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Is Advanced Age a Restriction in Urogynecological Operations?

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Abstract: Recent studies show an increase in pelvic floor disorders with the increasing advanced-age population. Comorbid chronic diseases in the advanced-age population increase the incidence of mortality and morbidity in surgical options, which are effective treatment methods for pelvic floor disorders. We analyzed the feasibility, reliability and outcomes of urogynaecology surgeries performed due to pelvic floor disorders in our study. This retrospective study analysed all females who had undergone any surgical operation for pelvic floor disorders at Atatürk University, Department of Obstetrics and Gynecology between January 2010 and December 2019. Only females over 65 years of age were included in the study. The data on the patients' age, gravida, parity, chronic diseases and degree of pelvic organ prolapse were obtained from medical records. Prolapse was assessed using the POP-Q grading system. The type of surgical procedures, operative parameters, and intraoperative or postoperative complications were determined from the records. Of 105 patients included in the study, the mean age was calculated as 70.32±4.59 years (range, 65-82 years), and body mass index (BMI) was calculated as 27.4±4.44 kg. Intraoperative blood loss exceeding 500 ml was observed only in four of 105 patients. No adjacent organ injury was observed in any of the patients during the operation. Only one case of hematoma at the sixth postoperative hour was observed, while three patients (2.86%) had recurrence in the postoperative follow-up period. We advocate that age should not be a restriction for the surgical treatment of pelvic floor disorders if patients are appropriately selected and operated on by a team of experts.

Keywords: Urogynaecology; Pelvic Organ Prolapse; Geriatrics; Advanced Age; Complication.

1. Introduction

Longevity is significantly increasing all over the world (1). In the United States, regular data recording systems calculated the total population growth rate as 9.7%, whereas the population over 65 years of age increased by 15.1% between 2000 and 2010 (2).

This rapidincrease in the geriatric population brings with it many problems, including pelvic floor disorders. A study has shown that the proportion of women with pelvic floor prolapse increases with age (26.5% in women aged 40-59, 36.8% in women aged 60-79, and

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49.7% in women over 80 years) (3). Pelvic floor disorders (PFD), which are common in women over 65 years of age, have necessitated correct evaluation and treatment of the disease (2).

Surgery is the most effective treatment method in symptomatic PFD (4). However, most women in this age group have at least one chronic disease, and it is well known that morbidity and mortality increase with advanced age. Surgical intervention may result in poor outcomes in advanced-age patients due to the risks it poses (4, 5). The literature is not clear on the consequences that urogynaecology surgery-related risks bear for the very elderly population, the increased risks, and whether these risks are age-specific factors.

The aim of this study was to determine perioperative adverse events in patients undergoing urogynaecology surgery, to demonstrate the effect of preoperative functional capacity on these events, and to analyse the feasibility, reliability and outcomes of surgical treatment for pelvic organ prolapse in women aged 65 years and over.

2. Material and Methods

All females who had undergone any surgical operation for pelvic floor disorders at Atatürk University, Department of Obstetrics and Gynecology between January 2010 and December 2019 were retrospectively analysed. The study was initiated after approval was obtained from the Atatürk University Faculty of Medicine Local Ethics Committee. The institutional ethics committee of our university hospital appropriated the retrospectively designed procedure, and informed-consent was surrendered (B.30.2.ATA.0.01.00/138). Research and Publication Ethics have been complied. Only females over 65 years of age were included in the study. The data on the patients' age, gravida, parity, chronic diseases and degree of pelvic organ prolapse were obtained from their medical records. The POP-Q grading system was used for prolapse assessment. The type of surgical procedures, operative parameters, and intraoperative or postoperative complications were also determined from the records. All patients had undergone pelvic examination, ultrasonography and cervical smear tests. Prior to the operation, the patients with symptomatic grade 2, 3 and 4 disease were discussed at the surgery council, and the type of surgery was decided. All patients were provided with the necessary information and signed informed consent forms before undergoing surgery. The medical records revealed that all patients received prophylactic antibiotics, low-molecular-weight heparin and compression stockings before the operation.

Major vascular or organ injuries and blood loss exceeding 500 ml during the operation were considered intraoperative complications, while embolism, abscess and hematoma development were accepted as postoperative complications. Failed first voiding trial after catheter removal or residual urine volume of 200 ml or more in the bladder was evaluated as postoperative urinary retention (6).

The patients were also called for annual control visits after the 1st, 6th and 12th postoperative month follow-ups. Recurrence was defined as the perception of prolapse described by the patient.

2.1. Statistical Analyses

The data were analysed using IBM SPSS 20 statistical analysis programme and presented as mean, standard deviation, median, minimum, maximum, percentage and number.

3. Results

The study included 105 patients with a mean age of 70.32±4.59 years (range, 65-82 years) and a body mass index (BMI) of 27.4±4.44 kg. A total of 48.7% had hypertension, 12.38% had heart disease, and 18.1% had diabetes mellitus. Demographic data of the patients and perioperative variables are shown in Table 1. Vaginal surgical procedures were found to be preferred in 88 of the patients (83.81%). Hysterectomy was previously performed, and the operation was planned due to cuff prolapse in 17 patients (16.19%). The surgical procedures performed in the patients are shown in Table 2. There was no significant difference between the surgical techniques.

Intraoperative blood loss exceeding 500 ml was observed only in four of the 105 patients. No adjacent organ injury was observed in any of the patients during the operation. Hematoma was observed in one case at the sixth postoperative hour, but no surgical revision was required. Regression of the hematoma was observed during the clinical follow-up of the patient. The records revealed that three patients (2.86%) had recurrence during the postoperative follow-up period. Preoperative evaluation showed that these were Grade 4 recurrences according to the POP-Q grading system-two patients had undergone only vaginal hysterectomy, and one had undergone a vaginal hysterectomy with sacrospinous fixation. One patient underwent a second surgical intervention. The other two recurrent patients were trained for pessary use. Intraoperative and postoperative complications are shown in Table 3.

Table 1: Demographic data of the patients and perioperative variables.

Variables	Mean ± SD	Median (Min-Max)
Age	70.32±4.59	70 (65–82)
Duration of surgery (min)	112.02± 34.11	110 (50–240)
Preoperative Hb (g/dl)	13:53±1.54	13.7 (9.6–16.3)
Postoperative Hb (g/dl)	12.08±1.45	12.1 (9.3–16.3)
BMI	27.4±4.44	26.2 (19.9–38)
Parity	3.14±1.53	3 (0–9)
	n	n %
POP-Q stage		
2	11	10.48
3	55	52.38
4	39	37.14
Presence of hypertension	51	48.57
Presence of heart disease	13	12.38
Presence of diabetes mellitus	19	18.10

Hb: haemoglobin concentration, BMI: body mass index

Table 2: Surgical procedures performed in the patients.

		n	n %
Anterior colporrhaphy		68	64.76
Posterior colporrhaphy		42	40.00
Sacrospinous fixation		35	33.33
Surgical method	Abdominal colposacropexy	14	13.33
	Laparoscopic colposacropexy	3	2.86
	Vaginal hysterectomy	88	83.81
Indication	Cuff prolapse	17	16.19
	Uterine prolapse	88	83.81

Table 3: Intraoperative and postoperative complications.

	n	n %
Recurrence	3	2.86
Urinary retention	5	4.76
Mortality	0	0
Bleeding	4	3.81
Adjacent organ injury during the operation	0	0
Pelvic abscess	0	0
Vulvovaginal hematoma	1	0.95
Embolism	2	1.90
Re-operation	0	0

4. Discussion

The findings of our study showed that intraoperative and postoperative complications encountered in advanced-age patients were not as high as feared in urogynaecology operations. Unfortunately, the geriatric population is generally considered a suboptimal candidate for surgery. As such, elderly patients who may obtain the greatest advantages from pelvic reconstructive procedures are often deprived of surgical options to correct pelvic dysfunction due to their age. Although the morbidity rates are found to be quite low in patients undergoing urogynaecology surgery in the literature, Elderly patients, especially in cases of reparative, non-life-saving procedures, are often considered inadequate candidates for surgical operations (1). However, some studies reported serious perioperative complications of nearly 25.8% in the group with a mean age of 79 years (SD±3.4). The most common complications were identified as blood

transfusion or significant blood loss, pulmonary oedema, and postoperative congestive heart failure (7). Solomon et al. found venous thromboembolism frequency of 0.3% in a large retrospective cohort study of 1104 women undergoing urogynaecology surgery in 2010 (8). Intraoperative and postoperative complications, including re-operation, were quite low in our study group. We advocate that age should not be a restriction for this surgical procedure if patients are appropriately selected, and the surgical team includes experts in the field.

Studies have demonstrated that conditions specific to geriatrics are associated with adverse surgical outcomes (9). Therefore, the detection of cardiovascular, pulmonary, renal, hepatic and cerebral pathologies before deciding on surgery will ensure infrequent and preventable postoperative complications (10). Detailed examination of the pelvic floor is of great importance in elderly patients. Thus, if non-surgical alternatives are available for a patient group with high comorbidity, the pessary, for example, can be considered in the foreground. However, although the pessary is used quite frequently in this age group, it has been found to be uncomfortable, probably due to long-term use by the patients, and did not eliminate the cause of the disease (11).

Obliterative methods are technically easier to apply; their operation time is shorter, and they provide a higher success rate compared to reconstructive methods. Although the studies on this subject are of low quality, the success rate of colpocleisis varies between 91% and 100% (12-14). Nygaard et al. recommended an obliterative procedure such as colpocleisis as a good treatment option in the elderly population (15, 16). One of the biggest advantages of this operation, which is the main limiting factor of loss of vaginal function, is that it can be performed with local anaesthetic methods (10). However, Huang et al. reported that moderate sexual desire persists in 30% of women over 65 years of age (17). Again, sexual desire has been shown to persist in advanced ages in the literature (1). Our medical records revealed that the obliterative method was applied in four patients; however, these patients were not included in the study as their data were incomplete, and they were lost to postoperative follow-up. It is noteworthy that this method was less applicable in our study group. Although reconstructive procedures seem to be more demanding, our centre prefers to preserve coital function even in elderly patients when deciding on the surgical procedure. We surmise that it is safe to perform conventional surgical procedures in this age group.

The main limitation of our study is its retrospective nature. However, the reliability of our medical records minimizes this limitation. Our centre is a tertiary referral hospital in the region, and the data collected are valuable. Conservative treatment is an acceptable method in advanced-age patients, and the data of advanced-age patients on this type of treatment could not be sufficiently obtained from our records. Selection bias may have occurred in the preoperative evaluations of the patients undergoing surgery and might be reflected by our low complication rates, which may not indicate the true incidence. Thus, it would be more useful to provide anatomical and subjective success rates and analyse prolapse recurrence analysis. In examining our data, we found that the operations were performed with conventional methods. We determined that other methods that could have been applied were not preferred in this population. Therefore, further studies should be performed to determine the functional outcomes of the surgical procedure performed in the elderly patient group.

5. Conclusions

Carbepenem resistance is increasing gradually and is a In conclusion, we argue that the complication rate of conventional pelvic organ prolapse (POP) surgery is low in patients over 65 years of age. Although clinicians are hesitant about surgical interventions in this age group of patients, surgical procedures that can improve pelvic floor restoration can be offered safely to these patients.

Limitations of the Study

It is our limitations that it is a retrospective study, the number of cases is low.

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None

Conflict of Interests

The authors declare no conflict of interest.

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Author Contributions

Conceived and designed the analysis: EPTY, OEY, GNCS. Collected the data: EPTY, GNCS, YET. Contributed data or analysis tools: RAA, MI. Performed the analysis: OEY, YK. Wrote the paper: EPTY, YET.

Ethical Approval

Ethics committee approval was received for this study from the ethics committee of Ataturk University.

Data sharing statement

All data relevant to the study are included in the article.

Informed Consent

Written informed consent was obtained from every patient at the time of the operation.

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Seroprevalence of galactomannan antigen in Erzurum and comparison of two different test kits for galactomannan detection

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Abstract: Early diagnosis of aspergillosis is important to initiate antifungal therapy and improve the prognosis of the disease. One of the commonly used tests for early diagnosis is the galactomannan antigen test. In this study, we aimed to determine the prevalence of galactomannan antigen in various risk groups; We aimed to compare the results of two different test kits used in diagnosis and to determine false positive rates. Bio-Rad Platelia Aspergillus Ag kit was used to detect Aspergillus galactomannan antigen in serum samples of patients who were hospitalized in various clinics or admitted to hospital for serious diseases. In order to detect false positives, some of the samples found positive in this test were studied with Bio Bio-Rad" kits as well as "Dynamiker Biotechnology (Tianjin) DNK-SM-1402-1" test kits for the second time. The same procedure was repeated for the third and fourth times. Galactomannan antigen was searched in 735 different cases. In 306 (41.6) cases were obtained in at least one positive result study. Galactomannan antigen was the most common in septicaemia (75.0%); the lowest rate was found in patients with pre-diagnosis of neoplasm (21.8%). Galactomannan antigen positivity was highest in patients over the age of 65. Galactomannan antigen positivity was found to be very similar in the second and third studies of positive samples. In the fourth repetition, both firms gave 100% similar results. From the first to the last, GM positivity rates gradually decreased and GM positivity of 98 (32.0%) out of 306 positive cases in the first study has continued. It was determined that the kits belonging to two companies can be used with the same reliability and the positive rates of both tests gradually decreased.

Keywords: Aspergillosis; Anemia; Galactomannan Antigen; Lymphoma; Leukemia; Septicemia.

1. Introduction

Aspergillus, which is mostly formed by Aspergillus species like Aspergillus fumigatus and Aspergillus niger, causes morbidity and mortality especially in immunosuppressed patients, and those who undergo solid and liquid organ transplantation and in hospitalized patients treated for serious diseases. It has been reported recently that the increase in fungal infections has reached alarming rates (1). Invasive

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Pulmonary Aspergillus (IPA), which is characterized by aspergillus hypha that invades lung tissue, is one of the most important fungal infections that can be mortal. The change of IPA incidence according to populations who are at risk and the diagnostic criteria make it difficult to show the incidence of this disease with numbers. In a meta-analysis, it has been shown that 29 studies covering the 2000-2018 period had an average of 16.3% (2.5%-57.1%) invasive Aspergillus prevalence based on PCR blood test results (2). It was reported that the incidence of IPA is 10%; in patients with Acute Myeloblastic Leukemia, between 3-15% in patients who undergo solid organ transplantation; and the mortality associated with IPA is approximately 45% (3). Actually, it was reported that despite the important advances in treatment and prevention, the incidence of IPC continues to increase and the mortality rate exceeds 50%.

The timely diagnosis of opportunistic fungal diseases, which often accompany serious diseases, is important for starting antifungal treatment. However, the diagnosis of fungal infections is difficult because of the symptoms, which are not partially featured. Although traditional diagnostic methods like histopathological examination and culture, which are still considered as a gold standard, maintain their importance in diagnosis, new serological and molecular techniques were also developed because the traditional ones have low sensitivity in detecting fungal pathogens (4). One of the oldest serological tests is the Aspergillus Platelia Aspergillus Enzyme-Linked GM Immunoassay (Bio-Rad, Hercules, CA) Antigen Test (5). GM is an exo-antigen that is released from cell walls during in vivo and in vitro reproductions of aspergillus species (6). GM, which is a soluble polysaccharide, is a biological marker that can be shown in samples like urine, cerebrospinal fluid (BOS), Broncho Alveolar Lavage (BAL) apart from GM serum samples (7). This test has the capability of detecting approximately 1 ng/mL antigen in serum. The sensitivity of this test, which does not necessitate an invasive procedure, varies between 50 and 92.6%, and its specificity varies between 94 and 99.6% in patients with hematological malignancies (7). Among the factors that affect the performance of this test include the use of antibiotics like piperacillin/tazobactam, especially the cross-reactions with other microorganisms and natural or parenteral foods (8-10). It was reported that GM test could give 38% false positivity among non-neutropenic patients when BAL samples were used (11).

No studies were conducted before on galactomannan antigen seropositivity in risk groups in our region. Although it does not fall off the agenda with its false-positive results, knowing the performance of the GM antigen test, which is recommended to be used in the diagnosis of invasive Aspergillus, will be a guide in the test selection. For this purpose, it was planned to compare the results of the GM antigen kits from two different companies, and to determine the results of repeated tests in serum samples taken on different days from patients who had GM antigen positivity.

2. Material and Methods

2.1. Scope *of the Study, Cases and Clinical Samples*

The study was conducted between March 2016 and March 2018 at the Routine Microbiology of the Laboratory Atatürk University Research Hospital. The serum samples of 735 different cases whose GM antigen tests were requested, whose preliminary diagnosis was acute and chronic lymphoma, anemia, idiopathic thrombocytopenic purpura (ITP), pulmonary Aspergillus (PA), leukemia, multiple myeloma, neoplasms, and septicemia, who referred to our hospital for treatment. Galactomannan antigens in the serum samples were studied daily, and the samples that were not studied on the same day were stored in the refrigerator (at +4°C) to be studied in three days at the latest.. This study was conducted in accordance with the Declaration of Helsinki Principles. Ethics committee approval was obtained [20.06.2020-317]. Research and Publication Ethics have been complied.

2.2. Commercial *kits used to detect GM antigen in serum*

The "Bio-Rad Platelia Aspergillus Ag Kit" was used to detect Aspergillus GM antigen in the serum samples of all patients who were admitted to the hospital for the first time in two years. In this test, 239 patients who were positive and whose identities were obtained were studies for the second time with the "Dynamiter Biotechnology (Tianjin) DNK-SM-1402-1" test kit as well as the "Dynamiker Biotechnology (Tianjin) DNK-SM-1402-1" kit. The same procedure was applied for the third time to the patients who were positive and was repeated for the fourth time in patients who were positive after this application.

2.3. Evaluation of serum *GM antigen tests and of results*

The "Bio-Rad Platelia Aspergillus Ag Kit" and "Dynamiker Biotechnology (Tianjin) DNK-SM-1402-1" test kits that were used in the detection of GM antigen were used according to the recommendations of the manufacturers. Galactomannan levels were considered positive in patient samples when the optical sites of the samples were 0.90 or above, or 0.5 or above the optical density index. In this study, a total of 5640 clinical samples of 735 cases were examined in two years in terms of GM with Bio-Rad Company Kits, and the patient results were reported according to these data.

2.4. Statistical Analysis

Chi square test applied. $P<0.05$ was considered statistically significant.

3. Results

The GM antigen was examined 5640 times in 735 different cases whose ages ranged from 1 to 92, whose mean age was 54.5, whose 413 (56.2%) were male, and 322 (43.8) were female. Out of 179 (24.4) of the male cases, and 127 (17.3) of the female cases had GM antigen positivity in 306 (41.6) cases at least in one examination. The distribution of galactomannan positivity between the genders according to disease groups is given in Table 1. GM positivity was detected to be higher in men; however, this difference was not statistically significant compared to women (P=0.2872). The highest positivity was detected in septicemia patients at a rate of 75.0%; followed by leukemia, lymphoma, multiple myeloma, pulmonary Aspergillus, ITP, and anemia patients. The lowest positivity was detected in patients with neoplasms. GM antigen positivity was significantly higher in septicemia patients than the patients with neoplasms (c2=12.2354; SD=1; p=0.0005).

The distribution of Galactomannan positivity is given in Table 2 according to age groups. As it can be understood in the table, the highest positivity in total was detected in patients aged 66 and older, and the lowest positivity was detected in the young group aged 1-17 who represented young participants.

However, galactomannan positivity between the age groups did not show a statistically significant difference (c2=1.1268; SD=3; p=0.7706).

In the present study, 5640 clinical samples of 735 cases were examined in terms of GM with Bio-Rad Company Kits, and the patient results were reported according to these data. The 239 of the positive samples in this first study were re-examined for the second time, 153 for the third time, and 98 for the fourth time. The "Dynamiker Biotechnology (Tianjin) DNK-SM-1402-1" test kits were included in the repetitions. At the end of these re-studies, the changes detected in galactomannan positivity are given in Table 3. As you can see, positive results obtained from the tests belonging to the two companies decreased, provided that the results were close to each other parallel to the increase in the examinations. In the fourth examination, 98 (32.0%) of the 306 patients who were determined to be positive insisted on GM positivity in the 4th examination.

