodemographic data

Participants were asked to fill out sociodemographic data forms along with CTQ, HAM-A, and HAM-D. Data on age, height, weight, and alcohol and cigarette use status were collected.

2.5. Statistical analysis

Statistical analysis was performed using the SPSS 15.0 software. The normality of the distributions was determined using visual graphs (e.g., histogram) and appropriate statistical methods. Student’s t-test was used to compare the mean of the two groups with normal distribution, and Mann–Whitney U test was used to compare the two groups without normal distribution. Kruskal–Wallis test was used to compare more than two groups with an abnormal distribution. Mann–Whitney U test was used for post hoc comparison of the groups. Bonferroni correction was made when the Mann–Whitney U test was used in post hoc comparisons. Chi-square test was used to compare categorical data. Spearman correlation analysis was performed to test the association between the two ranked variables. A P value < 0.05 was accepted as statistically significant.

3. RESULTS

There were 87 patients in both the study and the control groups with a total of 174 patients. The mean ages of the study and control groups were 36.8 ± 12.4 and 37.0 ± 11.8 , respectively. There were 76 (87.4%) females in the study group and 74 (85.1%) females in the control groups. There was no statistically significant difference between the two groups regarding age ($P=0.935$) and gender ($P=0.660$) (Table 1).

The mean body mass indices (BMI) of the study and control groups were 26.4 ± 7.3 and 24.9 ± 3.8 , respectively. There was no statistically significant between the two groups ($P=0.097$) (Table 1).

Of the groups, 29.9% of the study group was smoking regularly, whereas 21.8% of the control group had the same ratio. The alcohol dependency rates of the study and control groups were 6.9% and 1.1%, respectively. However, there was no statistically significant difference in the cigarette and alcohol use rates between the two groups ($P=0.226$ and $P=0.117$, respectively) (Table 1).

Table 1. Sociodemographic data of the study and control groups.

	Study group	Control group	P
Age (years)	36.8 ± 12.4	37.0 ± 11.8	$F=0.338, P=0.935^*$
BMI (kg/m ²)	26.4 ± 7.3	24.9 ± 3.8	$F=24.31, P=0.097^*$
Gender (female)	87.4%	85.1%	$\chi^2=1.193, P=0.660^{**}$
Cigarette (use)	29.9%	21.8%	$\chi^2=1.469, P=0.226^{**}$
Alcohol (use)	6.9%	1.1%	$\chi^2=2.382, P=0.117^{***}$

*Independent sample t-test.

**Chi-square test.

***Fisher’s exact test.

As previously mentioned, we categorized participants into three clustered childhood trauma pattern groups using the CTQ. Healthy controls consisted of 55.8% of pattern group 1 and 55% of pattern group 2. However, all of the participants who were in pattern group 3 had major depressive disorder (Table 2).

Table 2. Number of study and control participants in different pattern groups.

	Pattern group 1	Pattern group 2	Pattern group 3	Total
Study (n)	34	36	17	87
Control (n)	43	44	0	87

Anxiety and depression levels, which were assessed by HAM-A and HAM-D, respectively, both had positive correlations with emotional, physical, and sexual abuse (Table 3).

Table 3. Anxiety and depression levels in different classifications of childhood abuse and neglect.

	Emotional abuse	Emotional neglect	Physical abuse	Physical neglect	Sexual abuse
HAM-A	$rs=0.321$	$rs=0.050$	$rs=0.292$	$rs=-0.050$	$rs=0.225$
	$P<0.001$	$P=0.511$	$P<0.001$	$P=0.516$	$P=0.003$
HAM-D	$rs=0.371$	$rs=0.065$	$rs=0.360$	$rs=-0.026$	$rs=0.242$
	$P<0.001$	$P=0.396$	$P<0.001$	$P=0.731$	$P=0.001$

The only two differences between the inclusion criteria for pattern groups 2 and 3 are the cut-off scores for physical and sexual abuse. However, as shown in Table 4, all median

(minimum–maximum) CTQ scores of pattern group 3 were higher than those of pattern group 2. After post hoc analysis, we found that there was no statistically significant difference between pattern groups 2 and 3 only in physical neglect ($P=0.058$). There was a statistically significant difference between pattern groups 2 and 3 in emotional neglect ($P=0.005$) and all other comparisons between any of the two groups in all of the five main categories in CTQ ($P<0.001$).

Table 4. Median (minimum–maximum) CTQ scores of participants in different pattern groups.

	Emotional abuse	Emotional neglect	Physical abuse	Physical neglect	Sexual abuse
Pattern group 1	5 (5–7)	8 (5–12)	5 (5–5)	5 (5–7)	5 (5–5)
Pattern group 2	7 (5–17)	14 (5–25)	5 (5–9)	8 (5–16)	5 (5–7)
Pattern group 3	11 (5–24)	19 (6–24)	12 (5–16)	10 (5–14)	8 (5–14)
P	<0.001	<0.001	<0.001	<0.001	<0.001

Among patients with major depressive disorder, male ($n=11$) participants had a mean score of 5 (minimum 5 and maximum 11) on the sexual abuse category of CTQ. Female ($n=76$) participants also had a mean score of 5 (minimum 5 and maximum 14) in the same category. There was no statistically significant difference between the two genders ($P=0.902$).

4. DISCUSSION

Our hypothesis was that children who experienced childhood trauma, especially physical and/or sexual abuse, are more susceptible to major depressive disorder. To test our postulate, we used the clustered childhood trauma pattern groups suggested by Schilling et al. (19). Participants in pattern group 1 had no trauma history. Pattern group 2 consisted of participants who have experienced significant emotional abuse, emotional neglect, and/or physical neglect and encountered mild to no physical or sexual abuse. Finally, pattern group 3 included participants with a history of physical and/or sexual abuse.

Just as we hypothesized, the pattern group that included participants with a history of physical or sexual abuse consisted solely of patients with depression; approximately 55% of pattern groups 1 and 2 comprised healthy controls.

It is evident from our results and previous studies that a history of physical and sexual abuse drastically increases the frequency of major depressive disorder. However, attributing the entire risk of depression to separate incidents of molestation would be an over-simplification. In pursuit of finding an explanation for this argument, we first investigated the correlation between five different categories of childhood trauma, as used in the CTQ, and severity of depression and anxiety.

We found that anxiety and depression levels, which were assessed by HAM-A and HAM-D, respectively, both had positive

correlations with emotional, physical, and sexual abuse. However, there were no statistically significant correlations between HAM-A and HAM-D scores and emotional or physical neglect. This result was similar to various previous studies (22). Poole et al. established that out of every adverse childhood events, emotional abuse escalates the risk of major depressive disorder the most, by a factor of 3.5. In the same study, it is argued that emotional abuse is instrumental in the development of depressive cognitions (22).

This result only showed that emotional abuse also increased the risk of major depressive disorder, as an isolated incident. However, we argued that childhood traumas should not be considered as the sum of isolated incidents but a pattern of relationship (19). The results described in the previous study did not provide us much information on interrelation patterns. We then compared median CTQ scores of participants in different pattern groups to examine the pattern of relationship.

Except for physical neglect, all the comparisons between pattern groups 2 and 3 for median CTQ scores in all categories were statistically significant. These results supported our argument that isolated physical or sexual abuse incidents were not the only stressful events attributed to increasing the risk of depression. On top of the traumatic effects of physical and sexual abuse, they also indicate a defective pattern of emotional relationship. Median CTQ scores of pattern group 3 for emotional neglect and abuse were significantly higher than those of any of the other two pattern groups.

Stress and trauma usually are used in the same context; however, there is a distinct difference between the two. Stress is a disturbing life event, and (psychological) trauma is a distressing or disturbing experience. In other words, stress is an unprejudiced event, but trauma is the experience of the stressful incident.

CTQ is a tool that measures an individual's perception of their childhood traumas rather than actual stressful events, especially in other categories than physical and sexual abuse. Therefore, our data is limited to distinguish whether our results (median CTQ scores of pattern group 3 for emotional neglect and abuse being significantly higher than the other two pattern groups) were a consequence of an abused child's perception or inappropriate emotional relationship of a sexual and/or physical abuser. To provide a better insight into this debate, we plan to include the parents of the participants in our future studies.

If we investigate the limitations of our study further, psychiatric family histories were not included in our study. Our study only included patients who were admitted to our outpatient clinic, making our study susceptible to Berksonian bias. Since CTQ is a self-report questionnaire, self-report bias is another possible limitation of our study. Moreover, psychological resilience is another confounding factor, which is discussed in depth below.

Psychological resilience is another major factor that affects the clinical outcome of childhood trauma (22–24). Some

studies established the impact of adaptive strategies on specific types of traumas. For example, emotional abuse has shown correlation with maladaptive emotion regulation, and emotional neglect has been associated with deficient adaptive regulation (24). For eliminating the confounding effect of psychological resilience, we plan to add appropriate tools, such as Connor–Davidson Resilience Scale or Cognitive Emotion Regulation Questionnaire, to our future studies.

Bulbul et al. established in their study that childhood trauma increases the risk of recurrent depressive attacks (25). History of childhood abuse or trauma of a major depressive patient, especially if there are repetitive depressive periods, should be thoroughly investigated for better treatment. Such thorough investigation would not only help us to prescribe an adequate psychopharmacological agent but also help us to set more suitable psychotherapeutic goals for the patient.

5. DISCUSSION

In conclusion, to provide a better idea of childhood trauma, we should not evaluate the clinical outcome as the sum of isolated incidents but as a defective pattern of relationship. A relationship containing physical and/or sexual abuse is expected to be distinctly different from the rest. Physical and sexual abuse apparently increases the risk of depression on their own, but they also indicate an amplified risk of experiencing emotional neglect and abuse, which is another risk factor for major depressive disorder.

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Investigation of Px1 Gene Expression, Serum Gpx1 and Selenium Levels on Colorectal Cancer

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ABSTRACT

Objective: Colorectal cancer is one of the first lines when examined the death cause of cancer. It is well known that family history, and racial and ethnic background and daily life are related with colorectal cancer and its treatment options are surgery, chemotherapeutic agents, and radiotherapy. One of the factors that play a critical role in the development of colorectal cancer is the oxidative stress. In this research, we aimed to investigate the association of level of glutathione peroxidase 1 (GPX1) and selenium element with colon cancer.

Methods: In this study, we aimed to determine expression levels of GPX1 genes and selenium that maintain protection against oxidative stress, with 35 colon cancer patients and their normal and tumor tissues associated with clinical and prognostic aspects by using qRT-PCR and atomic absorption methods.

Results: The results of our study showed that GPX1 gene expression were found to be statistically significantly different (two-fold greater in normal tissue; $p < 0.05$) between normal and tumor tissue. Although there was a positive correlation between serum GPX1 and selenium levels and increase in expression of GPX1 gene and serum GPX1 levels, there was no statistical significance ($p > 0.05$).

Conclusion: Colorectal cancer, that many factors are involved in its etiology, we have found that our preliminary studies results might show the potential role of association between GPX1 gene expressions and selenium levels. For this reason, it has been suggested that the subject should be supported by a large-scale group of patients.

Keywords: Colorectal cancer, glutathione peroxidase 1, selenium.

1. INTRODUCTION

Colorectal cancer is one of the first cancer types when deaths are examined caused by cancer (1). Colorectal cancer is treated like other cancer disease with multiple and combine treatment options including surgery, radiotherapy and chemotherapy. It is well-known that colon cancer is related with patient's familial factors, ethnicity, and environmental factors and also lifestyle of the patient (2,3).

Cancer is a disease that possibly ends with death and characterized by uncontrolled cell proliferation and invasion of surrounding tissue and/or cells from the center of the damaged cells. The characteristics of cancer cells are such as escape from the apoptosis, cell proliferation, angiogenesis and metastasis (4,5). Due to the statistical result of the world, the number of cancer patients in the world in 2020 will be more than 15 million (6).

It is important to develop of new agents with low toxicity and high specificity for the targets because the developed chemotherapeutic agents induce the drug resistance mechanisms in tumor cells and the toxicity rates are high.

Free radicals and hypoxia both triggered the inflammation processes. These cause the change of formation the cellular micro-macro environment in oxidative damage. In addition to this oxidative damage mechanism, deforming the normal cell respiration and metabolism of xenobiotics could be ended up causing the cancer.

The body spends its energy to make homeostasis work with full capacity with oxidant and antioxidant enzyme systems for protection of the reactive oxygen species (ROS) products. In case of any corruption of the protective capacity of oxidant and antioxidant enzyme system, DNA damage might initiate and it might cause carcinogenesis and cell death (7-10). Some of these antioxidant enzyme systems are superoxide dismutase (SOD), glutathione peroxidase (GPX), myeloperoxidase (MPO) and nicotinamide adenine dinucleotide (phosphate) (NQO1), glutathione-S-transferase (GST) and non-enzymes antioxidants such as vitamin C, vitamin E, vitamin A, flavonoids etc.

GPX is an enzyme that isolated from mammalian red blood cells and has two subgroups; selenium-dependent and selenium-independent GPX. Selenium (Se)-dependent GPX is located in

the cell mostly in cytoplasm and mitochondria and it needs to selenium to be active. Even though GPX is active almost all tissues, most GPX activity occurs in liver and erythrocytes. GPX is responsible to protect the cells from oxidative damage by the reduction to lipid peroxides and H₂O₂ (11).

Se-dependent GPX has four subgroups; cytosolic/mitochondrial GPX (GPX1), gastrointestinal (GPX2), plasma/extracellular (GPX3) and phospholipid-hydro peroxide (GPX4). GPX1 is an important antioxidant enzyme that plays a protective role from hydrogen peroxide and reactive oxygen species. However, GPX1 metabolized cholesterol and hydro peroxides such as fatty acid peroxides, the enzyme doesn't metabolized the fatty acid peroxides absence of phospholipase A2. Se is an element that intake the body between 71µg and 152µg per day by daily products from varies resources such as, mainly grains, wheat, milk products, meat, fish, drinking water (12). Se is a trace element with a long history as a preservative for cancer (13). The hypotized for Se and carcinogenesis relation is focused on its action on apoptosis, arresting the cell cycle and supporting the DNA repair system (14). In addition, the researches are showed that low Se level was responsible and related for the risk of several cancers such as lung, esophagus, stomach, liver, breast, prostate, bladder and colorectal cancer (14-18).

