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TMSJ publishes original researches, interesting case reports and reviews regarding all fields of medicine. All of the published articles are open-access and reachable in our website. The primary aim of the journal is to publish original articles with high scientific and ethical quality and serve as a good example of medical publications for stimulating students, doctors, researchers. Our mission is to feature quality publications that will contribute to the progress of medical sciences as well as encourage medical students to think critically and share their hypotheses and research results internationally.

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## ***EDITORIAL***

***Dear readers,***

It is an honor to be able to meet again with our precious readers in the last issue of 2018. As the editors of Turkish Medical Student Journal, we attach importance to our journal being open-access, since one of our primary aims is to be able to reach to all of our readers freely, especially medical students. Considering the importance of open-access in this Information Age, It is a pleasure to publish our latest issue in the Open Access Week (22-28 October 2018). We also respect all the other open-access journals that have similar mission with our journal in this special week.

As the editorial board with all the efforts we made to raise the quality of the publication, I am very glad to announce that our journal has submitted an application to the Turkish local index (ULAKBİM/TR dizin). On the behalf of the editorial board, I express my gratitude to our editorial advisory board, our dear readers and everyone who has supported us so far to improve the quality of our journal.

In this issue you will find 5 original articles, 1 case report and 1 review. Şenyiğit et al. evaluated 657 patients with musculoskeletal system tumors and tumor-like lesions according to their ages and gender in order to assess the demographical profile of patients with musculoskeletal tumors first time in Thrace region. Meldonium is an anti-ischemic drug that functions by delaying beta-oxidation of fatty acids in cardiac muscle cells via inhibiting carnitine biosynthesis. It has also been popular on media due to its illegal use by professional athletes to benefit from its performance-enhancing effects. The efficiency of meldonium in the treatment of cardiovascular diseases such as myocardial infarction, heart failure has still been investigated by researchers. Vamsi et al. published their paper in this issue assuming meldonium strengthens the antianginal effect of basic therapy applied to patients with stable angina pectoris. Mutlu et al. conducted a research focusing on peer bullying, an issue that has negative effects on many children and adolescents globally. They trained secondary school students to raise awareness and to advise them on how to behave when they encounter bullying. As they analyzed the situation by conducting surveys before and after the training, they detected a drastic reduction in the rates of the victim and bully students. Elmacı et al. investigated the unnecessary tests ordered when the automation system of the hospital encountered with a shutdown. They revealed 2549 non-stat tests were ordered during the shutdown, despite the announcement of the laboratory that only stat tests should be ordered in that time, thus pointed out the inconvenient use of biochemical laboratory testing. Göztepe et al. presented a case report about a patient with secondary infertility who had subsequent miscarriages. More detailed information about the researches is available in the following pages.

Hope to meet you again in the next issue.

***Koray DEMİRCİ***  
***Editor-in-Chief***



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## THE EVALUATION OF MUSCULOSKELETAL SYSTEM TUMORS AND TUMOR LIKE LESIONS IN THRACE REGION

Ece Şenyiğit<sup>1</sup>, Begüm Söyleyici<sup>1</sup>, Nur Gülce İşkan<sup>1</sup>, Hilal Sena Çıfıbaşı<sup>1</sup>, Aslı Göztepe<sup>1</sup>, Mert Çiftdemir<sup>2</sup>

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### ABSTRACT

**Aims:** The aim of this study is to evaluate the data belonging to patients who were diagnosed with benign or malignant soft tissue and bone tumors and tumor-like lesions evaluated by musculoskeletal tumor study group of Trakya University Faculty of Medicine in between January 2013 and June 2017 and the relationship between the frequency of benign, malignant bone and soft tissue tumors and tumor-like lesions, with the patients' age and gender.

**Methods:** The data of 687 patients who were evaluated by the musculoskeletal tumor study group of Trakya University Faculty of Medicine between January 2013- June 2017 were analyzed retrospectively. All of the data was analyzed by using SPSS. Chi-square analysis was used to obtain categorical data in order to point out the distribution of age and gender of patients with musculoskeletal system tumors and tumor-like lesions.

**Results:** The number of patients over the period from January 2013 to June 2017 was 687. The number of patients who were evaluated by biopsy and acquired histopathologic confirmation of their condition was 341. The mean of patients' ages was  $44.3 \pm 21.4$  (4-92). Among 341 patients, 106 (47.1%) patients were female and 119 (52.9%) patients were male. The mean of females' ages was  $43.7 \pm 20.4$  (4-92). The mean of males' ages was  $44.7 \pm 22.4$  (5-90).

**Conclusion:** Benign bone and soft tissue tumors were more common than malignant tumors. Benign bone tumors were predominantly seen in young adults. Our results was consistent with the literature however due to some patients who did not need a pathological sampling, our sample size was smaller than intended. With better archived information, more consistent results could be obtained in further studies.

**Keywords:** Tumor, bone, tissue, epidemiology

### INTRODUCTION

The musculoskeletal system tumors and tumor-like lesions are categorized as benign, malignant tumors and tumor-like lesions. Osteoid osteoma, osteoblastoma, osteoma, osteochondroma, enchondroma, giant cell tumors are considered as benign bone tumors whereas osteosarcoma, Ewing's sarcoma and chondrosarcoma are considered as malignant bone tumors. Lipoma, rhabdomyoma, leiomyoma, hemangioma etc. are regarded as benign soft tissue tumors whereas liposarcomas, fibrosarcomas, leiomyosarcomas etc. are regarded as malignant soft tissue tumors. There are also tumor-like lesions such as bone cysts (1).

Malignant bone tumors are naturally primary or metastatic (2). Bone is a common place for metastasis of visceral cancers (3, 4). There are five visceral organ cancers which commonly metastasize to the bones. These are respectively lung, breast, prostate, kidney and thyroid cancers. In addition, bones can be affected by cancers that originate from the reticuloendothelial system and metastasize such as multiple myeloma. When cancer metastasizes on the bones, they usually become more susceptible to pathologic fractures. Since not all bone tumors are symptomatic, the incidence is frequently higher than detected rates (4).

Studies show that osteochondroma is the most common tumor of the bone. Lower limbs are the most common site for bone tumors. Other common areas are

pelvis and upper limbs (1). The most common primary malignant tumor of the bone is osteosarcoma and this tumor shows a bimodal age distribution which has its first peak at the 2nd decade and the second peak at the 7th decade. Chondrosarcoma is also one of the malignant tumors and the patients' ages are generally greater than 50 years (1).

Benign bone tumors are more common than malignant bone tumors and they are mostly seen in children and young adults (5).

On the other hand, some lesions imitate bone and soft tissue tumors. These are tumor-like lesions. Tumor-like lesions can be described as bone lesions which are not caused by a tumoral process. These are infections such as osteomyelitis, Brodie abscess and cystic lesions such as simple bone cysts (1). They are also kept in mind in differential diagnosis.

The aim of this study is to appraise the data belonging to patients who were evaluated regarding the musculoskeletal study group of Trakya University Faculty of Medicine between January 2013 and June 2017 and the relationship between the frequency of benign and malignant musculoskeletal system tumors and tumor-like lesions with the patients' age and gender.

## **MATERIAL AND METHODS**

This study was approved by Scientific Research Ethics Committee of Trakya University Faculty of Medicine. In this study, the data of all patients who were evaluated by the musculoskeletal study group of Trakya University Faculty of Medicine between January 2013- June 2017 were analyzed retrospectively. The number of the patients was 687. Informed consent was obtained from all of the subjects. Age and gender data of the patients who were pre-diagnosed with musculoskeletal system tumors and tumor-like lesions were obtained from General Archive Unit of Trakya University Hospital and only known by researchers. After data collection, pathological diagnoses were categorized into two basic classifications as bone tumors and soft tissue tumors. In both sections, three categories were identified as malignant, benign and tumor-like lesions. In the study; liposarcoma, periosteal osteosarcoma, adenocarcinoma, chondrosarcoma, metastatic carcinoma and myxoid liposarcoma were considered as malignant tumors. Lipoma, osteochondroma, enchondroma, schwannoma, traumatic and Morton's neuroma, giant cell tumor of the tendon sheath, osteoid

osteoma, plasmacytoma, keratinous cyst, enchondromatosis, fibroma of the tendon sheath, and intraosseous lipoma were added to the category of benign tumors. Simple bone cyst and ganglion cyst were categorized as tumor-like lesions.

All of the data were analyzed using IBM SPSS 20.0. In this study; numbers, percentages, arithmetic mean  $\pm$  standard deviation (minimum-maximum) were used as descriptive statistics. Chi-square analysis was used to obtain categorical data in order to point out the distribution of age and gender of patients with musculoskeletal system tumors and tumor-like lesions. A p-value  $<0.05$  was set for the statistically significance.

## **RESULTS**

The mean number of patients with a pre-diagnosis of musculoskeletal system tumor over the period from January 2013 to June 2017 was 687. 347 (50.5%) of the patients were male and 340 (49.5%) patients were female. Table 1 shows the numbers of patients who are pre-diagnosed with musculoskeletal system tumors and tumor-like lesions and also the number of patients whose pathology reports demonstrate the final diagnosis available in the system according to years. The number of patients who have pathology reports was 341. The mean of patients' ages was  $44.3 \pm 21.4$  (4-92). Among 341 patients, 106 (47.1%) patients were female and 119 (52.9%) patients were male. The mean age of female patients was  $43.7 \pm 20.4$  (4-92). The mean age of male patients was  $44.7 \pm 22.4$  (5-90). Table 2 summarizes the demographic data of genders. There is no statistically significant difference found between genders ( $p > 0.05$ ). Consistent with the data of patients with reports, the number of soft tissue tumors was 72. 146 patients were found as diagnosed with bone tumors and 6 patients had tumor-like lesions. Among all the data of tumor and tumor-like lesions, the type of the lesion was not written on one patient's pathology report. There were 142 benign tumors, 70 malignant tumors and 13 missing data for tumor type in pathology reports. Table 3 shows the distribution of tumors and tumor-like lesions according to years. Table 4 summarizes the variants of tumors and means of ages (Table 4 and 5). There is no statistically significant difference between the mean of ages in different types of tumors ( $p > 0.05$ ).



**Table 1: Numbers of pre-diagnosed and diagnosed patients.**

	2013	2014	2015	2016	2017	Total
Number of pre-diagnosed patients (n)	48	168	214	169	88	687
Number of pathology reports (n)	25	50	122	89	55	341

**Table 2: Distribution of tumors and ages.**

	Soft tissue tumors	Bone tumors	Tumor-like lesions
Male (n)	39	76	3
Female (n)	33	70	3
The mean of males' ages (years)	47.8	43.8	18.3
The mean of females' ages (years)	50.5	41	35.7

**Table 3: Distribution of tumors and tumor-like lesions according to years.**

Year	Bone tumors (n)			Soft tissue tumors (n)		Unidentified tumors*
	Malignant tumors	Benign tumors	Tumor-like lesions	Malignant tumors	Benign tumors	
2013	5	5	1	2	3	-
2014	13	17	1	14	11	-
2015	18	34	2	8	17	2
2016	5	13	2	4	10	4
2017	13	22	1	2	9	-

\*In 6 of the pathology reports, the diagnoses were given as 'soft tissue tumors' without any identification as malignant or benign.

**Table 4: Numbers of patients and means of ages according to soft tissue and bone tumors.**

	Soft tissue tumors		Bone tumors	
	n	mean of ages	n	mean of ages
Benign (n/mean of ages)	50	47.4	92	35.8
Malign (n/mean of ages)	16	53.9	54	54.1
Tumor-like lesions (n/mean of ages)	-	-	7	29.4

**Table 5: Numbers of patients and mean of ages according to benign and malign tumors.**

	Benign tumors		Malignant tumors		Tumor-like lesions	
	n	mean of ages	n	mean of ages	n	mean of ages
Male (n/mean of ages)	74	37.6	40	60.1	4	24.8
Female (n/mean of ages)	68	42.3	30	46.2	3	35.7

## DISCUSSION

Pathologic lesions in musculoskeletal tissue were grouped as tumor-like lesions, benign tumors and malignant tumors in this study. The data of 341 patients were analyzed and categorized as afore-mentioned. According to the results, bone tumors are more common than soft tissue tumors and benign tumors are more in number than malignant tumors in general.

The rate of tumors and tumor-like lesions was similar in both genders. In addition, the rate of bone tumors also did not show a significant difference in both genders. However, the studies of Kazi et al. (6) and Dabak et al. (7) showed that bone tumors are more common in males. The reason behind the difference between this study and the literature may be due to the number of patients. In the study of Kazi et al. (6), there are more male patients than this study. However, the results of this study are compatible with the literature according to the frequency of benign and malignant tumors. It is stated that benign bone tumors are more common than malignant tumors that is also valid for this study (6, 7).

According to the literature, benign bone tumors are more common in younger individuals (8). In this study, the mean age of patients with benign bone tumors was found 35.8 years that is younger by comparison with the mean ages found as of other tumors.

Dabak et al. (7) reported in their study that the frequency of bone tumors is more than soft tissue tumors which is also compatible with our study. Their study, which has the same methodology with our study has been conducted in the middle Black Sea region. Their study results show that benign and malignant tumors are more frequently seen in ages between 31-41 and 51-60 respectively (7). In our study, we found the mean age of patients with benign tumors is 39.9 years and the mean age of patients with malignant tumors is 53.1 years and they indicate that Trakya region also has similar results.

Dabak et al. (7) also reported the mean ages of bone and soft tissue tumors in their study. However, in our study, the mean ages of both types of tumors were found older than Dabak's results (7). The reason for this age gap might be relevant to the number of the patients evaluated.