Table 1: Galactomannan positivity according to disease groups.

Disease		**GM (+)**		**GM (-)**		**P value**
		Female	**Male**	**Female**	**Male**	
	n	**n (%)**	**n (%)**	**n (%)**	**n (%)**	
Septicaemia	8	4 (50.0)	2 (25.0)	1 (12.5)	1 (12.5)	
Leukemia	187	41 (21.9)	68 (36.4)	40 (21.4)	38 (20.3)	
Lymphoma	134	28 (20.9)	48 (35.8)	22 (16.4)	36 (26.9)	
Multipl myelom	44	12 (27.3)	11 (25.0)	11 (25.0)	10 (22.7)	
Pulmoner aspergilloz	8	1 (12.5)	2 (25.0)	2 (25.0)	3 (37.5)	
ITP	32	7 (21.9)	5 (15.6)	18 (56.3)	2 (6.3)	
Anemia	74	10 (13.5)	13 (17.6)	27 (36.5)	24 (32.4)	
Neoplasm	248	24 (9.7)	30 (12.1)	74 (29.8)	120 (48.4)	
Total	735	127 (17.3)	179 (24.4)	195 (26.5)	234 (31.8)	0.2872

GM: Galactomannan, ITP: Idiopathic thrombocytopenic Purpura

Table 2: Galactomannan positivity according to age groups.

Age Group		**GM (+)**	**GM (-)**	**P value**
	n	**n (%)**	**n (%)**	
1-17	10	3 (30.0)	7 (70.0)	
18-45	204	81 (39.7)	123 (60.3)	
46-65	287	121 (42.2)	166 (57.8)	
66 and older	234	101 (43.2)	133 (56.8)	
Total	735	306 (41.6)	429 (58.4)	0.7706

Table 3: Results obtained with the kits of two companies used to search for GM antigen.

Period of study	n	BIORAD		DNK-SM-1402-1	
		GM (+) n (%)	GM (-) n (%)	GM (+) n (%) (%)	GM (-) n (%)
Firs study	735	306 (41.6)	429 (58.4)	-	-
Second time study	239	230 (96.2)	9 (3.8)	229 (95.8)	10 (4.2)
Third time study	153	151 (98.7)	2 (1.3)	152 (99.3)	1 (0.7)
Four time study	98	98 (100.0)	0 (0.0)	98 (100.0)	0 (0.0)

4. Discussion

In the present study, GM antigen seroprevalence was detected in several disease groups in line with the preliminary diagnosis of clinics that requested GM antigen tests. The patients consisted of those who were at risk for leukemia, lymphoma, multiple myeloma, ITP, anemia, neoplasms, septicemia, invasive fungal infections that were pre-diagnosed with PA.

Interestingly, in the present study, the highest positivity rate was detected in septicemia patients; and positivity was detected below the overall average in PA cases who were expected to be represented at a higher rate than other diseases. We believe that the low number of cases in these two disease groups might have played a role in this result. Apart from these two groups, the highest positivity rates were detected in leukemia, followed by lymphoma, multiple myeloma, ITP and anemia, and the lowest positivity was detected in patients with neoplasms. It is possible to speculate that these results are similar to the general literature data.

When all the cases were considered, the prevalence of invasive Aspergillus in our region was 41.6% according to the results of the first GM antigen test. The datum that IPA prevalence varies according to the disease risk groups and the testing methods used in the diagnosis and their sensitivity and specificity has become classical knowledge. Linke et al. reported that the epidemiology and treatment practices of invasive fungal diseases following allogeneic hematopoietic stem cell transplantation are in constant change (12). Melancon et al. argued that the sensitivity of the galactomannan test was 44.8%, and its specificity was 100% in the diagnosis of acute invasive fungal sinusitis and reported that there were no significant associations between galactomannan condition and mortality in this patient population (13). In a study conducted in our country, the sensitivity of the GM antigen test was found to be 68%; specificity was 77% according to 0.5 ng/ml cut-off value in neutropenic pediatric patients (14). Chan et al. reported that the galactomannan antigen seropositivity rates increased from PA (24.1%) to chronic PA (35.7%) and IPA (54.9%) (15). Cai et al. reported that the most common underlying disease of IPA patients was Chronic Obstructive Pulmonary Disease, and the sensitivity of the GM test was 40.7% and its specificity was 61.1% (16). As in these studies, in many other studies, the sensitivity of the GM test was found to be lower. These results mean that the GM antigen test detects those with real diseases at a very low rate. Its specificity was found to be high in some studies; however, it was found to have low rates in some studies. According to Cai et al., who reported the specificity of this test as 61.1%, patients were not correctly identified by nearly 40% of those who were detected as negative. Although it has an important place in early diagnosis of IPA, it is difficult to argue that GM antigen tests can detect a completely safe prevalence rate. However, the results that will be obtained from the test will be guiding together with another laboratory, radiological and clinical findings.

Many studies were conducted on the relation between GM antigen positivity and age groups and gender. In one of these, Kaur et al. identified PA prevalence to be at the highest level in 21-40 age group (13.3%) in HIV-positive patients who were admitted with lower respiratory infection in India; and reported the prevalence as 18.7% in women, and 7.7% in men (17). Sun et al. argued the average IPA incidence in Taiwan as 1.51 per million people on an annual scale and noted that this rate increased at the end of one year and observed male dominance (M/F: 1.85/1.15) in the IPA incidence (18). In a study conducted in the Netherlands, Chai et al. detected that GM positivity was 64.8% in men, and 35.2% in women when they considered the galactomannan index of 0.5%; however, they also reported that this high prevalence was not statistically significant in men compared to women (19). Parallel to these results, GM positivity was higher in men than in women; however, there was no statistically significant difference between the genders ($p = 0.2872$). In the present study, the rate of positivity increased gradually as the ages of the patients increased. In this context, the highest GM positivity was detected in patients who were over the age of 65. However, this difference was found to be not statistically significant between age groups ($p = 0.7706$).

In the present study, GM antigen presence was mainly examined with the kits of Bio-Rad Company, and the results obtained with these kits were reported to the relevant clinics. The second, third and fourth repetitions for the GM antigen search also included the "Dynamiker Biotechnology (Tianjin) DNK-SM-1402-1" test kits; and the results of these tests were compared. In the second repetition, the same results were obtained from the tests of the two companies.

Although these results showed that GM positivity could last up to two years in risk groups, maybe even longer, and the two companies had similar performance.

As a result, GM antigen prevalence was as high as 41.6% in patients with the risk of invasive fungal infections like leukemia, lymphoma, multiple myeloma, ITP, anemia, neoplasms, septicemia and PA in Erzurum region. Proportionally, IPA risk was higher in men compared to women, and higher in the elderly compared to the young population, and GM positivity is long-term. It was determined that the GM antigen kits of both "Bio-Rad" and "Dynamiker Biotechnology" could be used with the same safety level. Invasive Aspergillus causes hospitalization durations to be extended, and risky patients have to undergo expensive antifungal treatment processes, especially those with immunodeficiency, which also causes a financial burden on the patient and the economy of the country. For this reason, it is necessary that the diagnosis of invasive Aspergillus is made without delay.

5. Conclusions

Invasive Aspergillus causes hospitalization durations to be extended, and risky patients have to undergo expensive antifungal treatment processes, especially those with immunodeficiency, which also causes a financial burden on the patient and the economy of the country. For this reason, it is necessary that the diagnosis of invasive Aspergillus is made without delay.

Limitations of the Study

Two kits have been compared within the possibilities.

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Conflict of Interests

The authors declare no conflict of interest.

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Ethical Approval

Ethics committee approval was received for this study from the ethics committee of Ataturk University.

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None

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None

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Burnout Levels of Medical Students in COVID-19 Pandemic: A Cross-Sectional Study

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Abstract: There is growing interest and strong evidence that the foundations of physician burnout were laid during the years of medical education. In this study, it was aimed to investigate burnout levels of preclinical medical students and associated factors. This cross-sectional study was carried out with 1009 preclinical medical students. The study data was collected through an online questionnaire using the sociodemographic information form and the Maslach Burnout Scale-Student Form. The average age of the students was 19.8±2.5 years, 52.2% were women, 61.9% had emotional exhaustion, 21.5% had depersonalization, and 53.5% had loss of competence. Grade I students' scores for emotional exhaustion and depersonalization were the lowest, while their competency scores were the highest. There was no significant association between age and burnout levels ($p>0.05$). Emotional exhaustion in women and depersonalization in men were significantly higher ($p=0.025$ and $p=0.031$, respectively). The frequency of exhaustion and depersonalization in students who did sports regularly was significantly lower and their competency scores were significantly higher ($p<0.001$, $p=0.022$, $p<0.001$, respectively). Burnout and depersonalization were significantly higher in students with pets ($p=0.010$, $p=0.036$, respectively). There was a significant association between academic achievement and all three dimensions of burnout. Academic achievement and emotional exhaustion and depersonalization scores were negatively ($r=-0.133$, $p<0.001$ and $r=-0.173$, $p<0.001$, respectively), competency scores were positively associated ($r=0.219$, $p<0.001$). There was a significant positive association between emotional exhaustion and depersonalization ($r=0.718$, $p<0.001$) and negative association ($r=-0.450$, $p<0.001$) between competency scores. Burnout of medical students should be recognized, individual and institutional preventive strategies should be developed.

Keywords: Medical Student; Burnout; Depersonalization; Competency; Emotional Exhaustion.

1. Introduction

Burnout syndrome is a serious condition that is increasingly common in healthcare workers which can reduce job satisfaction and productivity on the one hand and endanger patient safety by increasing the likelihood

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of mistakes on the other (1).

The concept of burnout which can also be defined as the "depletion of internal resources" of the individual due to a workload he can not handle, was first proposed by Freudenberger in 1974 and was addressed for professions that work face-to-face with human beings (2).

Burnout is evaluated in three sub-dimensions: emotional exhaustion (EE), depersonalization (DP) and loss of competence (C) (3). In EE, it is possible to have inability to adapt to difficulties, have excessive fatigue with emotional inability to cope and psychological resources can be depleted as a result of the stress that the individual is repeatedly exposed to. In DP, person puts a distance between others (patients, institution and colleagues for doctors; peers, classmates, educators and faculty administration for students). The stage of depersonalization is actually an individual's attempt to cope with burnout. In the loss of C (lack of personal achievement), low professional competence is perceived. The person feels incapable of performing his/her duties with a sense of inability to achieve. It arises as a result of the other two burnout parts. Increased burnout is accompanied by a decrease in competence (4).

Burnout of healthcare servers has been associated with hostile attitudes towards patients, worsening relationships with colleagues, erroneous medical practice, insomnia, fatigue, depression, anxiety, decreased job satisfaction, suicidal thoughts (5, 6).

Burnout is a frequently studied issue on doctors and other health workers but data on burnout of medical students is inadequate. Burnout in medical students who are physicians of the future is thought to start in faculty. Medical education is a difficult and long process that requires lifelong learning and can have debilitating consequences on students. Being a medical student has emotional challenges as well as physical. Studies carried out in physicians reveal that the foundations of burnout date back to the years of studentship and are based on the difficulties of medical education (7). Academic stress, peer competition, high academic performance expectations and fear of failure, course load, sleep disorders, economic problems, witnessing patients' lives, deaths and disabilities wear them down (8, 9).

It has been suggested that education program and curriculum factors are also effective in burnout of students (7). All of these factors cause medical students to experience conditions such as anxiety, stress, depression and burnout more often than other student groups (10). Studies show that students' mental health deteriorates as medical education progresses, even starting from the early years of studentship (11). It reports that more than half of medical students experience burnout somewhere in the medical education process (6, 11, 12) and widespread burnout is detected even in preclinical stage students (13). Burnout is associated with depression and dropouts in students and it has been reported to have very serious consequences such as suicidal thoughts (14).

Today's medical students are tomorrow's doctors. Another worrying aspect of burnout which occurs during the student years and is not intervened is the potential for its negative effects to be reflected in their future professional lives, patient communication, professionalism and empathy attitudes, patient safety (13). A study conducted on assistants reported that burnout affects their professional attitudes and the most negatively affecting burnout component is depersonalization (15). The emotional exhaustion phase of burnout shows that the individual lacks both physical and psychological support (3).

On the way to be a doctor, awareness of burnout from the early years of medical school, providing preventive and interventional measures when necessary is important in terms of increasing both professional satisfaction and patient safety in health care service.

The COVID-19 pandemic has profoundly affected higher education as well as in all areas of life. As of 11.03.2020 when the pandemic was declared and the first case was seen in Turkey, universities were first suspended for three weeks and then online education started. The students who sampled the study have been at home since the beginning of the pandemic and education has been going online for three-half years. COVID-19 measures, restrictions, pandemic conditions and the online education process are thought to further increase the stress on students (16). There has never been a study in our institution that investigates the burnout of preclinical students. In this study, it was aimed to investigate burnout levels of preclinical medical students and associated factors in COVID-19 Pandemic.

2. Material and Methods

2.1. Study Setting and Population

Research and Publication Ethics were followed at all stages of the study. Ethical permissions were taken for study. The study was carried out in accordance with the rules of the Helsinki Declaration. This study is a cross-sectional study carried out with preclinical students of Atatürk University Faculty of Medicine. The target population of the study is made up of students studying Turkish and English medicine programs. The study was conducted between 12.06.2021 and 20.06.2021. Participation in the research was done on a voluntary basis. No printed material was used due to pandemic conditions. The data was collected through an online survey which was created via Google forms (Google LLC, Mountain View, California, United States). Survey was shared with students via classroom WhatsApp groups. Students were informed about the purpose of the study and given a week to respond to the questionnaire. It was attempted to increase participation with reminder messages and data collection was terminated at the end of the period. The survey, which could be answered in about 10 minutes,

began with a question of online consent, and those who did not approve could not answer other questions.

2.2. Study size

The population of the study consisted of a total of 1197 students studying in the first (n=409), second (n=353) and third (n=335) grades. In the study, which was aimed to reach the whole target population of the study, 84% participation was achieved with 1009 volunteer students.

2.3. Data collection tools

2.3.1. Sociodemographic Characteristics

A two-part data collection form consisting of sociodemographic characteristics and Maslach Burnout Scale-Student Form (MBS-SF) was used. With the sociodemographic data form, the students' grade, age, gender, grade point average, student club membership, playing sports, playing a musical instrument, having pet and dating status were questioned.

2.3.2. Maslach Burnout Scale- Student Form

First developed by Schaufeli et al. in 1996, the Maslach Burnout Scale (17) was adapted as a student form by Schaufeli et al. in 2002 (8). The scale was adapted to Turkish (2011) by Çapri et al. (5). On scale, there are 3 sub-dimensions and a total of 13 articles, including emotional exhaustion (5 item), depersonalization (4 item) and competency (4 item). The scale is answered on a 5-point Likert scale as never, sometimes, usually, often, always and is scored between 0-4. Three separate burnout scores are obtained for each participant by calculating the sub-dimension scores separately. While scores are collected directly for exhaustion and depersonalization, reverse scoring is done for the competency sub-dimension. The total scores that can be obtained are between 0-20 points for EE and 0-16 points for DP and C sub-dimensions. High scores in the exhaustion and depersonalization sub-dimensions and low scores in the competence sub-dimensions indicate burnout. While there were 16 articles on the original scale, articles 6, 12 and 15 were removed in the Turkish adaptation study and the scale was given a final version of 13 articles. In the adaptation study, Cronbach Alpha internal consistency coefficients were reported as 0.76, 0.82 and 0.61 for EE, DP and C respectively, and test-retest reliability results were 0.76, 0.74 and 0.70 respectively (5). In our study, Cronbach's Alpha coefficients were found to be 0.83, 0.78, 0.68, respectively, for EE, DP, and C sub-dimensions. Accordingly, the data was considered to be sufficiently reliable and scale scores were calculated.

2.4. Statistical Analysis

Data were analyzed using the SPSS 25.0 (SPSS Inc., Chicago, IL, USA) statistical package program. Categorical variables were presented as numbers, percentages and numerical variables as mean and standard deviation. The suitability of numerical variables to normal distribution was investigated with the Kolmorov Smirnov Test and the calculated z values for skewness and kurtosis were investigated by graphing methods. In the analysis of continuous variables, Student T, One Way ANOVA, when necessary Kruskal Wallis, Mann Whitney U were used and Mann Whitney U with Bonferroni correction was used in post-hoc analyses while χ^2 tests were used for categorical variables. Spearman's rho correlation analysis was used to investigate the relationships between continuous variables. Ordinal logistic regression analysis was conducted to evaluate the independent variables affecting the probability of inclusion of participants in the EE, DP, and C groups determined according to defined cut-off points. A confidence analysis was conducted on the articles of both scales, the Cronbach Alpha coefficient was calculated. The statistical significance level was accepted as $p<0.05$.

3. Results

3.1. Participants' Sociodemographic Characteristics

1009 volunteer students participated in the study. Sociodemographic characteristics of students are presented in Table 1. The mean age was 19.8±2.5 years, 52.2% (n=527) were female. 352 (34.9%) were first graders, 349 (n=34.9%) were second and 308 (n=30.5%) were third graders. 59.8% of students do sports, 23.6% have pets, 24.3% play a musical instrument, 36.2% are members of a student club and 20.5% have a date.

3.2. Scores according to the sub-dimensions of burnout and their relationship with various variables

Students' EE score was 10.4±4.6, while DP score was 6.4±3.7 and C score was 9.2±2.9. Semester I students had the lowest EE (9.3±4.4) and DP (5.3±3.5) scores while their C scores (9.7±2.7) were highest and there was a significant difference between semesters in terms of all three score types ($p<0.001$). When evaluated in terms of genders, the mean EE score in students was significantly higher in favour of women ($p=0.025$) and the mean DP score was significantly higher in favour of men ($p=0.031$). The average score for the competency was higher in women, but no significant difference was observed ($p=0.061$). The EE and DP score averages of regular sports students were significantly lower than those who did not play sports and their C score averages were significantly higher ($p<0.001$, $p=0.022$, $p<0.001$, respectively). The mean scores of exhaustion and depersonalization were significantly higher in students who had pets. ($p=0.010$, $p=0.036$, respectively). Although the mean scores of EE and DP were high in students who could play a musical instrument, it was not significant ($p=0.457$, $p=0.914$, respectively). On the other hand, the mean C score was found to be significantly higher in students who could play musical instruments ($p=0.009$). The mean scores of EE, DP and

C were similar in terms of being a member of a student club and having a date (p>0.05) (Table 1).
There was no significant relationship between the ages of the students and their EE, DP and C scores (p>0.05). The overall grade point average of the study group was 79.9±8.9, which was the highest in first year students (83.8±8.9). EE (r=-0.133, p<0.001) and DP (r=-0.173, p<0.001) scores were negatively and C scores (r=0.0.219, p<0.001) were positively associated with grade point average. When looking at the relationship between the burnout subdimensions themselves, there was a positive relationship between EE and DP scores (r=0.718, p<0.001), negative between C scores (r=-0.450, p<0.001) and significant negative (r=-0.487, p<0.001) between DP and C scores. (Table 2).
In the evaluation made by accepting the median of the scores of the scale dimensions as the cut-off point, it was observed that 61.9% (n=625) of the students experienced emotional exhaustion, 21.5% (n=217) depersonalization and 53.5% (n=540) loss of competence (Figure 1).