According to this, in our study, it was aimed to investigate of GPX1 gene expression, serum GPX1 level and Se level to understand their role on the disease pathogenesis with colorectal cancer patients.

2. METHODS

2.1. Patients Selection

35 tumor tissue (25 male and 10 female) that diagnosed by colorectal cancer and their surrounding tissues were enrolled the study which received from XXX Hospital. The tissues were collected after obtaining written informed consent from the participants and approval from XXX Ethics Committee based on World Medical Association Declaration of Helsinki. Patient's medical records, and pathological reports were received to confirm the diagnosis and cancer status.

2.2. Isolation of RNA and determination of RNA purification

First of all, tumor tissues were homogenized. To homogenization procedure were completed according to kit procedure (Purelink(TM) RNA Mini Kit). MagNa Lyser Green Beads were used to start homogenization including an incubation period 60 seconds 6500 rpm. The tubes were included 25 mg tissue sample and 500 µL lysis buffer. After homogenization, RNA were isolated by using Purelink(TM) RNA Mini Kit due to the instruction. Quality and quantity of RNA was measured by using Nanodrop (Thermo Scientific, USA). The concentration maintained at the optical density (OD) of 260 nm and the purification level was detected at OD ratio of 260 nm/280 nm.

2.3. Synthesis of cDNA

After isolation of RNA, cDNA was synthesis was performed by using suitable oligo (dT) primers and High Capacity RNA-to-cDNA™ Kit. Samples were amplified at 37°C for 1 min and 95°C for 5 min.

2.4. Gene expressions by qRT-PCR

Glutathione peroxidase-1 (TaqMan® Gene Expression Assay, Assay ID: Hs00829989_gH) gene expressions were determined by using Real-Time PCR with Agilent Technologies Stratagene Mx3005p. Amplifications were completed with 20 µL reaction volume including cDNA, gene expression probe of TaqMan, suitable primers and TaqMan master mix. β-aktin (TaqMan® Gene Expression Assay, Assay ID: Hs99999903_m1) was used to normalized GPX1 gene expression. The results were analyzed by using "Relative Quantification" method. Due to the method, targeted gene from samples CT value and endogenous control HGPRT genes CT value were used to calculate the DCT.

Calculation procedure: $DDCT = [(C_{target}) - (C_{housekeeping})] - [(C_{control target}) - (C_{control housekeeping})]$

The results were examined by 2^{-DDCT} (19). GPX1 gene amplification for all tissues and their CT results were given in Figure 1.

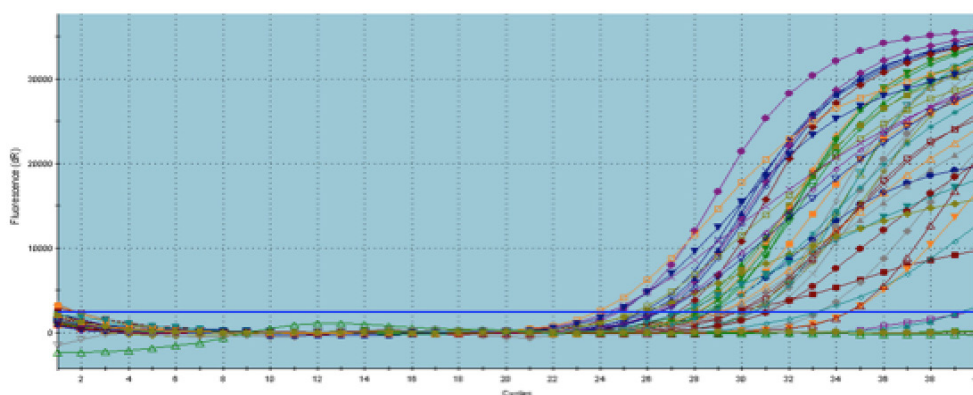


Figure 1. GPX1 gene amplification result

2.5. Level of Selenium with Atomic Absorption

Thermo Scientific Atomic Absorption Spectrophotometer was used to determine the Selenium level by using specific 'Selenium, Se' lamp. The calibration of the measurements was based on the copper standard (3.5 mg / L (ppm) copper standard measurement: 0.4 A).

2.6. Level of serum GPX1

Serum GPX1 level was determined by ELISA due to the kit instructions (USCN Life Science). Serum samples were isolated from patient blood. All patients and their serum were studied duplicate.

2.7. Statistical analysis

The statistical analyses were performed using the SPSS 21.0 statistical software package (SPSS, Chicago, IL). P values lower than 0.05 were assumed to be statistically significant. Analysis of relative expression data was performed according to the threshold cycle (CT) method. Differences in the fold changes of the tissues samples were analyzed using the Mann-Whitney U test.

3. RESULTS

The characteristics of the patients with colorectal cancer and their demographic data are given in Table 1. The main age were 63,57±10,74 for the patients.

Table 1. Demographic and clinical data of the patients

Parameters	Patients (n=35)
Age	63,57±10,74
Sex (Female/Male)	25/10
Level of Selenium	65,57± 21,93
Level of GPX1 (pg/ml)	155,14 ±19,81
Metastasis (%)	57,1
Stage (%)	
Early Stage (T1-T2)	6,7
Advanced (T3-T4)	93,3
Lymph nodes metastasis (%)	
N0	35,7
N1	42,9
N2	21,4
Tumor Size (%)	
<4cm	21,9
≥4 cm	78,1
Differentiation (%)	
Advanced	20,7
Middle	51,7
Week	27,6

GPX1: Glutathione peroxidase 1

It was statistically found that GPX1 gene expression were found in 2 times high level on tumor tissues in contrast to surrounding tissues (p=0,045) (Table 2).

Table 2. GPX1 gene expression on tumor tissues in contrast to surrounding tissues and their fold change

Gene	95% CI	P Value	Fold Change
GPX1	(0,19-0,80)	0,045*	-2,015

GPX1: Glutathione peroxidase 1

CI: Confidence interval

In addition, the relationship between serum GPX1 and selenium levels in contrast to the increase and decrease in the expression of GPX1 gene in the tumor tissue is shown in Table 3. Although there was a positive correlation between serum GPX1 levels and the increase in GPX1 gene expression there could not find statistical significance (p>0,05).

Table 3. The relation of level of Selenium, serum GPX1 level and GPX1 gene expression

Level of Serum	GPX1 gene expression		P Value
	Decrease Level (n:12)	Increased Level (n:23)	
Selenium	65.75±13.84	65.47±25.45	0.972
GPX1 (pg/ml)	129.17±40.11	168.70±140.92	0.351

GPX1: Glutathione peroxidase 1

The relationship between clinical parameters and serum GPX1, selenium levels were shown in Table 4. There was no statistical significance between the relation of expression and levels with clinical parameters.

Table 4. Clinical parameters and patients level of serum selenium and serum GPX1

Clinical Parameters	Level of Selenium	Level of GPX1 (pg/ml)
Tumor Size		
>4cm	64,84±23,15	140,20±62,87
<4cm	61,45±18,46	129,29±72,30
Stage		
1-2 (Erken)	69,09±9,75	212,50±81,37
3-4 (İleri)	64,37±23,14	128,57±60,22
Sex		
Male	63, 74±17,27	167,20±135,63
Female	70,13±31,45	125,00±38,22
Metastasis		
Yes	63,14±23,95	131,50±34,41
No	68,80±19,23	186,67±172,95

GPX1: Glutathione peroxidase 1

5. DISCUSSION

Individual differences in oxidant and antioxidant enzyme systems are thought to have a role in many cancer types. The system is responsible to remove of harmful compounds

that caused by reactive oxygen species (10). If the balance doesn't work properly between reactive oxygen species and antioxidant level, the pathological process begins even it ends up with cell damaged.

Understanding the antioxidant capacity and its mechanism for the organism might block the pathological conditions. The most effective antioxidants are SOD, CAT and GPX. SOD, CAT and GPX1 enzymes involved the primer endogenous antioxidant members and they work together to remove the impact of free radicals. While SOD is responsible especially to detoxification of ROS to hydrogen peroxide, CAT and GPX1 work for detoxification of hydrogen peroxide to H₂O and oxygen (20). The other antioxidants that non-enzymatic ones are vitamin C, vitamin E, carotenoids, thiol antioxidants (glutathione, thioredoxin ve lipoic acid), flavonoids, selenium and others (20).

There are a variety of studies on antioxidants and their role and the subject is still ongoing. Not only the level of antioxidant systems is important for all disease but also system is important in especially cancer patients. There are several contradictory results about specific antioxidant and the diseases. It might be related of the disease specific pathway. Hoffman et al. have studied with colorectal cancer patients and they resulted that the patients had not showed any change of GPX activities (21). Despite that Hasegawa et al. have worked with anaplastic and papillary thyroid tumors. Their results have shown that patient's GPX levels were found statistically low on mRNA expressions based (22). Malinowska et al. have studied the relation of colorectal cancer and antioxidants and the results have come up statistically increased level of glutathione peroxidase and superoxide dismutase (23).

In our study, we have found the similar results with the literature about GPX1 gene. Our results demonstrated that GPX1 gene expression was two times higher in normal tissue in contrast to tumor tissue ($p=0,04$). In addition to this, GPX1 have found 1,9 times less on tissue with lymphatic invasion in contrast to tissue without lymphatic invasion ($p=0,04$). Moreover, we have compared the GPX1 gene expression with tissues with metastasis. The results showed that GPX1 gene was found 1,34 less expressed on tissue with metastasis. In addition to the increase in GPX1 gene expression, we have observed that serum GPX1 levels also increased in a positive manner. In contrast to these results, there are some studies that indicate an increase in GPX activity related with tumor presence (24,25).

Selenium has a complex cellular biochemical system that contains the gene expression of a large number of selenium-dependent proteins such as GPX1. GPX1 is selenium-dependent proteins in its active side (26).

In many studies, selenium has been found to play a role in the activation and expression of GPX1(27,28). In different epidemiological studies, it has been shown that there is an inverse proportional relationship between serum selenium level and different cancer types although Se element has been

shown to inhibit some type of cancer (29,30). In a study of 169 colon cancer patients and 169 controls in Poland and Estonia, selenium levels in patients were reported to be at the lowest level. These results demonstrated that low level of selenium might be related high level of malignancy (31). 451 colorectal patients were enrolled the study and the results were ended up selenium protective capacity such as high selenium level has the positive effect on cancer (31). Nevertheless, serum selenium level has the protective role for cancer; the results are been thought to the mean level of selenium in the serum has the ability of protection. Other than these studies, in a Phase III cohort study with 35535 participants from 427 centers in the United States, Canada and Puerto Rico, it was suggested that selenium supplementation could not reduce the risk of prostate or colorectal cancer (32-34).

In our study, we could not have found any statistical result about serum selenium level on tumor tissues and normal tissues. In many studies, characteristics such as gender, epidemiological differences and dietary habits have led to conflicting results between colorectal cancer risk and selenium levels (31,35). Similarly, in our study has the results that there could not observe any correlation between serum selenium level or selenium and GPX1 levels. Another study suggests that there is an inverse link between dietary selenium levels and cancer-related deaths, including colon and rectum cancers (36). Other than that the study demonstrated that statistically high level of selenium related to decreased level of colorectal cancer (36). In addition to selenium protective capacity, it is also thought to that selenium is effective on cancer progression and metastasis (37,38). The mechanism might work on during the progression of cancer by blocking the carcinogenesis process on affecting the individual tumor like tumor specific effect (37,38).

It is believed that the tumor specific effect of selenium is caused by the fact that the extracellular area of the cancer cell is more reductive than the intracellular area. Furthermore, this differentiation of cells potential might promotes more selenium uptake into the cell. The other hypothesis is about the selenium roles on metastasis. It is believed that selenium inhibits metastasis by reducing the expression of genes such as osteoporosis and collagen (39).

5. CONCLUSION

In conclusion, we have found the statistically decreased level of GPX1 gene expression on tumor tissues. However serum GPX1 level has the similar changes with gene expression results, there could not find statistically important result when compared the clinical parameters.

According to literature, there are several contradictory results about specific antioxidant and the disease. In our study has the preliminary result about gene expression, serum GPX1 and selenium levels on colorectal cancer that could be related personal characteristics such as gender, epidemiological differences and dietary habits on Turkish patients. The area

needs to be lightened with large scale patient group and further studies to understand underlying pathological role.

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Resilience in Nursing Students: The Effect of Academic Stress and Social Support

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ABSTRACT

Objective: This study was conducted to evaluate the levels of psychological resilience, academic stress and social support available to nursing students and the relationship between these factors.

Methods: The population of the study, which had a descriptive and correlational research design, was made up of 1202 students, while the sample consisted of 322 students selected using the sample size formula for a known population. Data were collected using a Structured Questionnaire, the Psychological Resilience Scale for Adults, the Nursing Education Stress Scale and the Multidimensional Scale of Perceived Social Support.

Results: 76.7% of students were female and 23.3% were male. A statistically significant correlation was found between scores for psychological resilience and perceived social support ($p < 0.05$). It was found that the individual characteristics of students affected their psychological resilience. Levels of psychological resilience, academic stress, and social support among nursing students are at a moderate level.

Conclusion: The significance of resilience is clear, a better understanding is needed of what factors affect a student's level of resilience and how this resilience can best be improved.

Keywords: Resilience, academic stress, social support, nursing students

1. INTRODUCTION

Individuals generally encounter a number of challenges and problems over the course of their lives; these can range from day-to-day issues to specific crises or other events. Managing individuals' environment carefully to help them overcome any adversities is of vital importance (1). Some professionals employed in highly stressful situations are particularly at risk of suffering problems such as depression, anxiety, burnout and traumatic stress. One occupational group particularly vulnerable to high levels of stress at work are those working in health care (2).