Out of 687 patients who were evaluated by the council, there are only 341 patients whose diagnosis was confirmed by a pathological examination. Other patients

who did not have any pathological report were evaluated through radiological screenings and clinical examinations. In that respect, numbers of the pathology reports are less than the total patient population. Therefore, the results of the study may not be sufficient to reflect the expected population.

As a conclusion, the data from our study showed that benign bone tumors and benign soft tissue tumors are more common than malignant forms. Moreover, in both genders, bone tumors are more seen than soft tissue tumors. Our results have both differences and similarities with the literature. In that respect, bone and soft tissue tumors not only have some certain characteristics but also have regional differences in frequency. With more data of these types of studies from different centers may provide effective data for the epidemiological research of bone and soft tissue tumors.

**Ethics Committee Approval:** This study was approved by Scientific Researches Committee of Trakya University School of Medicine.

**Informed Consent:** Written informed consent was obtained from the participants of this study.

**Conflict of Interest:** The authors declared no conflict of interest.

**Author contributions:** Concept: EŞ, BS, NGİ, HSC, AG, MÇ. Design: EŞ, BS, NGİ, HSC, AG, MÇ. Supervision: EŞ, BS, NGİ, HSC, AG, MÇ. Resources: EŞ, BS, NGİ, HSC, AG, MÇ. Materials: EŞ, BS, NGİ, HSC, AG, MÇ. Data collection and/or processing: EŞ, BS, NGİ, HSC, AG, MÇ. Analysis and/or Interpretation: EŞ, BS, NGİ, HSC, AG, MÇ. Literature Search: EŞ, BS, NGİ, HSC, AG, MÇ. Writing Manuscript: EŞ, BS, NGİ, HSC, AG, MÇ. Critical Review: EŞ, BS, NGİ, HSC, AG, MÇ.

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## RESEARCH OF URGENT BIOCHEMISTRY TEST ORDERING HABIT

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### ABSTRACT

**Aims:** This study aims to reveal the inappropriate use of biochemical laboratory testing at Trakya University Hospital Biochemistry Laboratory, increase the awareness of the physicians and prevent time loss.

**Methods:** This study was descriptive, retrospective and carried out by scanning data resources. Two 48-hour intervals were chosen to evaluate the test ordering habits of the physicians working at Trakya University Hospital. Between the dates of 3rd - 5th of November 2017, Trakya University Hospital Biochemistry Laboratory was working fully functionally. However, between the dates of 10th - 12th of November 2017, the automation system of the hospital was scheduled to be shutdown due to a technical error. All the physicians working at Trakya University Hospital were informed about the technical error of the automation system and were told that they would need to order only stat tests by using old-fashioned test request forms. The data of ordered tests in these two-time intervals were analyzed and compared by using frequencies and percentages as descriptive statistics.

**Results:** The mean number of tests per patient was 23 between 3rd - 5th of November 2017 and 15.5 between 10th - 12th of November 2017. The number of patients who had at least one test order decreased only 13.1% between 10th - 12th of November 2017. The total number of departments who made at least one test order increased by one between 10th - 12th of November 2017.

**Conclusion:** This study indicates that physicians should be more careful while ordering tests which are necessary. Therefore, there is a need for better communication between the laboratory staff and physicians that also plays a significant role in providing better health care for the patients.

**Keywords:** Biochemistry, laboratories, emergencies

### INTRODUCTION

There is not a certain definition of urgent test in medical sciences. Generally, the word "stat" is being used to specify the urgent test. Stat, which comes from the Latin word statim, means immediately (1).

Laboratories have at least 2 priority levels for tests such as routine and stat. In addition, there is another priority level called as soon as possible (ASAP) that is the second most urgent category, placed between routine and stat. Volmar et al. (2) revealed that 44.2% of laboratories defined 3 priority levels that include routine, ASAP and stat in their study. Using more than 3 priority levels is not recommended due to its confusing effects on the laboratory staff (3).

In the past, the stat testing was only for the patient's convenience. However, nowadays the stat testing is being used for both the physician's and the institution's convenience besides the patient's convenience (4). This new usage of stat testing puts a heavy load on the shoulders of the laboratory staff. When laboratories cannot meet stat expectations both the physician and the laboratory workers become dissatisfied and this situation directly effects the patient's treatment (3).

Decreasing the turnaround time for stat testing is crucial for critical patients. Therefore, it is mandatory to give priority to urgent tests among thousands of tests that are ordered. To provide this priority, evidence-based use of laboratory testing by physicians carries an important role. Otherwise, piling up of stat tests extends expected

stat turnaround times and causes delays in necessary interventions.

The aim of this study is to investigate the usage of biochemistry laboratory testing according to necessity, raise the awareness of physicians and prevent time-consuming mistakes.

## MATERIAL AND METHODS

This descriptive, retrospective study was approved by Trakya University Faculty of Medicine Scientific Research Ethics Committee and carried out by scanning data resources of Trakya University Hospital Biochemistry Laboratory. In this study, biochemistry test ordering habits of the physicians in Trakya University Hospital were analyzed by comparing the amount and types of tests requested from Trakya University Hospital Biochemistry Laboratory in two consecutive weekends.

Biochemistry Laboratory of Trakya University Hospital accepts test samples from all services and policlinics of the hospital and consider the ones that are sent from emergency policlinic or defined as urgent by the physician as stat. Between the 3rd of November 2017, 18:30, and 5th of November 2017, 18:30, the laboratory was working fully functionally and this time interval was called weekend zero (W0) in the study. However, between the 10th of November 2017, 18:30 and 12th of November 2017, 18:30, the automation system of the hospital, that allows physicians to order tests online and review the results, was scheduled to be shutdown due to a technical error and this time interval was called as weekend one (W1) in the study.

All the physicians working at Trakya University Hospital were informed about the technical error of the automation system and they were requested to order only stat tests by using old-fashioned test request forms. The reason why they were requested to order only stat tests was to avoid any mistakes due to huge amount of test request forms circling around the laboratory. To determine the tests that were stat among the tests ordered in W1, the study by Sufov et al. (5) that was based on guidelines of American College of Emergency Physicians was used. All of the tests that are listed in Table 1 were considered as stat.

**Table 1: Biochemistry tests that were considered as stat.**

Stat Tests	
Activated partial thromboplastin time	D-Dimer
Ammoniac	Glucose
Amylase	N-terminal pro b type natriuretic peptide
Arterial blood gas	Prothrombin time
Beta human chorionic gonadotropin hormone	Serum chlorine level
Blood urea nitrogen	Serum potassium level
Carbon dioxide	Serum sodium level
Complete blood count	Troponin I
Complete urine examination	Valproic acid
Creatinine	

After W0 and W1, data of all the ordered biochemistry tests in W0 and W1 were obtained from the data processing unit of the laboratory. All the patients who were taking inpatient treatment in the hospital or brought to the emergency service of the hospital were included in the study if their physician ordered at least one biochemistry test for them. The data were classified by the demographical data of patients, the time when the test was ordered, the department where the test was ordered from and the name of the test. The results of W0 and W1 were compared by using arithmetic mean, frequencies and percentages as descriptive statistics.

## RESULTS

The total number of ordered tests in W0 and W1 were shown in Table 2. The mean number of tests per patient was 23 in W0, 15.5 in W1; the decrease was 32.6%. There were 5832 stat and 4477 non stat test orders in W0, 3510 stat and 2549 non stat test orders in W1. The percentage of ordered tests that were accepted as stat (shown in Table 1) to total was 56.6 in W0 and 58 in W1. The number of patients decreased only 13.1%, from 449 to 390. The total number of departments increased by one in W1, from 35 to 36. The percentage of ordered tests that were sent from the emergency department was 21.1 in W0 and 19.2 in W1.

**Table 2: Total number of ordered tests in W0 and W1.**

	W0	W1
Total Number of Ordered Tests (n)	10309	6059
Number of Patients (n)	449	390
Number of Different Types of Tests (n)	102	88
Number of Departments (n)	35	36

\*W0: 3rd of November 2017 18.30 - 5th of November 2017 18:30,

\*W1: 10th of November 2017 18.30 - 12th of November 2017 18:30



The most ordered non-stat tests in W0 and W1 were shown in Table 3. There was a decrease in the orders of all nine tests, the test order that decreased the most was total bilirubin by 57.3%, and the least decreased was serum aspartate aminotransferase (AST) by 30%. There were 4 non-stat test orders that increased in W1 (Table 4). The most ordered stat tests were shown in Table 5.

**Table 3: The most ordered non stat tests in W0 and W1.**

Type of Test	Number of Ordered Tests (n)	
	W0	W1
AST (SGOT)	502	351
ALT (SGPT)	501	348
CRP	491	329
Albumin	410	259
Total Protein	364	227
Total Bilirubin	295	126
Direct Bilirubin	292	128

AST: Aspartate aminotransferase, SGOT: Serum glutamic oxaloacetic transaminase, ALT: Alanine aminotransferase, SGPT: Serum glutamic pyruvic transaminase, CRP: C-Reactive protein, LDH: Lactate dehydrogenase, CK: Creatine kinase, ALP: Alkaline phosphatase, W0: 3rd of November 2017 18:30 - 5th of November 2017 18:30, W1: 10th of November 2017 18:30 - 12th of November 2017 18:30

**Table 4: Increased non stat tests in W1.**

Type of Test	Number of Ordered Tests (n)	
	W0	W1
HDL	9	13
LDL	9	13
Triglyceride	9	12
Cholesterol	8	12

HDL: High-density lipoprotein, LDL: Low-density lipoprotein, W0: 3rd of November 2017 18:30 - 5th of November 2017 18:30, W1: 10th of November 2017 18:30 - 12th of November 2017 18:30

**Table 5: The most ordered stat tests in W0 and W1.**

Type of Test	Number of Ordered Tests (n)		Type of Test	Number of Ordered Tests (n)	
	W0	W1		W0	W1
Complete Blood Count	702	446	Complete Blood Count	702	446
Serum Potassium Level	682	421	Blood Urea Nitrogen	682	421
Serum Sodium Level	682	419	Creatinine	682	419
Serum Chlorine Level	655	313	Glucose	655	313
Creatinine	633	303	Serum Sodium Level	633	303

## DISCUSSION

In this study, it was apparent that every ordered test in W1 had the possibility to be a stat test. It substantially depended on the patient's current condition. However, reaching every physician and patient to check the necessity of the ordered tests, was time-consuming and nearly impossible because of the missing data due to the technical error in the automation system of the hospital. That is why it was decided to form a list that contains the most probable stat tests to make a general comparison between W0 and W1.

It was hoped that physicians would only order stat tests in W1 otherwise it could be very challenging for both patients and staff of the hospital. Test results had to be delayed because of the excessive amount of test orders which were logged into machines manually in W1 and this extra workload affected the patients in critical condition negatively.

The proportion of the stat tests to total is 56.6% in W0 and 58% in W1. Since doctors were notified about the situation of the laboratory and asked to order only the stat tests, it was expected to see the ratio of stat tests much higher in W1. However, the results were not compatible with our hypothesis. The decrease in the ordered non-stat tests in W1 was ranging between 30% and 57.3% (Table 3). In fact, there were two possible tests that could be considered as stat in Table 3: creatine kinase (CK) and C-reactive protein (CRP). However, some conditions stated in Guideline on Pathology Testing in the Emergency Department had to be met to consider these tests as stat (6). There were 4 different conditions that CRP testing had to be considered as stat: atraumatic back pain, fever for investigation, fever for investigation with significant travel history and suspected septic joint. Besides that, there were two conditions where CK testing had to be considered/performed as stat; snake bite and significant overdose (6). Except for CK and CRP, other tests in Table 3 could have been ordered when the laboratory turned to its usual working. This way, the extra workload of the laboratory could have been eased and actual stat tests could have been resulted on time. There was an increase in non-stat tests that were shown in Table 4 in W1 despite the situation.

Volmar et al. (2) found that 16.3% of 52 participating biochemistry laboratories could not meet

the expected turnaround times of stat tests in their study in 2009. Andrew Sucof et al. (5) recorded a 25% decrease in test orders in the Emergency Department of Rochester University Hospital after reporting a newly prepared guideline, without any restriction, for ordering tests to physicians in between the years 1995 and 1997. Yilmaz et al. (7) observed a decrease, ranging between 12.6% and 85% in ordered tests in Ankara Numune Training and Research Hospital after only reorganizing the test ordering screen and this also saved 371,183 USD in one year. Ordered tests per patient were 15.8 at the beginning of their study (7). In our study, ordered tests per patient was 15.5 despite the fact that the laboratory asked to physicians to send only stat tests in W1.

The major limiting factor of this study was missing data of W1 due to ordering tests with old-fashioned test request form. This problem prevented us from making detailed analysis such as including departments to the comparison. In addition, to evaluate the use of biochemistry laboratory tests a more detailed study that includes tracking all patients' treatments and physicians' reasons for ordering tests needs to be carried out.

In conclusion, this study shows that physicians should be more careful while ordering tests which are necessary. Therefore, there is a need for better communication between the laboratory staff and physicians which also plays a significant role in providing better health care for the patients.

**Ethics Committee Approval:** This study was approved by Scientific Researches Committee of Trakya University School of Medicine.