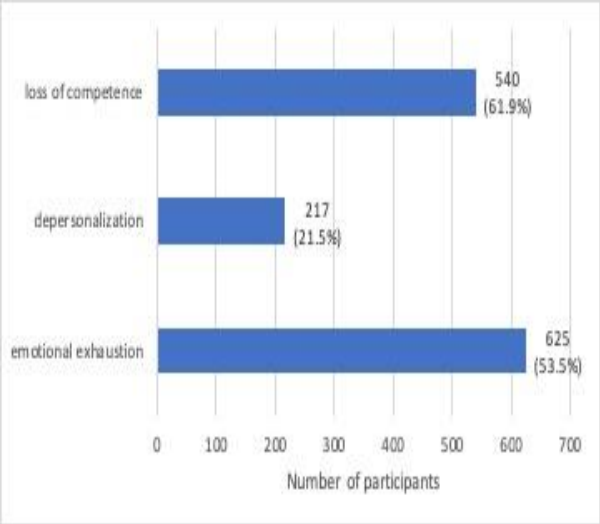

Figure 1: Frequency of emotional exhaustion, depersonalization and loss of competence.

Table 1: Scale scores according to sociodemographic characteristics.

		Emotional exhaustion	**Desensitization**	**Competence**
Sociodemographic characteristics	n (%)	Mean±SD	Mean±SD	Mean±SD
Grade (n=1009)		**p<0.001**	**p<0.001**	**p<0.001**
I	352 (34.9)	9.3±4.4[a,b]	5.3±3.5[a,b]	9.7±2.7[a]
II	349 (34.6)	10.9±4.7[a]	7.2±3.9[a]	8.7±3.2[a,b]
III	308 (30.5)	11.0±4.4[b]	6.8±3.5[b]	9.3±2.6[b]
Gender (n=1009)		**p=0.025**	**p=0.003**	p=0.061
Female	527 (52.2)	10.7±4.5	6.1±3.7	9.4±2.7
Male	482 (47.8)	10.1±4.6	6.8±3.8	9.0±3.0
Do you exercise regularly?(n=1009)		**p<0.001**	**p=0.022**	**p<0.001**
Yes	603 (59.8)	9.9±4.6	6.2±3.8	9.5±2.9
No	406 (40.2)	11.1±4.5	6.7±3.6	9.8±2.8
Do you have a pet? (n=1009)		**p=0.010**	**p=0.036**	p=0.611
Yes	238 (23.6)	11.1±4.8	6.9±3.6	9.3±3.0
No	771 (76.4)	10.2±4.5	6.3±3.8	9.2±2.8
Do you play a musical instrument? (n=1009)		p=0.457	p=0.914	**p=0.009**
Yes	245 (24.3)	10.2±4.6	6.4±3.9	9.7±3.0
No	764 (75.7)	10.5±4.6	6.4±3.7	9.1±2.8
Are you a member of a student club? (n=1009)		p=0.503	p=0.311	p=0.337
Yes	365 (36.2)	10.5±4.4	6.6±3.6	9.4±2.7
No	644 (63.8)	10.3±4.7	6.3±3.8	9.2±2.9
Do you have a date? (n=995)		p=0.974	p=0.525	p=0.974
Yes	204 (20.5)	10.4±4.6	6.6±3.6	9.2±3.0
No	791 (79.5)	10.4±4.6	6.4±3.8	9.2±2.8

[a, b]: There is a significant difference between the groups expressed with the same character.

Table 2: Correlations between participants' ages, grade point averages and scores of the scale sub-dimensions.

Variables		EE scores	DP scores	C scores
Age	r	-0.059	0.003	0.055
	p	0.061	0.921	0.083
Grade point average	r	-0.133	-0.173	0.219
	p	**<0.001**	**<0.001**	**<0.001**
Emotional exhaustion	r		0.718	-0.450
	p		**<0.001**	**<0.001**
Desensitization	r			-0.487
	p			**<0.001**

EE Emotional exhaustion, DP depersonalization, C competence.

4. Discussion

The findings of our study showed that intraoperative In this study, in which the burnout of preclinical medical students was investigated, emotional exhaustion and loss of competence were found in more than half of the students, and depersonalization was found in one of the five students.

Burnout is reportedly common among medical students in literature (13, 18). Dyrbye et al. (2010) found burnout in more than half of medical students (13). The rates found in our study are higher than the burnout rates reported in a meta-analysis of students' burnout (44%) (19).

In our study, it was observed that the mean scores of EE and DP were lower in the first grades than the other grades, and the mean scores of C were higher. Third graders experience EE more than first and second graders, and second graders experience more EE than first graders. This situation can be explained by the increase in the course load with the advancing class, the increasing difficulty of medical education, and the increase in academic concerns. Similarly, it was observed that C scores decreased in the second grades. Studies have reported that burnout is higher in third-year students than in first and second-year students. Our results are in parallel with the literature (20-22).

The increase in burnout and depersonalization with the increase in educational years supports the idea that the foundations of burnout syndrome seen in physicians are laid during student years (7, 23). In a study conducted with senior students at the same faculty, the fact that all three sub-dimension scores were higher than this study (23) can be interpreted as an increase in all dimensions of burnout with medical education. However, there are also studies reporting that there is no difference between classes in terms of burnout (24).

In our study, there was no significant relationship between the age of the students and the burnout sub-dimension scores. This may have been due to the fact that the ages of the students were close to each other. Findings on the relationship between age and burnout are contradictory in the literature. In two separate studies (25, 26) and another multicenter study conducted with interns, no relationship was found between age and burnout (7), and another study reported that EE and DP increase with age (27). In a study by Koşan et al. with physicians, it was found that C increased and DP decreased as age increased (28).

EE scores in women were significantly higher than in men. This may be related to gender characteristics such as women being more emotional. On the contrary, in the studies of Zheng et al (29) and Li et al. (30) it is reported that EE is higher in men. In our study, DP scores were significantly higher in males. Similar results were obtained in studies conducted with physicians (31, 32).

Although competency scores were higher in females than males in our study, it was not statistically significant. Datas in the literature on this subject are contradictory. Results which were similar to our results were reported in the study of Yang et al. (22). However, some studies report that there is no significant difference in the total burnout score between men and women (1, 24).

It is reported that burnout is less common in students who do sports regularly (18). In our study, EE and DP were significantly lower and competency scores were significantly higher in students who did sports compared to those who did not ($p<0.001$, $p=0.022$, $p<0.001$, respectively). According to this result, it can be said that physical activity is a protective factor on burnout and students who do sports feel more competent (Table 1). Our study results are compatible with the literature.

Supporting students in terms of both leisure time and facilities to enable them to do sports activities in institutions can be effective in preventing student burnout (18). In a study, it was reported that sports, music and socialization are effective as common coping strategies in preventing burnout (33). Datas on extracurricular activities are contradictory. While no relationship was found between extracurricular activities and burnout levels in one study (34), it was reported to reduce burnout in another study (35).

In our study, it was observed that the EE and DP scores of the students who had pets were significantly higher than those who did not. This situation may be related to the emotional personality characteristics of those who keep pets.

In this study, although the students' EE and DP score averages were similar according to their playing a musical instrument, their competence score averages were significantly higher. In various studies, participation in social, artistic and cultural activities was associated with higher levels of competence (36, 37). In this sense, it can be accepted that playing an instrument is a factor that increases students' self-confidence and sense of competence and prevents burnout.

Average scores for all three dimensions were similar according to membership in a student club and dating status. The fact that students spend time at home and stay away from some social activities due to pandemic conditions may have an impact on the results. In this study, the students with high grade point averages had significantly lower EE and DP mean scores, while their C mean scores were also significantly higher. It is seen that as the EE and DP scores of the students' decrease, their academic success increases and they feel more competent while academic failure causes a decrease in the competence of the students (Table 2).

In a study conducted in Nepal, similar results were obtained with our study and it was reported that academic achievement had a protective effect on burnout (38). In a study conducted with intern doctors, it is reported that burnout is higher in students who couldn't finish medical school on time (39).

In our study, it was observed that there was a significant and positive relationship between students' EE and DP scores. Emotional exhaustion also brings about depersonalization in students. Similarly, in this study, there were significant negative relationships between EE and DP with C scores. While students who do not experience emotional exhaustion and DP feel more competent, it is seen that there is a loss of competence in students who experience EE and DP. In a study conducted in healthcare professionals in our region, a positive relationship was found between EE and DP, and a negative relationship between EE and personal achievement in line with our findings together with high levels of burnout (1).

Factors such as dissatisfaction with lessons, lack of peer support, heavy workload, stress and lack of leisure time are reportedly important factors for burnout and social support is important in preventing burnout (7). Families and schools play an important role. Providing physical environments in schools where students can socialize, leaving free time in the curriculum where students can deal with their special interests and spare time for their hobbies can contribute to reducing burnout.

5. Conclusions

In this study conducted during the COVID-19 pandemic and during the online education process, emotional exhaustion was detected in 61.9% of students, depersonalization in 21.5% and loss of competence in 53.5%. These results show that more than half of the students' experience emotional exhaustion and loss of competence. The study is important in that burnout has not been investigated in the same population before and it provides data about medical students. It can be said that individual and institutional preventive strategies are needed to prevent the burnout of medical students who are the physicians of the future.

Limitations of the Study

The study has some limitations. Firstly, the results of our cross-sectional study with preclinical students of a single medical school cannot be generalized for medical school students. The scale used for the study is a self-report tool and prejudice is difficult to avoid. Students without internet access may not have been able to participate in the study because the data was collected online. The clinical students were not included in the study. Finally, the challenges of the pandemic and factors related to online education were not included in the study.

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Conflict of Interests

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Author Contributions

ECT, EBY designed the research, and participated in data collection. SY did the data analysis. ECT, SY, ZK, EBY, AA wrote the manuscript, read and approved the final script.

Ethical Approval

Ethical permissions were taken by the Atatürk University Clinical Research Ethical Committee (IRB No.B.30.2.ATA.0.01.00/252-04/70 Date: 27.05.2021). The study was carried out in accordance with the rules of the Helsinki Declaration.

Data sharing statement

None

Informed Consent

Informed consent was obtained from all participants included in the study.

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Comparison of Impulsivity and Eating Attitude According to Exercise Status

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Abstract: The aim of this study was to compare the impulsivity and eating attitudes of volleyball players and sedentary students, and determine the possible effects of regular exercise on these attitudes. A total of 65 participants, 32 volleyball players and 33 sedentary individuals voluntarily participated in this study. A Personal Information Form, Eating Attitudes Test (EAT-40), and Barratt Impulsiveness Scale were administered to the participants. Independent Samples t-test, Pearson Correlation test, and Multiple Regression analysis were used in the statistical analysis. No statistically significant differences were found between the total scores of the volleyball players and sedentary participants in terms of eating attitudes and impulsivity. However, significant differences were found in the sub-dimensions of non-planning and motor impulsivity ($p<0.05$). Moreover, a statistically significant positive correlation was found between the total scores of the Eating Attitudes Test and the total scores of the Barratt Impulsiveness Scale ($r=.378$, $p=.002$). Statistically significant positive correlation was found between the Eating Attitudes Test total scores and motor ($r=.448$, $p=.000$) and attentional impulsivity ($r=.263$, $p=.035$). A significant interaction was detected between the sub-dimensions of the Barratt Impulsiveness Scale (non-planning, motor and attention impulsivity), and the total scores of Eating Attitudes Test ($R=.455$, $R^2 = .207$, $p<0.01$). The t-test results regarding the significance of the regression coefficients showed that the motor impulsivity variable was an important predictor of eating attitude. This study demonstrated that regular exercise is a significant predictor of motor impulsivity on eating attitudes of regularly trained volleyball players as compared to sedentary participants.

Keywords: Volleyball; Athlete; Sedentary; Eating Attitude; Impulsivity.

1. Introduction

Exercise is a set of regular, planned and repetitive activities aimed at maintaining and improving cardiovascular endurance, hormonal balance, physical and mental fitness (1,2). Regular exercise has positive

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effects on physiological, metabolic and psychological health as well as beneficial effects on chronic diseases (3). Regular exercise is very important in both body weight and appetite control (4). It has been shown that exercise is also effective on the individual's self-esteem and stress management, and reduces depression level (5).

Impulsivity has been associated with many issues such as not making a plan, not taking risks in the face of events, and displaying reactive behaviors in the context of neurophysiological, psychological and behavioral characteristics that affect the individual's life (6). Impulsivity is defined as the inability to fully interpret the stimuli reaching the cerebral cortex and to generate the appropriate response, the responses result in a quick unplanned response, and the behavior becomes desensitized to the negative consequences of the given response (7). Impulsivity physiologically stimulates the urge to eat in individuals, causing uncontrolled eating behavior and enabling them to turn to foods (especially simple carbohydrates) that are more harmful than beneficial to the body. Individuals with impulsivity are more interested in appetizing, high-calorie foods because they cannot control their eating behavior (8,9). Eating behavior is associated with many complex regulations including social and emotional development, managed by the motor and sensory functions of the brain. Eating behavior is not only a behavior to meet the essential needs of the body, but also associated with pleasurable and painful patterns (10). Eating disorder is a condition that is related to body weight and appearance, but occurs with thought and eating behavior pathology (11). In this case, the individual's eating attitude and body image deteriorates (12). Several studies have indicated that regular exercise reduces body dissatisfaction (13), facilitates weight gain in anorexia nervosa (14), reverses cardiac abnormalities (15) and improves quality of life (16).

The current study evaluated the sub-dimensions of impulsiveness in volleyball players, and the relationship between impulsive consumption patterns and eating attitudes in athletes. Although exercise is an effective intervention for many psychological health problems, it has been overlooked as a potential aid in impulsivity and eating attitudes. Therefore, the aim of this study is to compare the impulsivity and eating attitude levels of volleyball players and sedentary students, and to determine the possible effects of regular exercise on these attitudes.

2. Material and Methods

The purpose of this study was to compare the impulsivity and eating attitude levels of volleyball players and sedentary students, and to determine the possible effects of regular exercise on these attitudes. The relational screening model, which is one of the general screening models, was used in the current study. This model is a screening method applied to the whole universe or a smaller group taken from the universe in order to have a general opinion about this universe from a universe with a large number of members (17). Also, relational screening model is a screening approach that detects common differentiation in two or more variables. Relational screening models aims at determining the presence and/or level of change between two or more variables and specifies the relationships between these variables. (18).

The study aimed at achieving the following sub-objectives:

- What are the eating attitude levels of the participants?
- What are the impulsivity levels of the participants?
- Is there a relationship between the eating attitudes of the participants and their impulsivity levels?
- What is the effect of impulsivity on eating attitude?

2.1. The hypotheses of the research

- H0= There is no relationship between the eating attitude of the participants and their level of impulsivity.
- H1= There is a strong relationship between the eating attitude of the participants and their level of impulsivity.

2.2. The universe and sample of the research

The universe of this research consisted of volleyball players (n:32) who study at different programs of a University and completed 60 minutes of volleyball training, and 20 minutes of strength training at least 3 days a week and sedentary students (n:33) who did not exercise regularly. The number of volleyball players and sedentary students and their descriptive data are shown in Table 1. The Barratt Impulsiveness Scale and Eating Attitudes Testcale were administered to the participants within the scope of the research, and the data were collected. Research and Publication Ethics have been complied. Permission was obtained from the University Sports Sciences Faculty Ethics Committee (Date: 17.03.2021, Number: 70400699-050.02.04-E.2100083816). In addition, individuals who agreed to participate in the study were asked to read and sign the Informed Consent Form, and the study was carried out in accordance with the Principles of the Declaration of Helsinki.

2.3. Data collection tools

The Personal Information Form, Barratt Impulsiveness Scale and the 'Eating Attitudes Test (YTT-40), which have reliability and validity were administered to the potential clients.

2.4. Personal Information Form

The personal information form designed by the researchers consisted of questions including gender, age, height, weight, body mass index, and exercise status of the participants.

2.5. Barratt Impulsiveness Scale

The Barratt Impulsiveness Scale was developed by Patton, Stanford, and Barrat (1995) to evaluate the personality/behavioral structure of impulsivity and measures motor, behavioral, cognitive, and thought impulsivity. The scale contains 30 items, and has three sub-dimensions-attentional, motor and non-planning. Four types of scores are achived in the scale, including the total score and the total scores of each sub-dimension (attentional, motor and non-planning). The Turkish validity and reliability study of this scale was conducted by Gulec et al. (2008), and the internal consistency coefficient of the scale was found to be 0.78 for students, and 0.81 for patients. The current study revealed that the internal consistency of the scale was tested using Cronbach's alpha (Cronbach α 0.77).

2.6. Eating Attitudes Scale (EAT-40)

EAT-40 is a scale developed with the aim of evaluating possible disorders in eating behavior and identifying problematic eating behaviors. The scale was developed by Garner and Garfinkel in 1979, and the validity and reliability of the Turkish version of the scale was established by Savasir and Erol (1989) (19). EAT-40 is a self-report format questionnaire with 40 items and each item is rated on a 6-point Likert Scale. A score of 30 and greater on this scale indicates greater disordered eating attitudes. Previous studies reported that individuals with a score above 30 except 7% of participants exhibited eating behavior disorder (20, 21). The total score is directly related to the level of psychopathology. EAT-40, in addition to detecting people who can be clinically determined as "patients", can also show the susceptibility to the risk of developing psychopathology. The internal consistency coefficient of the scale was found to be 0.70 in Turkish adaptation study conducted by Savasir and Erol (1989) (20). For the current study, the internal consistency of the scale was tested using Cronbach's alpha (Cronbach α 0.75).

2.7. Statistical Analysis

SPSS 20.0 package program was used in the analysis of the data. The normality of the data was evaluated with the Kolmogorov-Smirnov Test. According to this test result, all data showed normal distribution. Independent Sample t-test was used to compare the eating attitudes and impulsivity levels of volleyball players and sedentary participants. The relationship between the eating attitude of the participants and their level of impulsivity was analyzed with Pearson Correlation Test. Additionally, Multiple Regression Analysis was performed to show the level of impulsivity predicting eating attitude. Data obtained from the scales were reported as mean and standard deviation, and data obtained from demographic characteristics were reported as frequency distribution. The level of $p<0.05$ was accepted as statistically significant.

3. Results

The demographic characteristics of the participants, the scales scores, and the findings related to the research questions were included in this section.

3.1 The Demographic Characteristics of Participants

64.6% of the 65 students constituting the sample group of the study were female (n=42), while 35.4% were male (n=23). On the other hand, 32 of 65 students were volleyball players who exercised regularly, whereas 33 of them were sedentary participants who did not exercise regularly. The mean age, height, and body weight of the students were found to be 19.63±.99 years, 168.95±9.04 cm, and 62.27±11.93 kg, respectively (Table 1).

Table 1: The Descriptive Statistics of Volleyball Players and Sedentary Participants.

Descriptive Data	Volleyball players n (%)	Sedentary n (%)	Total (%)
Gender			
Female	16 (50)	26 (78.8)	42 (64.6)
Male	16 (50)	7 (21.2)	23 (35.4)
Age			
18-19	12 (37.5)	19 (57.6)	31 (47.7)
20-22	20 (62.5)	14 (42.4)	34 (52.3)
Body Mass Index			
Underweight (18.5 kg/m²)	2 (6.9)	3 (10.0)	5 (8.5)
Normal (18.5-25 kg/m²)	22 (75.9)	23 (76.7)	45 (76.3)
Overweight (25-30 kg/m²)	5 (17.2)	4 (13.3)	9 (15.3)

Table 2: Comparison of Eating Attitude Levels according to Exercise Status.

	Groups	N	Mean	S.D.	t	p
Eating Attitude Total Score	Volleyball players	32	18.97	10.83	.792	.431
	Sedentary	33	17.21	6.61		

As shown in Table 2, it was observed that there was no statistically significant difference in the comparison of the eating attitude levels of the volleyball players and sedentary participants (p>0.05).

Table 3: Comparison of Impulsivity Levels according to Exercise Status.

	Groups	N	Mean	S.D.	t	p
Total Score	Volleyball players	32	61.22	7.34	.661	.511
	Sedentary	33	60.00	7.51		
Non-planning impulsivity	Volleyball players	32	22.56	2.86	-2.905	.040*
	Sedentary	33	24.42	4.16		
Motor impulsivity	Volleyball players	32	21.06	3.99	2626	.011*
	Sedentary	33	18.70	3.23		
Attentional impulsivity	Volleyball players	32	17.28	3.44	.500	.619
	Sedentary	33	16.88	3.03		

* p< .005.

