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Comparison of patients presenting to the emergency department with psychiatric complaints before and after the covid-19 pandemic.

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ABSTRACT

Objectives: This study aims to investigate whether there was a difference in the psychiatric complaints of patients presenting to the emergency department before and after the COVID-19 pandemic.

Methods: All patients aged 18 years and over who presented to the adult emergency department of the University of Health Sciences Bursa Yüksek İhtisas Training and Research Hospital between 11.03.2019 and 11.03.2021 with psychiatric complaints, for whom psychiatry consultation was requested, and whose complete study data were available were retrospectively included in the study.

Results: There were 1508 patients in the study. Of the patients, 50.9% (n=768) were in the pre-pandemic group, 54.0% (n=815) were single, and 77.4% (n=1167) were unemployed. As a result of the statistical analysis, a significant correlation was found between diagnosed psychiatric diseases, depression, anxiety disorder, post-traumatic stress disorder, alcohol-substance withdrawal, panic disorder, delirium, and other psychiatric diseases with the pre-pandemic and post-pandemic periods respectively [($p=0.001$), ($p<0.05$), ($p<0.001$), ($p<0.05$), ($p<0.05$), ($p<0.05$), ($p<0.05$)]. In addition, a significant correlation was found between hallucinations, agitation, aggression, panic attacks, catatonic symptoms, delusions, depressive complaints, and the onset of these symptoms and findings with the pre-pandemic and post-pandemic periods [($p=0.001$), ($p<0.001$), ($p<0.001$), ($p<0.05$), ($p<0.001$), ($p<0.05$), ($p<0.05$), ($p<0.05$)]. Accordingly, in the post-pandemic group, the presentation rate of patients with a diagnosis of psychiatric illness, generalized anxiety disorder, panic disorder, and delirium, taking psychiatric medication, having agitation, panic, delusions and depressive complaints, who are single and unemployed was significantly higher than in the pre-pandemic period.

Conclusion: It has been understood that the COVID-19 disease, causing a worldwide pandemic, serious mortality, and morbidity, increased psychiatric complaints compared to the pre-pandemic period.

Keywords: Psychiatric complaints, COVID-19, anxiety, emergency department

How to cite this article

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COVID-19 was first detected in December 2019 in Wuhan, China, and then spread rapidly worldwide. On 11 March 2020, the World Health Organization (WHO) declared COVID-19 a pandemic. The virus has caused a major health crisis around the world due to its rapid spread and high mortality rate. Currently, many research and studies on COVID-19 are ongoing [1]. The COVID-19 pandemic has had significant psychological effects on people, which has led to emotional reactions such as anxiety, stress and fear in many people due to the high contagiousness, lethality, and uncontrolled nature of the disease [2].

During the pandemic, the sense of uncertainty in the community, concerns about the future of the health system and society, job losses, economic uncertainties, social isolation and quarantine have harmed people's mental health.

The COVID-19 pandemic has also posed an increased risk to people with mental health problems. These people have struggled to receive their current treatments during the pandemic, and their support systems and resources have decreased, which has led to an increase and worsening of symptoms in people with psychological problems [3].

However, people have developed ways to cope with their emotional reactions such as anxiety, stress, and fear. These include stress-reducing behaviors such as regular exercise, meditation, good sleep patterns, healthy nutrition, and social connections. In addition, psychological support services have also been an important resource to protect people's mental health during the pandemic [4].

Some people may also experience health problems after the pandemic. In particular, due to the measures taken during the pandemic, many people may not have been able to go for regular health checks and receive treatment, which may have negatively affected the health of people with chronic diseases or those who require treatment.

This study aims to investigate whether there was a difference in the psychiatric complaints of patients presenting to the emergency department before and after the COVID-19 pandemic.

METHODS

This single-center retrospective study was conducted with the protocol numbered 2011-KAEK-2021/02-11 approved by the Clinical Research Ethics Committee of the University of Health Sciences Bursa Yüksek İhtisas Training and Research Hospital.