Nurses in particular work in tense and demanding environments. They often experience conditions that are far from optimal (including lengthy or unpredictable hours) and these can increase their psychological vulnerability (3). During nursing education, nursing students can also be under stress as they attempt to deploy the new ideas and skills they have learned in a practical setting. As nursing students experience higher levels of stress than students in other health subjects it is essential to understand how their degree of resilience affects them (4).

Psychological resilience can be viewed as a multi-dimensional construct and it is critical that is clearly defined in order to differentiate it from related constructs, some of which may

have overlapping meanings (2). Psychological resilience can be defined as a person's capacity to adapt and cope in the face of difficult situations (5,6,7). Psychological resilience is a complicated and dynamic process that is affected by bio-physiological, psychological, socio-cultural and politico-economic factors (8,9). Psychological resilience is increased by becoming more healthy, improving the quality of life and developing and improving coping mechanisms (6,7,10,11).

Improving psychological resilience and managing stressful situations are capacities that society at large expects from nurses. These qualities can be fostered in nursing students with the aid of the educational process and educational experience. Like every university student, nursing students will have various stress-oriented experiences (7,12). However, worries concerning academic success remain one of the most important reasons for stress. Academic stress consists of the physical, mental and emotional responses that emerge because of the emotions and thoughts related to educational conflict, disappointment, pressure and the fear of being unsuccessful (13). It may have an impact on one's concentration, memory, and the processes making decisions and solving problems. As a result of this, it may also affect the level of academic success and resilience of nursing students. Increasing academic success and adapting

to changing situations require effective stress management and the use of various coping mechanisms (12,14).

Studies about protecting and improving the resilience of nursing students have reported that social support plays a significant role. The perception of social support is associated with an individual's appraisal of their value. An individual who thinks that they are loved, valued, helped when needed, and that their relationships are satisfying, perceives themselves as more supported. Social support systems have an important role in decreasing or balancing the damage caused by the stressful situations that individuals face (10,15,16). Studies note that one's perception of social support is related to the level of resilience felt and demonstrated (17-19).

In this context, it can be asserted that the concept of nursing students' resilience is important, that it is directly related to academic success and that it affects their coping mechanisms. However, there is limited research on this subject. Within this context, there is a clear need for studies aimed at determining the factors that affect resilience and that create strategies to improve it (20-22).

The aim of this study was to evaluate levels of psychological resilience, academic stress and social support among nursing students and determine the relationships between them. The research questions were as follows:

- What are the nursing students' psychological resilience levels?
- What are the nursing students' academic stress levels?
- What are the nursing students' social support levels?
- Is there any relationship between the nursing students' levels of resilience, academic stress and social support?
- Which factors affect levels of psychological resilience, academic stress and social support in nursing students?

2. METHODS

2.1 Design and Participants

This study used a descriptive and correlational research design. The population of the study was made up 1202 students studying in 2015-2016 academic year at the Istanbul University, Florence Nightingale Nursing Faculty, while the sample of study included 322 students selected using the sample size formula for a known population. Sampling was conducted by a stratified random sampling method. The stratification criteria were the classes which the subjects taking part were attending. Potential participants were selected and assigned at random by researchers from a table constructed of random numbers. The inclusion criteria was that students were willing to participate and did so voluntarily.

2.2. Data collection

Researchers collected data via one-on-one interviews. Investigators met with the students and explained the aim

and scope of the study, its duration and what was expected of the participants. In the data collection, a Structured Questionnaire Form, the Psychological Resilience Scale for Adults and the Nursing Education Stress Scale were used.

Structured Questionnaire Form: The questionnaire form was prepared by considering studies related to the literature (10,12,16). The form contains variables of gender, age, year of education, income, average success, marital status, number of siblings, working status, living area and health insurance.

Psychological Resilience Scale for Adults: The scale was developed by Friberg et al. to measure the level of adults' psychological resilience and a six-dimensional structure was then created by the same researchers in 2005. The scale has a total of 33 items with 6 dimensions including "structural style" and "perception of future" with 4 items each, "family cohesion", "perception of self" and "social competence" with 6 items each and "social resources" with 7 items. The Cronbach alpha internal consistency coefficient was found to be 0.86 in the Turkish version of the study conducted by Basım and Çetin in 2011 (9). A format was used in which positive and negative attributes were on different sides, and for answers, five separate options were given in order to avoid prejudiced evaluations of preference for items of scale. A score of 1 to 5 was accepted as showing that psychological resistance increased as the score increased. Questions 1, 3, 4, 8, 11, 12, 13, 14, 15, 16, 23, 24, 25, 27, 31 and 33 in the scale were accepted as inverse questions and scored accordingly.

Nursing Education Stress Scale: The scale was modified and developed by Rhead from the Nurse Stress Scale developed by Gray-Toft and Anderson. Karaca et al. conducted a Turkish validity and reliability study in 2014 (23). The scale is made up of two sub-dimensions and 32 items and is a quadratic (0-3 points) Likert type. For the "practice stress" sub-dimension, questions 4, 5, 7, 9, 11, 13, 15, 16, 18, 19, 21, 24, 25, 27, 29 and 32 are used; for the "academic stress" sub-dimension, questions 1, 2, 3, 6, 8, 10, 12, 14, 17, 20, 22, 23, 26, 28, 30 and 31 are used. Each subscale has a value from 0 to 48 and the total score obtainable from the scale is between 0 and 96. An increase in score indicates an increasing level of stress. Since the Cronbach's alpha values of the scale items are higher than 0.83, the internal consistency is high and the scale is reliable.

Multidimensional Scale of Perceived Social Support: This was developed in 1988 by Zimet and his colleagues. The validity and reliability studies in Turkey were carried by Eker and Arkar in 1995 (24). The scale is a Likert type instrument arranged in a range from 1 to 7, from "absolutely no" (1) to "absolutely yes" (7). There are three subgroups: "family", "friend" and "someone special" which reflect the support resources given in the scale. Each group consists of 4 items, and there is a total of 12 items. Support from family is measured by items 3, 4, 8 and 11 on the scale, support from friends is measured by items 6, 7, 9 and 12, and items 1, 2, 5 and 10 measure the support from a partner or someone very close. A high score on the scale indicates that perceived social support is high.

The internal consistency Cronbach alpha values are 0.85 for the “family” subscale, 0.88 for the “friend” subscale and 0.92 for the “someone special” subscale.

2.3. Ethical Considerations

Ethical approval for this study was granted by the Istanbul University Ethics Committee (Date: 25.05.2016 Number: 112). The researchers explained the purpose of the research, roles of participants, benefits and potential risks of the study and their right to withdraw at any time. Students’ written consents/approvals were received with Used Confidentiality Agreement Form.

2.4. Research Limitations

This study involved nursing students in only one nursing faculty. Therefore, the results cannot be generalized to all other nursing schools. The results might not be representative of the wider nursing student population.

2.5. Statistical analysis

Data were analysed using the Statistical Package for Social Sciences 22.0 (SPSS 22.0) using frequency, percentage, minimum, maximum, mean, standard deviation for descriptive analyses. Student t tests, the One way ANOVA test and Tukey HSD were used for comparison of the groups. The relationships between levels of psychological resilience, academic stress and perceived social support were analyzed using Pearson’s Correlation Analysis. $p < 0.05$ was considered statistically significant.

3. RESULTS

3.1. Students’ socio-demographic characteristics

The average age of the students was 20.65 ± 1.65 . 76.7% ($n=247$) of the students were female, and 23.3% ($n=75$) were male. 32.6% ($n=105$) were sophomore students and their average academic success level was 2.70 ± 0.41 (in a 4 point grading system). 48.8% ($n=157$) lived with their families and 38.8% ($n=125$) had 2 siblings. 88.5% ($n=285$) were not employed, 74.8% ($n=241$) were self-employed and 86% ($n=277$) had health insurance.

3.2 Average total scores and sub-dimension scores for the Psychological Resilience Scale For Adults, the Nursing Education Stress Scale and the Multidimensional Scale of Perceived Social Support

The average scores of the students for the Psychological Resilience Scale for Adults were as follows: 3.61 ± 0.76 for “structural style”, 3.79 ± 0.85 for “perception of future”, 3.77 ± 0.77 for “family cohesion”, 3.71 ± 0.69 for “perception of self”, 3.69 ± 0.71 for “social competence”, and 4.01 ± 0.67 for “social resources”. The average total score of the

Nursing Education Stress Scale was 63.84 ± 16.83 ; for its sub-dimensions, it was found to be 32.17 ± 8.81 for “practice stress” and 31.66 ± 8.86 for “academic stress”. The average total score for the Multidimensional Scale of Perceived Social Support was 65.16 ± 14.08 ; for the sub-dimensions, it was 22.84 ± 5.22 for “family”, 22.78 ± 5.16 for “friend”, and 19.54 ± 8.01 for “someone special” (Table 1).

Table 1. Average total scores and sub-dimension scores of the Psychological Resilience Scale for Adults, Nursing Education Stress Scale and Multidimensional Scale of Perceived Social Support ($n=322$)

Scale	Sub-dimension	Min.-Max.	Avg.±SD
Psychological Resilience Scale for Adults	Structural Style	1-5	3.61 ± 0.76
	Perception of Future	1-5	3.79 ± 0.85
	Family Cohesion	1.17-5	3.77 ± 0.77
	Self Perception	1.67-5	3.71 ± 0.69
	Social Competence	1.5-5	3.69 ± 0.71
	Social Resources	2-5	4.01 ± 0.67
Nursing Education Stress Scale	Practice Stress	3-48	32.17 ± 8.81
	Academic Stress	3-48	31.66 ± 8.86
	Total	6-96	63.84 ± 16.83
Multidimensional Scale of Perceived Social Support	Family	4-28	22.84 ± 5.22
	Friend	4-28	22.78 ± 5.16
	Someone Special	4-28	19.54 ± 8.01
	Total	18-84	65.16 ± 14.08

Min.:Minimum Max.:Maximum

Avg. Average, SD: Standard Deviation

3.3. Correlation of psychological resilience and academic stress

No statistically significant correlation was found between the nursing students’ average scores for the Psychological Resilience Scale for Adults and the Nursing Education Stress Scale and their sub-dimensions ($p > 0.05$; Table 2).

3.4. Correlation of psychological resilience and perceived social support

A statistically significant correlation was found between the scores for all the sub-dimensions of Psychological Resilience Scale for Adults and the “family” sub-dimension of the Multidimensional Scale of Perceived Social Support ($p < 0.05$). A significant correlation was found between the score for the “friend” sub-dimension of the Multidimensional Scale of Perceived Social Support, and the scores for “perception of future”, “family cohesion”, “perception of self”, “social competence” and “social resources” sub-dimensions of the Psychological Resilience Scale for Adults ($p < 0.05$). A significant correlation was found between the “someone special” sub-dimension of the Multidimensional Scale of Perceived Social Support, and the scores for “perception of future” and “social resources” sub-dimensions ($p < 0.05$; Table 2).

Table 2. Correlation analyses of Psychological Resilience Scale for Adults and Nursing Education Stress Scale and Multidimensional Scale of Perceived Social Support (n=322)

Scales	Sub-dimensions		Scales							
Psychological Resilience Scale for Adults	Nursing Education Stress Scale									
		Practice Stress		Academic Stress		Total		Practice Stress	Academic Stress	Total
		r	p	r	p	r	p	r	P	
	Structural Style	0.035	0.535	-0.009	0.876	0.014	0.809			
	Perception of Future	-0.041	0.462	-0.106	0.057	-0.077	0.166			
	Family Cohesion	-0.036	0.522	-0.091	0.104	-0.067	0.234			
	Self Perception	-0.105	0.060	-0.095	0.088	-0.105	0.060			
	Social Competence	-0.011	0.849	-0.066	0.237	-0.040	0.470			
	Social Resources	0.093	0.095	0.024	0.664	0.061	0.271			
Psychological Resilience Scale for Adults	Multidimensional Scale of Perceived Social Support									
		Family		Friend		Someone Special		Total		
		r	P	r	p	r	p	r	p	
	Structural Style	0.161	0.004**	0.099	0.075	0.065	0.242	0.134	0.016*	
	Perception of Future	0.289	0.001**	0.252	0.001**	0.125	0.024*	0.271	0.001**	
	Family Cohesion	0.628	0.001**	0.458	0.001**	0.105	0.060	0.460	0.001**	
	Self Perception	0.123	0.027*	0.171	0.002**	0.057	0.310	0.141	0.011*	
	Social Competence	0.231	0.001**	0.360	0.001**	0.094	0.091	0.271	0.001**	
	Social Resources	0.550	0.001**	0.556	0.001**	0.166	0.003**	0.502	0.001**	
Nursing Education Stress Scale	Multidimensional Scale of Perceived Social Support									
		Family		Friend		Someone Special		Total		
		r	P	r	p	r	p	r	p	
	Practice Stress	0.036	0.515	0.032	0.568	-0.040	0.475	0.002	0.964	
	Academic Stress	0.005	0.931	-0.039	0.491	-0.020	0.717	-0.024	0.670	
	Total	0.022	0.699	-0.004	0.949	-0.032	0.573	-0.011	0.841	

3.5. Correlation of nursing education stress and perceived social support

No statistically significant correlation was found between the total scores and sub-dimensions of the Multidimensional Scale of Perceived Social Support and total scores of “practice stress” and “academic stress” sub-dimensions and the Nursing Education Stress Scale ($p > 0.05$; Table 2).