As shown in Table 3, significant differences were found in the sub-dimensions of non-planning impulsivity and motor impulsivity between volleyball players and sedentary participants (p<0.05). There was no statistically significant difference in the total score and attentional impulsivity sub-dimension (p>0.05).

Table 4: The Relationship between Eating Attitudes and Impulsivity Levels.

			Total score	Non-planning	Motor	Attentional	Eating Attitude Total score
Barratt Impulsivity Scale	Total score	r	1				
		p	.				
	Non-planning	r	.594**	1			
		p	.000	.			
	Motor	r	.763**	.181	1		
		p	.000	.149	.		
	Attentional	r	.743**	.122	.456**	1	
		p	.000	.334	.000	.	
Eating Attitude Scale	Total score	r	.378**	.040	.448**	.263*	1
		p	.002	.753	.000	.035	.

*p< 0.05, **p< 0.01, *** p< 0.001.

According to Table 4, a statistically significant positive correlation was found between the total score of the eating attitude scale and the total score of the impulsivity scale (r=.378, p=.002). These results indicated that as impulsivity level increased, so did the eating attitude levels of the participants. Moreover, a statistically significant positive correlation was found between the Eating Attitude Test total score and motor (r=.448, p=.000), and attentional impulsivity (r=.263, p=.035).

Table 5: Multiple Regression Predicting Eating Attitudes.

Variables	**B**	**SE B**	**B**	**T**	**p**
(Constant)	-2.570	8.394		-.306	.760
Non-planning impulsivity	-.111	.282	-.046	-.395	.694
Motor impulsivity	.992	.304	.422	3.260	.002
Attentional impulsivity	.209	.354	.076	.589	.558
R = .455	R^2 = .207				
$F_{(3,61)}$ = 5313	p = .003				

Table 5 shows that there was a significant interaction between the sub-dimensions of the Barratt Impulsiveness Scale (non-planning, motor and attention impulsivity), and the total score of Eating Attitudes Test ($R=.455$, $R^2 = .207$, $p<.01$). These three variables jointly explain approximately 21% of the variance in eating attitudes. According to the standardized regression coefficient (β), the relative ranking of the predictor variables to the eating attitude was found to be motor, attentional and non-planning impulsivity. When the significance of the regression coefficients was analyzed in terms of the t-test results, it was found that the motor impulsivity variable played an important role as a predictor of the eating attitude. The study results demonstrated that the variables of non-planning and attentional impulsivity did not have a significant predictor.

4. Discussion

The aim of this study was to compare the impulsivity and eating attitudes of volleyball players and sedentary students, and to determine the possible effects of regular exercise on these attitudes. The present study showed that volleyball players and sedentary participants had similar levels in terms of total eating attitudes, total impulsivity, and attention impulsivity. It is a well-known fact that exercise affects our nervous system and especially our hormones, which play a role in our emotions and psychology (22). One of the hormones that increase production when exercising and making a person feel happier and more energetic is endorphins. (23). The present study also demonstrated that non-planning impulsiveness was higher in sedentary participants than volleyball players, and motor impulsivity scores were higher in volleyball players than sedentary participants.

Unplanned impulsivity indicates that sedentary students do not like to engage in tasks involving mental complexity and cognitive participation in planning their lives, they are focused on the moment they live in, and their instability in making plans by acting without thinking about the future. Similar to our study, it is stated that exercise positively affects behaviors and cognitive functions such as impulse control and decision-making functions, as well as reducing unplanned impulsivity (24).

On the other hand, the fact that the motor impulsivity scores of volleyball players were higher than those of sedentary participants indicates that the tendency of volleyball students to act without thinking is higher than sedentary students.

Previous studies showed that higher rates of motor impulsivity were reported in male university students compared to females in our country (25, 26). The higher number of male participants in the volleyball players group compared to the sedentary participants group may have been effective in this result. Furthermore, although body mass index and eating attitudes did not differ between the volleyball players group and the sedentary participants group, significant impulsivity differences were found. In contrast to our results, recent studies stated that high rates of overweight and obesity among university students were also reported to be associated with physical inactivity (27). Adding regular exercises to daily routines is defined as a health-promoting lifestyle (27). As obesity rates increase worldwide, there is a need for methods to adopt the lifestyle behaviors necessary for sustainable weight loss (28).

The results of this study have also shown that there was a positive and significant relationship between impulsivity and disorder in eating attitudes. The association of impulsive personality traits with impaired eating behaviors, binge eating disorders, and increased body mass index has attracted attention. Similar to our results, previous research have also demonstrated that high levels of impulsivity were observed in university students with impaired eating behaviors. (29, 30).

The present study also revealed that motor impulsivity was an important predictor of eating attitude. Motor impulsivity is characterized by a lack of behavioral control and acting quickly without adequate consideration of consequences. In one study, impulsive traits were shown to be indirectly related to obesity, and high-risk behaviors that cause an increase in addictive food consumption (30). Recent systematic reviews and meta-analyses have identified impulsive traits as a potential etiological and/or maintenance factor for binge eating behavior (31).

It was recommended that regular exercise, which was among the behavioral interventions that were effective in treating impulsivity, also associated with many psychopathologies, should be included in the improvement of psychosocial well-being (32). Also, increasing physical activity with regular exercise could help compensate and suppress the hedonic urge to overeat (33, 34). Considering that regulating behavior is based on the effectiveness of sufficiently suppressing impulsive responses to external stimuli, it seems surprising that motor impulsivity kept being a problem for the volleyball players group that regularly exercised. Motor impulsivity, which can be reflected as the tendency to be quick in reacting to the arrival of the ball in volleyball players in our study group, can also be reflected as agility in sports when combined with foresight, the cognitive component in which planning and position are well predicted (35). Motor impulsivity can be associated with the performance required for agility by providing rapid body movement with a change in speed or direction in response to a stimulus. On the other hand, if it is not balanced with the cognitive component, it can also be associated with the risk of injury by causing reckless behavior (36).

5. Conclusions

The present results support that impulsivity can be considered as a risk factor for individuals to develop eating psychopathology. There are some limitations in our study. The cross-sectional nature of the study is not sufficient to establish a cause-effect relationship. Our sample is relatively small and its average BMI is classified as normal. It may be useful to perform similar studies in larger groups of overweight or obese individuals and in more gender-balanced samples. Despite these limitations, to our knowledge this was the first study to evaluate the sub-dimensions of impulsiveness in volleyball players, and the relationship between impulsive consumption patterns and eating attitudes. Lastly, the present study revealed valuable findings that will encourage behavior change among those with a sedentary lifestyle.

Limitations of the Study

There are some limitations in our study. The cross-sectional nature of the study is not sufficient to establish a cause-effect relationship. Our sample is relatively small and its average BMI is classified as normal. It may be useful to perform similar studies in larger groups of overweight or obese individuals and in more gender-balanced samples.

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Conflict of Interests

The authors approved that they have no conflict of interest

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Author Contributions

Ozturk, D., Ceyhun Akgül, H. contributed to the constructing the idea for research. Ozturk, D., Ceyhun Akgül, H. and Oral M. contributed to the planning the design of the work. Data Collection and/or Processing- Ozturk D., Oral, M. Analysis and/or Interpretation – Oral M.; Literature Review Ozturk, D., Ceyhun Akgül, H. and Oral, M.; Writing Manuscript- Ozturk D.; Critical Review- Ozturk, D., Oral, M. and Ceyhun Akgül, H.

Ethical Approval

The study was approved by Atatürk University Sports Science Faculty Ethics Committee with the decision dated 17.03.2021 and numbered 70400699-050.02.04-E.2100083816.

Data sharing statement

None

Informed Consent

Informed consent was obtained from all individual participants included in the study.

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The Importance of Bıochemical and Hematological Parameters in Pleural Effusion Etiology

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Abstract: Pleural effusion, the pathological collection of fluid in the pleural space, is very widespread. Light's criteria are still the most commonly used initial laboratory test to determine the etiology of pleural effusion. We purposed to examine the usability of routine laboratory parameters in the differentiation of exudate-transudate. The 150 patients hospitalized in the chest diseases service due to pleural effusion etiology were retrospectively analyzed between January 2018 and December 2019. The patients were divided into two groups according to Light's criteria as exudate and transudate. The pleural fluid data, routine laboratory parameters and radiological image features compared between both groups. Significantly higher serum C-reactive protein (C-RP) values were found in patients with exudative pleural effusion, and significantly higher serum mean platelet volume (MPV) and lower serum platelet values were found in patients with transudative pleural effusion. The serum MPV was negatively correlated with serum platelet. The serum MPV, platelet and C-reactive protein values may be candidate parameters to support the Light's criteria in the differential diagnosis of transudate and exudate pleural fluid.
Keyword: Pleural Effusion; Exudate-Transudate; MPV, Platelet; C-RP.

1. Introduction

Pleural effusion, the pathological collection of fluid in the pleural space, is very widespread. The etiological distribution of pleural effusions is related to the age of the patient, the region, s/he lives in, clinic or hospital where the study was conducted and the advances in diagnostic methods (1). Its the most common causes are cancer, pneumonia and congestive heart failure. In addition, tuberculosis is a significant reason of pleural effusion in our country (2, 3).

Light's criteria are still the most commonly used initial laboratory test to determine the etiology of pleural effusion (4). Whether a pleural effusion is a transudate or an exudate determines its further evaluation and treatment. Laboratory parameters used for light criteria; LDH, total protein, and albumin. Also, when the cholesterol and LDH concentration are evaluated together, a very specific result is obtained in the presence of exudate (5, 6). However, sometimes these

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criteria may be insufficient to distinguish between exudate and transudate, and clinicians may have difficulties in approaching patients. therefore, there is a need for new parameters that are easily accessible, inexpensive and reproducible.

Biochemical and hematological blood parameters such as C-reactive protein (C-RP), albumin, platelet, neutrophil and MPV play important roles in reflecting reactions such as inflammation and immune response (7). Recently, the platelet-lymphocyte ratio (PLR), neutrophil-lymphocyte ratio (NLR), C-RP albumin ratio (CAR) obtained from routine laboratory parameters have been shown as new inflammatory biomarkers in many studies (8-10). There are many studies emphasizing that these parameters may be a diagnostic/prognostic factor in patients with pleural effusion (11-15).

In this study, we purposed to examine the usability of routine laboratory parameters and a new inflammatory biomarker obtained from these parameters in the differentiation of exudate-transudate.

2. Material and Methods

Research and Publication Ethics has been complied with at all stages, with the realization and preparation of the study.

The 150 patients hospitalized in the chest diseases service due to pleural effusion etiology were retrospectively analyzed between January 2018 and December 2019. The study protocol was approved by the Harran University Faculty of Medicine, Ethics Committee (Approval No: HRU/21.10.02 and Approval Date: 24.05.2021). Patients over 18 years of age with radiological pleural fluid, patients with pleural fluid laboratory data obtained by thoracentesis (pleural fluid protein, LDH, albumin, glucose, cell count, pH values), and patients with routine laboratory data were included in the study. Patients under 18 years of age, patients with radiological pleural fluid detected but not applied thoracentesis and/or patients without pleural fluid laboratory data were excluded from the study (thirty-six patients). As a result, a total of one hundred and fourteen patients were included in this study. Demographic and laboratory information of the patients were obtained from the recorded data. Age, gender, clinical diagnosis, pleural fluid characteristics, radiological image features (anatomical region and amount of effusion), biochemical and haematological laboratory data of all patients were recorded. According to the amount of effusion according to the PA chest X-ray; non-massive fluid if one or both costophrenic sinuses are closed; submassive fluid if the area from the diaphragm to the level of the hilum is radiopaque; the fluid above the hilus level was defined as massive fluid. Glucose, total protein, LDH and albumin levels were measured in pleural fluid taken by thoracentesis and in peripheral venous blood taken simultaneously. The patients were divided into two groups according to Light's criteria as exudate and transudate (4). The classic Light's criteria are; fluid is considered exudative if it meets one or more of the following criteria: the absolute pleural fluid lactate dehydrogenase (LDH) level is >200; the pleural: serum LDH ratio is >0.6; and/ or the pleural: serum protein ratio is >0.5. The pleural fluid data, routine laboratory parameters, radiological image features, adenosine deaminase (ADA) levels and values such as the NLR, PLR, LMR and CAR were accepted as new inflammatory biomarkers compared between both groups.

2.1. Statistical analysis

Descriptive statistics are presented as Means±Standard Deviation or medians (25-75 interquartile range). The Kolmogorov-Smirnov test was used to determine whether the data were normally distributed. The student's t-test test was used to compare normally distributed data and the Mann-Whitney U test was used for non-normally distributed data. Spearman's correlation coefficient was used for correlation analysis. To predict exudative fluid according to ADA, C-RP and platelet levels, the cut-off value was determined using receiver operating characteristic (ROC) curve analysis. To predict transudative fluid according to MPV the cut-off value was determined using receiver operating characteristic (ROC) curve analysis. The level of statistical significance was set at $p<0.05$.

3. Results

A total of 114 patients (48 women and 66 men) were included in the study. Table 1 shows the pleural fluid characters, anatomical localizations and volumes, and clinical diagnoses of the patients. There was transudate-qualified pleural fluid in 31 patients and exudate-qualified pleural fluid in 83 patients. The most common diseases in all patients were malignancy, parapneumonic effusion, congestive heart failure and tuberculous pleurisy.

It was statistically significant that the fluids were seen in the right pleural space and the fluid volume was non-massive in the exudate group. When both groups were compared in terms of cell characteristics of the pleural fluid, there was a significant lymphocyte and neutrophil dominance and low pH value in the exudate group (Table 2).

Demographic and laboratory data of the patients in both groups were compared in Table 3. There was a significant difference between the groups in gender ratio and the mean age ($p=0031$, $p<0.001$). When both groups were compared; urea, creatinine and MPV values were found to be significantly higher in patients in the transudate group, while C-RP, ADA, and platelet values were found to be statistically higher in patients in the exudate group.

Correlation between variables was demonstrated using Spearman's test. The serum MPV was negatively correlated with serum platelet (r:-0.563; p<0.001) (Table 4).

According to the roc analysis, the cut-off value of C-RP≥4.3 with a sensitivity of 55% and specificity of 70%, and the cut-off value of platelet ≥279.5 predicted exudate pleural fluid with a sensitivity of 64% and specificity of 63% (Figure 1).

According to the roc analysis, the cut-off value of MPV ≥7.0 predicted transudative pleural fluid with a sensitivity of 66% and specificity of 64% (Figure 2).

Table 1: Clinical and radiological data of patients with pleural fluid.

	Number of patients (n=114)
Fluid type	
Transudate	29
Exudate	85
Anatomical region of fluid	
Right	52
Left	26
Bilateral	36
Amount of Fluid	
Nonmassive	49
Submassive	46
Massive	19
Clinical diagnosis	
CHF	21
PPE	25
TB pleurisy	14
Malignancy	35
Empyema	10
CKF	4
PTE	5

CHF, Congestive heart failure; PPE, parapneumonic effusion; TB, tuberculosis; CKF, chronic kidney failure; PTE, pulmonary thromboembolism.

Table 2: Comparison of pleural fluid features between groups.

	Transuda (n=29)	Exuda (n=85)	P
Amount of Fluid (%)			
Nonmassive	13 (44.8)	36 (42.4)	0.069
Submassive	15 (51.7)	31 (36.5)	
Massive	1 (3.4)	18 (21.2)	
Anatomical region of fluid (%)			
Right	5 (17.2)	47 (55.3)	**<0.001**
Left	2 (6.9)	24 (28.2)	
Bilateral	22 (75.9)	14 (16.5)	
Pleural fluid lymphocyte, $\times 10^3$/mL	0.01 (0.0-0.23)	0.07 (0.03-0.22)	**0.007**
Pleural fluid neutrophil, $\times 10^3$/mL	0.0 (0.0-0.05)	0.02 (0.01-0.13)	**0.032**
Pleural fluid monocyte, $\times 10^3$/mL	0.0 (0.0-0.04)	0.0 (0.0-0.05)	0.188
Pleural fluid pH	7.43 ± 0.06	7.35 ± 0.17	**0.004**
ADA levels, U/L	12.2 (7.3-35.7)	38.6 (24.6-58.0)	**0.004**
Clinicals diagnosis			
CHF	21	0	
PPE	0	25	
TB pleurisy	0	14	**<0.001**
Malignancy	0	35	
Empyema	0	10	
CKF	4	0	
PTE	4	1	

ADA, adenosine deaminase; CHF, Congestive heart failure; PPE, parapneumonic effusion; TB, tuberculosis; CKF, chronic kidney failure; PTE, pulmonary thromboembolism.

Table 3: Comparison of demografic and laboratory data between groups.

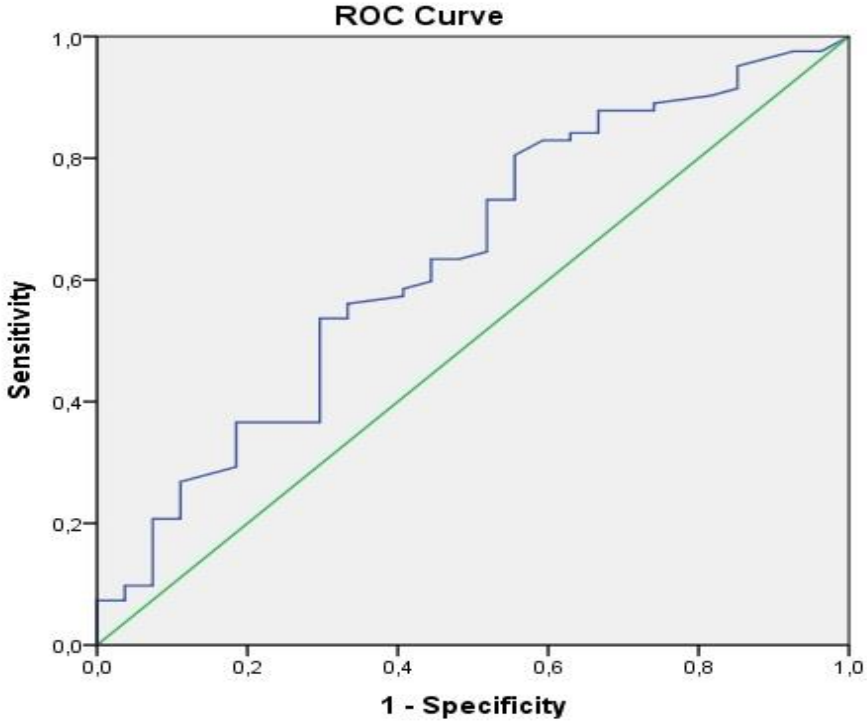
	Transuda (n=29)	Exuda (n=85)	P
Age, years	70.0 (57.5-79.5)	51.0 (32.0-69.0)	**<0.001**
Gender, f/m	8/21	40/45	0.067
Glucose, mg/dl	121.0 (95.0-169.5)	109.0 (91.0-138.5)	0.172
Urea, mg/dl	59.0 (42.8-107.0)	28.5 (20.0-40.2)	**<0.001**
Creatinine, mg/dl	1.2 (0.7-1.8)	0.7 (0.6-0.8)	**<0.001**
AST, U/L	20.0 (12.0-35.0)	20.0 (13.2-27.7)	0.493
ALT, U/L	19.0 (14.0-41.0)	21.0 (12.0-30.7)	0.677
T.Bilirubin, mg/dl	0.7 (0.4-0.9)	0.5 (0.3-0.7)	0.094
Albümin, g/dl	2.7 ± 0.8	3.2 ± 0.5	0.059
Sodium, meq/l	137.8 ± 3.8	136.7 ± 3.7	0.756
Potassium, meq/l	4.4 ± 0.8	4.2 ± 0.5	0.089
CRP, mg/dL	3.0 (0.6-8.6)	5.2 (1.6-12.3)	**0.036**
WBC count, $\times 10^3$/mL	8.0 (7.1-12.5)	10.3 (7.8-13.2)	0.166
Lymphocytes, $\times 10^3$/mL	1.5 (0.8-2.3)	1.6 (0.9-2.4)	0.851
Neutrophils, $\times 10^3$/mL	6.1 (4.6-10.0)	7.2 (5.1-10.3)	0.325
Monocytes, $\times 10^3$/mL	0.7 (0.4-0.8)	0.7 (0.5-1.1)	0.141
Eosinophils, $\times 10^3$/mL	0.0 (0.0-0.2)	0.1 (0.0-0.3)	0.060
Hemoglobin, g/dL	10.9 ± 2.6	11.9 ± 2.3	0.206
Hemotocrit, %	35.1 ± 7.9	38.4 ± 7.2	0.189
MPV, fL	7.6 (6.6-8.2)	6.6 (5.8-7.4)	**0.005**
MCV, fL	86.8 ± 8.6	84.2 ± 7.9	0.977
Platelet count, $\times 10^3$/mL	227.0 (177.5 -346.0)	334.0 (235.7-444.7)	**0.009**
RDW, %	14.0 ± 2.1	13.6 ± 2.6	0.210
ERS, h	29.5 (4.5-72.0)	50.0 (20.5-64.5)	0.220
NLR	4.9 (2.9-8.5)	4.5 (2.5-9.6)	0.981
LMR	2.0 (1.2-3.5)	2.1 (1.1-3.5)	0.975
PLR	160.0 (114.3-269.2)	211.6 (133.9-314.7)	0.085
CAR	1.3 (0.2-3.3)	1.6 (0.5-4.0)	0.228

AST, aspartate transaminase; ALT, alanine transaminase; CRP, C-reactiveprotein; WBC, white blood cell; MPV, mean platelet volume; MCV, mean corpuscular volume; RDW, red cell distribution width; ESR, erythrocyte sedimentation rate; NLR, neutrophil-lymphocyte ratio; LMR, lymphocyte-monocyte ratio; PLR, platelet-lymphocyte ratio; CAR, C-reactive protein to albumin ratio.