All patients aged 18 years and over who presented to the Adult Emergency Department of University of Health Sciences Bursa Yüksek İhtisas Training and Research Hospital

between 11.03.2019 and 11.03.2021 with psychiatric complaints, for whom psychiatry consultation was requested, and for whom complete study data were available were retrospectively included in the study. Patients under 18 years of age, who did not have psychiatric complaints, and whose complete study data could not be accessed were excluded from the study.

A standardized data entry form was created. The data of the patients were obtained from emergency patient files through the Hospital Information Management System. Using the hospital automation system and patient cards, patients' age, gender, marital status, employment status, presenting complaint, history of psychiatric illness, alcohol and/or substance use, comorbidities, medications, mode of onset of symptoms (acute-chronic), whether they were a diagnosed psychiatric patient, whether they had thoughts or attempts of self-mutilation, whether they were forensic cases, whether they had COVID-19 infection, whether they were open to communication, treatment compliance, whether neurological symptoms and signs accompany, general physical examination and neurological examination characteristics, pathological features in imaging (brain tomography, magnetic resonance imaging) tests requested to rule out organic pathologies, psychiatry consultation results and recommendations, treatment performed in the emergency department, diagnosis, consultations requested from other departments, and outcome status (discharge, hospitalization) were investigated. The study was recorded in the standard study data entry form.

Statistical Analysis

IBM SPSS Statistics for Windows, Version 21.0 (IBM Corp. Armonk, NY: USA. Released 2012) package program was used for statistical analyses. Descriptive statistics were expressed as mean ± standard deviation (minimum - maximum), median and range and/or interquartile range (IQR) for numerical variables, while categorical variables were expressed as number of cases and (%). Kolmogorov-Smirnov test was used for normality distribution of the data. Levene's test was used to determine whether the assumption of homogeneity of variances was met. The

significance of the difference between the groups in terms of continuous numerical variables for which parametric test statistical assumptions were met was examined by Student's t-test, while the significance of the difference in terms of continuous numerical variables for which parametric test statistical assumptions were not met was evaluated by Mann-Whitney U test. Chi-square and Fisher's exact test were used to analyze whether there was a relationship between categorical variables. $p<0.05$ was considered statistically significant. The results were given at 95% confidence interval.

Table 1. Clinical and Demographic Information

Age (year) *		**36 (28-46)**
Gender #	Male	820 (54,4)
	Female	688 (45,6)
Groups by Pandemic #	Pre-Pandemic	768 (50,9)
	Post-Pandemic	740 (49,1)
PCR Test Result#	Negative	1451 (96,2)
	Positive	57 (3,8)
Marital Status#	Single	815 (54,0)
	Married	674 (44,7)
	Other	19 (1,3)
Employment Status#	Unemployed	1167 (77,4)
	Employed	301 (20,0)
	Other	40 (2,6)
Family History of Psychiatric Disease#		372 (24,7)
Diagnosis of Psychiatric Disease#		756 (50,1)
Psychiatric Diseases#	Psychosis	318 (21,1)
	Adjustment Disorder	305 (20,2)
	Bipolar Disorder	208 (13,8)
	Depression	205 (13,6)
	Anxiety Disorder	171 (11,3)
	Alcohol-Substance Addiction	130 (8,6)
	Schizophrenia	101 (6,7)
	Post Traumatic Stress Disorder	42 (2,8)
	Panic Attack	31 (2,1)
	Conversion	29 (1,9)
	Delirium	26 (1,7)
	Obsessive Compulsive Disorder	25 (1,7)
	Attention Deficit Hyperactivity Disorder	15 (1,0)
	Somatoform Disorder	14 (0,9)
	Other	58 (3,8)
Non-Psychiatric Co-morbidity#		365 (24,2)
	Hypertension	170 (11,3)
	Diabetes Mellitus	45 (3,0)
	Epilepsy	31 (2,1)
	Mental Retardation	29 (1,9)
Co-morbidity #	Coronary Artery Disease	22 (1,5)
	Asthma/COPD	19 (1,3)
	Dementia	13 (0,9)
	Cerebrovascular Disease	13 (0,9)
	Other	69 (4,6)
Alcohol Use#		295 (19,6)
Drug Use#		261 (17,3)
Total#		1508 (100)

n (%), * Median, (IQR 25-75), COPD: Chronic Obstructive Pulmonary Disease

RESULTS

A total of 1508 patients were included in the study. The median age of the patients was 36 (IQR, 25-75: 28-46) years and 54.4% (n=820) of the patients were male. While 50.9% (n=768) of the patients were in the pre-pandemic group, 3.8% (n=57) had positive PCR test results. While 50.1% (n=756) of the patients had a diagnosed psychiatric illness, 24.7% (n=372) had a family history of psychiatric illness. The most common psychiatric disorders were psychosis (21.1%, n= 318) and adjustment disorder (20.2%, n=305) (Table 1).