3.6. Socio-demographic characteristics and psychological resilience levels

The score for the Psychological Resilience Scale for Adults for 20 years-old and younger students was found to be significantly higher than the scores for the “family cohesion” and “social resources” subscales ($p < 0.01$). The average scores of women for the sub-dimensions of the Psychological Resilience Scale for Adults were higher than that of men at a statistically significant level ($p < 0.05$). The average scores of sophomore students in the Social Resources and Family Cohesion sub-dimensions of Psychological Resilience Scale

for Adults are higher than that of students in other classes and this difference was statistically significant ($p < 0.05$). There was no significant difference between the resilience levels of the individuals that had nuclear families or extended families ($p > 0.05$). The mean score for the “structural style” subscale scores of those who had four or more siblings was significantly higher than the others ($p < 0.05$). The mean score for the “social sufficiency” subscale of individuals who had 2 siblings or fewer was found to be statistically significantly higher than those had four siblings or more ($p < 0.01$). The mean score for the “social resource” subscale of those whose income matched their expenditure was found to be statistically significantly higher than those who could not meet their expenses ($p < 0.01$). The “social assistance” subscale mean score of those with social security was found to be statistically significantly higher than those without social security ($p < 0.05$). The mean score for the “family cohesion”, “social qualification” and “social resources” subscales of the unemployed were found to be statistically significantly higher than those who were employed ($p < 0.01$, Table 3).

Table 3. Comparison of socio-demographic characteristics and sub-dimension scores of Psychological Resilience Scale for Adults (n=322)

Socio-demographic Characteristics		Psychological Resilience Scale for Adults						
		n	Structured Style	Perception of Future	Family Cohesion	Self Perception	Social Competence	Social Resources
			Avg.±SD	Avg.±SD	Avg.±SD	Avg.±SD	Avg.±SD	Avg.±SD
Age	≤20	157	3.65±0.76	3.79±0.83	3.94±0.69	3.68±0.72	3.72±0.71	4.13±0.60
	>20	165	3.57±0.76	3.79±0.87	3.61±0.82	3.74±0.67	3.66±0.72	3.90±0.71
	t; p		0.945; 0.345	-0.077; 0.939	3.986; 0.001**	-0.805; 0.421	0.714; 0.476	3.091; 0.002**
Gender	Women	247	3.67±0.76	3.86±0.82	3.84±0.77	3.72±0.67	3.76±0.69	4.13±0.63
	Man	75	3.42±0.75	3.55±0.91	3.54±0.75	3.67±0.75	3.48±0.76	3.63±0.64
	t; p		2.558; 0.011*	2.823; 0.005**	3.001; 0.003**	0.519; 0.604	2.911; 0.004**	5.980; 0.001**
Class	1.Class	85	3.56±0.69	3.82±0.85	3.87±0.74	3.73±0.76	3.80±0.65	4.03±0.67
	2.Class	105	3.65±0.83	3.82±0.85	3.89±0.75	3.68±0.67	3.66±0.73	4.15±0.60
	3.Class	85	3.59±0.78	3.78±0.82	3.61±0.78	3.76±0.70	3.69±0.74	3.92±0.69
	4.Class	47	3.65±0.73	3.70±0.93	3.62±0.81	3.65±0.61	3.59±0.74	3.82±0.72
	F; p		0.279; 0.841	0.243; 0.866	3.181; 0.024*	0.341; 0.796	1.017; 0.385	3.508; 0.016*
Family Type	Elementary family	262	3.61±0.75	3.79±0.85	3.80±0.77	3.72±0.67	3.71±0.71	4.01±0.67
	Extended family and others	60	3.64±0.81	3.78±0.85	3.66±0.79	3.68±0.78	3.64±0.71	3.99±0.64
	t; p		-0.290; 0.772	0.071; 0.944	1.240; 0.216	0.400; 0.689	0.681; 0.497	0.280; 0.780
Number of Siblings	2 siblings or less	140	3.69±0.78	3.89±0.80	3.77±0.78	3.75±0.65	3.81±0.69	4.12±0.63
	3 siblings	83	3.70±0.73	3.82±0.88	3.89±0.76	3.73±0.74	3.71±0.72	4.05±0.74
	4 sibling or more	99	3.43±0.74	3.63±0.89	3.66±0.77	3.63±0.70	3.51±0.72	3.82±0.62
	F; p		4.317; 0.014*	2.708; 0.068	1.976; 0.140	0.889; 0.412	5.414; 0.005**	6.041; 0.003**
Income Status	Welcomes expense income	241	3.65±0.73	3.82±0.87	3.82±0.74	3.72±0.66	3.73±0.68	4.08±0.65
	Revenue does not meet expenses	81	3.51±0.85	3.70±0.78	3.62±0.86	3.68±0.77	3.57±0.80	3.81±0.68
Health Insurance	Yes	277	3.63±0.75	3.82±0.83	3.78±0.78	3.74±0.69	3.72±0.71	4.03±0.68
	No	45	3.49±0.82	3.61±0.97	3.69±0.72	3.56±0.68	3.50±0.71	3.90±0.61
	t; p		1.116; 0.265	1.527; 0.128	0.758; 0.449	1.623; 0.106	1.998; 0.047*	1.199; 0.231
Employment Status	Working	37	3.62±0.64	3.78±0.94	3.43±0.68	3.76±0.61	3.39±0.72	3.72±0.69
	Not working	285	3.61±0.78	3.79±0.84	3.81±0.78	3.70±0.70	3.73±0.70	4.05±0.66
	t; p		0.083; 0.934	-0.050; 0.960	2.889-; 0.004**	0.472; 0.637	-2.792; 0.006**	-2.876; 0.004**

Avg.: Average t: student t tests' value F:One way ANOVA test value *p<0.05

**p<0.01

4. DISCUSSION

Nursing students have to cope with various stressors in both educational and the clinical environments. A high level of resistance is needed to be able to manage this and progress. Psychological resilience is an important factor affecting the academic life of nursing students. Learning to limit stress and developing psychological resilience in the clinical practice environment are important topics in helping students to gain new perspectives and to cope with stress during clinical practice (20,24,25). This research was carried out to evaluate levels of psychological resilience of nursing students, explain the relationship of these to academic stress, which is thought to have an important effect on resilience, and also to examine the effect of social support, which is an external factor.

In this study, the scores obtained from the subscales of the Psychological Resilience Scale showed that the psychological

resilience of the students was at medium level. In the research by Smith and Yang, and Rios-Risques et al., the resilience level of nursing students was also found to be moderate (26,27). The finding obtained from this research was thus similar to other research findings. In this respect, it can be said that the psychological resilience of the students was not at a sufficient level and that it needs to be increased. Academics are an important resource for increasing the resilience level of students. Professional resilience should begin by developing acute care areas and educational strategies within nursing education and it should continue with postgraduate experience. New nurses may increase their level of resilience as they become familiar with the social environment of the clinic and develop their own skills, but they may also need more time to develop (28).

Stress in nursing education is a very controversial issue. Stress is an issue that can negatively affect the psychological

and physiological health of students and their academic achievement. Students with high stress levels also have low levels of coping (29,30). When the findings obtained from this research related to the academic stress experienced by students were examined, it was determined that the academic stress levels of the students were slightly above medium, and the academic and practice stress subscale scores were also similar and slightly above the moderate level. In Pines et al.'s study, the students' stress susceptibility scores were found to be around average as well (31). The stress levels of nursing students were higher in similar studies conducted in Turkey. In these studies, many internal and external factors which may cause stress, such as the assessment and examination system in Turkey, problems in clinical practice environments, the attitudes of educators and the individual characteristics of students were identified (32-34). Another study conducted with the aim of determining and comparing stress levels of nursing students in five countries showed that stress is a common problem for nursing students (35). In the light of these findings, there is a need to develop programs for strengthening students' ability to cope with stress, to provide university and clinical orientation, and to plan the initiatives necessary by examining each institution-specific stressor.

Social support is one of the most significant external factors having an impact on an individuals' capacity to handle stressful situations (16,29,30). In this study, it was determined that the level of social support students perceived themselves to have was moderate, and the subscales of "family", "friends" and "someone special" were also found to be moderate and close to each other. Activities could be planned within a Faculty to increase the social support provided to students. For example, organizing social club activities to increase the level of support from friends will also increase the interaction of students with each other. Moreover, unlike the findings in the literature, in this study, there was no significant relationship between the stress level of students and level of perceived social support. It will be necessary to carry out repeated studies to explain the reasons for this finding.

There is a mutual and negative relationship between stress and resilience. Studies have shown that the resilience level of stressed individuals is low. In the study by Pines et al., it was found that students with higher scores for "psychological refreshment" had higher resilience scores (31). In this respect, it has been proposed that strategies be developed for the psychological strengthening of students. It has also been determined in research conducted with nursing students that the levels of resilience and academic success are negatively affected by academic stress (20,21,29). Smith and Yang found a negative relationship between nursing students' resilience, stress and psychological well-being (27). However, in this study, a relationship was not found between resilience and the stress levels of students.

In this study, the level of resilience, social support the six dimensions of psychological resilience of the students were found to be significantly correlated. This finding supports the literature showing that the level of social support is higher

for students that have a high level of psychological resilience (20,29,36). Programs should aim increase the level of social support and thus to strengthen the resilience of students.

The research demonstrated that the socio-demographic characteristics of the students affected the resilience level. Age is an individual characteristic that affects psychological resilience and perceived stress level (26,37). The mean score for the "family cohesion" and "social resources" scores of students aged 20 and under in this study was found to be significantly higher than that of those aged 20 and over. The lower "family cohesion" and "social resources" scores for younger people may be considered as a reflection of the socio-cultural characteristics of the society in which the students live.

In the research, the level of resilience demonstrated by female students was significantly higher than that of male students. This difference may be related to the fact that the social support level of female students was higher than that of male students (30). In a study conducted by Altıok and Üstün in Turkey, it was revealed that male students experienced different behaviors from other nurses and patients during clinical practice because they were male, and this was determined to be an important stressor (33). Male students participating in the research may have experienced more stress, which may have negatively affected their resilience levels.

As the students' amount of education increases, it is expected that the ability to cope with stressful situations will also increase. In a study on the psychological well-being and resilience of nursing students, it was determined that upper-class students experienced more psychological well-being than other students (27). In this study, the sophomore students were found to be stronger and have significantly greater social resources in the "family adjustment" subscales than the other students. In this context, initiatives to increase levels of social support may be useful for increasing levels of resilience.

In the study, the number of siblings, income status, access to social security and employment situation were also found to affect psychological resilience levels of students. However, family type did not affect resilience levels. Taking individual characteristics into account in efforts to increase the resilience of students will have an effect on the success of social and institutional support.

5. CONCLUSION

The levels of psychological resilience, stress and social support experienced by the students in the sample group were moderate. It is thus necessary to increase the students' levels of resilience. It is suggested that nurse educators and school administrators plan activities such as mentoring and group education sessions, and that they increase the number of social activities available and set clear organizational strategies.

The resilience of nursing students needs to be strengthened, and their education needs to incorporate ways of doing this. Although the significance of resilience is clear, a better understanding is needed of which factors affect a student's level of resilience and how this resilience can best be improved. For this to happen, a more explicit definition of which resilience in nursing students involves should be formulated and applied in a consistent manner. This will allow better theoretical models to be developed and evaluated.

Conflict of Interest: The author's declare that they have no conflict of interest. There are no other potential conflicts of interest pertaining to this work.









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Physical Self-Perception, Body Posture of Nursing Students and Associated Factors

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ABSTRACT

Objective: In this study, it was aimed to determine the relationships between physical self-perception, body posture disorders, age, gender and BMI categories and nursing students' physical self-perception and body posture disorders.

Methods: This cross sectional study was conducted. The study population was comprised of 1202 students studying at the Nursing Faculty, the sample consisted of 341 students. The data were collected by using "Structured Question Form", "Symmetrigrif", "Posture Aware by Center Road Software LLC" and "Physical Self-Description Questionnaire (PSDQ)".

Results: Students' average age was 20.33±1.60. Body posture analysis through symmetrigrif showed that the students suffered from kyphosis, lordosis, scoliosis, flattening and curvature. Analysis of shoulder, spine, hip, wrist, neck, upper back, torso, abdomen, and back showed first-degree deformation. According to Body Posture Aware App, there was first-degree deformation on the head, the shoulder and the hip. When the scale scores of PSDQ of the students are examined; it was seen that the average score of PSDQ of female students was 265.96 ± 40.28 and that of male students was 294.64 ± 42.97.

Conclusion: The students had problems with body posture and gender played a role in posture and self-perception. Considering the period of life students go through and the fact that they will be a member of health personnel, utmost attention needs to be paid to this issue.

Keywords: Nursing students, gender, physical self-perception, body posture

1. INTRODUCTION

"Physical self-concept" or "physical self-perception" is of great importance in terms of getting in contact with the physical world, ability to specialize and healthy development (1,2,3). This type of drive leads people to perceive their body negatively or positively (1,4). Especially the university life which coincides with the period between adolescence and adulthood turn out to be a quite demanding, turbulent and painful process for the students. The fact that students discover their identities and individualize in a healthy way comes into prominence in this period (5,6).

Physical self or physical perception is a fundamental component of self-confidence and self-concept. It is usual for a person who considers oneself physically sufficient or who is perceived likewise by others to like his/her own body and think that he/she will be physically sufficient on his/her own. In addition, it is also ordinary for basic structures such as self-esteem to be at high level as a result of the high level of perceived physical self-sufficiency (7,8).

Ideal body-build requires both being thin and physically proper. In other words, the body needs to be proportional and healthy.

In this context, especially proper body posture turns out to be a factor that directly affects physical self-concept for both male and female students (8). American Orthopaedic Association describes posture "the state of balance in which muscles and bones can protect other body structures from injuries in upright position, sitting and lying positions (9,10). In other words, posture is described as the composite of the positions of all the joints of the body at any given movement (11,12). Posture is the mechanical alignment between the parts of the body. It is divided into two categories: static posture (in resting or stationary positions) and dynamic posture (in movement). Human body achieves a proper posture through the workings of muscles in coordination to ensure stability or adjust to a movement. Good posture refers to the positioning of the body in a way that balance point of each body segment is vertically situated from top to the bottom. There is an anterior convex in the neck in ideal cervical standing. Gravity falls through the earlobe in sidelong standing (10,13-15).