Table 4: Spearsman Correlation of Variables.

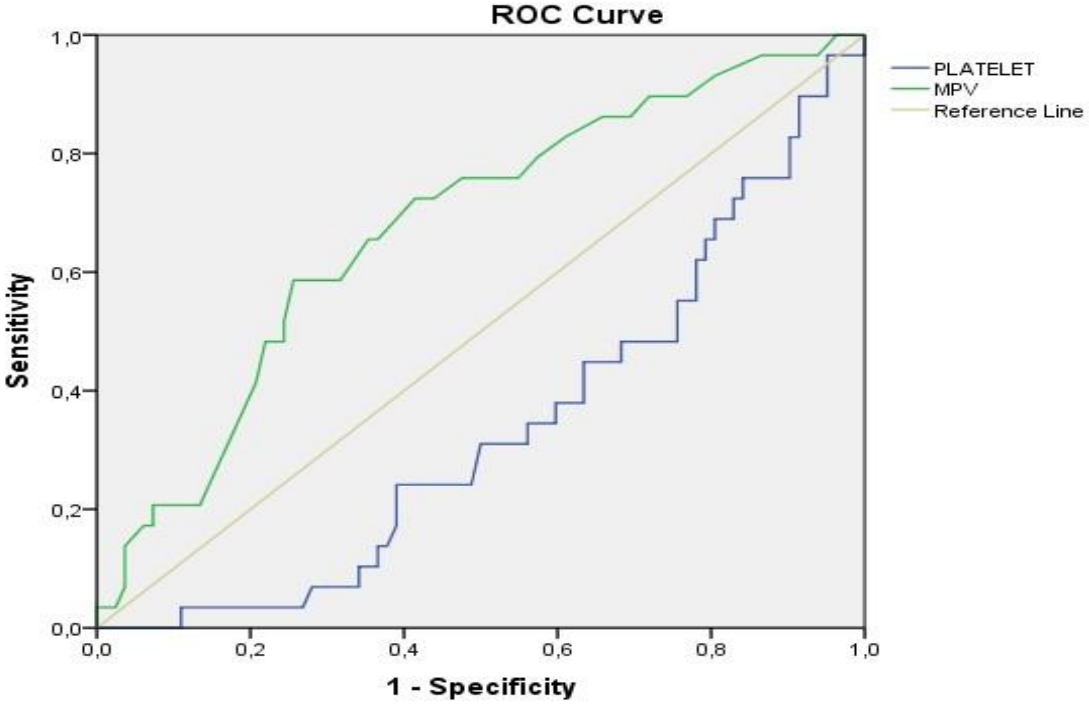
Variables	**Mean**	**SD**	**1**	**2**	**3**
1. MPV, fL	7.0	1.4	—	- 0.563**	- 0. 043*
2. Platelet,$\times 10^3$/mL	324.2	150.4		—	0.069*
3. C-RP, mg/dL	7.3	8.0			—

*p>0.05, **p<0,001.



Variables	AUC	95%Cl	P
C-rp	0.635	0.512-0.757	0.036

Figure 1: Receiver operating characteristics (ROC) curve of C-rp for predicting the exudate fluid.



Variables	AUC	95%Cl	P
MPV	0.676	0.564-0.788	0.005
Platelet	0.337	0.229-0.445	0.009

Figure 2: Receiver operating characteristics (ROC) curve of MPV and platelet for predicting the transudative fluid.

4. Discussion

In this study, we found significantly higher serum C-RP values in patients with exudative pleural effusions, while we found significantly higher serum MPV and lower serum platelet values in patients with transudative pleural effusions.

Pleural effusion is a common pathological condition that may occur due to many different underlying diseases. The first step in determining the cause of an effusion is to differentiate the fluid from transudate to exudate. In many clinical studies performed, it has been observed that pleural effusions with exudate characteristics are caused by malignancy, parapneumonic effusion and tuberculosis, respectively, while pleural effusions with transudate characteristics are mostly caused by CHF (16-19). Our study was consistent with the literature data. The most transudate fluid was found in CHF, and the exudate fluid was most intense in malignancy, PPE, and tuberculosis. Pleural fluid cell analysis and pH value can also help detect fluid character. Neutrophil (parapneumonic effusion and empyema) and lymphocyte cell dominance (tuberculosis and malignancy) are more common in exudate-characterized pleural fluids (5, 20). In transudative effusions, the pH is usually alkalosis (21). pH<7.2 is one of the typical findings for complicated parapneumonic effusion with exudate character (22). In our study, there was significant neutrophil and lymphocyte cell dominance in exudate-qualified pleural effusions and transudate-qualified fluid pH was significantly prone to alkalosis.

Adenosine deaminase (ADA) is a hydrolytic enzyme that plays an important role in purine metabolism. Many studies are showing that pleural fluid ADA (p-ADA) is especially associated with tuberculous (TB) pleurisy. (23, 24). The pleural ADA cut-off value >40 is widely accepted for the diagnosis of TB pleurisy (25). However, in different studies, it has been stated that p-ADA can be a biomarker that can be used to differentiate pleural transudates from exudates (26, 27). In our study, p-ADA levels were found to be significantly higher in the exudate pleural fluid group. this is because inflammatory diseases with lymphocyte dominance are included in this group (TB, empyema cancer, etc).

Separation of exudate and transudate in pleural effusion is very important in patient management. Sometimes the Light criteria may not be sufficient for this distinction. Therefore, there is a need to evaluate other biochemical and haematological parameters. It has been shown that in inflammatory status, IL-6, IL-1, and TNF-α can stimulate precursor cells of blood platelets (28). Therefore, blood platelets are the first cells to accumulate at the site of injury in inflammatory conditions. Mean platelet volume (MPV), which is easily calculated by haematological analyzers, is one of the routine blood parameters. During inflammation, there is an inverse relationship between platelets and MPV values. While platelets undergo activation and ageing at the site of inflammation, mean platelet volume (MPV) decreases in patients with ongoing inflammation (29). This means that increased platelet production is accompanied by a decrease in the mean platelet volume. When we searched the literature, there were very few studies investigating the relationship between MPV and platelet in patients with pleural effusion. In a study conducted with transudative-qualified pleural effusion patients, it was emphasized that high MPV and low platelet might be poor prognostic criteria (30). Hyperreactivity of blood platelets has been shown to markedly increase patients' susceptibility to acute cardiovascular events (31, 32). Ohuchi et al. stated that increased platelet count and decreased MPV values are prognostic factors in exudate-qualified malignant pleural effusion patients (15). As we know, MPV and platelet values were compared for the first time in our study between transudate and exudate qualified pleural effusion patients. Patients with transudative effusion had significantly higher MPV and low platelet values and there was a negative correlation between MPV and platelet the according to Spearman's test. This may be explained by the presence of cardiovascular and low-grade inflammatory diseases in this group. Therefore high MPV and low platelet count can be laboratory parameters that can be used in the separation of transudate and exudate.

CRP is a biomarker of inflammation and infection. It is synthesized in hepatocytes after stimulation by different cytokines and released into the blood in response to the inflammation (33). Many studies are showing that CRP can be used as prognostic and diagnostic in patients with malignant and parapneumonic pleural effusion (34-36). In two different studies, it has been suggested that pleural fluid HsCRP values and CRP values are parameters that can be used in the separation of transudate and exudate (37, 38). In our study, there was a significant difference between the two groups in terms of serum CRP value. Therefore, serum CRP value can be a non-invasive, inexpensive and easily accessible parameter that can be used to differentiate between transuda and exudate.

In recent studies, new inflammatory biomarkers such as NLR, LMR, PLR, and CAR have been found that can be easily calculated from routine parameters. These biomarkers have been observed to have diagnostic and prognostic values in many pathologic states (39-41). In a study, it was shown that the pleural fluid neutrophil-lymphocyte ratio is an inexpensive and easily calculated haematological parameter that can be used in the differential diagnosis of pleural effusion (42). Studies are showing that NLR and PLR can predict survival in malignant effusions (43, 44). In our study,

NLR, PLR, LMR and CAR biomarkers were compared for the first time in the differentiation of transudate exudate, but no significant results were obtained. This may be due to the small number of our patients.

5. Conclusions

As a result, we found high serum MPV and low serum platelet levels significant for transudate pleural fluids, and high serum C-reative protein levels for exudate pleural fluids. In the differential diagnosis of transudate and exudate pleural fluid serum MPV, platelet and C-reactive protein values may be candidate parameters to support the Light's criteria. We think that our study may lead to studies being conducted in larger populations.

Limitations of the Study

There are some limitations of our study. It can be listed as being a single-centre-retrospective study and inclusion of fewer patients in the study due to insufficient registered laboratory data.

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None.

Conflict of Interests

The all authors have no conflicts of interest to declare.

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Author Contributions

Concept- Hocanli I.; Design- Hocanli I.; Supervision- Hocanli I., Sahin A.; Data Collection and/or Processing- Hocanli I.; Analysis and/or Interpretation - Hocanli I.; Literature Search- Hocanli I., Sahin A.; Writing Manuscript- Hocanli I.; Critical Review- Hocanli I., Sahin A.

Ethical Approval

The study protocol was approved by the Harran University Faculty of Medicine, Ethics Committee (Approval No: HRU/21.10.02 and Approval Date: 24.05.2021).

Data sharing statement

Data and mareials are available upon request. Hyperlink: 'mail to: iclalhocanli@2163mail.com

Consent to participate

Consent for the study was obtained from all participants for the study.

Informed Consent

Informed consent form was obtained from all participants for the study.

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Multiple injections of PRP/steroid combination result in better clinical outcomes in advanced osteoarthritis: A prospective randomized study

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Abstract: The impact of PRP/steroid combination in advanced osteoarthritis is unclear. Multiple intraarticular injections are thought to sustain better clinical scores. The objective of this prospective study is to evaluate the effect after repeated injections of corticosteroid (CS) and platelet-rich plasma (PRP) treatment compared to single dose PRP/steroid injection in patients affected by advanced osteoarthritis. A total of 98 patients affected by clinically and radiographically documented with grade 3-4 gonarthrosis according to Kellgren- Lawrence classification were included. The patients were randomized into 2 study groups. Forty-nine patients (Group 1) received three intra-articular injections of PRP (5mL) and steroid (1 cc-5 mgr triamcinolone). Forty-nine patients (Group 2) received one intra-articular injection of PRP/steroid (5 mL). In multiple injection group, an unblinded physician performed the injection once a week for three weeks into the affected knee in both groups. All patients were evaluated with the VAS score and the Knee injury and Osteoarthritis Outcome Score (KOOS) subscales before the infiltration, at 2 and 6 months after the first injection. The combination of intra-articular PRP with steroids resulted in a significantly superior clinical outcome. This study demonstrated that multiple intraarticular injections of PRP/steroid combination are more effective in advanced osteoarthritis when compared to single injection.

Keywords: Platelet Rich Plasma; Corticosteroid; Intraarticular Injection; Advanced Arthritis.

1. Introduction

Osteoarthritis (OA) is a degenerative disorder that leads to loss of function and increased pain. It also causes work loss and increased dependency. This condition affects 38% to 47% of the population aged older than 60 years (1). Many factors are thought to play in its pathogenesis. These can be summarized as age, gender, obesity, genetic predisposition, and activity level. The treatment options can be classified into nonoperative

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and operative treatment. Operative treatment includes high tibial osteotomy, unicondylar prosthesis, and total knee arthroplasty (2). In nonoperative treatment, non-steroidal anti-inflammatory drugs (NSAIDs), analgesic drugs, and physical rehabilitation is started. Second-line treatment are intraarticular therapies (3).

Intraarticular injections maintain their role for nearly half a century in the treatment of osteoarthritis. Its first use begins with corticosteroid injections (4). Thanks to advances in injection therapies, hyaluronic acids, platelet-rich plasma (PRP), and stem cell-based therapies have been recently performed. Although approved by Food and Drug Administration, AAOS does not recommend its use of these therapies. However, recent articles suggested the positive factors of intraarticular injections (5). One recent meta-analysis indicated the superiority of PRP over steroid and hyaluronic acids (6). These therapies have different characteristics regarding dose and preparation method, the number of injections, the content of active agent (i.e., platelet and white blood cell content). Available studies report different clinical efficieny and preparation formulas. Therefore, it is difficult to compare these results (7, 8).

It is plausible to consider that the improvement in pain relief is less as the grade of arthritis increases. In our practice, we observed that some patients are reluctant to undergo surgery due to increased risk of arthroplasty and other alternative surgeries. Corticosteroids have been demonstrated to detrimental to cartilage tissue but this would be not important in end-stage arthritis with extensive cartilage loss (9, 10). Corticosteroids decrease pain in short-term and is costeffective. PRP injection provides clinical improvement up to one year, but its clinical effect in advanced osteoarthritis is lacking (11).

The pain relief obtained after multiple injections of hyaluronic acid or PRP injections have been shown (12, 13). However, it needs further investigation (14). It can be assumed that the simultaneous use of longlasting PRP and steroids providing shortterm intense pain relief, this combination can be palliative in advanced arthritis. Also, it is unknown whether multiple PRP steroid combinations result in improved clinical outcomes in patients with advanced osteoarthritis. This study aims to compare multiple versus single PRP-steroid combination concerning clinical outcomes in advanced knee osteoarthritis.

2. Material and Methods

Research and Publication Ethics were followed at all stages of the study. The study is in compliance with the Helsinki Declaration. Ethics committee approval was received from the ethics committee of Ataturk University Medical Studies Department Head on 04.10.2018 at the 6th meeting with regards to the document written on 04.10.2018 with number 25. Informed consent was obtained from every participant. A priori power analysis indicated that a study population of 98 patients was planned with an alfa level 0.05 and beta level 0.2. The patients were randomized by opening a sealed envelope. The envelopes were prepared by a health professional blinded to the study. 98 patients with advanced arthrosis (grade 3-4 osteoarthritis) were randomized to receive either three dose PRP/steroid injection or a single PRP/steroid injections. Patients were informed about the study. Randomization was performed by opening a sealed envelope.

This double-blind prospective randomized study was conducted between October 2018 and March 2021. Radiographs of the affected knees were evaluated by a blinded physician with ten-year experience in orthopedic practice. Anterior-posterior radiographs were graded by the examining surgeon using the Kellgren- Lawrence classification. Patients with level 3-4 arthritis (advanced osteoarthritis) were included. Inclusion criteria were advanced osteoarthritis of the knee (Kellgren-Lawrence Grade 3-4), intraarticular injection of unilateral knee, age >65 years, having BMI >30 (morbid obesity), resistant pain unresponsive to NSAIDs more than 1 year, normal coagulation profile and whole blood count, no history of surgery on bilateral knees, history of septic arthritis, local superficial lesion and infection on the knee, presence of complete outcome and demographic data. Exclusion criteria included NSAID use within last 30 days prior to injection, previous intraarticular injection within 6 months, rheumatoid or autoimmune disease, immunodeficiency, existing hip osteoarthritis, systemic metabolic disease, use of corticosteroid, presence of smoking habitus and any agents affecting platelet activation.

Patients received an injection into unilateral knee. Home exercises were routinely prescribed to all patients. Informed consents were given by the patients about intraarticular steroid and PRP treatment with its advantages and disadvantages. One patient for each group had local superficial lesion. Therefore, they are excluded from the study. First group received three PRP/steroid injections. Group 2 received single PRP/steroid injection.

Demographic data such as gender, age, BMI, and follow-up were collected. Clinical evaluation: Functional assessment of patients was made based on pretreatment as well as 2nd and 6th month posttreatment results of the Knee injury and Osteoarthritis Outcome Score (KOOS) scores with its subscales and the Visual Analog Scale (VAS). All injections were routinely performed by one physician using standard protocol. Using aseptic procedures, the injection was performed in an anterolateral approach (along the patellar tendon) with the knee in 90 degrees flexion. If effusion is present, joint aspiration was made before injection. The injections were repeated three times with one week intervals in Group 1. Group 2 received only one injection. In both groups, after the injection of PRP (5 cc), 1 mL triamcinolone acetonide was injected with the same needle No local anesthetic agent was used in all patients due to its possible chondrotoxic effect, which

could deteriorate clinical outcomes in the arthritic knee. Possible side effects like mild swelling and pain were recorded within 48 hours after drug administration. Physical activity was prohibited in this time period.

At the beginning of intraarticular PRP treatment in our clinic, our biochemical laboratory gave technical support in PRP preparation. Peripheral blood (60 mL) was taken from all patients. Three tubes of 20 mL syringes were prepared by adding 2 mL of acid citrate dextrose (ACD-A) to each. These tubes were placed into a centrifuge system with symmetric configuration to avoid unequal distribution of turning forces in centrifugation applied to samples. The double spinning method was applied as described by Mazzocca (15). This method has been found to be comparable to the other two methods applied in the same study. The first centrifugation was performed for five minutes at 1500 rpm. After the removal of upper layers of plasma, samples were centrifuged for twenty minutes at 6300 rpm. We did not activate PRP before injections. Leucocyte filtration was not performed. The preparation process was repeated for every application, and intraarticular injection was performed within 4-6 hours after preparation because an open system was used. PRP solution was not stored. The platelet number, number of red blood cells, and white blood cell components were measured by an automated hematology analyzer (Beckman Coulter, Brea, CA). Complete blood count was performed for the first ten patients with advanced osteoarthritis to determine whole blood/PRP platelet and white blood cell count. PRP's platelet and white blood cell levels were compared with levels of the peripheral blood. The mean platelet counts in the peripheral whole blood and PRP were 140.3±45.4x103/μL and 550.8±287.9x103/μL, respectively. The mean white blood counts in the peripheral whole blood and PRP were 5.1±1.4x103/μL and 9.76±2.8x103/μL, respectively.

2.1. Statistical Analysis

Analyses were conducted using SPSS Statistics 21.0 (IBM Corp, Armonk, NY). Data normality was checked using the Shapiro-Wilkins test. Categorical and continuous variables were given as frequencies, mean and standard deviation, respectively. The Chi-square test was used to compare categoric variables (gender, paracetamol use). An independent t-test was used to compare two treatment groups based on continuous data (BMI, age) and comparison of two treatment arms based on outcome scores. Temporal changes in the groups' outcome scores (KOOS, VAS) were evaluated using a general linear model for repeated measures test. Statistical significance was set as $p<0.05$. T-test was used to compare quantitative variables between groups.