The most common symptoms and signs in the presentation were delusions (31.5%, n= 475) and depressive symptoms (30.8%, n= 464), and 56.2% (n=848) of these symptoms/findings were sudden onset. In the psychiatric evaluation of the patients, 75.1% (n=1132) were open to communication and 50.9% (n=767) were compliant with treatment. Consultation from other departments was requested for 18.7% (n=282) of these patients (Table 2).

In the analysis performed to determine the relationship between the gender, marital and employment sta-

Table 2. Clinical and Demographic Information

Onset Status of Symptoms[#]	Acute	848 (56,2)
	Chronic	660 (43,8)
Admission Symptoms/Findings [#]	Delusion	475 (31,5)
	Depressive Symptoms (Complaints)	464 (30,8)
	Anxiety	439 (29,1)
	Hallucination	422 (28,0)
	Self-Harm	409 (27,1)
	Agitation	369 (24,5)
	Catatonic Symptoms	283 (18,8)
	Aggression	137 (9,1)
	Panic Attack	101 (6,7)
	Deprivation	72 (4,8)
Psychiatric Drug Use [#]		557 (36,9)
Psychiatric Drugs[#]	Antidepressant Agents	430 (28,5)
	Antipsychotic Agents	372 (24,7)
	Mood Regulatory Agents	103 (6,8)
	Anxiolytic Agents	53 (3,5)
Psychiatric Evaluation Findings [#]	Openness to Communication	1132 (75,1)
	Treatment Compliance	767 (50,9)
	Presence of Suicidal Thoughts	334 (22,1)
	Aggression Status	152 (10,1)
	Presence of Neurological Findings	152 (10,1)
Forensic Status [#]		337 (22,3)
Other Consultation Request[#]		282 (18,7)
	No	1226 (81,3)
	Internal Medicine	179 (11,9)
	Neurology	67 (4,4)
	Orthopedics and Traumatology	9 (0,6)
Other Consultation [#]	Infectious Diseases	7 (0,5)
	General Surgery	7 (0,5)
	Anesthesia and Reanimation	6 (0,4)
	Brain and Nerve Surgery	4 (0,3)
	Other	4 (0,3)
	Plastic and Reconstructive Surgery	2 (0,1)
Computed Tomography of the Brain[#]		153 (10,1)
Cranial Magnetic Resonance Imaging [#]		120 (8,1)
Total[#]		1508 (100)

n (%)

Table 3. Analysis of Variables by Groups

Variables			Groups		Total	Chi-square/ Fisher's exact test
			Pre-Pandemic	Post-Pandemic		
Gender	Female	n (%)	362 (52,6)	326 (47,4)	688 (100)	p>0,05*
	Male	n (%)	406 (49,5)	414 (50,5)	820 (100)	
Marital Status	Single	n (%)	379 (46,5)	436 (53,5)	815 (100)	**p=0,001&**
	Married	n (%)	379 (56,2)	295 (43,8)	674 (100)	
	Other	n (%)	10 (52,6)	9 (47,4)	19 (100)	
Employment Status	Unemployed	n (%)	540 (46,3)	627 (53,7)	1167 (100)	**p<0,001&**
	Employed	n (%)	199 (66,1)	102 (33,9)	301 (100)	
	Other	n (%)	29 (72,5)	11 (27,5)	40 (100)	
History of Psychiatric Illness	No	n (%)	381 (55,3)	308 (44,7)	689 (100)	**p<0,05***
	Yes	n (%)	387 (47,3)	432 (52,7)	819 (100)	
Family History of Psychiatric Illness	No	n (%)	582 (51,2)	554 (48,8)	1136 (100)	p>0,05*
	Yes	n (%)	186 (50,0)	186 (50,0)	372 (100)	
Total		n (%)	768 (50,9)	740 (49,1)	1508 (100)	