**Informed Consent:** Written informed consent was obtained from the participants of this study.

**Conflict of Interest:** The authors declared no conflict of interest.

**Author contributions:** Concept: KE, Bİ, SE, EÖ. Design: KE, Bİ, SE, EÖ. Supervision: KE, Bİ, SE, EÖ. Resources: KE, Bİ, SE, EÖ. Materials: KE, Bİ, SE, EÖ. Data collection and/or processing: KE, Bİ, SE, EÖ. Analysis and/or Interpretation: KE, Bİ, SE, EÖ. Literature Search: KE, Bİ, SE, EÖ. Writing Manuscript: KE, Bİ, SE, EÖ. Critical Review: KE, Bİ, SE, EÖ.

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## THE INFLUENCE OF METABOLIC THERAPY ON CLINICAL AND HEMODYNAMIC PARAMETERS IN PATIENTS WITH STABLE ANGINA

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### ABSTRACT

**Aims:** The objective of our study is to investigate the antianginal activity of meldonium and its influence on the hemodynamics and clinical parameters in patients with stable angina who fall under III-IV functional classes according to the classification of the Canadian Heart Association.

**Methods:** The study was carried out including 105 patients with stable angina pectoris who were in III-IV functional classes at the age of 42-72 years. The first group (n=52) was administered the standard treatment (beta-blockers, aspirin, atorvastatin). The second group of patients (n=53) were given a combination of basic therapy along with meldonium 10% solution of 5 ml intravenously for 10 days then 1000 mg per day orally for 10-12 weeks. Suitable healthy people were selected as the control group (n=36).

**Results:** Patients with stable angina pectoris were characterized with the reduction of workload, double work, time loading on bicycle ergometer, increased specific and total peripheral vascular resistance, increased central sympathetic activity on heart, decreased vagal and humoral activity on heart rate. The analysis of the data indicated a decrease in the frequency of anginal attacks after treatment in the first group by 45% and reduced daily nitroglycerin requirement by 48%. Combination therapy resulted in a decrease of the parameters by 71.8% and 76%, respectively.

**Conclusion:** After the treatment in both groups, we detected an improvement in physical exertion tolerance, reduction in total peripheral vascular resistance and sympathetic activity of the heart. Combination therapy with meldonium significantly reduced the central sympathetic activity and peripheral vascular resistance, also increased the workload, run time compared to the basic therapy.

**Keywords:** Hemodynamics, stable angina, carnitine

### INTRODUCTION

Cardiovascular diseases are the number one cause of death globally. In 2016, an estimated 17.9 million people died from cardiovascular diseases, representing 35% of all global deaths (1). Most of the cardiovascular diseases can be prevented by changing behavioral risk factors such as tobacco use, unhealthy diet and obesity, physical inactivity and alcohol abuse. Nowadays metabolic therapy is an important direction of treatment for ischemic heart diseases (2).

Angina pectoris is one of the life-threatening cardiovascular conditions affecting the global population. Four national cross-sectional health examination stu-

dies found recently that among the United States, in 40-74 years of age population, the prevalence rate of stable angina pectoris is higher among the females than in males (2).

With the data obtained from several clinical studies and drug trials, meldonium was identified as an anti-ischemic drug with several indications in neurological degeneration, pulmonary system dysfunction and cardiomyocyte protection (3). It provides the biochemical protection of cells from the effects of ischemia by effecting the carnitine metabolism. Despite imbalance in the need of the myocardial oxygen supply and its delivery, cardiomyocytes remain viable and function actively (3).

The mechanism of meldonium is well understood; being a partial inhibitor of fatty acids oxidation and an analog structurally to the precursor of the gamma-butyrobetaine (GBB) (4). It inhibits carnitine metabolism and biosynthesis by competing with GBB hydroxylase enzyme, that catalyzes the last step in carnitine biosynthesis pathway, also inhibiting kidneys' reabsorption (5). Meldonium's other effect is the inhibition the long chain fatty acids transportation through the mitochondrial membranes. This progresses in the complete transport of cytosolic ATP and further delaying the beta-oxidation of fatty acids. This prevents the mitochondrial accumulation of the unoxidized fatty acids and acetyl carnitine and acetyl coenzyme-A. The increased cytosolic fatty oxidation is a specific signal for the activation of glucose oxidation (5).

Reduction in carnitine leads to situmilation of its precursor GBB synthesis, simultaneously activating the nitric oxide (NO) synthase, possibly is responsible for meldonium's antianginal and vasospastic effect (5).

A study conducted by Dzerve et al. (6) demonstrated the efficiency of meldonium in combination with the standard therapy at doses of 500mg, twice daily for the duration of 10-12 weeks. There was an improvement in the exercise tolerance in patients with stable angina and the positive dynamics were dose-dependent (6).

The data from different publishers around the globe, gave evidence that meldonium's efficiency in myocardial ischemia by improving the systolic function of the myocardial cells, the inhibition of the occurrence of myocardial hypertrophy and dilatation, increased contractility of the smooth muscles of arterioles, increased tolerance to stress, reduction of angina symptoms (7).

The aim of this study is to investigate the antianginal activity of meldonium and its influence on the hemodynamics and clinical parameters in patients with stable angina that were III-IV functional classes.

## **MATERIAL AND METHODS**

The study was carried out with 105 patients (66 males and 39 females) whose conditions are defined as stable angina III-IV functional classes (FC) according to the classification of the Canadian Heart Association (CHA) and was approved by the local ethics committee of Zaporozhye State Medical University (8). The

mean age was  $60.0 \pm 0.88$  years. The diagnosis of stable angina along with differential diagnosis was made with the following parameters: anamnesis data, risk factors, data of objective examination and the results of examinations using laboratory and instrumental methods. 27 patients had medical history of myocardial infarction. All the patients were assigned to the basic therapy, including  $\beta$ -blockers, calcium antagonists, antiplatelet agents and statins. Patients were distributed into two groups. The first group consisted of 52 people, who received conventional therapy, whereas 53 patients in the second group received the basic treatment along with a combination of meldonium 5 ml of 10% solution intravenously for 10 days then converted to oral 1000 mg per day for 10-12 weeks. The course of treatment was 10-12 weeks. Suitable healthy people were selected as the control group (n=36).

The patients, who had stable angina pectoris FC III-IV classified by CHA with a disease duration more than 1 year, were included in the study (8). All patients gave their consent to participate in the study. On the other hand, the patients represented with hypertension, heart failure, sino-auricular and atrioventricular blocks, diabetes, liver and kidney disorders were excluded from the study.

Antianginal effect was estimated with the help of a self-observation diary, with the number of angina attacks and the number of nitroglycerin tablets taken per day.

Assessment of peripheral hemodynamics was performed using computer diagnostic complex "REO-KOM" developed in laboratory and computer diagnostic systems of Kharkov National Aerospace University. Among all parameters, Systolic blood pressure-SBP (mm Hg), Total peripheral vascular resistance-TPVR ( $\text{din} \times \text{sm}^{-5} \times \text{sec}$ ), Diastolic blood pressure-DBP (mm Hg), Specific peripheral vascular resistance-SPVR (relative units) and Heart rate-HR (bpm) were selected.

The measurement of cardiac rhythm was carried out using computer cardiographic systems "Cardiolabs 2000" HAI MÉDICA (Ukraine) (9). CARDIOLAB is a computer-aided echocardiographic complex intended for conducting a wide range of cardiographic studies. The most informative parameters were: the average value of RR interval - RR average (sec), variational span of RR intervals - VS (sec), mode (relative units) - Mo, amplitude of Mode - AMo (%), index of vegetative balance - IVB (relative units), vegetative indicator rhythm



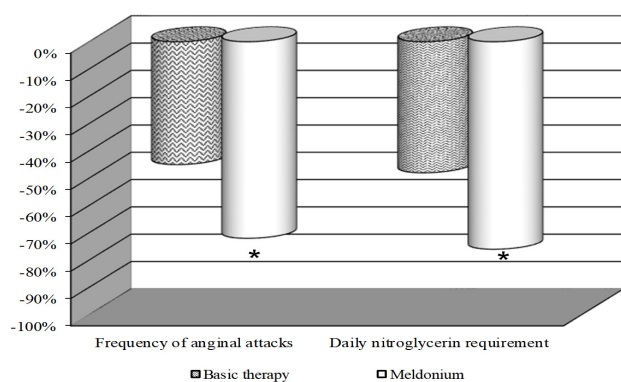
- VIR (relative units), Baevskiy tension index - TI (relative units).

Bicycle ergometer test (BET) was performed using SECA CARDIOTEST 100 (HÖRMANN, German) (10). Among all parameters, workload - WL (W), max - heart rate at the threshold of tolerance - HR (bpm), blood pressure at the threshold of tolerance - BPmax (mm Hg), loading time T (min), double work - DW were selected. DW was calculated as an indicator that indirectly reflects the oxygen consumption of the myocardium by the formula:  $DW = HR_{max} \times BP_{max} / 100$ .

When comparing the study groups student t test was performed. Numbers, percentages, arithmetic mean  $\pm$  standard deviation were used as descriptive statistics. A p-value  $<0.05$  was set for statistically significance.

## RESULTS

Analysis of the data indicates a decrease in frequency of anginal attacks after the treatment in the first group by 45% and reduced daily nitroglycerin requirement by 48%. Combination therapy resulted in more significantly decrease of the parameters by 71.8% and 76%, respectively ( $p=0.0007794$ ,  $p=0.008145$ ) (Figure 1).



\* - confidence interval compared to basic therapy  $P < 0.001$

**Figure 1: Dynamics of antianginal effect in patients after treatment.**

In the second group, TPVR and SPVR decreased by 35% and 23% respectively than in the first group (Table 1).

**Table 1: Dynamics of peripheral hemodynamics parameters in patients after treatment.**

Parameters	Basic therapy	Meldonium	Healthy group
	1	2	
TPVR	2159 $\pm$ 93.8	1859 $\pm$ 36.2 $P_{1,2}=0.0009668$	1846 $\pm$ 114
SPVR	51.7 $\pm$ 2.57	44.6 $\pm$ 1.16 $P_{1,2}=0.000123$	44.5 $\pm$ 2.74

\*TPVR= Total peripheral vascular resistance, SPVR= Specific peripheral vascular resistance

Changes in heart rate are characterized by the following changes: VS variation rate increased by 11%, AMo mode amplitude decreased by 7% in both groups, TI stress index decreased by 34% in the first group and 45% in the second group. This indicated a decrease in the central sympathetic activity, which led to a decrease in vascular tone, a decrease in peripheral resistance, and, as a consequence, an increase in exercise tolerance (Table 2).

**Table 2: Dynamics of cardiac rhythm in patients after treatment.**

Parameters	Basic therapy	Meldonium	Healthy group
	1	2	
RR average (sec)	0.815 $\pm$ 0.032	0.814 $\pm$ 0.028	0.804 $\pm$ 0.013
VS (sec)	0.048 $\pm$ 0.004	0.047 $\pm$ 0.006	0.169 $\pm$ 0.014
Mo (relative units)	0.831 $\pm$ 0.028	0.834 $\pm$ 0.029	0.816 $\pm$ 0.027
AMo (%)	53.5 $\pm$ 2.02	51.3 $\pm$ 1.82 $P_{1,2}=0.02780$	49.5 $\pm$ 1.68
IVB (relative units)	289.8 $\pm$ 14.5	291.4 $\pm$ 14.1 $P_{1,2}=0.00932$	285.3 $\pm$ 20.1
VIR (relative units)	7.53 $\pm$ 0.500	7.74 $\pm$ 1.13 $P_{1,2}=0.8336$	6.74 $\pm$ 0.443
TI (relative units)	215.5 $\pm$ 17.4	201.7 $\pm$ 12.1 $P_{1,2}=0.000244$	177.2 $\pm$ 14.6

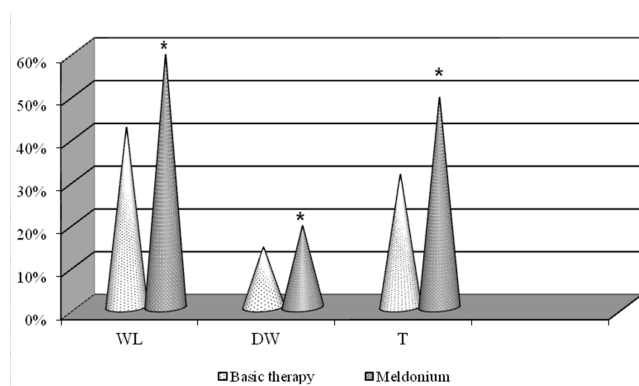
\*RR average - the average value of RR interval (sec), VS - variational span of RR intervals (sec), Mo - mode (relative units), AMo - amplitude of Mode (%), IVB - index of vegetative balance (relative units), VIR - vegetative indicator rhythm (relative units), TI - Baevskiy tension index (relative units)

Measurement on BET after treatment; the absolute magnitude of the power transferred to the threshold load was increased in patients of both groups. However, the addition of meldonium to conventional therapy contributed to a more substantial and a significant increase of WL compared with the isolated use of basic therapy ( $p=0.00061$ ). On the background of standard therapy, WL was increased by 42%, SBP and HR at the threshold of tolerance by 6%, while the growth of double work was 14%, and the loading time was increased by 31% (Table 3).

**Table 3: Comparison of bicycle ergometer results between healthy subjects and stable angina patients.**

Parameters	Healthy subjects	SA patients
	1	2
WL (W)	106.9±1.08	45.8±1.16 $P_{1,2}=0.00061$
HR max (BPM)	137.6±1.28	110.2±1.06 $P_{1,2}=0.00301$
BP max (mmhg)	183.8±1.87	163.8±1.69 $P_{1,2}=0.02275$
Double work (DW)	262.1±2.09	169.8±2.27 $P_{1,2}=0.00005$
T (min)	8.34±0.105	5.56±0.122 $P_{1,2}=0.00543$

The addition of meldonium increased WL by 59%. The parameters HRmax and BPmax, as well as dual works were increased by 9.8%, 8% and 8.6%, respectively and demonstrated a significant increase of T on bicycle ergometer at 49%, which was close to that of the control group ( $p=0.00543$ ). As the results in Figure 2 shows, the increase of T on bicycle ergometer was close to the control group. This leads to the functional enhancement of patients with coronary heart disease improving their tolerance to the physical stress and quality of life.