Physical self-concept and ideal body posture might lead university students to suffer from social physical anxiety. Study findings show that girls feel social physical anxiety more than boys and they report that such anxiety is influential in their

behaviors (2). At the same time, it is emphasized that boys have higher levels of self-esteem than girls. The number of studies on such an important and current issue is insufficient (5,8,16).

Aim

In this study, it was aimed to determine the relationships between physical self-perception, body posture disorders, age, gender and BMI categories and nursing students' physical self-perception and body posture disorders.

2. METHODS

2.1. Study Design

The students in the sample group were determined through stratified random sampling (the stratum criteria are the classes the students are studying at). The samples from the targeted sub-strata were chosen by using random number tables.

2.2. Participants

The study population was comprised of 1202 students studying at the Istanbul University Florence Nightingale Nursing Faculty in the academic year 2015 – 2016; on the other hand, the sample consisted of 322 students, which was calculated through the formulation of sample size calculation for an existing population (95% confidence interval, 5% margin of error, 50% frequency). To prevent any data loss, the number of the students that would be included in the sample was determined to be 341 by calculating 10% and including it to the sample. A total of 341 students, 232 female and 109 male, participated in the study. In the study using stratified sampling method, all the students whose aimed and important explanations were studied were included. 105 students are first class, 111 students are second class, 92 students are third class and 33 students are fourth class participated in the study. The criteria for participation in the study was students' voluntariness/willingness and allowing their photos to be taken; while the criteria for exclusion from the study was having undergone a surgical operation on spine, not being voluntary or willing, and not consenting one's photos to be taken.

2.3. Data Collection

The data were collected by using "Structured Question Form", "Symmetrigrاف", "Posture Aware by Center Road Software LLC" and "Physical Self-Description Questionnaire (PSDQ)".

Structured Question Form: The form consists of questions related to age, gender, The Body Mass Index (BMI), marital status, grade/class, family type, income statues, place of residence, substance use, chronic disease, regular medication use and doing regular exercise.

Symmetrigrاف: Postural analysis was conducted through Symmetrigrاف, a clear chart divided into squares. Symmetrigrاف is a practical tool consisting of 10 cm side-squares, 9 in horizontal and 27 in vertical positions, and it enables us to

spot the asymmetry in spinal cord in lateral and front plan (Figure 1). The assessment was done by stabilizing the feet at a certain spot. The person to be assessed stood behind the tool. In the posterior analysis, the mid-point between the ankles was immobilized; and in the lateral analysis, the slight tip of lateral malleolar was stabilized. The posture assessment was conducted through three scales: "normal", "1st degree deformity" and "2nd degree deformity". According to the points of references, deviations up to 3 cm was considered as 1st degree deformity; and deviations more than 3 cm were referred as 2nd degree deformity. In lateral appearance, the points of reference are slightly tip of lateral malleolar, shoulder midpoint, slightly back of hip joint, and ear tragus (11,17). In postural analysis, Symmetrigrاف and Bragg posture chart were used together; the person was placed on a step put behind the symmetrigrاف; and the person's posture was then compared to the shapes in Bragg posture chart, and assessed as "good, moderate, and poor" (10,11).



Figure 1. Symmetrigrاف (11)

Posture Aware by Center Road Software LLC (App Store, United States): This application, which was developed to determine the body posture and can be downloaded to smart phones/tablets or computers, enables people to upload their body posture photos to the app to be assessed. The app gives scores visually to the ideal postural analysis of the spots marked as red on the photos taken (18). In the study, the analysis of the visual was conducted by the researchers (Figure 2).

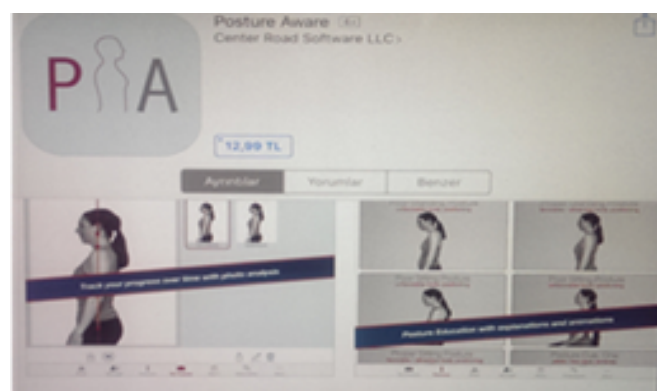


Figure 2. Body Posture Aware Application (18)

PSDQ: The instrument was developed by Marsh, Richards, Johson, Roche and Tremayne in 1994 (19). Its Turkish reliability and validity studies were completed by Aşçı (3,20). It consists of 9 subscales related to Strength, Body Fat, Physical Activity, Endurance, Sports Competence, Coordination, Health, Appearance, Flexibility as well as two global measures of Global Physical Self-concept and Global Esteem. The PSDQ is a 70-item test and it uses a 6-point likert scale with "1: Completely False" and "6: Completely True". Reverse Scoring was applied for the following subscales: Health (1.,12.,23.,45.,56.,67.), Body Fat (4.,15.,26.,37.,48.,59.), Appearance (40.,62.), Strengths (41.,31.), Flexibility and Global Esteem (22.,33.,44.,68.,70.). The scale gives scores ranging from 6 to 24, for each dimension, in 5 different dimensions of physical perception. The high score on the scale shows a high level of physical perception in the high individual whereas the low score shows low physical perception. Internal consistency coefficient of PSDQ subscales which were adapted to Turkish ranges from Cronbach Alpha 0.87 to 0.98 (3,5). In this study, Cronbach Alpha coefficient for PSDQ was found to be 0.893.

2.4. Procedures

Students' written and oral informed consents were taken within the scope of the study. After measuring students' height and weight, "Structured Question Form" was filled in. Then, students' body posture analysis was completed by using "Symmetrigrاف". Following this, students' photos were taken with the use of tablet laptops to use them in "Body Posture Aware App". After body posture analysis was completed through both methods under the guidance of an orthopedist, students were asked to fill in PSDQ, which was the final step in data collection.

2.5. Ethical Considerations

Ethical approval for this study was obtained from the Istanbul University Ethics Committee (16.03.2016/401). The researchers explained the purpose of the research, roles of participants, benefits and potential risks of the study, their right to withdraw at any time. Students' written consents/approvals were received with Used Confidentiality Agreement Form.

2.6. Statistical Analysis

For data analysis, IBM SPSS Statistics 22 (IBM SPSS, Turkey) was utilized for statistical analysis. Data were analyzed via Shapiro Wilks test and it was observed to be normally distributed. In addition to descriptive statistical methods (mean, standard deviation, frequency), Student t Test was used to examine quantitative data for inter-group analysis. To analyze the data for groups of more than two, one way ANOVA test was used whereas Tukey HSH Post Hoc test was preferred to detect which group caused the difference. Chi-square test, Yates Continuity Correction and Fisher Absolute Chi-square test were used for analysis of qualitative data. Significance level was determined to be at $p < 0.05$.

3. RESULTS

3.1. Students' Individual Characteristics

68% of the participant students were female and average age was 20.34 ± 1.69 years. 98.8% of them were single and 32.6% were second graders. As for family, 79.2% lived in nuclear family and 33.1% had at least 4 siblings. In addition, 49.9% lived with their family. 87.7% had health insurance while 89.7% did not hold any job. 9.1% of them suffered from a chronic disease while 9.4% were on regular medication. When it comes to habits, 9.1% smoked and abused alcohol and 27% did not do regular exercise. BMI was found to be 22.47 ± 3.66 kg/m² for the female students and 23.57 ± 3.50 for the male (Table 1).

Table 1. Individual Characteristics of Students (N = 341)

		n	%
Age (years)	Avg. \pm SD	17-32	20,34 \pm 1,69
Gender	Girl	232	68,0
	Boy	109	32,0
BMI Categories	Weak	24	7,0
	Normal weight	240	70,4
	Overweight	65	19,1
	1st degree obese	8	2,3
	2nd degree obese	3	0,9
Marital status	Morbid obese	1	0,3
	Married	4	1,2
Class	Single	337	98,8
	1st class	105	30,8
	2 nd class	111	32,6
	3rd class	92	27,0
Family type	4 th class	33	9,7
	Nucleus	270	79,2
Number of siblings	Wide	61	17,9
	Single child	27	7,9
	2 siblings	133	39,0
	3 brothers	68	19,9
Life location	4 and over siblings	113	33,1
	Alone	5	1,5
	Family	170	49,9
	Friend	37	10,9
	Dorm	112	32,8
Health security	Relative	17	5,0
	There is	299	87,7
Working Status	No	42	12,3
	Working	35	10,3
Chronic disease	Not working	306	89,7
	There is	31	9,1
Smoking	No	310	89,7
	Yes	31	9,1
Alcohol use	No	310	90,9
	Yes	31	9,1
Continuous drug use	No	309	90,6
	Yes	32	9,4
Sports activity	No	249	73,0
	Yes	92	27,0

3.2. Results of Body Posture Analysis with Respect to Symmetrigrاف and Body Posture Aware App

Posture analysis via symmetrigrاف showed that 10% of the students suffered from kyphosis, 2.9% from lordosis, 1.5% from scoliosis, 19.9% from flattening, 1.2% from curvature.

First-degree deformations were diagnosed on shoulder, spine, hip, wrist, neck, upper back, torso, abdomen, and back at the respective rates: 41.1%, 6.2%, 8.2%, 7%, 5.6%, and 0.3%. According to Body Posture Aware App, there was first-degree deformation on the head with 1.2%, on the shoulder with 36.7% and on the hip with 2.3% (Table 3).

3.3. PSDQ Scores and Comparison of PSDQ Scores with respect to Individual Characteristics

Total average score obtained from PSDQ was 275.13±43.23. Average score for Health subscale was 33.65±6.73; 23.62±5.02 for Coordination, 18.72±6.40 for Physical Activity, 26.48±6.84 for Body Fat, 21.14±6.45 for Sports Competence, 25.85±5.48 for Global Physical Self-concept, 23.82±4.88 for Appearance, 23.94±5.40 for Strength, 22.88±6.00 for Flexibility, 20.53±6.21 for Endurance and 34.51±6.34 for Global Esteem (Table 2).

When Table 2 is taken into consideration, it can be seen that 20-21 age group obtained statistically higher average scores of PSDQ ($p<0.05$) in total and higher average scores from subscales of Body Fat ($p<0.05$), Flexibility ($p<0.05$) and Global Esteem ($p<0.05$) compared to the students aged 19 and below (Table 3).

Male students had statistically higher scores at significant level than girls from PSDQ ($p<0.01$), and subscales of Health ($p<0.01$), Coordination ($p<0.01$), Physical Activity ($p<0.01$), Sports Competence ($p<0.01$), Global Physical Self-concept ($p<0.01$), Strength ($p<0.01$), Flexibility ($p<0.01$), Endurance ($p<0.01$) (Table 2).

Regarding BMI measures, overweight and obese students had statistically significant higher scores than underweight and normal weight students from Strength subscale

($p<0.01$) just like normal students' grades were higher than underweight students from Strength subscale ($p<0.01$). Also, underweight students had statistically significant higher scores from Flexibility subscale than overweight and obese students ($p<0.05$) (Table 2).

3.4. Comparison of Students' Individual Characteristics with Symmetrigrاف and Body Posture Aware App Results

Table 3 shows that Symmetrigrاف did not indicate any statistically significant difference among the ratios of physical deformity in terms of age groups ($p>0.05$). The rate of kyphosis ($p<0.01$) and flattening ($p<0.05$) among male students is statistically significantly higher than the female ones. The frequency rate of second-degree deformity on shoulder ($p<0.01$), spine ($p<0.05$), and the neck ($p<0.05$) was statistically significantly higher among the male than the female. On the other hand, the rate of first-degree deformity for the female is statistically higher at a significant level than the male students ($p<0.01$). Posture Aware App has shown that the rate of second-degree deformity on shoulder among the male is statistically significantly higher than that of the female students ($p<0.05$).

Based on BMI categories, 25% of the underweight students, 7.5% of the ones with normal weight and 13% of the overweight and obese students were diagnosed to suffer from kyphosis. The frequency of flattening cases showed statistically significant differences ($p<0.05$) with 33.3% for underweight students, 16.3% for normal weight students and 27.3% for the overweight and obese. Likewise, statistically significant differences were observed in cases of physical deformities on shoulder based on BMI ($p<0.01$). 8.3% of the underweight students and 0.4% of the normal weight ones suffered from physical should deformity in the second degree.