3. Results

Age and gender were similar in both groups. (p>0,05). VAS scores were different in both groups at each time point. Decrease in VAS scores was significantly more in multiple injection group. (Table 2) KOOS-Pain, KOOS-Symptom, KOOS-Sport Activities, and KOOS-Activities of Daily Living subscales demonstrated a significant increase in multiple injection group at each time point. KOOS QoL scores were similar at each time point in both groups. (p>0,05) (Table 3-7).

Table 1: Demographic Characteristics in two groups.

	Group		p
	multiple injection (PRP/steroid)	single injection (PRP/steroid)	
Age	68.12±7.34	67.78 ±7.62	.819
Body mass index	32.04±1.59	31.43±1.29	.039*
Gender (male/female)	15/22 (%30.6/44.9)	34/27 (%69.4/55.1)	.211

* indicates p<0.05.

Table 2: Comparison of VAS scores in two groups.

	Group		p
	multiple injection (PRP/steroid)	single injection (PRP/steroid)	
VAS Baseline	7,47±1,12	8,59±1,1	.000*
VAS 2-months	3,24±1,13	4,63±1,51	.000*
VAS 6- months	5,08±1,54	6,73±1,47	.000*

* indicates p<0.05.

Table 3: Comparison of KOOS-pain scores in two groups.

	Group		p
	multiple injection (PRP/steroid)	single injection (PRP/steroid)	
KOOS Pain Baseline	7.47±1.12	24.18±5.89	.328
KOOS Pain 2 months	41±10.02	28.61±8.95	.000*
KOOS6 Pain 6 months	43.69±8.79	33.14±7.21	.000*

* indicates p<0.05.

Table 4: Comparison of KOOS- symptom scores in two groups.

	Group		p
	multiple injection (PRP/steroid)	single injection (PRP/steroid)	
KOOS Symptom Baseline	47.63±6.42	40.76±6.77	.000*
KOOS Symptom 2 months	52.53±6.59	45.86±6.17	.000*
KOOS Symptom 6 months	61.63±7.9	52.31±8.13	.000*

* indicates p<0.05.

Table 5: Comparison of KOOS-Activities of Daily Living subscores in two groups.

	Grup		p
	multiple injection (PRP/steroid)	single injection (PRP/steroid)	
KOOS ADL Baseline	23.69±4.66	23.57±5.3	.904
KOOS ADL 2 months	38.49±8.52	29.78±7.91	.000*
KOOS ADL 6 months	47.45±7.3	38.65±7.31	.000*

* indicates p<0.05.

Table 6: Comparison of KOOS- Sport Activities subscores in two groups.

	Grup		p
	multiple injection (PRP/steroid)	single injection (PRP/steroid)	
KOOS SA Baseline	6.61±2.31	8.06±1.75	.001*
KOOS SA Baseline 2 months	13.29±3.89	12.67±2.71	.369
KOOS SA Baseline 6 months	17.92±4.15	16.22±3.06	.024*

* indicates p<0.05.

Table 7: Comparison of KOOS- Quality of Life in two groups.

	Grup		p
	PRP Stereoid 3lü enjeksiyon	PRP Steroid tek enjeksiyon	
KOOS QoL Baseline	8.2±2.71	9.43±2.18	.015*
KOOS QoL 2 months	19.61±5.44	18.9±4.43	.478
KOOS QoL 6 months	25.04±5.42	24.29±4.02	.435

* indicates p<0.05.

4. Discussion

The most important finding of this study was that multiple injection of PRP and steroid combination gives better KOOS scores and pain relief at 6 months in advanced osteoarthritis (p<0.05).

There are many studies which demonstrated the beneficial effects of PRP. A review concluded that multiple PRP injections decreases pain at 6 months in patienst with mild to moderate knee osteoarthritis (16). Patel et al showed that PRP injection gives better WOMAC scores at 6 months after injection. To note, he didn't find any difference between single and double PRP injections (17). Yaradilmis found better results with the use LR-PRP over hyaluronic acid at 12 months follow-up (18). In a network meta-analysis, Migliorini found that PRP injections are superior relative to steroids, hyaluronic acid and placebo at 3, 6, and 12 months after injection. There was no significant difference between corticosteroids, hyaluronic acid and placebo (6). Güvendi compared the effect of corticosteroid and PRP in grade 3 osteoarthritis. Both agents are effective, but the patients had more prolonged pain relief after PRP injections (19).

In a meta-analysis, Concoff suggested clinical improvement after 2-4 injections of hyaluronic acid compared to single injection (20). Smith pooled data regarding intra-articular corticosteroid and hyaluronic

acid combination. Based on 8 trials, he concluded that combination injections reduces pain to hyaluronic acid alone (21).

In mild to moderate osteoarthritis, Camurcu et al suggested that methlyprednisolone one week before to PRP injection resulted in significantly better clinical outcomes at 6 months but no significant difference at 12 months between combined injection, PRP and methlyprednisolone alone compared to PRP and MP injections alone in patients who had mild to moderate knee OA (22). In a prospective randomized study, Simental-Mendía found better VAS scores in triple PRP injection group compared to single injections at 12 months of follow-up (23). Kavadar et al randomized 102 patients with grade 3 arthritis according to number of PRP injections. Clinical improvement in VAS, WOMAC, Timed Up and Go Tests was noted in both groups, with greatest improvement in triple injection group (24). In a prospective study, Gormeli suggested the benefit of multiple PRP injections in mild to moderate arthritis over single PRP and hyaluronic acid in mild arthrits. But, he didn't observe any improvement in advanced arthritis (25). Munde et al found that three PRP injections with grade 3 osteoarthritis provided more pain relief compared to single and double injections (26). Rai et al investigated the use of combined injection including HA along with PRP and corticosteroid). In younger patients with mild-to-moderate osteoarthritis, improved function, pain relief, and quality of life are observed (27).

All these studies demonstrated the potential benefit of PRP and steroid injections. In the present study, improved VAS and KOOS scores after combined injection in advanced osteoarthritis are never evaluated before. Our results are in line with previous studies supporting the effect of multiple injections. Advanced arthritis is an endstage with extensive cartilage damage. The inflammatory cascade can be transiently blocked by simultaneous PRP and steroid injection. We didnt evaluate the need for arthroplasty and need for NSAID use in both groups. But, it seems that the decrease in VAS scores and improved KOOS scores are indicative of synergistic effect of PRP and steroid treatment.

5. Conclusions

In conclusion, our results demonstrated that multiple intraarticuler PRP and steroid injections result in clinical improvement compared to single injection. This injection regiment can be an alternative for patients unwilling to surgery or have high risk for anesthesia.

Limitations of the Study

Limitations include lack of comparison of different PRP preparation methods and evaluation of the need for arthroplasty at the end of the treatment.

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Conflict of Interests
No potential conflict of interest relevant to this article was reported.

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Ethics committee approval was received from the ethics committee of Ataturk University Medical Studies Department Head on 04.10.2018 at the 6th meeting with regards to the document written on 04.10.2018 with number 25.

Data sharing statement
None

Consent to participate
Informed consent was obtained from the patients

Informed Consent
The study complies with the Declaration of Helsinki. Consent of all patients was obtained before the article.

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Determination of miRNA Expression Levels Involved in WNT Signaling Pathway in Multiple Sclerosis Patients

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Abstract: Multiple Sclerosis (MS) is an autoimmune central nervous system disease characterized by inflammation, demyelination, and axon damage. Recent studies have shown that the WNT signaling pathway is a negative factor in the process. miRNAs are non-protein-coding RNAs that play a role in processes such as cell development, differentiation, proliferation, and cell death by repressing target genes. As with many pathways, miRNAs are also effective in regulating the WNT signaling pathway. In our study, the expression levels of miRNAs (miR-145, miR-301b, miR214, miR-190a, miR-1304) targeting genes involved in the WNT signaling pathway were examined. Our study was carried out in order to comprehend the relationship between MS and the WNT signaling pathway, to contribute to the clinic and the literature in elucidating the etiology of MS, and determining treatment strategies with the results to be obtained. Blood samples were taken from patients with MS (17) included in our study during both attack and remission periods. Blood samples were taken from the control group (16) participating in the study, and the expression levels of miRNAs included in our study were quantitatively analyzed using the RT-PCR method. When compared with the control group, no statistically significant difference was observed in terms of fold increase values in the miRNA levels (miR-145, miR-301b, miR-214, miR-190a ve miR-1304) of the MS attack period, while statistically significant differences (respectively; p=0.010, p=0.023, p=0.002, p=0.006, p=0.003) were found in terms of fold increase values of all miRNA levels in the remission period. Considering the medications used by the patients and the number of attacks, there was no statistically significant difference in miRNA expression levels. In our study, it was deduced that miRNA expression levels, which are effective in the WNT signaling pathway, may play a role in elucidating the clinical course and genetic mechanism of MS, particularly during the remission period.
Keywords: miRNA; Multiple Sclerosis; WNT Signaling Pathway.

1. Introduction

Multiple Sclerosis (MS) is defined as an autoimmune disease involving the central nervous system, characterized by demyelination, axonal damage, and inflammation. The etiology of MS disease has not been

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fully elucidated. Myelin sheaths, oligodendrocytes, axons, and nerve cells are damaged. There are many types of signal transduction pathways involved in the development and repair of oligodendrocytes (1). One of the signaling pathways is the evolutionarily conserved WNT signaling pathway. The WNT signaling pathway is significant in the adhesion of cells capable of renewing themselves in adulthood, in the control of transcription of target cell genes, and in maintaining cell polarity and proliferation, cell differentiation, and migration in the embryonic period (2). literature studies demonstrate that the WNT signaling pathway is a negative factor in the myelination process.

miRNAs are non-protein coding RNAs. They are encoded by genes that are transcribed from DNA but not transformed into protein. miRNAs can be found in exonic, intronic regions of protein-coding genes and in intergene regions. miRNAs play a role in processes such as cellular development, differentiation, proliferation, and death by suppressing one or more target genes (3).

The WNT signaling pathway plays a negative role in the myelination process in the CNS. Myelin loss and impaired axonal conduction elicit various neurological deficits such as numbness, weakness, visual defect, and paresis. Damaged myelin can be repaired or remyelinated, consistent with clinical remission. Remyelinated sheaths are susceptible to subsequent demyelination and are characterized by recurrent remyelination and demyelination, clinical relapse, and remission in MS. As a result, it can lead to irreversible disability. To target the autoimmune inflammatory mechanism of MS in the peripheral and CNS, current medications for this disease are immunomodulators. Immunomodulatory therapy is important in alleviating inflammation. They can stop the course of demyelination and prevent clinical exacerbation. However, approaches to support repair for pre-established demyelinated lesions are still deficient. The role of the WNT signaling pathway in the myelination process has been demonstrated. Oligodendrocytes are cells that make remyelination in the CNS and the effects of the WNT signaling pathway on the development of oligodendrocytes have been indicated in studies. Considering its relationship with inflammatory and autoimmunity, studies with the WNT signaling pathway MS will contribute to the literature in order to develop approaches that will lead to timely and effective remyelination (4-6).

As with many cellular signaling pathways, it has essential functions in the regulation of the WNT signaling pathway. miRNAs are very significant in regulating the functioning of all kinds of signaling pathways in our bodies. As a result of the increase or decrease in the expression levels of miRNAs, the functioning of the signaling pathways is affected. Defects in signal pathways play a role in the etiology of many diseases, particularly cancers and neurodegenerative diseases.

Five miRNAs that have a function in the WNT signaling pathway were included in the study. miRNA-145.2 regulating the expression of the FZD7 gene acting on the Frizzled (FZD) receptor miR-301b regulating the expression of the TCF4 gene acting on the TCF/LEF transcription factor miR-214.4 acting on the 3 β catenin protein regulating the CTNNB1 gene MiR-190a, which regulates the expression of the MAPK8 gene acting on MAPK signal, and miRNA-13046, which regulates the expression of the WNT3A gene, acts on the 5 WNT ligand, were included. It was aimed to determine whether there was a genetic relationship between miRNAs involved in the WNT signaling pathway and MS disease.

2. Material and Methods

2.1. Materials

This study was approved by the Atatürk University Faculty of Medicine Clinical Research Ethics Committee (06/15-30.11.2017). Research and Publication Ethics were followed at all stages of the study. The study included 17 MS patients who were admitted to the Atatürk University Health Research and Application Center Neurology Outpatient Clinic, who was in the attack phase and were hospitalized and received attack treatment. A written informed consent form was obtained from the patients. Detailed systemic and neurologic examinations were performed. Clinical, laboratory, and medication information were recorded. Their blood was taken into an EDTA tube. The patients were called for control 3 months after their remission period, and detailed examinations were again made and their blood was taken into an EDTA tube. Demographic data of the patient and control groups in our study is given in Table. 1.

Furthermore, 4 (23.6%) of 17 RRMS patients were newly diagnosed and had not started medication treatment yet, and received solely attack treatment. Five (29.4%) of our patients were using subcutaneous interferon beta-1b (IFN-β-1b), 3 (17.6%) were using subcutaneous glatiramer acetate, and 5 (29.4%) were using oral fingolimod. The average number of attacks of the patients is 5.29. The mean disease duration of our MS patients is 3.35 years.

Table 1: Demographic data of groups.

	MS	Control
Number of patıents/controls	17	16
Age	28.64±7.34	28.81±6.70
Gender F/M n(%)	12(70.6%)/5 (29.4%)	11(68.75%)/5 (31.25%)

2.2. Methods

2.2.3. Quantitative real-time PCR

miRNA was isolated from peripheral blood samples using the miScript RNeasy Mini Kit (Hilden, Germany) according to the manufacturer's instructions and its quality was assessed by spectrophotometric analysis (Maestrogen, MaestroNano Spectrophotometer, USA). cDNA was then synthesized by reverse transcription from 2 µg of total RNA using the QiagenmiScript II Reverse Transcription Kit (Hilden, Germany) with a Labcycler Thermal Cycler (SenSoquest). Diluted cDNA was used as a template for quantitative real-time polymerase chain reaction (RT-PCR) analysis.

The cDNA was used in combination with QiagenmiScript SYBR Green PCR Kit (Qiagen, Germantown, MD, USA) and miScript primer assays. Quantitative rt-PCR was run in a Rotor-Disc 72 with 25-µl reaction volumes for 40 cycles of 95°C for 2 min, 94°C for 15 s, 55°C for 30 s in a QiagenRotorgene Q (Qiagen, Hilden, Germany). The reaction mixture contained 12.5 µL of miScript SYBR Green Master Mix, 1 µL of each primer (forward and reverse primer), 6.5 µL of DNase/RNase-free distilled water, and 5 µL of cDNA template. SNORD61 was chosen as the reference gene for this study. Reference sequence numbers for all primers were obtained from the GenBank.

2.3. Statistical Analysis

Changes in gene expressions of miRNAs were calculated. The 2ΔΔCt analyzes of all miRNAs were analyzed using the GeneGlobe Data Analysis Center online analysis program by entering data into the Excel program of the Ct values given in the Real-Time analysis. SNORD61 98was accepted as reference genes and delta Ct values were calculated first. The p-value was calculated with the Saturn T-test in the same program. A $p< 0.05$ was considered significant. These values were made for all genes included in our study. Descriptive statistics for continuous variables are tabulated as mean and standard deviation.

3. Results

A total of 50 blood samples were taken from the patient and control groups included in our study. cDNA synthesis and enrichment were performed by isolation of miRNA from the collected samples. The expression levels of the miRNAs that we determined (miR-145, miR-301b, miR-214, miR-190a, and miR-1304) were quantitatively identified. According to the statistical analysis; fold differences were observed for miRNAs (miR-145, miR-301b, miR-214, miR-190a, miR-1304) compared between groups compared to the control group.

When miRNA expression levels of the control group were accepted as 1, an increase was observed in 3 miRNA levels (miR-145, miR-214, and miR-1304) of Group 1, while a decrease was observed in 2 miRNA levels (miR-301b and miR-190a). On the other hand, in accordance with the fold increase analysis made by accepting the miRNA expression levels of the control group as 1, all miRNA expression levels of Group 2 were increased. Numerical data of the fold increase is shown in Table 2.

Table 2: Fold increase values between miRNA expression levels of study groups miRNA.

miRNA type	Group 1* fold increase	Group 2* fold increase
hsa-miR-145	1.3431	3.435
hsa-miR-301b	0.7887**	1.4385
hsa-miR-214	1.2509	3.0889
hsa-miR-190a	0.9727**	1.7895
hsa-miR-1304	1.7727	3.7293

*The fold increase values were compared to the control group.
** Fold decrease was observed instead of fold increase.

In the statistical analysis, the significance of the change between the Attack period (Group 1) and Remission (Group 2) MS patients and the control group was evaluated over the 2' Delta CT (2-ΔCT) values normalized with the SNORD61 control.

When compared to the control group, no statistically significant difference (respectively; p=0.833, p=0.704, p=0.738, p=0.759, and p=0.274) was observed in terms of fold increase values in all miRNA levels (miR-145, miR-301b, miR-214, miR-190a ve miR-1304) of Group 1, while a statistically significant difference was found in terms of fold increase values of all miRNA levels of Group 2 (respectively; p=0.010, p=0.023, p=0.002, p=0.006, and p=0.003) (Table.3).

Table 3: P values of the groups and statistical significance.

miRNA type	Group 1 p value	Group 2 p value
hsa-miR-145	0.833	0.010*
hsa-miR-301b	0.704	0.023*
hsa-miR-214	0.738	0.002*
hsa-miR-190a	0.759	0.006*
hsa-miR-1304	0.274	0.003*

*Expresses statistical significance.

The significance of the change between the MS patients in the Attack and Remission period and the control group in the statistical analyzes we made according to the medications used is given in Table 4.

According to the data obtained, of miRNA types analyzed in Group 1, up-regulation was observed in miR-145, miR-214, and miR-1304 expression levels, and down-regulation in miR-301b and miR-190a expression levels. Up-regulation was observed in the expression levels of all miRNA types analyzed in Group 2. The medications used did not have an effect on miRNA gene expressions in our study.

Table 4: P values and statistical significance according to the number of attacks.

ATTACK	miR-145		miR-301b		miR-214		miR-190a		miR-1034	
At S.	G1	G2	G1	G2	G1	G2	G1	G2	G1	G2
≥6	0.836	0.016*	0.744	0.019*	0.711	0.004*	0.723	0.007*	0.235	0.002*
2-5	0.872	0.029*	0.706	0.029*	0.821	0.003*	0.753	0.006*	0.291	0.003*
1	0.790	0.013*	0.823	0.019*	0.711	0.001*	0.717	0.005*	0.391	0.002*

G1: Group1, G2: Group2 *Indicates statistical significance.

Table 5: P values and statistical significance according to the drugs used.

	miR-145		miR-301b		miR-214		miR-190a		miR-1034	
DRUG	G1	G2	G1	G2	G1	G2	G1	G2	G1	G2
IFN-β-1b	0.887	0.011*	0.77	0.027*	0.749	0.004*	0.769	0.006*	0.238	0.002*
FTY720	0.902	0.017*	0.713	0.021*	0.724	0.005*	0.787	0.006*	0.127	0.003*
GA	0.822	0.022*	0.692	0.032*	0.830	0.002*	0.743	0.007*	0.280	0.003*
OTHER	0.790	0.013*	0.823	0.019*	0.711	0.001*	0.717	0.005*	0.391	0.002*

G1: Group1, G2: Group2 *Indicates statistical significance.

4. Discussion

MS is one of the most common neurological diseases affecting the CNS, with attacks of inflammation in the brain and spinal cord and demyelination of the myelin sheaths surrounding the axons, with multifactorial etiopathogenesis and often affecting young adults. Demyelination often occurs as a result of chronic inflammation in the CNS. In recent years, it has been shown that the WNT signaling pathway has an important role in myelination and remyelination (7).