\* - confidence interval compared to basic therapy  $P < 0.001$

\*WL: Workload

\*DW: Double work

**Figure 2: The change of bicycle ergometer test values in patients after treatment.**

## DISCUSSION

The modern literature highlights the favorable effects of meldonium on the cardiovascular system (11). Many authors pointed out the advantages of this drug indicating its antianginal, anti-arrhythmic effects, also its role in acid-base regulation in blood and NO metabolism (12). Sakharchuk et al. (13) pointed out that meldonium was an effective drug for the treatment of cardiac insufficiency due to ischemic heart disease. Their study on meldonium showed a positive effect on the blood hemodynamics, normalization of NO content and increased quantity of the membrane-bound erythrocytic enzymes.

Dudko et al. (14) indicated in their study that meldonium's effects against a placebo background in 50 patients revealed its antianginal effects and increased physical workload capacity in patients.

Ol'binskaia et al. (15) reported antianginal and anti-arrhythmic action of meldonium, by evaluating its ability to prevent ventricular extrasystoles, enhancement of physical capacity in the administered patient group.

Karpov et al. (16) revealed that the drug had a positive effect in improving the coronary circulation in patients with atherosclerosis.

Teplyakov et al. (17) demonstrated the anti-ischemic effects of meldonium in postinfarction left ventricular dysfunction patients in whom chronic hypoxia developed due to chronic pulmonary congestion, having an improved dynamic in their acid-base balance of their blood.

Enina et al. (18) reported that there was a transient decrease in the arterial blood pressure after 30 minutes of the drug administration in patients. The clinical parameters of blood changed after 60-90 minutes after bolus injection normalizing the cerebrovascular activity.

The obtained data from our study show that meldonium is capable of reserving additional ways of energy metabolism, contributes to an optimization of energy usage to facilitate the hemodynamic condition of heart. More studies on higher risk populations should be carried out to investigate the safety and efficacy of this drug proving its positive dynamics in patients with cardiovascular diseases.

In conclusion the inhibitor of carnitine-dependent fatty acid oxidation, meldonium, strengthens the antianginal effect of basic therapy. It leads to the expansion of the functional capabilities of patients with IHD and increases their tolerance to the physical exertion. Meldonium contributes to a more pronounced decrease in central sympathetic activity system and the total peripheral resistance of the vessels. The course of treatment with meldonium improves antianginal effect of basic therapy and significantly reduces the total peripheral resistance in the vessels ( $p=0.0009668$ ). Combination treatment of meldonium contributes to a more pronounced exercise test tolerance when compared with basic therapy.

**Ethics Committee Approval:** This study was approved by the local ethics committee of Zaporozhye State Medical University.

**Informed Consent:** Written informed consent was obtained from the participants of this study.

**Conflict of Interest:** The authors declared no conflict of interest.

**Author contributions:** Concept: GNV. Design: GNV. Supervision: GNV, VT. Resources: GNV. Materials: GNV. Data collection and/or processing: GNV, VT, VV. Analysis and/or Interpretation: GNV, VT, VV. Literature Search: GNV, VT, VV. Writing Manuscript: VT, VV. Critical Review: GNV, VT, VV.

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## THE EFFECT OF PREVENTION FOR PEER BULLYING IN SECONDARY SCHOOL

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### ABSTRACT

**Aims:** Peer bullying is a frequent problem among adolescents. The aim of this study is to evaluate the effectiveness of complementary prevention for peer bullying in 11-14-year-old adolescents with family, teacher, student collaboration and to assess the effect of peer bullying on the quality of life.

**Methods:** Seven hundred sixty students registered in school between ages 11-14, and who accepted to participate in the study were included in our investigation. Olweus Bully/Victim Questionnaire and Pediatric Quality of Life Inventory were used as data collection tools in the study. After the pre-test, school teachers and two selected students from each class; a total of 48 students were trained in peer bullying in small group. Interactive awareness activities were organized for the students at the school with all trained students and teachers to raise awareness of peer bullying. Afterwards, information brochures were distributed to the children and parents. 3 weeks after the training post-test was applied. The statistical evaluation of the study was carried out by using Chi-square and Student's t-tests.

**Results:** The questions about bullying and victimization were analyzed. In the study, the rate of victim students reduced from 43.2% to 30.4%; the rate of bully students reduced from 23.4% to 21.7%. There was a significant reduction in the rate of people involved in peer bullying. Nevertheless, Pediatric Quality of Life Inventory assessment of health-related quality of life in our group showed that the quality of life of students who were not involved in peer bullying was significantly higher. After our training, quality of life significantly increased in students who were not involved in bullying, compared to the ones who are involved in bullying.

**Conclusion:** In our study group, it was observed that the quality of life of students who were not involved in peer bullying was significantly higher. The number of people involved in peer bullying decreased significantly. The low number of invalid surveys revealed that our research was successful in attracting the attention of the target group.

**Keywords:** Awareness, bullying, adolescent

### INTRODUCTION

The 'bullying' behavior can be described as "intentional, repeated long term negative (unpleasant or hurtful) behavior or attitude by one person or a group of people directed against a person having difficulty defending himself or herself" (1). This definition has gained acceptance among researchers and practitioners. Therefore, the phenomenon of bullying can be

explained as three separate attitudes: aggressive behavior, carried out repeatedly and over time; intentional "harm doing", carried out repeatedly and over time; an interpersonal relationship that is characterized as an actual, perceived imbalance of power, strength. Therefore, it can be stated; much of the bullying can/ may occur without any apparent provocation from the person being targeted (2).



In the literature, we see different results for peer bullying. Inequalities in Young People's Health, Health behavior in the school-aged children international report from the 2005/2006 survey indicates that there are large cross-national variations in the proportion, ranging between 4% (Sweden) to 33% (Turkey), of youngsters reporting as having been a victim of bullying in their school minimum two or three times in the past months. Currie C et al. (3) states that boys more often report being a victim of bullying, the experience is reported less often with increasing age.

There are large differences in the extent of reports of bullying others at school at least two times in the past couple of months. While in some countries this behavior is almost nonexistent, it is reported by up to a third in others: 11-year-olds from 2% (Sweden) to 24% (Greenland), boys 3% (Sweden, Czech Republic, Hungary) to 27% (Greenland, Romania, Estonia), girls 1% (Norway, Sweden) to 22% (Greenland). Usually bullying others is more common among boys and decreases with age in most countries (3). Peer bullying is an important determinant of adolescent health-related quality of life (HR-QOL) with a negative impact on psychosocial well-being (4).

As a result, peer bullying causes a negative effect that reduces the quality of human life. Nevertheless, peer violence and quality of life have not been studied together with a holistic education method. The aim of this study is to evaluate the effectiveness of complementary prevention for peer bullying in 11-14-year-old adolescents with family, teacher, student collaboration and to assess the effect of peer bullying on the quality of life.

## **MATERIAL AND METHODS**

This work is being supported by the European Union Delegation to Turkey Civil Imagine program "International, strengthening the existing child rights network at the national and local level to ensure more be heard children's voices" was funded by the International Children's Center Project. This project financed by Manisa Provincial Directorate of National Education and Governorship has been realized with permission. This study was approved by the ethical committee of Manisa Celal Bayar University of Medical Sciences. The research was conducted on a voluntary basis. Forms were handed out in the classroom. The students filled the forms voluntarily in class, in silence with the teach-

er in presence without interrupting.

The study was designed in accordance with the pre-test-post-test method. We applied pre-test before our intervention. Among the first and second surveys, school teachers and two students from each class; a total of 48 students were trained in the definition, types of peer bullying and the best possible reactions that have to be given when experiencing peer bullying. The reason of this training was to create role model peer students for awareness activities of peer bullying from each class. We organized interactive awareness activities, such as icebreaking activities and awareness videos for peer bullying with cake and lemonade, lasting at least 45 minutes were organized for the students at the school with all trained students and teachers to raise awareness of peer bullying. Three weeks after the training and awareness activities, post-test was applied. Information brochures including information about the best possible reactions when experiencing peer bullying were given to the children and parents at the date of the post-test.

Olweus Bully/Victim Questionnaire and the Pediatric Quality of Life Inventory were used as data collection tools in the study. The universe of this research is the students in a secondary school in Manisa (n=760). The sample of the research was 5, 6, 7, 8th-grade Secondary School students aged 11 to 14 who accepted to participate in the study pre-test (n=603), post-test (n=549).

Olweus Bully/Victim Questionnaire includes general or global questions about being bullied in the past months (or bullying other students, in a different section). The students were asked to respond to the questions about all specific forms of bullying. The forms of bullying included in the study are direct physical, verbal, emotional, social harassment and threatening or/and coercive behaviors. In the terms of intentional social isolation, the bullying also includes more indirect or relational ways of harassment, manipulation of friendship relationships and having rumors spread (2). Some questions about digital or cyberbullying are also included (2). Turkish validity and reliability studies were conducted elsewhere (5).

Pediatric Quality of Life Inventory (PedsQI): Examined the reliability and validity of the PedsQI in the assessment of health-related quality of life in pediatric patients (6). There are two different forms as parental scale and self-report. The scale consists of four subdivisions in which physical, emotional, social, and school-related functionality is questioned (6). The increase

in points, ranging from zero to 100 points, describe the high level of quality of life. In our country, Turkish validity and reliability study of PedsQL was performed for all age groups (7).

The statistical evaluation of the study was carried out using the SPSS 15.0 package program, the responses to pre- and post-tests were compared with Chi-square and Student's t-tests. Numbers, percentages, arithmetic mean  $\pm$  standard deviation were used as descriptive statistics. A p value  $<0.05$  was set for statistically significance.

## RESULTS

The peer bullying was assessed using the Olweus Bully / Victim Questionnaire, the Turkish translation (6). Questions related to peer bullying were analyzed. As the result of the performed statistical analysis the rate of victim students reduced from 43.2% to 30.4%; rate of bully students reduced from 23.4% to 21.7% in the post-test. There was a reduction of the rate of victims and bullies

**Table 1: Answers about bullying and victimization in pre and post tests.**

Questions	Victim		Bully	
	Pre Test (n= 592) %	Post Test (n=543) %	Pre Test (n= 586) %	Post Test (n= 530) %
In the past months at school did not suffer/make peer bullying	56.8	69.6	76.6	79.3
It happened only once or twice	25.3	18.6	15.5	12.2
It happened 2 or 3 times in a month	6.3	3.1	3.1	3.8
The average was once a week	4.4	3.3	1.9	1.9
It happened several times a week	7.3	5.3	2.9	2.6

in the post-test. However, the decrease of bullying was higher for victim-students than bullies in the post-test. Table 1 shows all answers of the pre and post tests about bullying or victimization.

When peer bullying and gender relations were investigated, it was found out that the difference in terms of peer bullying among gender groups had lost statistical meaning after training (as for pre-test:  $p<0.01$ , post-test:  $p>0.05$ ). According to the answers given by the students in the questionnaires on physical, verbal, emotional and cyberbullying in the pre and post-test, gender and the proportions of the victim and bullying students together can be seen in Table 2.

**Table 2: Gender and the proportions of the bullying and victim students in the pre and post tests.**

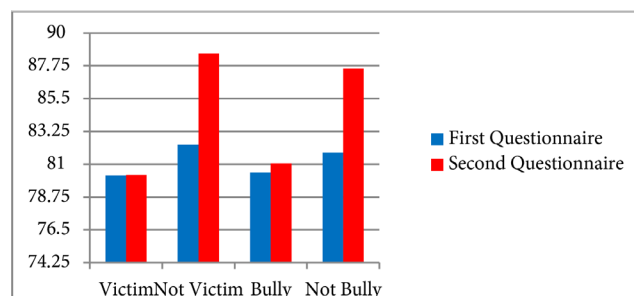
Items	Girls		Boys	
	Pre Test n (%)	Post Test n (%)	Pre Test n (%)	Post Test n(%)
That all the questions in questionnaire indicated students have not been bullied	85 (29.9)	108 (41.2)	52 (19.1)	95 (40.3)
At least one of the question in questionnaire indicates that students have been bullied at least once or twice recently	199 (70.1)	154 (58.8)	220 (80.9)	141 (59.7)
That all the questions in questionnaire indicated students have not been bullied others	157 (58.4)	180 (68.2)	124 (47.3)	149 (63.9)
At least one of the question in questionnaire indicates that students have been bullying others at least once or twice recently	112 (41.6)	84 (31.8)	138 (52.7)	84 (36.1)

Physical health, emotional functioning, social functioning, and school functioning were analyzed using the PedsQL. Scale total score (STS), physical health total score (PHTS) and psychosocial score (PSTS) were calculated. The results showed that the quality of life of bully or victim-students were significantly lower ( $p<0.001$ ). After our training activity, the quality of life scores of students who were not bully or victims were significantly increased ( $p<0.001$ ). All results of students who were bullied or victimized are shown in Table 3. Pre and post-tests results are shown in Figure 1.