Table 2. Student scores from subscales of Physical Self-Description Questionnaire and Physical Self-Description Questionnaire levels based on individual characteristics (N=341)

Physical Self-Description Questionnaire Subscales	Age Group	Age Group				Gender			BMI Categories			
		19-↓	20-21	22-↑	p	Female	Male	p	Underweight	Normal	Overweight and obese	p
	Avg.±SD (Min.-Maks.)	Avg.±SD	Avg.±SD	Avg.±SD		Avg.±SD	Avg.±SD		Avg.±SD	Avg.±SD	Avg.±SD	
Health	33,65±6,7 (39-48)	32,35±6,42	34,21±7,08	34,25±5,98	0,059	32,66±6,73	35,77±6,24	0,001**	32,58±8,83	33,46±6,70	34,57±6,05	0,328
Coordination	23,62±5,02(8-36)	22,78±5,18	24,25±4,92	23,30±4,86	0,055	22,90±4,68	25,16±5,38	0,001**	24,50±4,48	23,87±5,03	22,57±5,04	0,095
Physical Activity	18,72±6,40(6-35)	17,95±5,93	19,41±6,75	18,08±6,01	0,125	17,86±6,29	20,54±6,26	0,001**	16,08±6,70	18,83±6,34	19,19±6,38	0,102
Body Fat	26,48±6,84(6-36)	25,14±6,69	27,49±6,97	25,91±6,37	0,016*	26,05±6,84	27,39±6,78	0,093	34,75±3,52	27,67±5,99	20,18±5,16	0,001**
Sports Competence	21,14±6,45(6-36)	20,02±6,61	21,40±6,51	22,23±5,84	0,071	19,53±5,90	24,57±6,27	0,001**	20,46±5,76	21,13±6,20	21,38±7,45	0,831
Global Physical Self-concept	25,85±5,48(9-36)	25,20±5,78	26,00±5,50	26,52±4,88	0,283	25,21±5,47	27,22±5,27	0,002**	26,75±6,02	26,33±5,09	24,10±6,15	0,006**
Appearance	23,82±4,88(11-85)	23,31±3,17	23,90±3,88	24,41±8,40	0,348	23,63±3,38	24,21±7,10	0,306	26,50±12,90	24,00±3,41	22,42±3,91	0,001**
Strength	23,94±5,40(9-36)	23,33±5,58	24,05±5,50	24,63±4,80	0,297	22,97±5,19	25,98±5,30	0,001**	20,96±5,12	23,75±5,21	25,43±5,66	0,001**
Flexibility	22,88±6,00(7-36)	21,51±6,07	23,62±5,82	23,09±6,08	0,016*	21,80±5,80	25,18±5,79	0,001**	23,04±5,27	23,38±5,83	21,26±6,49	0,025*
Endurance	20,53±6,21(6-36)	19,52±5,96	20,81±6,25	21,42±6,36	0,109	18,86±5,69	24,08±5,79	0,001**	19,08±6,63	20,93±6,27	19,74±5,82	0,171
Global Esteem	34,51±6,34(18-84)	33,52±6,21	35,40±6,61	33,70±5,50	0,029*	34,50±6,22	34,54±6,61	0,951	35,17±5,06	34,57±6,61	34,12±5,85	0,751
Total	275,13±43,23(165-390)	264,63±44,06	280,55±42,89	277,53±40,26	0,011*	265,96±40,29	294,64±42,97	0,001**	279,88±43,72	277,92±42,52	264,96±44,26	0,062

Min: Minimum,; Max: Maximum, Avg.: Average; SD: Standart Deviation
One Way ANOVA, Student t Test * $p<0,05$ ** $p<0,01$

Table 3. State of physical deformity and analysis of physical deformities in terms of individual characteristics based on Symmetrigrاف and Body Posture Aware App Results (N=341)

			Age Groups			p	Gender		p	BMI Categories			p	
			n(%)	19-↓ n(%)	20-21 n(%)		22-↑ n(%)	Female n(%)		Male n(%)	Underweight n(%)	Normal n(%)		Overweight and obese n(%)
Symmetrigrاف	Kyphosis	Yes	34(10,0)	9 (8,7)	14(8,1)	11 (17,2)	0,101	12 (5,2)	22 (20,2)	0,001**	6 (25)	18 (7,5)	10 (13)	0,015*
		No	307(90,0)	95 (91,3)	159 (91,9)	53 (82,8)		220 (94,8)	87 (79,8)		18(75)	222 (92,5)	67 (87)	
	Lordosis	Yes	10(2,9)	1 (1)	8 (4,6)	1 (1,6)	0,167	9 (3,9)	1 (0,9)	0,178	2 (8,3)	7 (2,9)	1 (1,3)	0,204
		No	331(97,1)	103(99)	165 (95,4)	63 (98,4)		223 (96,1)	108 (99,1)		22 (91,7)	233 (97,1)	76 (98,7)	
	Scoliosis	Yes	5(1,5)	3 (2,9)	2 (1,2)	0 (0)	0,284	5(2,2)	0 (0)	0,181	0 (0)	5 (2,1)	0 (0)	0,344
		No	336(98,5)	101 (97,1)	171(98,8)	64(100)		227 (97,8)	109 (100)		24 (100)	235 (97,9)	77 (100)	
	Flattening	Yes	68(19,9)	1 (15,4)	41 (23,7)	11 (17,2)	0,203	39 (16,8)	29 (26,6)	0,035	8 (33,3)	39 (16,3)	21 (27,3)	0,026*
		No	273(80,1)	8 (84,6)	132 (76,3)	53 (82,8)		193 (83,2)	80 (73,4)		16 (66,7)	201 (83,8)	56 (72,7)	
	Curvature	Yes	4(1,2)	2 (1,9)	1 (0,6)	1 (1,6)	0,572	2 (0,9)	2 (1,8)	0,595	1 (4,2)	2 (0,8)	1 (1,3)	0,349
		No	337(80,1)	102 (98,1)	172 (99,4)	63 (98,4)		230 (99,1)	107 (98,2)		23 (95,8)	238 (99,2)	76 (98,7)	
	Shoulder	Normal	198(58,1)	69 (66,3)	92 (53,2)	37 (57,8)	0,229	147 (63,4)	51 (46,8)	0,009**	9 (37,5)	148 (61,7)	41 (53,2)	0,001**
		First-degree deformity	140(41,1)	35 (33,7)	79 (45,7)	26 (40,6)		84 (36,2)	56 (51,4)		13 (54,2)	91 (37,9)	36 (46,8)	
		Second-degree deformity	3(0,9)	0 (0)	2 (1,2)	1 (1,6)		1 (0,4)	2 (1,8)		2 (8,3)	1 (0,4)	0 (0)	
	Spine	Normal	308(90,3)	95 (91,3)	155 (89,6)	58 (90,6)	0,752	214 (92,2)	94 (86,2)	0,048*	19 (79,2)	220 (91,7)	69 (89,6)	0,084
		First-degree deformity	31(9,1)	9 (8,7)	17 (9,8)	5 (7,8)		18 (7,8)	13 (11,9)		4 (16,7)	19 (7,9)	8 (10,4)	
		Second-degree deformity	2(0,6)	0 (0)	1 (0,6)	1 (1,6)		0 (0)	2 (1,8)		1 (4,3)	1 (0,4)	0 (0)	
	Hip	Normal	335(98,2)	104 (100)	169 (97,7)	62 (96,9)	0,483	229 (98,7)	106 (97,2)	0,113	23 (95,8)	236 (98,3)	76 (98,7)	0,189
		First-degree deformity	4(1,3)	0 (0)	3 (1,7)	1 (1,6)		3 (1,3)	1 (0,9)		0 (0)	3 (1,3)	1 (1,3)	
Second-degree deformity		2(0,6)	0 (0)	1 (0,6)	1 (1,6)	0 (0)		2 (1,8)	1 (4,2)		1 (0,4)	0 (0)		
Wrist	Normal	318(93,3)	101 (97,1)	160 (92,5)	57 (89,1)	0,287	219 (94,4)	99 (90,8)	0,094	22 (91,7)	222 (92,5)	74 (96,1)	0,134	
	First-degree deformity	21(6,2)	3 (2,9)	12 (6,9)	6 (9,4)		13 (5,6)	8 (7,3)		1 (4,2)	17 (7,1)	3 (3,9)		
	Second-degree deformity	2(0,6)	0 (0)	1 (0,6)	1 (1,6)		0 (0)	2 (1,8)		1 (4,2)	1 (0,4)	0 (0)		
Neck	Normal	311(91,2)	97 (93,3)	155 (9,8)	59 (92,2)	0,578	217 (93,5)	94 (86,2)	0,025*	18(75)	220 (91,7)	73 (94,8)	0,016*	
	First-degree deformity	28(8,2)	7 (6,7)	17 (89,6)	4 (6,3)		15 (6,5)	13 (11,9)		5 (20,8)	19 (7,9)	4 (5,2)		
	Second-degree deformity	2(0,6)	0 (0)	1 (0,6)	1 (1,6)		0 (0)	2 (1,8)		1 (4,2)	1 (0,4)	0 (0)		
Upper Back	Normal	315(92,4)	95 (91,3)	158 (91,3)	62 (96,9)	0,267	215 (92,7)	100 (91,7)	0,114	19 (79,2)	224 (93,3)	72 (93,5)	0,046*	
	First-degree deformity	24(7,0)	9 (8,7)	14 (8,1)	1 (1,6)		17 (7,3)	7 (6,4)		4 (16,7)	15 (6,3)	5 (6,5)		
	Second-degree deformity	2(0,6)	0 (0)	1 (0,6)	1 (1,6)		0 (0)	2 (1,8)		1 (4,2)	1 (0,4)	0 (0)		
Torso	Normal	320(93,8)	97 (93,3)	161 (93,1)	62 (96,9)	0,404	219 (94,4)	101 (92,7)	0,118	20 (83,3)	227 (94,6)	73 (94,8)	0,080	
	First-degree deformity	19(5,6)	7 (6,7)	11 (6,4)	1 (1,6)		13 (5,6)	6 (5,5)		3 (12,5)	12 (5)	4(5,2)		
	Second-degree deformity	2(0,6)	0 (0)	1 (0,6)	1 (1,6)		0 (0)	2 (1,8)		1 (4,2)	1 (0,4)	0 (0)		
Abdomen	Normal	340(99,7)	103 (99)	173 (100)	64 (100)	0,319	231 (99,6)	109 (100)	0,001**	24 (100)	239 (99,6)	77 (100)	0,810	
	First-degree deformity	1(0,3)	1 (1)	0 (0)	0 (0)		1 (0,4)	0 (0)		0 (0)	1 (0,4)	0 (0)		
Waist	Normal	319(93)	99 (95,2)	160 (92,5)	60 (93,8)	0,655	219 (94,4)	100 (91,7)	0,111	20 (83,3)	225 (93,8)	74 (96,1)	0,076	
	First-degree deformity	20(5,9)	5 (4,8)	12 (6,9)	3 (4,7)		13 (5,6)	7 (6,4)		3 (12,5)	14 (5,8)	3 (3,9)		
	Second-degree deformity	2(0,6)	0 (0)	1 (0,6)	1 (1,6)		0 (0)	2 (1,8)		1 (4,2)	1 (0,4)	0 (0)		
Body posture Aware App	Head	Normal	335(98,2)	102 (98,1)	172 (99,4)	61 (95,3)	0,175	230 (99,1)	105 (96,3)	0,086	22 (91,7)	237 (98,8)	76 (98,7)	0,091
		First-degree deformity	4(1,2)	2 (1,9)	0 (0)	2 (3,1)		2 (0,9)	2 (1,8)		1 (4,2)	2 (0,8)	1 (1,3)	
		Second-degree deformity	2(0,6)	0 (0)	1 (0,6)	1 (1,6)		0 (0)	2 (1,8)		1 (4,2)	1 (0,4)	0 (0)	
	Shoulder	Normal	214(62,8)	71 (68,3)	103 (59,5)	40 (62,5)	0,459	115 (66,8)	59 (54,1)	0,014*	10 (41,7)	160 (66,7)	44 (57,1)	0,016*
		First-degree deformity	125(36,7)	33 (31,7)	69 (39,9)	23 (35,9)		77 (33,2)	48 (44)		13 (54,2)	79 (32,9)	33 (42,9)	
		Second-degree deformity	2(0,6)	0 (0)	1 (0,6)	1 (1,6)		0 (0)	2 (1,8)		1 (4,2)	1 (0,4)	0 (0)	
	Hip	Normal	331(97,1)	102 (98,1)	167 (96,5)	62 (96,9)	0,712	226 (97,4)	105 (96,3)	0,108	22 (91,7)	234 (97,5)	75 (97,4)	0,176
		First-degree deformity	8(2,3)	2 (1,9)	5 (2,9)	1 (1,6)		6 (2,6)	2 (1,8)		1 (4,2)	5 (2,1)	2 (2,6)	
		Second-degree deformity	2(0,6)	0 (0)	1 (0,6)	1 (1,6)		0 (0)	2 (1,8)		1 (4,2)	1 (0,4)	0 (0)	

Chi-square Test, Yates Continuity Correction and Fisher Absolute Chi-square Test

*p<0,05 **p<0,01

In the same manner, there were statistically significant differences in physical neck deformity cases ($p < 0.05$) in the second degree at the rates of 4.2% among underweight ones and 0.4% among the normal weight students (Table 3).

Based on Body Posture Aware App results, statistically significant differences were observed among BMI categories in the rates regarding physical deformity ($p < 0.05$). That is, 4.2% of the underweight participants and 0.4% of the students with normal weight suffered from neck deformity in the second degree (Table 3).

4. DISCUSSION

Symmetrigrاف assessments showed that kyphosis in 10% of the students, lordosis in 2,9%, scoliosis in 1,5%, flattening in 19,9% and curvature in 1,2% were identified while there was first-degree deformity in shoulder, spine, hip, wrist, upper back, torso, abdomen and back parts. Similarly, body posture analysis of Body Posture Aware App revealed first-degree deformities in the head, shoulder and hip. The fact that body posture analysis through Symmetrigrاف and Posture Aware App showed similar physical deformities indicates that both methods are reliable. In today's world, university students, called Generation Y, often use technological tools related to the Internet in their daily lives, which might reach addiction levels. Today, problems in body posture have occurred in addition to the obesity problem that has increased in ratio due to reduction in physical activities and increasing use of technological tools, which is one of the findings of this study that was expected in relation to students' technology use (21-24).

20-21 year-old students' total scores of PSDQ and average scores of the subscales Body Fat, Flexibility, and Global Esteem were found to be higher than those of the group aged 19 year old and below. This finding can be attributed to the fact that students who are training to be nurses are professionally more conscious and have increased their accumulation of knowledge thanks to the courses they take in the university and accordingly have made changes in their lives.

Male students' total scores of PSDQ and average scores of the subscales Health, Coordination, Physical Activity, Sports Competence, General Physical Self-Concept, Strength, Flexibility and Endurance were found to be higher than the scores female students obtained. This finding demonstrates that female students consider themselves less able compared to male students when it comes to physical self-perception levels in terms of health, coordination, physical activity, sports competence, general physical self-concept, strength, flexibility and endurance. The finding along these lines is attributable to the fact that male students perceive themselves to be better in the fields mentioned above and that they consider themselves privileged in such areas because of gender. Previous studies show that the male participants obtain higher scores than the female (5,25-28).