* Chi-square/ Fisher's exact test

tus of the patients, and the history of psychiatric illness in their background and family history with the period before and after the pandemic, a significant difference was found between pre pandemic and post pandemic period in terms of marital status, employment status, and having a history of psychiatric illness in their background respectively [(p=0.001), (p<0.001), (p<0.05)]. The rates of singles in the post-pandemic group and married and other groups in the pre-pandemic group were significantly higher. In the post-pandemic period, the rates of unemployed and having a history of psychiatric illness were significantly higher (Table 3).

In the Chi-square / Fisher's exact analysis to determine the relationship between the patients' diagnosed psychiatric illness status and current psychiatric illness diagnoses and the period before and after the pandemic, a statistically significant correlation was found between depression, anxiety disorder, post-traumatic stress disorder, alcohol-substance addiction, panic attacks, delirium, other psychiatric disorders (sleep disorder, eating disorders), and alcohol use with the pre- and post- pandemic period respectively [(p=0.001), (p<0.05), (p<0.001), (p<0.05), (p<0.05), (p<0.05), (p<0.05), (p<0.05)]. In the post-pandemic period, the rates of anxiety disorder, panic attacks, delirium and alcohol use were significantly higher in those with diagnosed psychiatric diseases. In the pre-pandemic group, the rates of depression, post-traumatic stress disorder, alcohol-substance abuse and other psychiatric diseases were significantly higher (Table 4).

In the analysis conducted to determine the relationship between the admission symptoms and findings, baseline status in terms of the period before and after the pandemic, a significant correlation was found between hallucinations, agitation, aggression, panic attacks, catatonic symptoms, delusions, depressive complaints, and the onset of these symptoms and signs with the period before and after the pandemic [(p=0.001), (p<0.001), (p<0.001), (p<0.05), (p<0.001), (p<0.05), (p<0.05), (p<0.05)]. In the pre-pandemic group, the rates of acute admission symptoms and signs, hallucinations and aggression were found to be significantly higher, whereas the rates of agitation, panic attacks, catatonic symptoms, delusions and depressive complaints were significantly higher in the post-pandemic group (Table 5).

In the analysis conducted to determine the relationship between the patients' psychiatric drug use status and medications, psychiatric evaluation findings, forensic case status, request for consultation outside of psychiatry, and cranial CT and MRI requests with the period before and after the pandemic, a significant correlation was found between the use of psychiatric drugs, use of anxiolytics, hallucinations and aggression, and request for other consultation with the period before and after the pandemic [(p<0.05), (p=0.001),(p<0.05), (p<0.05), (p<0.05)]. The rates of hallucinations and aggression among psychiatric evaluation findings were significantly higher in the pre-pandemic group, whereas the rates of psychiatric drug use, anxiolytic use and request for other consultation were significantly higher in the post-pandemic