**Table 3: Results of pediatric quality of life inventory.**

Variables		Physical health score	Psychosocial score	Scale total score
		Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD
Victim	Yes	82.22 $\pm$ 15.92	78.72 $\pm$ 17.35	80.25 $\pm$ 15.37
	No	86.29 $\pm$ 14.22	84.95 $\pm$ 14.45	85.62 $\pm$ 13.25
	p value	$<0.001$	$<0.001$	$<0.001$
Bully	Yes	81.90 $\pm$ 16.84	79.51 $\pm$ 17.10	80.70 $\pm$ 15.19
	No	85.66 $\pm$ 14.28	83.61 $\pm$ 15.35	84.57 $\pm$ 13.89
	p value	$<0.001$	$<0.001$	$<0.001$

\*SD: Standard Deviation



**Figure 1: Pre and post test sts score of pediatric quality of life inventory.**

## DISCUSSION

The researchers found that there was an association of bullying with impairment in social role, lower mental health and adverse effects on families which provides additional information and background for peer bullying (4). In our study, there were similar results in different level, we found a relationship between peer bullying and quality of life. It was observed that the quality of life of students who were not included in peer bullying was significantly higher ( $p < 0.001$ ).

Many governments throughout the world with schools and educators invest money and time for anti-bullying interventions. Generally, these planned interventions showed some decrease in the rate of bullying. The whole-school interventions including complementary components and multiple disciplines directed at different levels of the school organization, more often reduced bullying and victimization rather than the interventions that only includes classroom-level interventions (8). Our pre and post-test assessment coupled with the training of the students and teachers in small groups then the interactive activities in the classroom reduced victimization and bullying in our study. The school based interventions on bullying as a systemic problem usually ends up with a solution. These school based approaches alter the school's entire environment which includes classrooms, teachers, administration, peer groups and individuals in a systematic way. The success of the whole-school interventions remind us that bullying results from external factors directed to individual children's psychosocial problems (9). At our training, we saw that teaching the negative outcomes of peer bullying to bullying students and teaching the basic solutions to victims with interactive classroom activities were successful. In addition, working with teachers, families and school administration was helpful to solve problems.

Peer bullying is a frequent problem among adolescents with different outcomes. The solution to this problem should include multiple variables, such as financial, social, legal and psychological commitments. However, when we consider the high number of students affected and the personal and economic costs of bullying, these efforts are important and necessary (9). In our study setting, students had a variety of different economic, social and cultural status. Cooperating with teachers and administrators in school was important for reaching and changing the school environment; awareness of students and their families, school teach-

ers and administrators were improved about peer bullying. We believe this cooperation supported to decrease the problem of peer bullying and increase the quality of children's lives.

Our study shows that the rate of victim students reduced from 43.2% to 30.4%; rate of bullying students reduced from 23.4% to 21.7%. There is a reduction in the number of people involved in peer bullying in the post-test which was an effective method for the target group as a whole. It is a limiting factor that the socio-demographic characteristics of students are not examined even if our study has reached the purpose.

Our results show that our training was an effective method for the target group. The low number of invalid surveys reveals that our research is successful in attracting the attention of the target group. To the best of our knowledge, it is the first survey research in our region about peer bullying. The results obtained from this research carried out in one cosmopolitan school for 720 children can give an insight into the big picture. We hope that other researchers will apply similar methods at the national level and our study attracts attention in this field.

**Ethics Committee Approval:** This study was approved by the ethical committee of Manisa Celal Bayar University of Medical Sciences

**Informed Consent:** Written informed consent was obtained from the participants of this study.

**Conflict of Interest:** The authors declared no conflict of interest.

**Author contributions:** Concept: CU. Design: ŞYS. Supervision: HK, BM. Resources: BM, İŞ, EM, MS, RS. Materials: BM, İŞ, EM, MS, RS. Data collection and/or processing: BM, İŞ, EM, MS, RS. Analysis and/or Interpretation: BÖ. Literature Search: CU, BM. Writing Manuscript: BM. Critical Review: CU.

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## THE INVESTIGATION OF UNIVERSITY STUDENTS' KNOWLEDGE ON NUTRITION AND EATING HABITS

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### ABSTRACT

**Aims:** The aim of this study is to analyze Trakya University School of Medicine students' knowledge on nutrition and their eating habits. In addition, it is aimed to determine whether there is a relation between knowledge and nutrition habits and whether medical education is enough to learn the correct information.

**Methods:** The study conducted in May 2018 was carried out by questionnaires given to 681 students, which were composed of 240 first graders, 98 second graders, 78 third graders, 143 fourth graders, and 110 fifth graders. Chi-square method was used to determine the relation between the class and the gender.

**Results:** Out of all students 30.4% of them thought that it is harmful to eat fish and yogurt together. 80.3% of them had the idea that consuming calcium in their diet does not increase iron absorption. 66.9% of the participants declared that they drink tea without sugar.

**Conclusion:** It was determined that the students do not apply the information they know correctly to their daily lives. In some questions, it was observed that the students' knowledge about nutrition is insufficient. In order to correct the eating habits and to create public awareness of nutrition, courses about nutrition should be included in the curriculum of medical students.

**Keywords:** Eating habit, student, survey

### INTRODUCTION

Nutrition is essential for every living organism to survive. Gender, age and body mass index are the factors that should be considered for a proper diet. In addition, healthy foods are necessary for a better nutrition. It is known that many diseases, growth and development disorders occur as a result of an improper diet (1).

Proper nutrition should be determined by taking into consideration the economic and socio-cultural status of the person as well as the nutritional value of the food. The conditions in which the person is facing may not be suitable for proper and adequate nutrition. In this case, the person needs to consume the most economical and achievable foods with adequate nutritional values (2).

Misleading done by the firms to sell their own products, the absence of the courses about proper nutrition in the curriculums of many universities, and the economic situation of university students can be the reasons for poor nutrition.

In this study, it is aimed to analyze Trakya University School of Medicine students' knowledge on nutrition and their eating habits. It is also aimed to determine the effect of the absence of courses about proper nutrition in the curriculum of medical students, on their eating habits.

## MATERIAL AND METHODS

This study has been approved by Scientific Research Ethics Committee of Trakya University School of Medicine. The research was conducted in May 2018 and it is a descriptive cross-sectional study. The participants of the study are 1st, 2nd, 3rd, 4th, and 5th grade students in Trakya University School of Medicine. The study was conducted by questionnaires consisting of 8 questions which were given by hand to the participants (Table 1). The participants were selected on a voluntary basis and the necessary information was written on the questionnaire. It was planned to be conducted on 1257 students however the number of students participating in the survey was 681. Of these students, 240 of them were first graders, 98 were second graders, 78 were 3rd graders, 143 were 4th graders and 110 were 5th graders. 12 students left the class section blank in the questionnaire and those students were not included in the study.

In the questionnaire distributed to the participants, the classes they are in was asked in order to determine whether the knowledge on nutrition was related to the level of received education. Participants were asked to indicate their gender in order to determine the role of gender in daily nutrition. The presence of chronic diseases was also asked to determine whether participants' habits were related to the diseases or not. Some of the questions were about knowledge or habits whereas some of them were questioned both of them in order to determine whether the knowledge is applied to their habits.

Question 1, 2, 3, 7A and 8A were asked to analyze the knowledge of the students whereas question 4, 5, 6, 7B and 8B were asked to analyze the habits of the participants.

As WHO indicates, 24.8% of the world population has iron deficiency anemia (3). Therefore, question 3 was asked to determine the knowledge of medical students about the foods which should be consumed in order to decrease the prevalence of this disease.

Since salt consumption is one of the factors which plays a role in hypertension, question 4 was asked to the students in order to analyze the prevalence of salt consumption (4).

The relationship between sugary drinks and body mass index is directly proportional (5). In addition,

Turkey has the highest tea consumption per person in the world with 2.5 kg per capita (6). With this information in mind, in order to examine the sugar consumption with tea, question 5 was asked to the students where the tea is consumed the most.

Turkey has also the highest bread consumption in the world with 199.6 kg per capita in a year (7). Not only the amount of bread consumed but also, the type of the bread is important for health. Question 7A and 7B were included in the questionnaire in order to determine both the knowledge and habits of the students about bread consumption.

It has been suggested that coronary artery diseases are more common in men who do not have breakfast (8). Thus, questions 8a and 8b were asked to determine whether the students studying at Trakya University School of Medicine have breakfast and the right information about the importance of breakfast.

**Table 1: The questionnaire.**

1- Is it harmful to eat fish and yoghurt together? Yes, it is. No, it is not.
2- What is the effect of eating yoghurt besides iron-containing foods on iron absorption? Increases No effect Decreases
3- Which of the following contains more iron element? Meatballs Milk Molasses Spinach Fruits
4- Which describes your salt consumption? I do not add salt to my meals. I add it according to the taste of the meal. I add it without tasting the meal.
5- How many sugar do you add to a glass of tea? None 1 or 2 3 or more
6- Which of the following describes your sweets consumption? None 1-2 times a week 3-5 times a week More than 5 times a week
7- A) Which type of the bread is healthier than the others? White bread Whole wheat bread Bran bread Multigrain bread Other B) Which type of the bread you consume the most? White bread Whole wheat bread Bran bread Multigrain bread Other
8- A) Which meal is more important during the day? Breakfast Lunch Dinner B) Which meal do you care more? Breakfast Lunch Dinner

The data were analyzed using Chi-square test on IBM SPSS Software 20.0 to compare the categorical data. Numbers and percentages were used as descriptive statistics to evaluate the given answers.

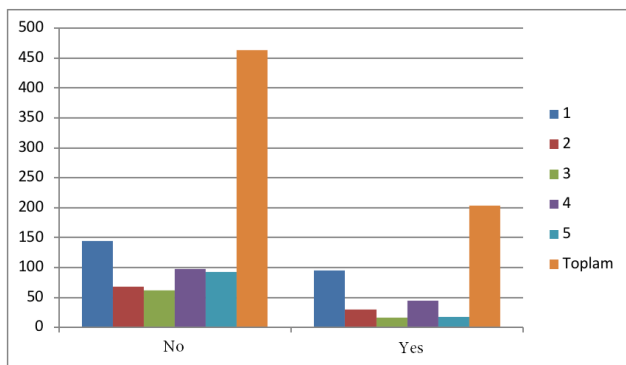
## RESULTS

Demographic features of the students participated in the study are given in Table 2.

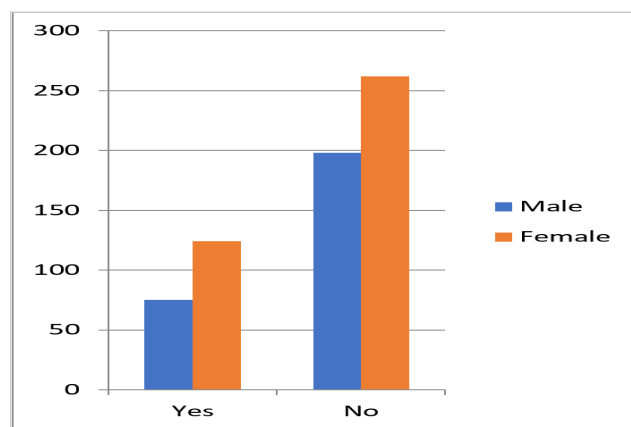
**Table 2: Demographic features of the students.**

	Number (n)	Percentage (%)
<b>Gender</b>		
Male	273	41.4
Female	388	58.6
<b>Classes</b>		
1	240	35.9
2	98	14.6
3	78	11.7
4	143	21.4
5	110	16.4

For the first question ('Is it harmful to eat fish and yogurt together?'), there were 472 (69.6%) students who said 'no, it is not' while 206 (30.4%) students said 'yes, it is'. The distribution of the answers according to the classes is given in Figure 1. The distribution of answers among classes was statistically significant ( $p < 0.001$ ). The distribution of the answers according to gender is given in Figure 2. The comparison of the answers among the gender groups was not statistically significant ( $p > 0.05$ ).

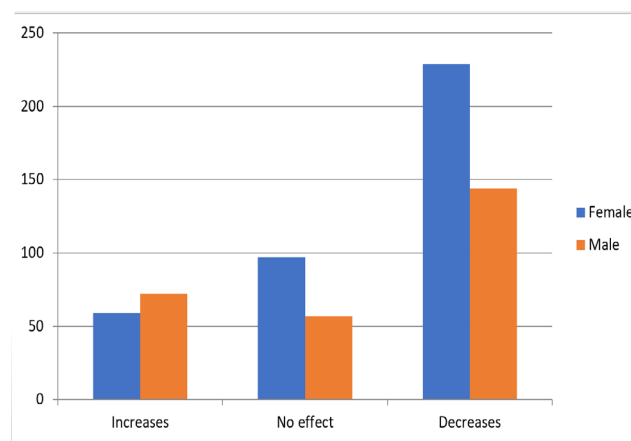


**Figure 1: The distribution of the answers to the first question according to the classes.**

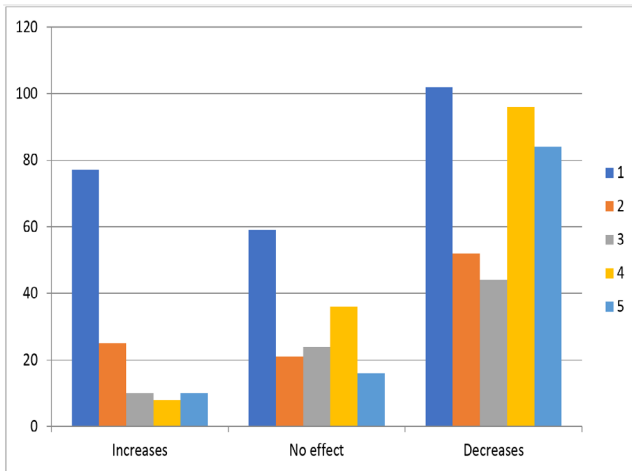


**Figure 2: The distribution of the answers to the first question according to gender.**

When the effect of calcium intake to iron absorption was asked in question 2 ('What is the effect of eating yogurt besides iron-containing foods on iron absorption?'), 133 (19.7%) students chose 'increases', 157 (23.2%) of them chose 'no effect' and 386 (57.1%) students chose 'decreases'. The distribution of the answers according to gender is given in Figure 3. There was a statistically significant difference among the gender groups regarding the given answers ( $p < 0.01$ ). The distribution of answers according to the classes is given in Figure 4.