According to BMI measures, students who are overweight and obese scored higher on average in Strength subscale than underweight and normal weight students. Also, normal weight students scored significantly higher in Strength subscale compared to underweight students. However, underweight students' average scores of Flexibility subscale were significantly higher than overweight and obese students. Currently, standards for being physical attractive are increasing more and more. The female pay attention to thinness and flexibility whereas the male care about muscular and strong body build and cultures impose standards for physical attractiveness, body weight and body build (2,29,30). This finding of the study can be assumed as the reflection of existing perceptions of the society on students.

Based on Symmetrigrاف assessment, the rate of kyphosis and flattening as well as second-degree deformities in the shoulder, spine and neck is higher among the male than the female. On the other hand, the rate of first-degree neck deformity among the female is higher than the male counterparts. Body Posture Aware App shows that second-degree shoulder deformity was identified in male students more often than female students. There might be various causes of posture-related problems. Among the primary ones come the following: having experienced an accident or trauma, weakness in lower back, abdomen and upper back muscles, sitting position, posture and movements incompatible with body mechanics, carrying heavy stuff, non-ergonomic desks, carelessness about body posture starting from adolescence, girls' desire to hide physical changes in their body or sitting slanted due to having big breasts, computer use for long periods and placing computer not on the head level (13,31,32). The finding of the study can be explained with the fact that female or male students do not pay attention to the practices mentioned above.

Symmetrigrاف measurements show that underweight, normal weight, overweight and obese students suffer from flattening whereas underweight students and the ones with normal weight suffer from second degree shoulder and neck deformities. According to Posture Aware App, underweight and normal weight students suffer a second-degree abnormality in shoulder. According to Body Mass Index, similar problems were diagnosed through both methods. The BMI is the value of the body mass divided by the square of the body height, and is universally expressed in units of kg/m^2 . It is used to predict body weight based on height. Assessment was conducted in line with BMI intersecting values suggested by World Health Organization (33). If BMI is 25 and over, the risk of hypertension (HT), type 2 Diabetes Mellitus (DM) and cardiovascular disease increases depending on obesity level. Therefore, assessment of university students' BMI is quite crucial in terms diagnosing future problems related to Internet and technological tool use. Similarly, the study conducted by Briggs et al. (34) reveals that the body parts where the most severe pain is felt are the neck and shoulder areas among children and adolescents who use computers.

These findings are believed to result from limitations in physical activities and changes in dietary habits because of increasing use of technology.

It was observed that average scores that students obtained from PSDQ were at intermediate level, they encounter problems related to body posture and gender is influential in posture and self-perception. In the light of the findings, it is recommended that;

- Physical activities be planned and a conducive environment be provided so that students can develop their physical self-perception and minimize the deformation of body posture.
- Courses that can boost physical self-perception be integrated into the curriculum.

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Text Messages Based Interventions for Pregnant Women's Health: Systematic Review

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ABSTRACT

Objective: The aim of this systematic review was to summarize evidence for the effectiveness of text message-based randomized controlled studies for the health of pregnant women.

Methods: We searched the following databases from 2005 and 2015, using databases Google Scholar, Pubmed, Ovid, Cochrane Library. The question of this systematic review; what are results of text message-based interventions on the health of pregnant women? Total of 15 articles was received that met the inclusion criteria for the study. After each full article was read, fifteen articles were included in this review.

Results: Text message were effective on smoking cessation, weight control, diabetes management, motherhood readiness, developing negative attitudes towards alcohol consumption.

Conclusion: This systematic review suggests use of text message is more practical and cost-effective method for promoting the health of pregnant women and they had a positive effect on health practices of pregnant women.

Keywords: health applications, mobile health, pregnant women, primary care, text message.

1. INTRODUCTION

Use of mobile health applications (mHealth) in developing healthcare and healthy lifestyle behaviors has increased in recent years (1, 2). World Health Organization (WHO) defines mHealth applications as supporting the public health and medical practices through mobile phones, patient follow-up monitors, personal digital assistant, other wireless devices (3). Some of the mobile health applications are formed as a reminder system in the smoking cessation, weight control and disease management and treatment for diabetes (4, 5). Mobile phones have a privileged place among the other mobile applications due to their properties such as being ubiquity, mobility, continuity and multi-media methods (2, 6). Sending a text message (SMS) is the simpler format commonly used among mobile health applications (7, 8). Health-related functions of the text messages include reminding health behaviors, reminding scheduled appointments and medication intake, notification of clinical test results, notification of health status, promotion of positive health behaviors, and increasing self-efficacy by giving information about access to information and sources (9, 10). Promotion of maternal-infant health is one of the fields where the mobile health applications has increased. Pregnant women and mothers can be encouraged by this way for many health behaviors during prenatal and postpartum periods (11,

12). SMS intervention studies on the importance of mobile technology in health promotion and pregnancy complication readiness, pregnant woman viewed the SMS intervention as useful in maternal healthcare services (13). The aim of this systematic review was to summarize evidence for the effectiveness of text message-based randomized controlled studies for the health of pregnant women.

2. METHODS

The question of this systematic review was "What are results of short message-based interventions on the health of pregnant women?"

2.1. Search Strategy

The systematic review included articles published between 2005 and 2015 and was performed in accordance with the Centre for Reviews and Dissemination 2009 (CRD)'s guideline (14). The question of this systematic review, "What are results of text message-based interventions on the health of pregnant women? We used for data summarizing "Checklist of Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement (PRISMA) which is a valid and reliable guideline (15, 16). We performed searches on:

Google Scholar, Pubmed, Ovid, Cochrane Library databases with the keywords of “pregnancy” and “text message” .

Inclusion criteria for the review included studies focused on the use of text messages with randomized controlled trial interventions for pregnant health.

2.2. Critical Appraisal

Quality evaluation of randomized controlled trials was conducted independently by the two authors. The methodological quality of eligible randomized controlled trials was assessed using tool developed by the Cochrane Collaboration (17).

According to our systematic literature review, 15 randomized controlled studies were included in the review. Ten of the articles examined within the scope of this review had low risk in Random Sequence Generation. Eight studies had low risk in Allocation concealment; whereas, 7 had uncertain risk (Figure 1).

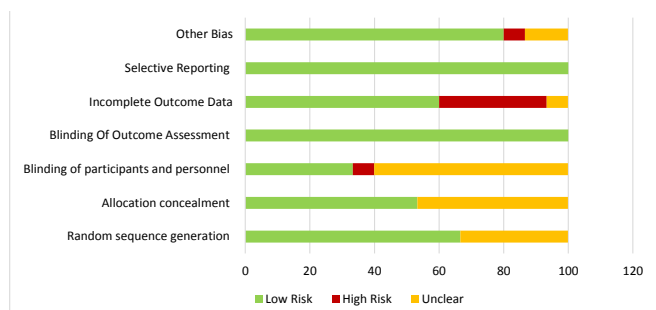


Figure 1. Risk of bias

3. RESULTS

After reading each one full article 15 randomized controlled studies were involved in this systematic review study (Figure 2). There were three studies Text4 baby program, three studies having influenza vaccine, two studies smoking reduction and cessation, two studies prevention of gestational diabetes, two studies increasing of health knowledge and awareness

in pregnancy, one studies reducing anxiety in screening tests, one studies prevention of obesity, one studies having HIV test.

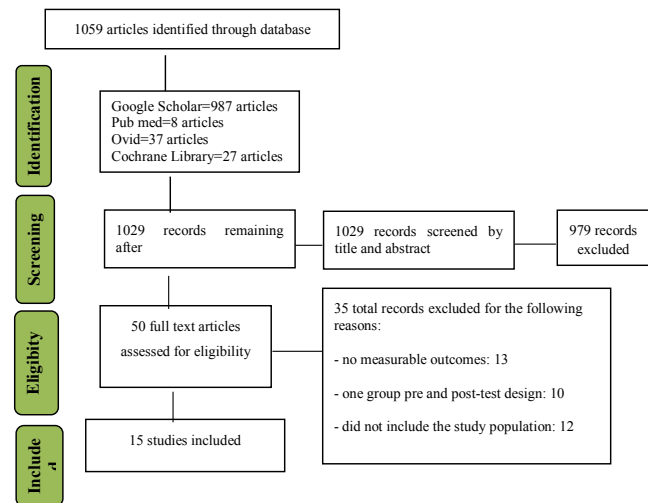


Figure 2. PRISMA Flow diagram for literature search

3.1. Effect of Text Messages on Smoking Cessation-Reduction

Result of studies pregnant woman’s self-efficacy, beliefs about its harms and quitting commitment scores increased, frequency of 7 day staying away from smoking of the was found to be increased. The amount of smoking was decreased. Also warning messages about reducing smoking gradually were found more effective (18, 19) (Table 1).

3.2. Effect of Text Messages on Influenza vaccine

Vaccination in pregnancy helps to protect newborns both through passive transfer of immunity (20). Result of one studies was determined that text message did not affect the influenza vaccination (21). Jordan et al. (2015) was found that vaccination rate was increased with text messages. Also reminder messages increased the vaccination possibility among pregnant women and mothers who thought to be vaccinated (22).

Table 1. Summary of literature review

Research	Sampling	Program Applied	Results
Naughton et al. (2012)	Experimental Group =102 Control Group =105	Text messages were sent two times daily to help the experimental group to quit smoking by themselves for 11 weeks, A general brochure was sent to the control group.	The probability of setting a date to quit smoking ($p=0.04$), self-efficacy ($p=0.02$), beliefs about its harms ($p=0.05$) and quitting commitment ($p=0.01$) scores were found to be higher for the experimental group than the control group.
Pollak et al. (2013)	Support message (group I)= 15 Support Text message+ gradually smoking cessation text messages (group II)=16	5 messages were sent daily for 5 weeks to the group I to choose a date to quit smoking within 2-3 weeks. Warning messages were sent to the group II for 5 weeks to quit smoking completely at the end of the 4 th week.	Frequency of 7 day staying away from smoking of the first group (7.5%) was found to be lower than the second group (13.4%). The amount of smoking in the first group (12 ± 07) was found to be lower than the second group (16 ± 11).
Moniz et al. (2013)	General Care Group=100 General Care+text message group=104	General care group was received general health text messages during pregnancy for 12 weeks, General care+text message group was received text messages about health+ influenza vaccine during pregnancy for 12 weeks.	At the end of the study, no difference was found between the influenza vaccination rate of the general care group (31%) and the influenza vaccination rate (33%) of the general care+ influenza vaccine group ($p>0.05$).
Stockwell et al. (2014)	Experimental Group=576 Control group=577	Test group was received 5 text messages containing information about influenza vaccine and 2 reminder messages for 5 weeks, Control group was received 2 reminder messages.	At the end of the study, the vaccination rate of the experimental group (61.9%) was found to be higher than the control group (49%).
Jordan et al. (2015)	Text message group = 3021 Education group =3820	Encouraging and reminder messages were sent to the one group, specific health education messages were sent to the other group.	It was found that the reminder messages increased the vaccination probability in mothers at the end of the year and pregnant women thinking to have vaccine. Health education not effective plan to have vaccine.
Cheng et al. (2008)	Text messages group = 1360 Control Group = 1422	Screening test results were sent to the group receiving text messages before the appointment, Test results were given to the group not receiving text messages during the appointment. Their anxiety status were evaluated before and 3 days after the appointment.	Anxiety level of text messages group was found to be lower before the appointment (33.8 ± 7.9) than those (39.1 ± 10.1) who did not ($p=0.02$).
Evans et al. (2012)	Intervention group= 48 Control group=38	Text messages about healthy lifestyle behaviors were sent to the intervention group during the pregnancy. Any application was not performed on control group. Pregnant women were evaluated again 2-3 months after the intervention.	The statement "I am ready to be a mother" for the pregnant women receiving Text4 baby sms contents increased compared to the beginning and follow-up ($p=0.04$). A positive development was determined in their attitudes towards alcohol consumption ($p=0.02$). No change occurred in the control group ($p>0.05$).
Evans et al. (2014)	Intervention group =229 Control group=230	text message about healthy lifestyle behaviors during the pregnancy were weekly sent to intervention group for 4 weeks according to their gestational week, No application was applied to the control group.	Beliefs of the pregnant women receiving vitamin intake during pregnancy increased (OR 1.91, 95% $p=0.02$). Additionally, their beliefs towards the importance of prenatal care ($p=0.04$) and the harms of alcohol consumption ($p=0.05$) were found to increase.
Evans et al. (2015)	Intervention group= 230 Control group=220	Women in the intervention group were followed up 3 times (after 4 weeks, in 28 th week and right after the birth) and they received weekly 3 text messages according to their gestational weeks. No intervention was applied to the control group.	At the end of the study, text messages were found to affect postpartum alcohol consumption of women in the intervention group ($p=0.04$).
Lau et al. (2014)	Intervention group =102 Control group =104	Starting to send 3-4 messages in a week to the women in the intervention group about increasing their health knowledge in pregnancy. No intervention was applied to the control group.	No significant difference was found between the pregnancy health knowledge scores of intervention and control groups ($p>0.05$).
Lund (2014) et al.	Intervention group = 1311 Control group = 1239	Weekly text messages about the subjects like the changes in the pregnancy in the intervention group. No intervention was applied to the control group.	Mortality rate of the intervention group (19 %) was lower than the control group (36 %) at the end of the study. In addition, the intervention was found to be associated with a significant reduction in perinatal mortality rate (OR0.50, CI:0.27-0.93, confidence interval of 95).