In this context, we conducted our current study in order to examine the relationship between the WNT signaling pathway, which is involved in the development and repair of oligodendrocytes, and MS disease, and to contribute to the etiology and treatment of MS with possible results. While genetic studies on Multiple Sclerosis have increased significantly in the last 10 years, there are limited studies in the current literature on the role of miRNAs in the development of MS (1, 4, 6-9).

MiR-145 was expressed at a higher rate in the blood samples taken during the attack and remission periods of RRMS patients compared to the control group. While the increase in miR-145 expression level was not significant in Group 1, the expression level was found more than 3 times in Group 2 and it was found to be statistically significant. In the expression study by Sondergaard et al. in the literature, in addition to the fact that miR-145 is expressed 3 times more in MS patients compared to healthy patients, they stated that miR-145 can be used as a possible diagnostic biomarker of miR-145, which can be found in serum and plasma in Peripheral Blood Mononuclear Cells (PBMC). In the study conducted by Keller et al., consisting of 20 MS patients and 19 healthy individuals, 866 different miRNA profiles were examined. They found that 10 miRNA types, including miR-145, were dysregulated in MS patients. As a result of their analysis, they reported that 9 miRNA types, including miR-145, were overexpressed in MS patients, and down-regulation was detected merely in miR-20b. 112 It has been shown that the up-regulation of miR-145, which is known to have a role in the WNT signaling pathway, its up-regulation 122 detected in MS patients has been shown to regulate the differentiation of oligodendrocytes by targeting the FZD7 receptor, which interacts with the WNT signaling pathway (10-11**).** The expression levels of miR-301b and miR-190a were different from each other in Group 1, Group 2, and Control groups. In both miRNA types, downregulation was detected in the attack period of MS patients compared to the control group. Up-expression level was identified in Group 2 compared to both Group 1 and the control group. As a conclusion of analyzes performed on blood samples taken during the remission period, it was ascertained that miR-301b and 38 miR-190a were expressed 1.4385 and 1.7895 times, respectively. In the literature, a hierarchical cluster graph is presented with down-regulation of miR-190 between 0.6 and 2-fold in the control group and up-regulation between 0.2 and 2-fold in the MS patient group (12-13). In another study, it was stated that the expression of miR301b, which is in the miR-130 family in MS patients, induces the release of TNF-alpha and IFN-gamma, thereby negatively affecting the brain functions.

MiR-214, another miRNA type evaluated in our study, was expressed at a higher rate in samples taken from patients in both attack and remission periods compared to the control group. Two different studies also demonstrated that ovarian expression of miR-214 in oligodendrocytes has a significant role in remyelination and axon regeneration (14).

No study has been found in the existing literature on the relationship between miR-1304 included in the study and MS disease. Considering the miR-1304 expression

value detected in both Group 1 and Group 2 in our study, it is understood that there is over-expression.
When the data obtained from other miRNAs in our study is analyzed, we encounter the miRNA with the highest fold increase in both Group 1 and Group 2 compared to the control group (15).
The number of publications in the literature on the relationship between immunomodulatory therapies used in MS and miRNAs is quite limited. There are some studies on the relationship between IFN-Beta-1b (IFN-β-1b), Fingolimod (FTY720), and Glatiramer Acetate (GA) treatments and miRNA expression levels in MS patients (16-17).

5. Conclusions

It is seen that there has been a significant increase in the number of studies on MS-miRNAs in recent years. As a result of these studies, it is predicted that the disease arises as a result of the interaction between environmental stimuli, susceptibility to disease, and determining genes. In our study, the effects of treatments applied to patients on miRNA profiles were analyzed, however statistically significant results were not found. Our study will shed light on future studies on the investigation of miR-145, miR-301b, miR-214, miR-190a, and miR-1304 miRNAs, which are involved in the WNT signaling pathway, which may have significant roles in the development of MS, as well as on the analysis of the course and mechanism of the disease.

Limitations of the Study

There are two major limitations in this study that can be addressed in future research. First, the sample size is larger. Second, the miRNAs of other target genes identified in the wnt signaling pathway inclusıon in the study

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Conflict of Interests

The authors declare that there is no potential conflict of interest for the research, authorship, and/or publication of this article. All authors read and approved the final manuscript.

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Author Contributions

Design of the study: EB, Sample collection: NB, Performed the experiments: EY, Data Collection and/or Processing: EB, NB, EY, Writing Original Manuscript: EB, NB, EY. EB contributed to revising the work and final approval of the final version of the manuscript.

Ethical Approval

This study was approved by the Atatürk University Faculty of Medicine Clinical Research Ethics Committee (06/15 30.11.2017).

Data sharing statement

The data that support the findings of this study are available on request from the corresponding author.

Consent to participate

Consent was obtained from the patient and control groups participating in the study.

Informed Consent

The patient and control group who agreed to participate in the study signed the informed consent form.

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Comparison of Rt-Pcr Test and Chest Computed Tomography in Diagnosis of Covid-19

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Abstract: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) caused an acute lower respiratory tract infection epidemic. To detect diagnostic performance of British Society of Thoracic Imaging (BSTI) SARS-CoV-2 Disease CT classification criteria in diagnosis of the disease. Adult patients who presented our pandemic clinic with suspected SARS-CoV-2 Disease and underwent chest CT between March 14, 2020 and June 09, 2020 were included in the study. The chest CT images of the patients were evaluated according to the BSTI SARS-CoV-2 Disease CT classification criteria. The diagnostic performance of chest CT was calculated using the reverse transcription polymerase chain reaction (RT-PCR) test as the gold standard in the diagnosis of SARS-CoV-2 Disease. Of the 386 patients included in the study, 49.2% were diagnosed with SARS-CoV-2 Disease. According to the BSTI Covit-19 CT classification criteria, the number of patients in the classic SARS-CoV-2 Disease, probable Covit-19, indeterminate and non-COVID diagnosis groups were 32.6%, 14.2%, 18.9% and 34.2%, respectively. The BSTI Covit-19 CT classification criteria showed very high diagnostic performance in the diagnosis of SARS-CoV-2 Disease. The use of these criteria to differentiate SARS-CoV-2 Disease pneumonia can standardize and optimize the diagnosis of SARS-CoV-2 Disease and management of the disease. © 2022 NTMS.

Keywords: Coronavirus Disease 2019; Computed Tomography; Diagnosis; BSTI.

1. Introduction

An acute lower respiratory tract infection epidemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first reported in Wuhan, China, in the last days of 2019 (1). Later, this disease was named coronavirus disease 2019 (Covit-19) by the World Health Organization and declared a pandemic (2). Within one year after the declaration of pandemic, the number of patients that contracted SARS-CoV-2 Disease had exceeded 100 million, and nearly 2.5 million people died (3).

The gold standard diagnostic test for SARS-CoV-2 Disease is the real-time reverse transcription polymerase chain reaction (RT-PCR) assay of a nasopharyngeal swab, oropharyngeal swab, or endotracheal lavage (4). This test is highly specific but has low sensitivity, ranging from 37 to 71%, in the early

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stages of the disease or in patients with insufficient samples (5-7). Therefore, it can cause false negative results; i.e., even if the patient is infected, the RT-PCR test may be negative. In addition, existing RT-PCR tests can take up to two days to produce results, and access to such tests is limited in some regions. Chest computed tomography (CT) is not recommended as a routine screening tool, but it is used as a diagnostic tool for SARS-CoV-2 Disease pneumonia, especially in regions where access to RT-PCR tests is limited, as well as in early-stage patients with false negative RT-PCR results (8, 9). With the widespread use of chest CT in the diagnosis and management of SARS-CoV-2 Disease, many guidelines have been published for this purpose (10-12). One of them is the Covit-19 CT classification of the British Society of Thoracic Imaging (BSTI) criteria.

This study aimed to measure the diagnostic performance of the BSTI Covit-19 CT classification criteria in the diagnosis of SARS-CoV-2 Disease.

2. Material and Methods

This retrospective and single center study was carried out in a University Training and Research Hospital after receiving approval from the SARS-COV-2 Scientific Research Committee of the Republic of Turkey Ministry of Health and the Local Ethics Committee (2020/06-70). Research and Publication Ethics has been complied with at all stages, with the realization and preparation of the study. Patients aged 18 years and over who presented to our emergency department with complaints such as fever, cough, sore throat, dyspnea, and loss of taste and smell between March 14, 2020 and June 09, 2020, underwent the RT-PCR test and chest CT due to suspected SARS-CoV-2 Disease were included in the study. The exclusion criteria were as follows: pregnancy, not having an RT-PCR test, not undergoing chest CT, or chest CT images not being available. The patients' symptoms, physical examination findings, RT-PCR results, and laboratory test results (such as white blood cell count and C-reactive protein) were obtained from the hospital's electronic medical records. The patients were divided into two groups as RT-PCR (+) and RT-PCR (-). Patients that had an initial negative RT-PCR test result but underwent this test again due to clinical suspicion, this time having a positive test result, were included in the RT-PCR (+) group.

The chest CT images of the patients were evaluated by two experienced radiologists blinded to the purpose of the study and the RT-PCR results of the patients. The radiologists evaluated the chest CT images in consensus and classified the patients into classic Covit-19, probable Covit-19, indeterminate and non-COVID groups according to the BSTI Covit-19 CT classification criteria (10).

2.1. Statistical Analyses

The statistical analysis of the data was performed using the Statistical Package for the Social Sciences version 15.0 (SPSS Inc., Chicago, IL, USA). The conformance of continuous data to normal distribution was determined with the Kolmogorov-Smirnov test. Continuous data conforming to normal distribution were expressed as mean±standard deviation (SD) while those without normal distribution were obtained as median and interquartile range (IQR) values. Categorical data were expressed as the number (n) and percentage (%) of patients. Student's t-test and the Mann-Whitney U test were used to compare continuous data between the two groups. The chi-square test was used to compare categorical data between the two groups. The RT-PCR results were used as the gold standard to evaluate the performance of chest CT in the diagnosis of SARS-CoV-2 Disease. Agreement between the chest CT diagnosis and the RT-PCR test results was determined by performing Cohen's kappa analysis. In addition, to measure the diagnostic performance of chest CT in the diagnosis of SARS-CoV-2 Disease, the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the BSTI Covit-19 CT classification were calculated. A p value of less than 0.05 was considered statistically significant.

3. Results

Throughout the study period, 386 patients were included in the study. The ages of the patients ranged from 18-95 years, with a median value of 54 (IQR:37-69) years. While 229 (59.3%) of the patients were male, 157 (40.7%) were female. According to the results of the RT-PCR test, 190 (49.2%) of the 386 patients were RT-PCR (+). There was no statistically significant difference in age and gender between the RT-PCR (+) and RT-PCR (-) groups. The C-reactive protein level was statistically significantly higher in the patients diagnosed with RT-PCR (+) group ($p<0.001$). Conversely the lymphocyte level was statistically significantly lower in the patients diagnosed with RT-PCR (+) group ($p=0.01$). The demographic characteristics and laboratory findings at the time of presentation are summarized in Table 1.

According to the BSTI Covit-19 CT classification, the CT findings were consistent with classic Covit-19 in 126 (32.6%) patients, probable Covit-19 in 55 (14.2%), indeterminate in 73 (18.9%), and non-COVID in 132 (34.2%). A SARS-COV-2 diagnosis was made based on a positive RT-PCR test in 118 of the 126 patients classified as classic Covit-19 and 12 of the 132 patients classified as non-COVID (Table 2 and Figure 1 and 2). The classic SARS-CoV-2 Disease category of the BSTI Covit-19 CT classification system had a sensitivity of 61.2%, specificity of 95.9%, PPV of 93.7%, and NPV of 72.3% in the diagnosis of the disease.

Table 1: Patients' demographic characteristics and laboratory findings at the time of presentation according to their RT-PCR test result.

	RT-PCR Test Result		
Variables	**Positive**	**Negative**	**p**
Gender, n (%)			
Male	106 (55.8%)	123 (62.8%)	0.16
Female	84 (44.2%)	73 (37.2%)	
Age, years	57 (39-68.3)	48.5 (33-70)	0.13
White blood cell count, $x10^9$/L	5.6 (4.2–7.6)	5.2 (3.9–6.8)	0.44
Neutrophil count, $x10^9$/L	4.25 (2.9–6.7)	3.7 (2.5–4.6)	0.18
Lymphocyte count, $x10^9$/L	0.7 (0.4–0.9)	1.1 (0.8–1.3)	0.01
C-reactive protein, mg/L	59.3 (42.4–94.6)	24.6 (5.1–39.8)	< 0.001
Hemoglobin, (g/dl)	13.2 ± 3.4	13.5 ± 2.5	0.67

Data are presented as n (%), mean (SD), or median (interquartile range). RT-PCR: reverse- transcriptionase polymerase chain reaction.

Table 2: Distribution of the RT-PCR-positive and RT-PCR-negative patients according to the BSTI COVID-19 CT classification.

	RT-PCR Test Result		
BSTI COVID-19 CT Classification	**Positive**	**Negative**	**Total**
Classic COVID-19	118 (30.6%)	8 (2.1%)	126 (32.6%)
Probable COVID-19	39 (10.1%)	16 (4.1%)	55 (14.2%)
Indeterminate	21 (5.4%)	52 (13.5%)	73 (18.9%)
Non-COVID	12 (3.1%)	120 (31.1%)	132 (34.2%)
Total	190 (49.2%)	196 (50.8%)	386 (100%)

RT-PCR: Reverse transcription polymerase chain reaction; BSTI: British Society of Thoracic Imaging; CT: computed tomography

Table 3: Diagnostic performance of the BSTI COVID-19 CT classification system.

BSTI COVID-19 CT Classification	**Sensitivity**	**Specificity**	**PPV**	**NPV**	**Accuracy**
Classic COVID-19[a]	62.1% (118/190)	95.9% (188/196)	93.7% (118/126)	72.3% (188/260)	79.3% (306/386)
Classic COVID-19 or Probable COVID-19[b]	82.6% (157/190)	87.8% (172/196)	86.7% (157/181)	83.9% (172/205)	85.2% (329/386)
Classic COVID-19, Probable COVID-19, or Indeterminate[c]	93.7% (178/190)	61.2% (120/196)	70.1% (178/254)	90.9% (120/132)	77.2% (298/386)

BSTI: British Society of Thoracic Imaging; CT: computed tomography; PPV: positive predictive value; NPV: negative predictive value. [a] Kappa=0.583, p<0.001; [b] Kappa=0.704, p<0.001; [c] Kappa=0.546, p<0.001

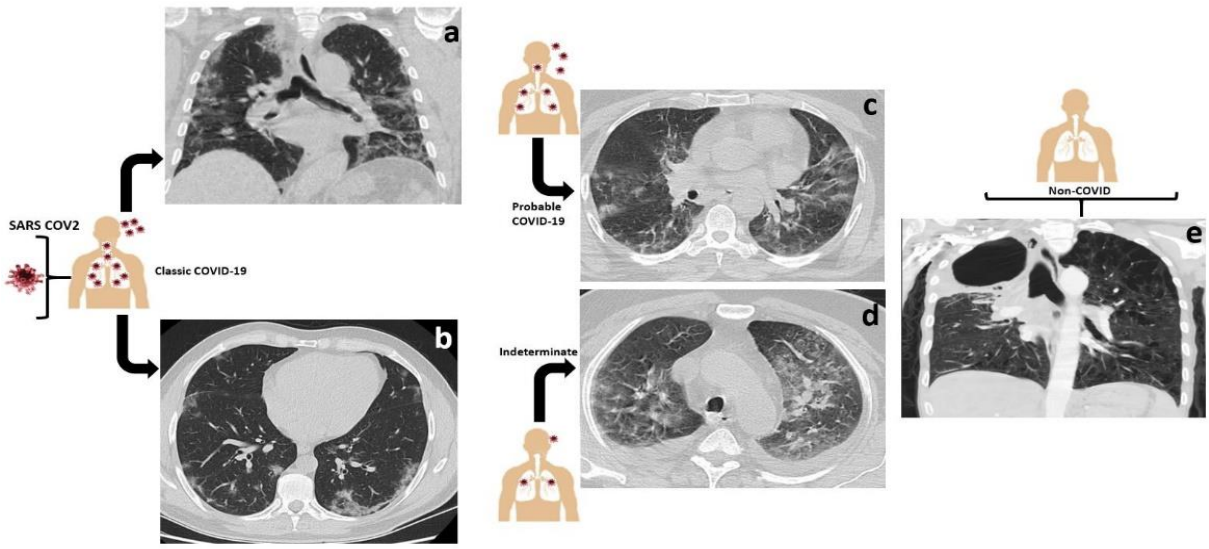

Figure 1: Experimental demonstration of SARS-CoV-2 infection according to diagnostic performance of the BSTI COVID-19 CT classification system. In the coronal and axial sections, peripheral predominantly multifocal ground-glass opacities are observed more prominent in the middle and lower lobes of bilateral lung parenchyma areas, which accompanied by diffuse interlobular septal thickening and subpleural lines. Findings were considered typical for COVID-19 pneumonia. CT findings of the patient were evaluated as Classic COVID-19 (a and b). Lower lobe dominant, bronchocentric and peripheral consolidation in both lungs; limited number of ground glass opacities are observed. CT findings of the patient were evaluated as probable Covid 19 pneumonia (c). Bilateral pleural effusion, more prominent ground-glass opacities in the central and upper zone, and accompanying nodular infiltration were present, which was evaluated clinically in accordance with the findings suggesting an alternative diagnosis (indeterminate) (d). Cavitation accompanied by volume loss in the right lung upper zone; right hilar soft tissue density, more prominent focal emphysematous aeration increases are observed on the left and apex. It was accepted as non-Covid 19 CT findings in the patient who had no sign of pneumonia (e).

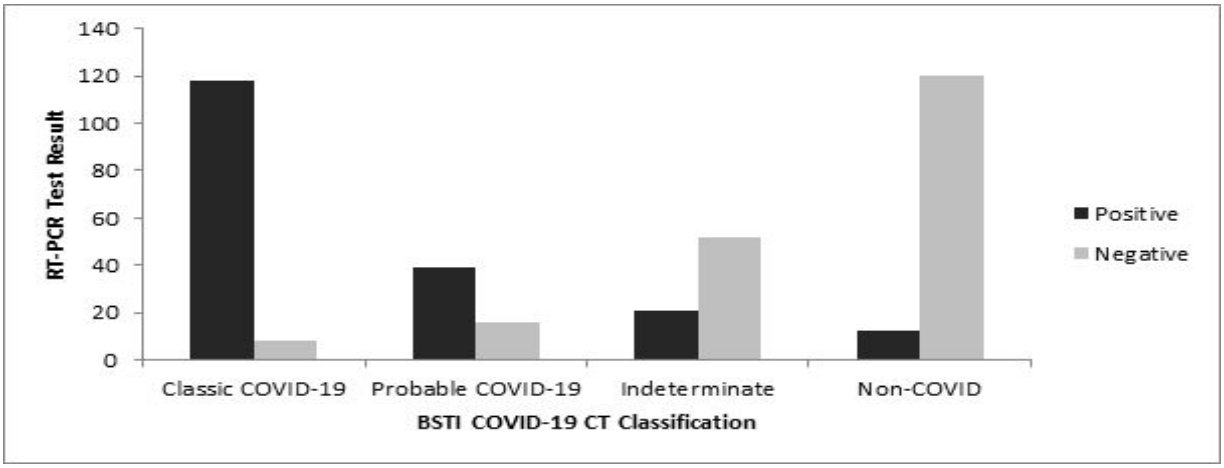

Figure 2: The ratio of CT findings according to the BSTI Covit-19 CT classification.

When the classic Covit-19 and probable Covit-19 categories were combined, the sensitivity of this classification system was determined as 82.6%, specificity 87.8%, and accuracy 85.2%. When the three groups other than the non-COVID category were combined, the sensitivity of this classification system was found to be 93.7%, specificity 61.2%, PPV 70.1%, NPV 90.9%, and accuracy 77.2% (Table 3).