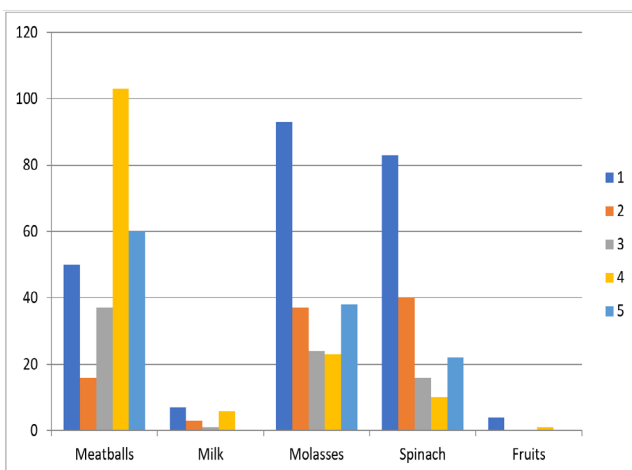
**Figure 3: The distribution of the answers to question 2 according to gender.**



**Figure 4: The distribution of the answers to question 2 according to classes.**

For the third question ('Which of the following contains more iron element?'), 241 (40.1%) students chose meatballs, 17 (2.5%) students chose milk, 207 (30.6%) students chose molasses, 176 (26%) students chose spinach and 5 (0.7%) students chose fruits. The distribution of the answers according to genders are as follows: 166 (42.9%) female students and 97 (35.9%) male students chose meatballs, 7 (1.8%) female students and 9 (3.3%) male students chose milk, 128 (33.1%) female students and 74 (27.4%) male students chose molasses, 83 (21.4%) female students and 89 (33%) chose spinach, 3 (0.8%) female students and 1 (0.4%) male students chose fruits.

The distribution of the answers according to the classes is given in Figure 5.



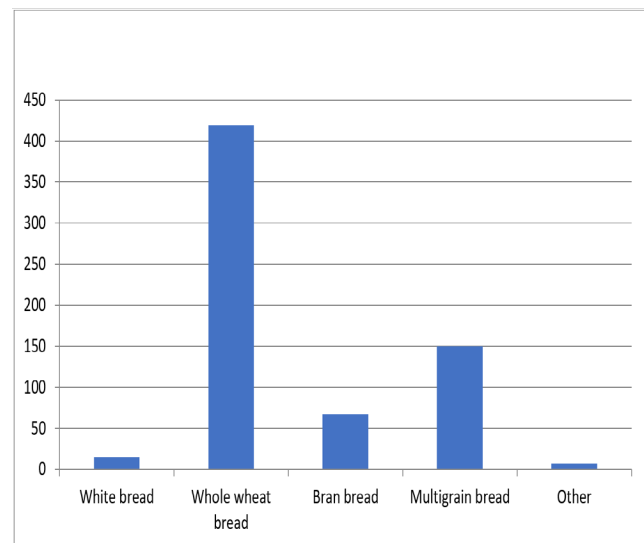
**Figure 5: The distribution of the answers to question 3 according to classes.**

In the questionnaire, the participants were asked whether salt, which is one of the main causes of cardiovascular diseases, was used as a habit in their daily lives. 166 (24.4%) of the participants stated that they have never used it. 464 (68.3%) participants said that they add it according to the taste of the meal and 49 (7.1%) participants stated that they add it without tasting the meal.

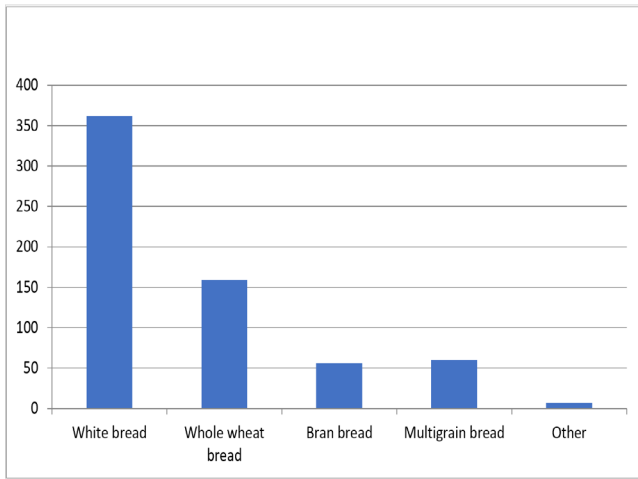
Four-hundred-fifty-three (66.9%) participants drink tea without sugar, whereas 196 (28.8%) students use 1 or 2 cubes of sugar. 29 (4.2%) participants drink tea with 3 or more cubes of sugar.

When sweet consumption was asked, the answers were as follows: 31 (4.6%) students do not eat any sweets, 304 (44.7%) students eat sweets 1 or 2 times in a week, 215 (31.6%) students eat sweets 3 to 5 times in a week, and 131 (19.2%) students eat sweets more than 5 times a week.

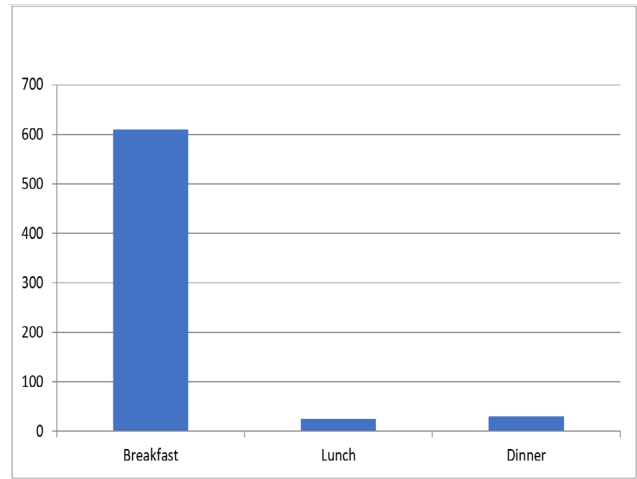
In order to analyze the effect of knowledge on habits, the answers to the questions about 'Bread Consumption' and 'Meal Preference' are given in Figure 6a, 6b, 9a, 9b respectively. The distribution of the answers according to gender is given in Figure 7. There was no statistically significant difference found between the answers when the gender groups were compared ( $p > 0.05$ ). The distribution of the answers according to the classes is given in Figure 8 and 10.



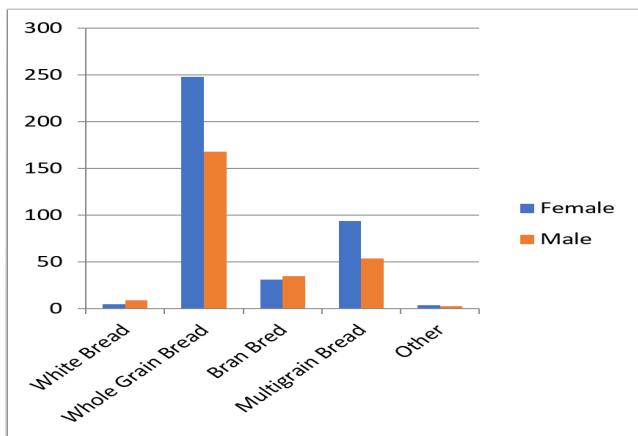
**Figure 6a: The distribution of the answers given to the question 7a (Which type of the bread is healthier than the others?).**



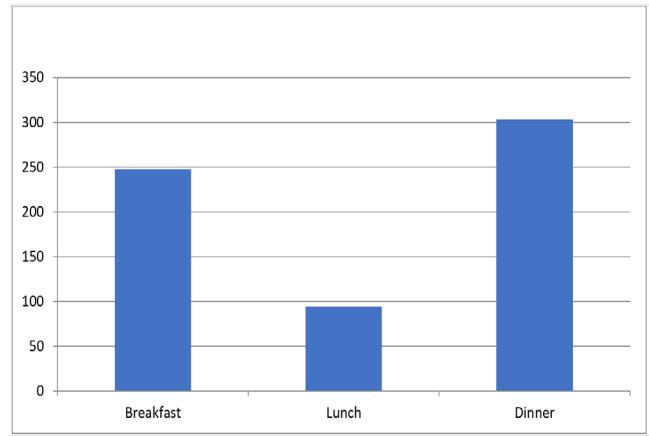
**Figure 6b:** The distribution of the answers given to the question 7b (Which type of the bread you consume the most?).



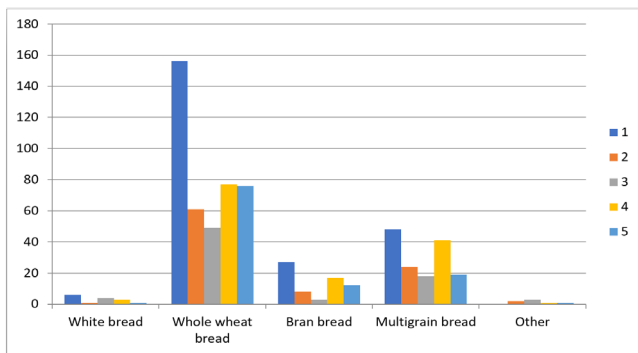
**Figure 9a:** The answers to question 8A.



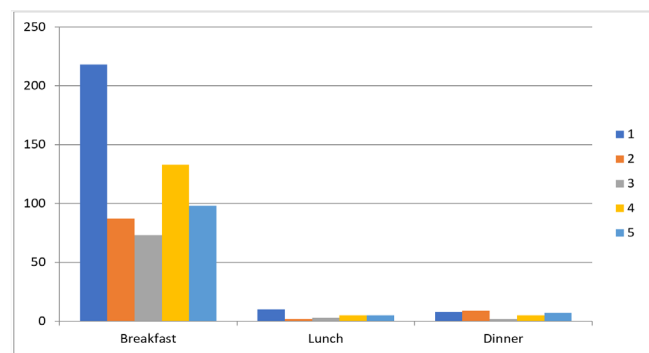
**Figure 7:** The distribution of the answers to question 7A according to gender.



**Figure 9b:** The answers to question 8B.



**Figure 8:** The distribution of the answers to question 7B according to the classes.



**Figure 10:** The distribution of the answers to question 8A according to classes.



## DISCUSSION

Today, there is a considerable number of people who have health problems due to insufficient and unconscious nutrition. Malnutrition is among the causes of many diseases such as cardiovascular diseases, obesity, and cancer. The treatment for these diseases is taking a sufficient amount of nutrients that the body needs (2).

Proper food preferences have great importance in preventing such diseases (9). One of doctors' primary tasks is to protect public health and to guide the public in the subject of nutrition. For this reason, it will be appropriate for doctors to take nutrition education as well as medical education. For example, Çalıştır et al (1) conducted a research on 792 students in Muğla University Central Campus. The top score was 25 and according to the results of the study, the ratio of the students whose score was between 18 and 20 was just 21.09% (1). Therefore, with this study, it is aimed to determine whether the education in Trakya University School of Medicine is enough to learn the proper and sufficient nutrition and to adapt this knowledge to their lives.

For the question about eating of fish and yogurt together, 69.6% of the students answered that it is not harmful. Therefore, it can be said that this common misconception is not widespread among medical students. However, every 3 students out of 10 students think that eating both fish and yogurt together is harmful. Based on this result, it can be said that medical education reduces misinformation.

It is known that calcium taken at pharmacological level reduces the absorption of iron by competing with iron in DMT-1 (Divalent metal transporter-1) mediated transport, but it has been proved that there is no negative effect of the amount of calcium that can be taken with nutrients in iron absorption (8). However, 57.1% of the participants thought that consuming meat and yogurt would reduce iron absorption. Only 23.2% of the participants thought that the amount of calcium taken with nutrients will not change the absorption of iron.

In question 3, 40.1% of the students gave the right answer by saying that meatballs contain more iron element than the other foods. However, there was no significant difference between the given answers among the classes ( $p=6,98$ ). Therefore, it could be said that

medical education may not have a contribution in that subject.

In Turkey, 14.3% of men and 23.4% of women have hypertension (4). It is known that salt intake increases blood pressure and causes hypertension. According to the results of the survey, it is seen that the 'taste of food' is the criteria for salt consumption.

As it is mentioned before, the consumption of sugary drinks and body mass index are related (5). Additionally, Turkey has the highest tea consumption per capita (6).

In our study, 66.9% of the students which is the majority of the students do not add sugar to their tea. The last two questions in the survey were composed of two sub-questions which were given as A and B. The aim of these two questions was to reveal whether the students' knowledge is reflected in the habits. 97.8% of the students thought that the consumption of white bread is not healthy whereas 56.4% of them consume white bread in their daily life. The reason behind white bread being so widespread may be the economic situation of the students and the difficulty of accessing other bread varieties can be shown. The contents of whole wheat bread are defined as complex carbohydrates. Digestion time of complex carbohydrates is longer than simple carbohydrates. They do not increase blood sugar quickly and do not over-stimulate insulin release from the pancreas. Since they do not cause hyperinsulinemia, blood sugar does not drop rapidly after meals and do not cause to eat more. The proportion of women who think that it is beneficial to consume whole-wheat bread is higher than men (10).