Soltani (2015) et al.	Intervention group = 14 Control group = 15	Daily messages encouraging healthy diet and physical activities were sent to the women from the intervention group. No intervention was applied to the control group.	Mean weight gain of women in the intervention group during the pregnancy (6.65 kg) was found to be lower than the control group (9.74 kg).
Odeny (2014) et al.	Intervention group = 195 Control group = 193	8 text messages during the pregnancy period and 8 text messages during the postpartum period were sent to the women in the intervention group. No intervention was applied to the control group.	As a result of the study, 19.6% of women in the intervention group and 11.8% of women in the control group applied to clinic during the postpartum period.
Van Ryswyk et al. (2015)	Intervention group = 140 Control group = 136	Messages were sent to women in the intervention group for reminding to have OGTT test in postpartum 6 th week and 3 rd and 6 th months; reminder message was sent to women in control group in postpartum 6 th month.	OGTT participation of the intervention group (77.6%) were found not to increase in postpartum 6 th month compared to the control group (76.8%) at the end of the study.
Perez Ferre (2010) et al.	Intervention group = 48 Control group = 49	Glucometers and mobile phones were given to the women in the intervention group. No intervention was applied to the control group.	At the end of the study, clinical visit of the experimental group reduced at the rate of 2%. While the average clinic visit number was 4.25 in the experimental group, it was 9.11 in the control group.

3.3. Effect on Reducing Anxiety

Pregnancy is one of the most important periods in a woman's life; not only in physical directions, but also in a number of social and psychological changes. Table 1 shows studies on the effect of text messages on reducing anxiety. Study subjects included come clinic for prenatal screen test. Result of one studies was determined text messages not effective for reducing anxiety (23).

3.4. Effect on The Text4 Baby Program

Result of studies text4 baby program increased pregnant women state ready to be a mother, developed negative attitudes towards alcohol consumption (24). Also text4 baby program increased pregnant women beliefs about taking vitamin during pregnancy, the importance of prenatal care, and the harms of alcohol consumption increased (24, 25) (Table 1).

3.5. Effect on Text Messages Antenatal Health Knowledge and Awareness

Adequate antenatal care is important to both the health of a pregnant woman and her unborn baby. Result of this study text messages found to be not effective for antenatal health knowledge and awareness (26, 27) (Table 1).

3.6. Effect on Text Messages Reducing Obesity

Mother obesity and excessive gestational weight gain (GWG) negatively affect pregnancy and delivery outcomes. Result of this study text messages found to be effective for weight gain during pregnancy (28) (Table 1).

3.7. Effect on Text Messages Having HIV Test

Mobile health (mHealth) interventions have been shown to improve adherence to HIV test among adults and improve

health service usage (29). The result of this review text messages found to be increased having HIV test pregnant woman (30) (Table 1).

3.8. Effect on Text Messages Diabetes Management

Gestational diabetes mellitus is defined as new onset or recognition of glucose intolerance in pregnancy (31). The result of this review text messages found to reduced clinical visits diabetic pregnant woman (32) (Table 1).

4. DISCUSSION

Our results suggest that text messages interventions that appear to have positive effects on pregnant women's health. For example that text messages were found to have positive effects on on smoking cessation and reduction of pregnant women (33-35).

It was found that only sending short text messages to pregnant women was not effective in influenza vaccination (17), but in addition to short messages, the use of reminder messages was found to be effective (21, 36).

Result of this review text4 baby program increased pregnant women's motherhood readiness, negative attitudes against alcohol usage, beliefs about vitamin intake during pregnancy (23, 24).

Result of this review found that text messages are effective in antenatal health knowledge and awareness, increasing nutrition knowledge and creating behavioral changes in the fight against obesity among the individuals (27, 28, 37, 38).

Text messages are suitable and useful in the self-management of diabetes (39). One of studies on the use of text message in diabetes management in pregnancy, reminder messages for Oral Glucose Tolerance Test (OGTT) were determined not to be effective in pregnant women, but decreased the clinic visit rates (40).

Our results show that some of the positive effects of text message interventions on pregnant women's health, however text message not effective for reducing anxiety. Although there is suggestive evidence of benefit in pregnant health, more research is needed to identify the other areas effect on pregnant health.

The limitation of our review is that we excluded all studies that did not report RCT results, another limitation of the review process may lead to a restriction (English).

5. CONCLUSION

Our review including the 15 studies results of RCTs of interventions that text messages interventions for pregnant women. This systematic review suggests use of text message is more practical and cost-effective method for promoting the health of pregnant women and they had a positive effect on health practices of pregnant women.

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Refractory Urticarial Vasculitis Responsive to Methotrexate: Could It Be a New Treatment Option?

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ABSTRACT

Objective: Urticarial vasculitis is a chronic clinicopathologic entity characterized by clinically characterized urticarial rash, histopathologically characterized by leukocytoclastic vasculitis. The pathogenesis is thought to be developed by a type III hypersensitivity reaction similar to leukocytoclastic vasculitis.

Methods: Antihistamines and/or corticosteroids (systemic/local) may be used in patients with limited normocomplementemic urticarial vasculitis. In the literature, severe cases treated with dapsone, colchicine, hydroxychloroquine, pentoxifylline, omalizumab, mycophenolate mofetil, rituximab, cyclosporine, intravenous immunoglobulin, and cyclophosphamide have been reported in the case reports.

Results: In this case, the patient, whose symptoms had not previously responded to treatment with antihistamines, steroids, cyclosporine, and omalizumab, responded to treatment with methotrexate.

Conclusion: This case report recommends that methotrexate therapy may be a treatment option for cases of resistant urticarial vasculitis.

Keywords: Urticarial vasculitis, methotrexate, omalizumab

1. INTRODUCTION

Urticarial vasculitis (UV) is a chronic clinicopathologic entity characterized by clinically characterized urticarial rash, histopathologically characterized by leukocytoclastic vasculitis (1). About 5% to 10% of patients with urticarial lesions have UV. The pathogenesis is thought to be developed by a type III hypersensitivity reaction similar to leukocytoclastic vasculitis (2).

Methotrexate (MTX) is an immunosuppressive drug that has been successfully used in dermatology to treat many inflammatory diseases for almost forty years (3). In this study, the use of MTX was described for vasculitis (4).

Herein, the case of resistant urticarial vasculitis responding to MTX therapy is presented.

2. CASE PRESENTATION

A 31-year-old woman presented complaining of suffering from urticaria for three months. A dermatologic examination revealed common urticarial plaques on her body (Figure 1) with no angioedema. As learned from the patient's medical history, the patient's urticarial plaques lasted longer than 24 hours. There was no illness other than Hashimoto's thyroiditis in her medical history. The patient had been using 75 mcg of Levothyroxine sodium for many years. There was no new medication use that could have triggered attacks of urticaria.

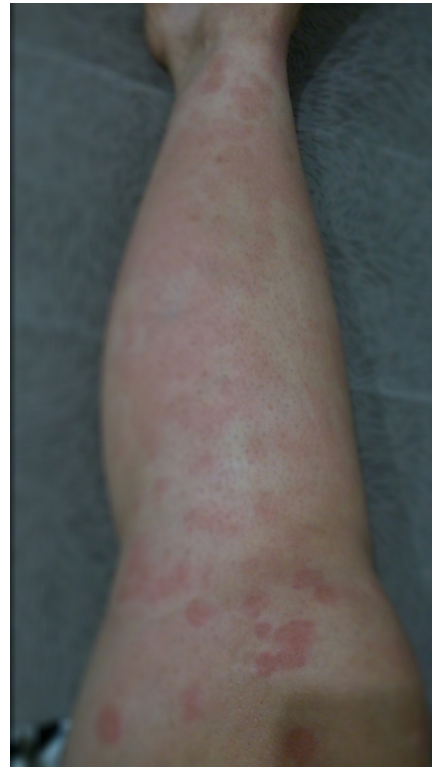


Figure 1. Common urticarial plaques on the leg.

The patient was medicated with a Rupatadine 10 mg tablet twice a day. After two weeks in which the symptoms did not diminish, the dosage was augmented to 10 mg tb of Rupatadine four times a day. When the patient's symptoms were not relieved after one month of Rupatadine tablet use, a twice a day dose of Cyclosporine 100 mg was added. After two months of an illness-free period with Cyclosporine, the urticarial attacks returned. Then, a subcutaneous treatment of Omalizumab (300 mg/28 day) was started. A 10 mg tablet of Montelukast sodium and a 5 mg tablet of Levocetirizine were simultaneously added to the dose. The patient's symptoms were not relieved after twelve doses of Omalizumab. Then, the Omalizumab dose was increased, and the patient received twelve doses of the Omalizumab treatment (300 mg/14 day) in six months.

A skin biopsy was taken from the patient's urticarial plaques for a differential diagnosis. Preliminary diagnoses from the biopsy were urticaria and UV. A histopathological examination showed mononuclear inflammatory infiltration in the papillary dermis with a swollen anterior fibrinoid necrosis perivascular area with eosinophils in the endothelium; as a result, it was compatible with vasculitis (Figure 2), and a direct immunofluorescence test was negative. At the laboratory review, ANA (antinuclear antibody) and other rheumatologic investigations were negative. Serum complement factors (C3, C4) levels were not found to be low.

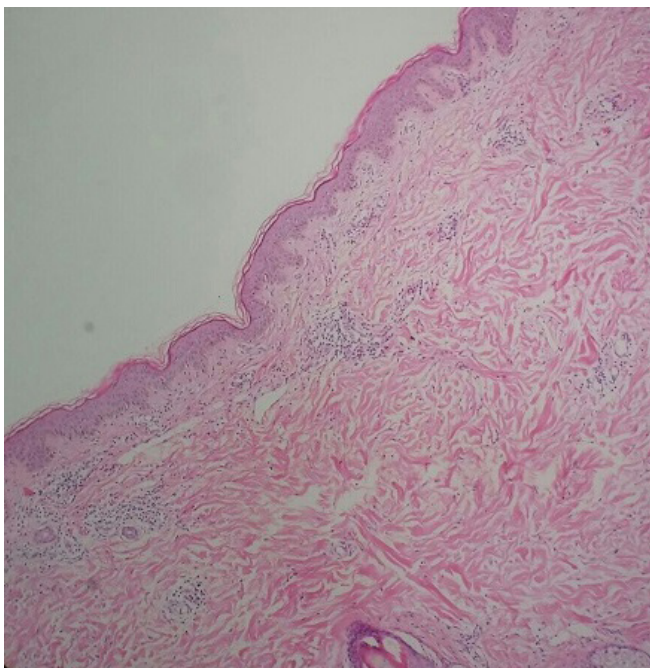


Figure 2. Mononuclear inflammatory infiltration in the papillary dermis with a swollen anterior fibrinoid necrosis, perivascular area eosinophils in endothelium, as a result it was compatible with vasculitis.

Systemic steroid therapy was added to the patient's treatment. Oral Prednisolone 48 mg/day was started, the dose was gradually decreased, and the treatment was continued for

two months. Since the patient's symptoms did not improve with systemic steroid therapy, it was decided to switch to MTX therapy. Subcutaneous MTX 10 mg/week treatment was started, and other treatments were discontinued. The patient's complaints were retreated in the second week. The patient's symptoms have not recurred for five months after methotrexate therapy. Liver and kidney function tests were normal during methotrexate treatment. MTX therapy was discontinued at the fifth month, and there was no recurrence of the patient's symptoms at the follow-up after the fifth drug-free month. The patient provided informed consent for the publication of this case report and the included images.

3. DISCUSSION

UV is characterized by a cutaneous presentation resembling urticaria and inflammation of the dermal capillaries on a skin biopsy. A finding of UV recorded over long periods of 24 hours were accompanied by extreme itching, violet coloration, and purpuric foci in the center (5,6). 20-30% of cases of UV are hypocomplemented (2). Normocomplementemic types of urticarial vasculitis are often idiopathic (7). The case was followed up clinically with an urticaria diagnosis. Then, by clinical suspicion, the case was diagnosed with normocomplemented urticarial vasculitis by biopsy and laboratory examinations.

UV treatment is planned according to the diffusiveness of skin lesions and accompanying systemic findings. Antihistamines and/or corticosteroids (systemic/local) may be used in patients with limited normocomplementemic UV. In the literature, severe cases treated with dapsons, colchicine, hydroxychloroquine, pentoxifylline, omalizumab, mycophenolate mofetil, rituximab, cyclosporine, IVIG, and cyclophosphamide have been reported in case reports (8,9).

MTX has antiproliferative, immunosuppressive, and anti-inflammatory effects. MTX is the most commonly used immunosuppressive agent after Prednisolone in the treatment of various skin diseases by experienced dermatologists. The fact that MTX is inexpensive, that its toxicity and side effects are well known, and that its efficacy data is easily available increases its use in dermatology (10). MTX has been used successfully in cutaneous vasculitis (11), but case reporting on use of urticarial vasculitis is limited. The MTX dose and its usage duration in the treatment of urticarial vasculitis is not clear due to the scarcity of reported cases in the literature. In the studies by Khasnis et al and Shen et al, the use of MTX as a 15 mg of intramuscular treatment for cutaneous vasculitis is mentioned (9,10), but for how many months MTX should be used is not mentioned. In this case, a patient suffering from cutaneous vasculitis was treated for five months with a subcutaneous MTX dosage of 10 mg/week MTX and had a successful outcome. Treatment of urticarial vasculitis with methotrexate was first mentioned by Stack in the literature (12). There is another case series in which MTX was successfully used for resistant urticaria (13).

MTX is a reliable treatment for other autoimmune diseases, and low doses seem to carry an admissible safety profile (14). The beneficial effects of methotrexate may be anti-inflammatory and immunosuppressive on urticarial vasculitis (15).

4. CONCLUSION

The patient, whose symptoms did not respond to previous treatment with antihistamines, steroids, Cyclosporine, and Omalizumab, had a positive response to treatment with methotrexate. MTX use in UV may be suitable in selected patients. This case report recommends that MTX therapy may be a treatment option for resistant UV. The limitation of this study was that it only examined a single case. There is a need for controlled clinical trials with larger patient numbers.

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