4. Discussion

Since the report of the first case, SARS-CoV-2 Disease has spread all over the world in a short time, infecting millions of people from different continents. Although more than a year has passed since the onset of the pandemic, a large number of patients infected with or suspected of being infected with SARS-CoV-2 Disease still present to hospitals every day. There is not

sufficient RT-PCR test capacity worldwide to detect SARS-CoV-2 Disease, the causative agent of SARS-CoV-2 Disease, and therefore hospitals have difficulties in triage, diagnosis, management or treatment of these patients. Since SARS-CoV-2 Disease primarily involves lungs, chest CT has become the preferred auxiliary diagnostic method in the diagnosis of SARS-CoV-2 Disease (13-15).

The results of our study showed that the classic SARS-CoV-2 Disease category of the BSTI Covit-19 CT classification system was highly specific and moderately sensitive in the diagnosis of the disease. The lower sensitivity compared to specificity may be due to the RT-PCR test being performed in the early period of the infection. Previous studies have shown that in patients with CT findings of SARS-CoV-2 Disease, early RT-PCR tests can produce false negative results, and serial RT-PCR tests should be performed for the diagnosis of SARS-CoV-2 Disease in these patients (16, 17).

In a study by Inui et al., it was reported that the sensitivity of BSTI classic Covit-19 category was 64.5% and its specificity was 92% (8). In the same study, it was shown that when the BSTI classic Covit-19 and probable Covit-19 categories were combined, the sensitivity increased to 71% and the specificity decreased to 87% (8). Our results support these findings. We determined that when combined, the classic Covit-19 and probable Covit-19 categories had increased sensitivity and reduced specificity in diagnosing the disease. Another important result of our study is that although 3% of the patients were in the non-COVID category according to the BSTI Covit-19 CT classification criteria, the RT-PCR tests of these patients were positive. This confirms the BSTI non-COVID categorization emphasizing SARS-CoV-2 Disease cannot be definitively ruled out in these cases and the RT-PCR test may be required.

Structured chest CT reporting is recommended for the diagnosis of SARS-CoV-2 Disease since it facilitates radiological diagnosis, reduces variability in interpretation of chest CT reports by clinicians, and standardizes the reporting language. To date, in addition to BSTI, several other structured reporting systems, such as the SARS-COV-2 Reporting and Data System (CO-RADS), SARS-COV-2 imaging reporting and data system (COVID-RADS), and the Radiological Society of North America Expert Consensus statement have been defined (11, 12, 18). These systems are reported to have similar diagnostic performance in SARS-CoV-2 Disease (8). If the patient has underlying interstitial lung disease, emphysema, non-specific interstitial pneumonia, chronic obstructive pulmonary disease, or interstitial pneumonitis, the performance of all chest CT reporting systems decreases in the diagnosis of SARS-CoV-2 Disease. This is due to chest CT findings of Covit-19 pneumonia being similar to those seen in above-mentioned diseases and other viral pneumonias (19). In the BTSI Covit-19 CT classification system, if there is an underlying disease such as interstitial lung disease and emphysema, it becomes difficult to make a diagnosis, and thus the patient is classified into the indeterminate category (10), which reduces the diagnostic performance of the BSTI classification system. The results of our study are in agreement with this information. In our study, of the patients in the BTSI indeterminate category, 29% had a positive RT-PCR test result while 71% had a negative RT-PCR test result.

5. Conclusions

The BSTI Covit-19 CT classification criteria showed reasonable diagnostic performance for SARS-CoV-2 Disease. In particular, the classic Covit-19 category was highly specific and moderately sensitive for the diagnosis of the disease. Further studies are needed to validate the BSTI Covit-19 CT classification system in larger and more diverse populations.

Limitations of the Study

This study has certain limitations. First, due to the retrospective nature of the study, there may have been selection bias. Second, the study being conducted in a single center may have affected the generalizability of the results. Another limitation is that SARS-CoV-2 Disease can be asymptomatic. The inclusion of only symptomatic patients in the sample may have affected the calculated diagnostic performance value of chest CT findings.

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Conflict of Interests

The authors declare that there is no conflict of interest.

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Author Contributions

KY, KK, DO, EA, ETS, HM, AS: Manuscript writing, coordination of the study, database management and analysis, KY, KK, DO, EA, ETS, HM, AS: Data collection, statistical analysis, KY, KK, DO, EA, ETS, HM, AS: contribution to the concept, design and critical revision of article.

Ethical Approval

The study was approved by the SARS-COV-2 Scientific Research Committee of the Republic of Turkey Ministry of Health and the Local Ethics Committee (2020/06-70).

Data sharing statement: The data sets generated and analyzed during the present study are included in this published article. Further details are available for noncommercial purposes from the corresponding author on reasonable request.

Informed Statement

Individuals who consented to participate were included in the study.

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Acinetobacteria Baumannıı Infection in the Intensive Care Unit-Risk Factors and Antibiotic Resistance

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Abstract:, In this study, we tried to elucidate the increased carbepenem resistance in healthcare-associated acinetobacter baummani infections and the factors affecting mortality in the intensive care unit. A total of 70 subjects that were positive for acinetobacter baumannii colonisation have been included in the analysis. The data on age, gender, smoking, comorbidities, steroid usage and antibiotic treatment within the first 24 hours has been recorded. Septic shock patients who did not respond to intense fluid replacement and required dopamine infusion for the treatment of hypotension were also interpreted. The results of antibiogram culture, duration of noninvasive and invazive mechanical ventilation, hospital stay and mortality information have all been investigated. The APACHE and SOFA scores of the first admission day have been calculated. Invasive mechanical ventilation has been conducted to 66 patients and the median duration of administration was 19.5±23.94 (1-138, range: 138) days. The APACHE II score was 24.69±8.37 and SOFA score was 10.43±3.42. The mean hospital stay was 26.03±24.23 (1-139, range 138) days. The mean time to observe positive culture from hospital admission was 15.55±1.19 days. Patients with both meropenem and imipenem resistance were considered carbapenem resistant. By 2010, it was observed that both imipenem and meronem resistance reached 100%. Meronem resistance was 58.3% in 2007, 71.4% in 2008, 81.5% in 2009, and 100% in 2010. Imipenem resistance was 61.5% in 2007, 74.3% in 2008, 81.5% in 2009, and 100% in 2010. © 2022 NTMS.

Keywords: A. baumannii; Antibiotics Resistance; Intensive Care Unit.

1. Introduction

Healthcare-associated infections are more prevalent in intensive care unit patients. The risk factors associated with *acinetobacteria baumannii* at ICU can be elaborated as longer hospital stay, immune supression, older age, comorbid disease, major trauma or burn, previous antibiotic usage, invasive procedures, long term catheterization and mechanical ventilation (1). The rate of healthcare-associated infections are 5-10 times higher in the intensive care unit compared to inpatient clinics. The other importance lies beneath the

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fact that healthcare-associated infections are related with increased mortality, morbidity and healthcare costs (2). Hospital acquired infections are major health problem in intensive care units (3). *Acinetobacteria baumannii* is a gram negative, aerob cocobasilius and is one of the most frequent reasons of nasocomial infections (4). Although *acinetobacteria baumannii* has been identified as a beneficial species previously, currently it is treated as a health status threat due to its resistance to polypharmacy (5).

In this study we aimed to evaluate the *acinetobacteria baumannii* infection in our respiratory ICU with the annual parameters, demographics data and the change of carbepenem and other antibiotic resistance.

2. Material and Methods

The current study has been conducted in the respiratory intensive care unit between August 2006-July 2010 as a retrospective analysis. Ethical approval was obtained from the ethics committee of Dicle University Medical Faculty (Ethics Committee Number:190-21.09.10). Research and Publication Ethics was complied with in our study. The bacterial cultural analysis have been conducted to all patients and 70 subjects that were positive for *acinetobacter baumannii* reproduction have been included in the analysis.

The data on age, gender, smoking, comorbidities, steroid usage and antibiotic treatment within the first 24 hours has been recorded in the analysis. Septic shock patients who did not respond to intense fluid replacement and required dopamine infusion for the treatment of hypotension were also interpreted. The results of antibiogram culture, duration of non-invasive and invazive mechanical ventilation, hospital stay and mortality information have all been investigated for the analyis. Age, smoking, duration of IMV, hospital stay,

2.1. Statistical Analyses

Statistical analysis was performed using SPSS 15.0 for Windows (SPSS Inc., Chicago, IL, USA). Descriptive statistics of continuous variables were shown with mean and standard deviation (SD) values. The chi-square test was used to compare the nominal variables between the two groups. Student's t test was used to compare the mean values of scalar data between the two groups. Shapiro-Wilk test was performed to evaluate whether the data is distributed normally. The hypotheses were bidirectional and $p \leq 0.05$ value was accepted as statistically significant at 95% confidence interval.

3. Results

We had 84 samples of 70 patients *acinetobacter baumanni* cultures. The details of baseline demographic parameters of the patients are shown in Table 1.

Non-invasive mechanical ventilation has been conducted to 43 patients and the median duration of administration was 5.15±6.52 (1-39, range: 38) days. Invasive mechanical ventilation has been conducted to 66 patients and the median duration of administration was 19.5±23.94 (1-138, range: 138) days.

The APACHE scores has been calculated according to lowest figures at the admission of ICU. The APACHE II score was 24.69±8.37 and SOFA score was 10.43±3.42. The mean hospital stay was 26.03±24.23 (1-139, range 138) days.

The mean time to observe positive culture from hospital admission was 15.55±1.19 days. The distribution of 84 samples were as follows: n=40 (47.6) from blood, n=26 (31%) deep tracheal aspiration material, n=7 (8.3%) from urine, n=7 (8.3%) from wound, n=4 (4.8%) from catheter. The antibiotics used within the first 48 hours of ICU stay were ceftriaxone n=29 (41.4), cefoperazone/sulbactam n=7 (9.9%), piperacillin/tazobactam n=3 (4.3%), levofloxacin n=6 (8.6%), meropenem n=8 (11.5%) and imipenem n=6 (8.5%).

3.1. Annual Resistance Rates

The annual resistance rates are shown in Table 2. There was a positive trend of bacterial colonisation starting from 2007 to 2009. We did not analyze 2006 due to limited number of cases n=1 (1.2%). The annual resistance distribution was n=14 (16.7%) in 2007, n=35 (41.7%) in 2008, n=27 (32.1%) in 2009 and n=7 (8.3%) in in 2010 (until June).

3.2. Carbepenem resistance

Patients with both meropenem and imipenem resistance were considered carbapenem resistant. By 2010, it was seen that both imipenem and meronem resistance reached 100%. Meronem resistance was 58.3% in 2007, 71.4% in 2008, 81.5% in 2009, and 100% in 2010. Imipenem resistance was 61.5% in 2007, 74.3% in 2008, 81.5% in 2009, and 100% in 2010 (Table 2).

3.3. Mortality Rate

The mortality rate, age, smoking, duration of IMV, hospital stay, APACHE II and SOFA scores were elaborared in Table 3. Regarding all the patients with acinetobacter baumannii colonisation the mortality rate has been observed as 87.1% (n=61). Age, smoking, duration of IMV, hospital stay, APACHE II and SOFA scores did not Show any statistical correlation with mortality.

Table 1: Baseline Demographics of the Study Population.

Baseline Demographics	*n (%)*
Gender	
Female	25 (35.7%)
Male	45 (64.3%)
Smoking	
Yes	30 (42.9%)
No	40 (57.1%)
Steroid Usage	
Yes	32 (45.7%)
No	37 (52.9%)
Dopamine Requirement	
Yes	60 (85.7%)
No	10 (14.3%)
Hospital Stay	
Yes	55 (78.6%)
No	15 (21.4%)
Outcome	
Alive	9 (12.9%)
Exitus	61 (87.1%)
Comorbid Disease	66(94.3%)
Chronic Obstructive Pulmonary Disease	26 (37.1%)
Congestive Heart Failure/Coronary Artery Disease	15 (21.4%)
Renal Failure	
Pulmonary thromboembolism	14 (20%)
Diabetes mellitus	9 (12.9%)
Cerebro-vascular event	9 (12.9%)
Pulmonary Tuberculosis History	9 (12.9%)
Malignity	6 (8.6%)
Hypertension	6 (8.6%)
Para-pulmonary effusion	5 (7.1%)
Bronchiectasia	4 (5.7%)
Muscle Disease	4 (5.7%)
	4 (5.7%)

Table 2: Annual antibiotic resistance rates (%).

Antibiotic	2007	2008	2009	2010
Cefotaxime	100	100	100	100
Trimethoprim + Sulfamethoxazole	92.3	85.7	96.3	71.4
Piperacillin Sodium	100	100	100	100
PiperacillinTazobactam	No Data	95.5	100	85.7
Chloramphenicol	100	100	No Data	No Data
Aztreonam	100	91.7	No Data	No Data
Cefepime Hydrochloride	61.5	80	100	100
Ceftazidime	92.3	91.4	96.3	100
Levofloksasin	100	90.3	95.8	71.4
Cefoperazone/Sulbactam Sodium	No Data	0	9.1	16.7
Ciprofloxacin	92.3	91.4	96.3	100
Imipenem	61.5	74.3	81.5	100
Meropenem	58.3	71.4	81.5	100
Colistin	No Data	0	No Data	0

Table 3: Comparison of risk factors on alive and exitus patients.

	EXITUS	ALIVE	P
Age (year)	63.34±15.9	55.67±22.09	0.20
Smoking (packs/year)	61.22±32.75	21.67±10.40	0.05
APACHE II	24.4±8.7	26±5.4	0.50
SOFA	10.49±3.46	10.0±3.31	0.69
IMV (days)	15,84±17.25	42.25±46.76	0.15
Duration of hospital stay (days)	21.5±17.8	56.6±38.36	0.03

$p \leq 0.05$ statistical significance.

A majority of the patient with smoking habit died (n=27/30). A statistical sginificance has been observed in the annual cigarette consumption was 61.22±32.75 packs in the mortality group and 21.67±10.40 packs/year in the alive individuals (p=0.05). One other significant data was duration of hospital stay between mortality group and alive subjects (p=0.03). Systemic steroid utilization, hospital stay, dopamin infusion, comorbid disease and gender differences did not generate any significance on dead and alive patients.

4. Discussion

In this study we have analyzed bacterial colonisation in order to detect the antibiotic resistance to acinetobacter baumannii. In our study, it was seen that the carbenem resistance of *A. Baumannii* reached 100%. In a recent systematic review, 24 studies were evaluated and, A. baumannii and carbapenem resistant strains were reported to account for 20.9% (95% CI 16.5-26.2) and 13.6% (95% CI 9.7-18.7) of all nosocomial infections, respectively (6).

We have investigated the *acinetobacter baumannii* treatment resistance in our intensive care unit with respect to mortality factors in the literature. We assume that the outcomes of this study will contribute to the patient management in the ICU.

The selection of edfective antibiotic at a sufficient dose is crucial forthe treatment success of healthcare-associated infections (7). At this stage the importance of resistance rates plays an important role for convenient treatment at the intensive care unit (8). The acinetobacter baumannii has developed resistance to dysinfectants and major antimicrobial agents thus becoming a severe healthcare-associated infection (9). *Acinetobacter baumannii* has developed strong resistance to sefthazidime 92.5% *(n=37/40)* and izolated *acinetobacter baumannii* cultivates this resistance to this antibiotic group (10). Since carbapenem group antibiotics are the last option in the treatment of *A. baumannii* infections, carbapenem resistance is of particular importance. In the study of Deveci et al., among 127 *A. baumannii* strains isolated from patients diagnosed with healthcare-associated infections between 2007 and 2010, 5 of 26 strains in 2007, 18 of 31 strains in 2008, 10 of 35 strains in 2009. In 2010, 20 of 35 strains and 20 of 35 strains were obtained from intensive care patients. While the sensitivity rate for imipenem was 50% in 2007, it was 20% in 2010. Similarly, increased carbepenem resistance was noted in our study. In the current research, by 2010, it was seen that *A.baumani* resistance reached 100% both imipenem and meronem resistance. Meronem resistance was 58.3% in 2007, 71.4% in 2008, 81.5% in 2009, and 100% in 2010. Imipenem resistance was 61.5% in 2007, 74.3% in 2008, 81.5% in 2009, and 100% in 2010. However lower resistance rates has been achieved in the European studies as mortalities was not always clearly identified due to comorbidities (12). In a previous article by Jang et al, they have declared that comorbid diseases played a major role than infection itself on mortality rates (13). Lahmer et al published that the rate mortality due to *acinetobacter baumannii* was 100% on sepsis cases (14). Similarly Leão et al emphasized that there is a relation between mortality and *acinetobecter baumanii* in sepsis patients at intensive care unit (15). A cohort study with septic shock patients in ICU has shown a mortality rate of 49.6% (16). On the contrary, no statistical significance has been achieved between the patients in septic shock that required dopamine and individuals with no sepsis in our study.

If the risk factors of *acinetobacter baumannii* infection was analyzed one can see that being male, comorbid disease *(respiratory and renal failure)*, high APACHE II score, longer stay at ICU, invasive mechanical ventilation, previous antibiotic usage, immuno-supression and septic shock were the major factors (17).

In another study conducted in burnt patients, a total of 30 patients infected with Multi-drug resistant *acinetobacter baummani* (MDR-AB) and 60 uninfected control cases were included in the study. This study showed that many factors contribute to multidrug resistance in *A. baumannii*. A combination of early detection of wound infections, appropriate antimicrobial treatments, surgical debridement and early wound closure may be effective in treatment (18). In another study in which a total of 70 newborns with extensive drug-resistant (XDR) *acinetobacter baummani* growth and 118 control newborns were included in the study, gestational age, mechanical ventilation, transfusion, parenteral nutrition, glycopeptide use, carbapenems, and aminoglycosides were found to be significantly associated associated with mortality (19).

On the contrary we did not found any statistical significance between exitus and alive individuals on age, comorbid disease, gender, hospital stay, systemic steroid usage, dopamine infusion requirement, systemic steroid administration duration of invasive mechanical ventilation, APACHE II and SOFA scores. The limited number of study population, heterogeneous patient profiles might be the reason of this issue. On the other hand all the risk factors above were not evenly present in the ICU patients.

According to previous research, the mortality rate of patients with *acinetobacter baumannii* colonisation ranges between 30-76% (20). In our study the mortality rate in *acinetobacter baumannii* clonized patients were 87.1% (n=61) (n=9, 12.9% were alive). The high rate of mortality in this study could be elaborated with 3 factors: older age, presence of comorbidities and being in the respiratory ICU.

Male gender has been elaborated as one of the risk factors in previous studies and this rationwas 64.3% in our research (21). The rate of smoking was 42.9% in our population and Wah-Shing Leung et al found a similar figure as 55.4% previously (22). The high rate of smoking could be attribured to the respiratory intensive care unit.

Preventing antibiotic resistance development to acinetobacter *baumannii* is one of the main objectives of intensive care patient management. A bacterial culture analysis should be conducted prior to initiating antibotic treatment on hospitalized patients. did not have a placebo group and the absence of a control group that did not receive both treatments.

5. Conclusions

Carbepenem resistance is increasing gradually and is a problem in terms of treatment. Having information about resistance would lead the physician in a more appropriate way for better treatment success. The antimicrobial regimen must be reassigned according to bacterial culture results. Increased carbapenem resistance is currently trending and this causes longer duration of hospital stay and increased mortality. Further studies should be conducted in this era with larger number of patients.

Limitations of the Study

The mail limitation of this study can be elaborated as the population only consisted of acinetobacter baumannii colonized individuals and lacking a control group. Nonetheless we still assume that this study will provide certain guidance to intensive care management.

Conflict of Interests

We do not have any conflicts of interest

Financial Support

We do not have financial resources to declare

Author Contributions

Data collection B.Ç, statistics E.K, spelling B.Ç and E.K, edit İ.H and M.K, translation and coordination T.K

Ethical Approval

Ethical approval was obtained from the ethics committee of Dicle University Ethics committee number: 192:21.09.10.

Data sharing statement

Data and materials are Available upon reguest: HYPERLINK "mailto:drbariscil@hotmail.com"drbariscil@hotmail.com

Consent to participate

Consent to participate was obtained from the participants.

Informed Consent

Informed consent was obtained from the participants

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