The second question which the habits of students were investigated, were composed of two sub-questions: 'Which meal is more important during the day?' and 'Which meal do you care more?'. Energy is needed to perform daily activities and 15%-20% of this energy is met by the first meal of the day. Skipping breakfast, which is the first meal of the day, leads to significant health problems. For example, the risk of coronary heart disease has been shown to be 27% higher in men who do not have breakfast than men who have breakfast (11). 91.6% of the students think that breakfast is the most important meal, but 38.2% of them have breakfast as a habit. According to the survey conducted on 357 male students studying at Qassim University Faculty of Health Sciences in Saudi Arabia, 49.9% of the students stated that they have breakfast every day (12).

In a survey conducted by Yılmaz et al (2) on 175 students studying in Balıkesir University Bandırma School of Health Nursing and Bandırma Vocational School of Child Development departments, 59.4% of the research group gives importance to breakfast and 29.7% of the students do not have breakfast. One of the reasons why students cannot pay attention to breakfast can be that breakfast preparation cannot be done in the dormitory or apart conditions. In this question, as in the previous habit-knowledge question, the rate of women who think that the most important meal is breakfast is more than that of men.

As a conclusion, having a course about proper nutrition in the curriculum of medical schools may have a contribution to increase the rate of right answers in the survey. Medical students who know proper nutrition may influence the public in the future as well. It may lead to a decrease in diseases which were caused by poor nutrition in our country for future generations. Giving courses about nutrition to the public may contribute the knowledge of new generations.

**Ethics Committee Approval:** This study was approved by Scientific Researches Committee of Trakya University School of Medicine.

**Informed Consent:** Written informed consent was obtained from the participants of this study.

**Conflict of Interest:** The authors declared no conflict of interest.

**Author contributions:** Concept: EK, AMP, OSK, BB, MEK, SE. Design: EK, SE. Supervision: EK, SE. Resources: EK, SE. Materials: EK, AMP, OSK, BB, MEK, SE. Data collection and/or processing: EK, AMP, OSK, BB, MEK, SE. Analysis and/or Interpretation: EK, AMP, OSK, BB, MEK, SE. Literature Search: EK, AMP, OSK, BB, MEK, SE. Writing Manuscript: EK, SE. Critical Review: EK, SE.

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## A CASE REPORT: A MOTHER WITH SECONDARY INFERTILITY

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### ABSTRACT

**Aims:** Secondary infertility is a disease where women with a firstborn are not able to have a child again. In this case report, we wanted to observe a whole process of a patient with secondary infertility and investigate the causes and whether there are any solutions for it.

**Case Report:** A 41-year-old female patient presented to the clinic with the complaint of not being able to get pregnant. First thoughts about the patient were focused on infertility however, she had a child before. Therefore, further investigations were needed. After the investigations, she was diagnosed with secondary infertility because no rational reasons were able to clarify her disease.

**Conclusion:** Nowadays, secondary infertility is still a major health problem and no medications or treatments are enough to resolve this problem. The most common theory is the H-Y antigen hypothesis, but still, there is not enough evidence for this theory to be proven.

**Keywords:** Infertility, pregnancy, immune system

### INTRODUCTION

Infertility is the failure of achieving a clinical pregnancy after 12 months or more of unprotected sexual intercourse. Infertility can be divided into two major categories: physiological and pathological. Physiological - process is where a woman can not get pregnant due to her biological timing or pregnancy. Pathological - condition has two types; primary and secondary infertility. A woman who never got pregnant in spite of having repetitive intercourse is diagnosed with primary infertility. Unlike this situation, women with secondary infertility get diagnosed after giving birth to a child (1).

Secondary infertility is the disability of the mother to get pregnant following the birth of her first child that was conceived without any reproductive technologies or fertility treats. Secondary infertility could also be defined as a process which includes recurrent miscarriages. This medical problem mostly comes out after birth, where cells of the fetus are able to pass through maternal circulation (2). During pregnancy placenta becomes permeable to fetal cells and even, after pregnancy, male DNA becomes sensible in the maternal

circulation. Women which are suffering from secondary recurrent miscarriages (SRM) are mostly mothers of boys where their immune systems are against a protein called male-specific minor histocompatibility (H-Y) antigens (2).

A specific gene on Y chromosome that encodes H-Y antigen; male, fetal and trophoblast cells express them in a ubiquitous manner (2). These antigens are very specific for H-Y immunity which becomes functional and is seen mostly after stem-cell transplantation.

In this case report it is aimed to present a forty-one-year-old female patient who had subsequent miscarriages after having given birth to her first son, thus was diagnosed with secondary infertility after the examinations.

### CASE REPORT

A forty-one-year-old female patient admitted to the Department of Gynecology and Obstetrics in Trakya University Hospital with unexpected and continued abortions is presented. According to her anamnesis,

she had two miscarriages and one medical abortion. She was healthy, not on any medication and had no known allergies. She did not have a history of alcohol or any other substance abuse.

Patient has an eight-year-old boy. For her previous pregnancy, no fertility medications or reproductive technologies were used. The patient stated that since her first born she has been trying to get pregnant, but she could not. Some genetic tests were needed to determine her diagnosis and treatment.

Polymerase Chain Reaction analysis was performed using genomic gene-specific DNA primers derived from the peripheral blood sample of the patient, which was later on directed to the Genetic Disease Diagnosis Center of Trakya University. 8 polymorphisms in 8 different gene regions were evaluated by the Pyrosequencing technique.

Prothrombin, factor V leiden, MTHFR C677T, beta fibrinogen genes were considered as normal; MTHFR A1298C homozygous mutant, factor XIII and GPIIIa heterozygous mutant, PAI-1 homozygote 5G.

The peripheral blood sample has been also sent to Istanbul Genetic Diagnosis Center for her chromosomal analysis. In the cytogenetic analysis report, no anomaly was detected performed on the metaphases obtained from the peripheral blood but pericentric inversion was detected in the region of p11q13 of chromosome 9. This change was evaluated as polymorphism and the phenotypic effect was not expected. Still, genetic counseling was suggested to the patient.

Simultaneous chromosome analysis of the patient's partner was also seen necessary and no numerical or structural anomaly was detected in the chromosome analysis performed on peripheral metaphases. With the results gathered together, it was decided that the patient did not have any disability for having a child and the patient was discharged.

After 4 years, the patient was presented again to Trakya University Hospital Department of Gynecology with the same complaints she had 4 years ago. Patient's husband was also admitted to the clinic for in-vitro fertilization treatment. For their microbiological evaluation venous blood samples were taken. The patient's AMH, Anti tox. IgM and CMV IgM levels were examined and the values according to the laboratory test results were found to be within normal limits. The ELISA

test was used to detect AntiHIV, HBsAg and AntiHCV values on patients' partner which were found to be negative.

## DISCUSSION

Secondary infertility is an unaccountable health problem. Still to this day, reasons for secondary infertility remain unclear while studies on possible causes continue.

This type of infertility is also characterized by having a male child. Resolving patients with secondary infertilities are much more difficult than patients with primary infertility, which often leads to discharge with an undefined cause of infertility diagnosis (3, 4).

Usually, patients have very similar complaints as Primary Recurrent Miscarriage (PRM) patients. Research shows that there are similar discomforts between PRM and secondary infertility patients (5). Another research found that immunotherapy method used for treating infertility did not affect PRM patients. On the other hand, it was observed that patients with SRM had a significant increase in birth rate (2).

Studies on the cause of secondary infertility are mostly focused on the H-Y hypothesis. According to this hypothesis immune reactions lead to a male-specific histopathological disorder. The role of gender in SRM was found 20 years ago. Based on the data and the information obtained from the study, a male-specific factor can be found in a woman with a male fetus (2).

Maternal carriage of HLA-class II alleles causes the production of H-Y antigens in patients with a first-born. Especially HLA-DRB1 is a part of the family gene called the human leukocyte antigen (HLA) complex which helps the immune system distinguish the body's own proteins from the ones made by foreign invaders. Providing instructions for building a protein that plays an important in our immune system (6).

It is also thought that recurrent miscarriage patients, in contrast to PRM, are carrying the immunological high responder alleles HLA-DR1 \*03 and HLA-DRB1 \*15 times more frequently (2). So SRM patients immune system is more selective and aggressive than normal peoples. This information predicts that H-Y antigens passing to blood after the first-born child may reduce the chances of having a healthy pregnancy. However,

this still remains an issue to be researched further considering the fact that the effects are not seen in every woman who has had a male child before.

In conclusion, we are hoping that this case report will lead to an increase in further research about this topic and be a path for the treatment of this condition.

**Ethics Committee Approval:** N/A

**Informed Consent:** Written informed consent was obtained from the participants of this study.

**Conflict of Interest:** The authors declared no conflict of interest.

**Author contributions:** Concept: AG, MAG, KE. Design: AG, MAG, KE. Supervision: AG, MAG, KE. Resources: AG, MAG, KE. Materials: AG, MAG, KE. Data collection and/or processing: AG, MAG, KE. Analysis and/or Interpretation: AG, MAG, KE. Literature Search: AG, MAG, KE. Writing Manuscript: AG, MAG, KE. Critical Review: AG, MAG, KE.

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## OTOSCOPIC EXAMINATION

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**Abstract:** Ear related diseases are common in both otolaryngology clinics and family practice since all age groups can get affected. Due to the frequency and the range of diseases of the ear, it is very important to carry out a thorough examination and make a correct diagnosis. Oscopes are very useful tools used for otoscopic examination. Although head mirrors and head lamps can be used for the examination of the ear, otoscopes provide a better field of vision and a more detailed sight. There are two main types of otoscopes; portable and wall-mounted. However, the examination should not be limited to the outer ear. It is the examiner's responsibility to check the area around the ear for abnormalities. Otoscopic examination is a convenient method for making a correct diagnosis. Therefore, every medical doctor should be able to perform a proper otoscopic examination and make a correct diagnosis.

**Keywords:** Ear, otitis, otoscopes, tympanic membrane

## INTRODUCTION

Diseases regarding the ear are common in not only otolaryngology clinics but also in family practice. It is an important disease group that alarms patients and their families (especially in pediatric age groups) to consult an emergency service for treatment. Detailly taken medical history of the patient is important as in all diseases (1).

Ear: Consists of 3 anatomical parts; Outer Ear: Auricle (pinna) and the ear canal, and Middle Ear: Tympanic membrane, the ossicles, tympanic cavity, mastoid cavity and the Eustachian tube and Inner Ear: Cochlea and vestibular structures.

Otosopic examination is essential for examining the ear canal and the eardrum with a light source. Examination of the eardrum can reveal information about some of the middle ear pathologies (2). Many tools and light sources are used for this purpose. Otoscopic examination can also be performed by reflecting the light from the light source into the ear canal through an ear spectrum via a head mirror. For this examination chair for the patient's head to rest on, a head mirror, various sizes of spectrums and a light source are needed. This method provides a better sense of depth due to its binocular view. However, carrying the equipment for the inpatients, examining non-cooperative patients and

children can be difficult. This method does not provide any magnification; ear canal and the eardrum are seen in their actual size. Directing the light with the head mirror also takes practice.

Otoscope: Today, otolaryngologists and family practitioners prefer using an otoscope. Oscopes are light, portable tools that include a light source and a lens system, providing magnification. Fiber optic lights or small light bulbs are used as the light source. There are many types of portable otoscopes as well as wall mounted otoscopes in the clinics (Figure 1A, B, C). Advances in the field of medical engineering provide more variety and lower prices.



**Figure 1: A) Portable otoscope in its case with various sizes of spare speculums, B) Portable otoscope, C) Wall mounted otoscopes.**



Otosopes generate brighter light (compared to head mirrors) and magnify the image. They can be carried easily for inpatient examination. However, interventions of the outer ear and the eardrum are harder. There is no sense of depth due to monocular vision.

Otolaryngology microscopes and endoscopes of proper size can also be used to examine the ear. Microscopic and endoscopic examination provide a clearer, magnified view. For troubled cases where a surgery is considered it is a must to use microscopes and endoscopes. Otoscopes are preferred in clinical use due to their convenience.

**Auricle: Pinna (external ear)** comes in all shape and sizes and changes from person to person. It has an elastic cartilaginous structure. The overlying skin is firmly attached to the cartilage. Only the earlobe has fatty tissue and skin instead of cartilage. Prominent ear occurs in the absence of antihelix or when the angle between the head and the ear is greater than 30°. There are no physiological disadvantages of prominent ear (3). Auricle must also be checked before examining the ear canal. Congenital anomalies, symmetry, size, hypoplasia or atresia, the presence of hematoma must be evaluated. Discoloration of the skin, tophus, skin eruption, infection, tumor lesions, scar tissue, chondrite and perichondritis allergic reaction symptoms, periauricular fistulas and vascular pathologies must be taken into consideration (4-7). Pressure should be applied to tragus to check for pain (pain is present in; otitis externa in adults and acute otitis in children). The pain and the clicking sound when pressure is applied to the front end of tragus are signs of temporomandibular joint disorders (Costen Syndrome) (8). The backside of the auricle and the upper surface of mastoid must be evaluated. Mastoid surface and the nearby area must be checked for lymphadenopathy, edema, swelling, rash, depression (caused by mastoidectomy), scar tissue, trauma and signs of tumor (Figure 2, 3, 4).



**Figure 2: Herpetic eruption (*Herpes zoster oticus*).**



**Figure 3: Fistula on the front side of the ear.**

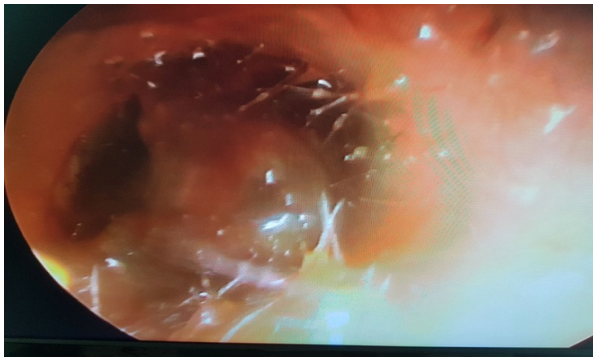


**Figure 4: Psoriasis lesions on the backside of the ear.**

**Ear Canal:** There are two structures present; outer cartilaginous canal and inner bony canal. The canal is not straight. It has an “S” shape. The length of the back wall is 25 mm and the front wall is 30 mm in adults. Hence the eardrum is placed at an angle from back to the front. One-third of the ear canal is composed of the cartilaginous canal, the overlying skin and cutaneous adnexa. There are two fissures on the front wall of the cartilaginous canal (Santorini fissures). The cartilage is not enclosed postero-superiorly (incisura terminalis). The skin on the cartilaginous region is thick. It contains ceruminous glands that are not present anywhere else in the body. Sebaceous glands and hair follicles are also present in this region. Skin is very thin in the bony canal. Since it is firmly attached to the bone, careless and harsh interventions cause bleeding and severe pain (2). There are no cutaneous adnexa in the bony canal. The radius of the canal is 7 to 9 mm. Vertical radius is larger. Innervation of the ear canal is provided by the 5th, 8th, 10th cranial nerves and 3rd cervical nerve. Branch of Vagus in this region is called the Arnold nerve (4). It might cause a fit of coughing and bradycardia while operating on the ear canal. Intense coughing might occur especially in elder patients preventing the perfor-



ming of the operation. The ear canal must be examined without using a speculum or an otoscope at first. Bleeding at the canal, mucoid or purulent discharges must be evaluated (9). Serous discharges following a head trauma might be a sign for cerebrospinal fluid leakage. Temporal fractures must come to mind in the presence of bloody discharge. Middle and external ear tumors and bullous hemorrhage otitis, foreign bodies inside the ear must be considered if trauma is not present in the patient's history (10). Furuncle, osteoma, otitis externa with severe pain, foreign bodies, cerumen accumulation and rigid plugs can be seen early on (Figure 5) (11).



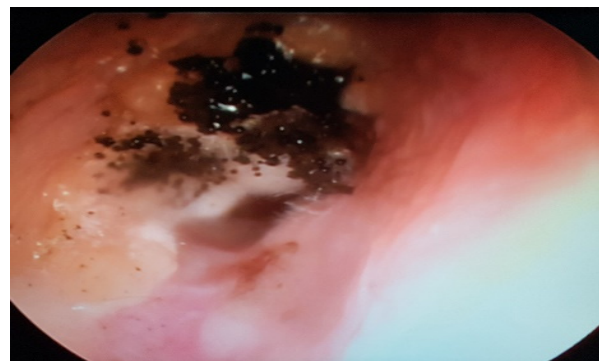
**Figure 5: Earwax blockage.**

### Otoscopic Examination

During otoscopic examination, the patient should be sitting on the examination chair and his head should be stable. The patient should be asked to turn his head left while the practitioner is examining the right ear and turn right while examining the left ear. Children should be examined while they are seated on one of their parent's lap and their heads should be held on the chest of the parent and turned to other side. The speculum which is used in ear canal should not be oversized. However, it should be broad enough to provide a good image and to insert an aspirator or other tools in necessary conditions. The auricle should be pulled backwards and upwards in adults because of the curve in the ear canal. In children, there are two methods: pulling the auricle backwards and downwards while the entrance of ear canal is observed, or it should be pulled backwards. The otoscope should be led through the ear canal. The speculum which is at the end of the otoscope may cause severe pain or bleeding if it is pushed quickly. Therefore, the movements of the practitioner should be smooth and controlled. Otoscope should be held as close to the front end as possible, similar to

holding a pencil. The otoscope should be led looking into the ear. The examination of babies and children are more difficult than adults' examination. The practitioner should be slow and careful so as not to frighten the children during the examination. It is difficult to properly examine a crying and anxious child. Especially in the examinations in primary care units, the color change – rash due to crying in tympanic membrane may lead to misdiagnosis (12).

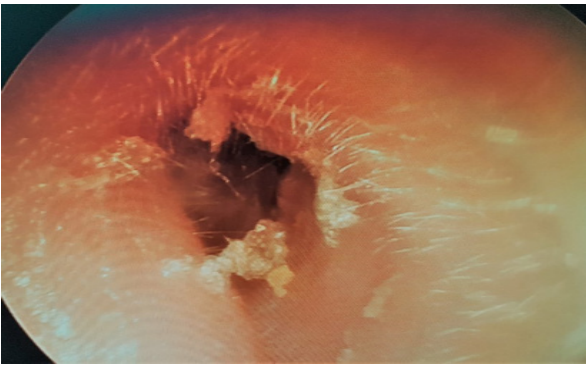
Ear canal (EA): Obstructions in the ear canal, stenosis, pushed-in earwax, foreign bodies, localized or diffuse external otitis, furuncle formation, otomycosis, fracture line due to trauma, serous, purulent, hemorrhagic discharge, exostosis or osteoma, tumoral changes or tumors should be examined (13-15). Posterosuperior meatal wall should be examined whether for any signs of depression. Earwax or foreign bodies which are blocking the ear canal should be removed properly. Living foreign bodies such as insects or flies in the ear canal should be killed by applying eardrops and then, aspirated or taken out with an alligator forceps (16). In severe external otitis that causes narrowness, tympanic membrane may be difficult to examine. If the otoscope is forced forwards in order to see the tympanic membrane, severe pain or bleeding might occur. Initially, external otitis should be treated (Figure 6-9) (13, 17, 18).



**Figure 6: Otomycosis in the external auditory canal.**



**Figure 7: Foreign body.**



**Figure 8: Seborrheic dermatitis.**



**Figure 9: A, B: Extreme narrowness of the ear canal due to an untreated infection.**

**Eardrum:** It is placed at the end of the ear canal and the border of middle ear. It is iridescent, transparent and oval. It has an oblique placement according to the ear canal. It is sloping from top to bottom and front to back. Its vertical diameter is 9-10 mm, horizontal diameter is 8-9 mm. The surface which is facing the canal is covered with epithelium. This surface is considered to be included in the outer ear. The surface which is facing the middle ear is covered with endothelium. In the middle of these surfaces, there is a fibrous layer. It has two different parts: Pars tensa and Pars flaccida. The fibrous layer is very small in pars flaccida (Shrapnell's membrane) (3). Therefore, it is neglected. In addition, there is no fibrous ligament in this layer. The different structure of pars flaccida is important in the formation of retraction pockets and cholesteatomas. It is defined in 4 quadrants as upper front, lower front, upper back and lower back according to the vertical line passing through the long arm of malleus and the horizontal imaginary line passing perpendicular to this line. The tip of the eardrum is conical towards the middle ear. The most depressed part is umbo which is formed by the tip of malleus. It reflects the light because of its structure. This triangle of light is called the Politzer's

triangle whose apex is in umbo and base is towards the front to the annulus. This shows that the structure of the eardrum and its placement angle in the ear canal is normal (3, 4).

The otoscopic evaluation of eardrum: All of the quadrants mentioned above and the general structure of the eardrum should be evaluated. Pneumatic otoscope or Siegel's speculum can be used for evaluating its mobility (19). Rash due to infection, hemotympanum, discharge, perforation, retraction pockets, the posture of malleus, umbo, the presence of Politzer's triangle are evaluated. Air-fluid levels behind the earlobe, presence of red-blue reflection in glomus tympanicum and glomus jugulare, the long arm of incus should be examined to the extent that the transparent structure of the membrane permits. Perforations should be evaluated for central or marginal formation. Marginal perforations have a risk for cholesteatoma formation. In congenital cholesteatomas, a white-colored mass image may be seen. If there is no active infection, the Eustachian tube can be examined by Valsalva maneuver in otoscopic examination. In newly formed traumatic perforations, blood on the perforation edges and tympanic membrane leaves which are curled backwards may be seen. Calcifications, thickenings, thinned areas due to the infections in tympanic membrane might be seen. The presence of Brown's sign or Schwartz sign should be evaluated (9). If there is a broad perforation, mucosa of the middle ear, promontorium, fenestrae and ossicles may be examined (Figure 10-14).

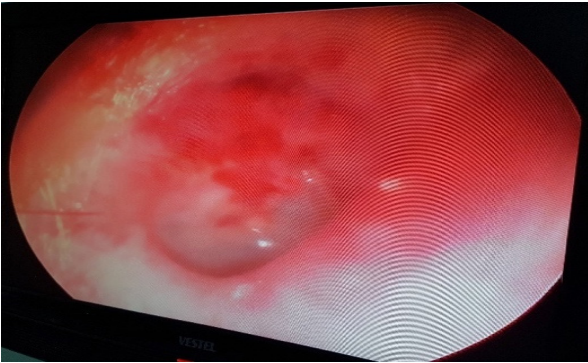


**Figure 10: Bullous myringitis.**

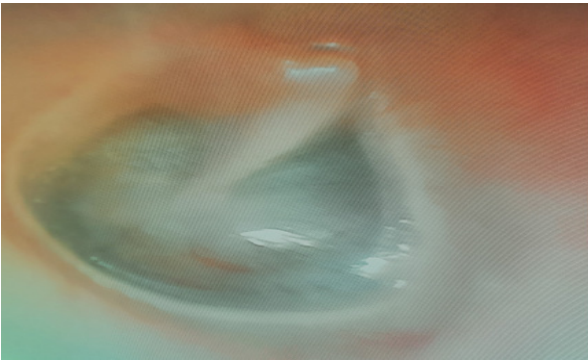




**Figure 11: Acute otitis.**



**Figure 12: Serous otitis.**



**Figure 13: Serous otitis, "blue" tympanic membrane due to delayed treatment.**



**Figure 14: Central traumatic perforation.**

## CONCLUSION

Since ear related diseases are very common and patients from all age groups can get affected, it is necessary to carry out a proper examination and make a correct diagnosis. Oscopes provide a good field of vision for the examination of the ear. Therefore, every medical doctor should be able to perform a proper otoscopic examination in order to make a correct diagnosis.

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2. Consulting fee or honorarium					
3. Support for travel to meetings for the study or other purposes					
4. Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like					
5. Payment for writing or reviewing the manuscript					
6. Provisions of writing assistance, medicines, equipment, or administrative support					
7. Other					

\*This means money that your institution received for your efforts this study.

**Section 3. Relevant financial activities outside the submitted work.**

Please indicate whether you have financial relationships (regardless of amount of compensation) with entities as described in the instructions. You should report relationships that were present during the 36 months prior to submission.

Complete each row by checking "No" or providing the requested information in the white boxes.

Relevant Financial Activities Outside the Submitted Work

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your Institution*	Name of Entity	Comments
1. Board membership					
2. Consultancy					
3. Employment					
4. Expert testimony					
5. Grants/grants pending					
6. Payment for lectures including service on speakers bureaus					
7. Payment for manuscript preparation					
8. Patents (planned, pending or issued)					
9. Royalties					
10. Payment for development of educational presentations					
11. Stock/stock options					
12. Travel/accommodations/meeting expenses unrelated to activities listed**					
13. Other (err on the side of full disclosure)					

\*This means money that your institution received for your efforts.

\*\*For example, if you report a consultancy above there is no need to report travel related to that consultancy on this line.

**Section 4. Other Relationships**

Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work?

\_\_\_ No other relationships/conditions/circumstances that present a potential conflict of interest.

\_\_\_ Yes, the following relationships/conditions/circumstances are present (explain below):

At the time of manuscript acceptance, we ask that you update your disclosure statements if anything has changed. On occasion, we may ask you to disclose further information about reported relationships.

This form is adapted from the Author Disclosure Form created by the International Committee of Medical Journal Editors (ICMJE). The IC has not endorsed nor approved the contents here. The official version of the ICMJE Author Disclosure Form is located at

[http://www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf)





## CONSENT FORM for CASE REPORT

Title of Project: \_\_\_\_\_

1. I have read, and understood the Participant Information Sheet dated \_\_\_\_\_
2. I freely agree to the use of my medical records for the purpose of this study.
3. I understand that the case report will be published without my name attached and researchers will make every attempt to ensure my anonymity. I understand, however, that complete anonymity cannot be guaranteed.
4. I have been given a copy of the Participant Information Sheet and Consent Form to keep.

Name of Participant \_\_\_\_\_

Signature of Participant \_\_\_\_\_ Date \_\_\_\_\_

The participant was informed through phone call and a verbal consent was obtained.

The following section regarding the witness is not essential but may be appropriate for patients where the research teams feel that the participant should have a witness to the consent procedure.

Name of witness (if appropriate) \_\_\_\_\_

Signature of witness \_\_\_\_\_ Date \_\_\_\_\_

Name of Researcher \_\_\_\_\_

Signature of Researcher \_\_\_\_\_ Date \_\_\_\_\_

Name of Researcher

Signature of Researcher \_\_\_\_\_ Date \_\_\_\_\_