Table 4. Analysis of Psychiatric Disease Diagnoses by Groups

Variables			Groups		Total	Chi-square/ Fisher's exact test
			Pre-Pandemic	Post-Pandemic		
Diagnosed Psychiatric Disease Status	No	n (%)	415 (55,2)	337 (44,8)	752 (100)	**p=0,001***
	Yes	n (%)	353 (46,7)	403 (53,3)	756 (100)	
Psychosis	No	n (%)	606 (50,9)	584 (49,1)	1190 (100)	p>0,05*
	Yes	n (%)	162 (50,9)	156 (49,1)	318 (100)	
Depression	No	n (%)	647 (49,7)	656 (50,3)	1303 (100)	**p<0,05***
	Yes	n (%)	121 (59,0)	84 (41,0)	205 (100)	
Bipolar Disorder	No	n (%)	654 (50,3)	646 (49,7)	1300 (100)	p>0,05*
	Yes	n (%)	114 (54,8)	94 (45,2)	208 (100)	
Obsessive Compulsive Disorder	No	n (%)	756 (51,0)	727 (49,0)	1483 (100)	p>0,05&
	Yes	n (%)	12 (48,0)	13 (52,0)	25 (100)	
Somatoform Disorder	No	n (%)	759 (50,8)	735 (49,2)	1494 (100)	p>0,05&
	Yes	n (%)	9 (64,3)	5 (35,7)	14 (100)	
Anxiety Disorder	No	n (%)	713 (53,3)	624 (46,7)	1337 (100)	**p<0,001***
	Yes	n (%)	55 (32,2)	116 (67,8)	171 (100)	
Post Traumatic Stress Disorder	No	n (%)	739 (50,4)	727 (49,6)	1466 (100)	**p<0,05&**
	Yes	n (%)	29 (69,0)	13 (31,0)	42 (100)	
Alcohol-Substance Addiction	No	n (%)	685 (49,7)	693 (50,3)	1378 (100)	**p<0,05***
	Yes	n (%)	83 (63,8)	47 (36,2)	130 (100)	
Attention Deficit Hyperactivity Disorder	No	n (%)	757 (50,7)	736 (49,3)	1493 (100)	p>0,05&
	Yes	n (%)	11 (73,3)	4 (26,7)	15 (100)	
Panic Disorder	No	n (%)	761 (51,5)	716 (48,5)	1477 (100)	**p<0,05&**
	Yes	n (%)	7 (22,6)	24 (77,4)	31 (100)	
Delirium	No	n (%)	760 (51,3)	722 (48,7)	1482 (100)	**p<0,05&**
	Yes	n (%)	8 (30,8)	18 (69,2)	26 (100)	
Conversion	No	n (%)	749 (50,6)	730 (49,4)	1479 (100)	p>0,05&
	Yes	n (%)	19 (65,5)	10 (34,5)	29 (100)	
Adjustment Disorder	No	n (%)	616 (51,2)	587 (48,8)	1203 (100)	p>0,05*
	Yes	n (%)	152 (49,8)	153 (50,2)	305 (100)	
Schizophrenia	No	n (%)	719 (51,1)	688 (48,9)	1407 (100)	p>0,05*
	Yes	n (%)	49 (48,5)	52 (51,5)	101 (100)	
Other	No	n (%)	729 (50,3)	721 (49,7)	1450 (100)	**p<0,05&**
	Yes	n (%)	39 (67,2)	19 (32,8)	58 (100)	
Alcohol Use	No	n (%)	596 (49,1)	617 (50,9)	1213 (100)	**p<0,05***
	Yes	n (%)	172 (58,3)	123 (41,7)	295 (100)	
Total		n (%)	768 (50,9)	740 (49,1)	1508 (100)	

* Chi-square/ Fisher's exact test

Table 5. Analysis of Symptoms by Groups

Variables			Groups		Total	Chi-square/ Fisher's exact Test
			Pre-Pandemic	Post-Pandemic		
Onset of Symptoms	Acute	n (%)	458 (54,0)	390 (46,0)	848 (100)	**p<0,05***
	Chronic	n (%)	310 (47,0)	350 (53,0)	660 (100)	
Hallucination	No	n (%)	524 (48,3)	562 (51,7)	1086 (100)	**p=0,001***
	Yes	n (%)	244 (57,8)	178 (42,2)	422 (100)	
Agitation	No	n (%)	614 (53,9)	525 (46,1)	1139 (100)	**p<0,001***
	Yes	n (%)	154 (41,7)	215 (58,3)	369 (100)	
Aggression	No	n (%)	673 (49,1)	698 (50,9)	1371 (100)	**p<0,001***
	Yes	n (%)	95 (69,3)	42 (30,7)	137 (100)	
Anxiety	No	n (%)	546 (51,1)	523 (48,9)	1069 (100)	p>0,05*
	Yes	n (%)	222 (50,6)	217 (49,4)	439 (100)	
Panic Attack	No	n (%)	730 (51,9)	677 (48,1)	1407 (100)	**p<0,05***
	Yes	n (%)	38 (37,6)	63 (62,4)	101 (100)	
Catatonic Symptoms	No	n (%)	673 (54,9)	552 (45,1)	1225 (100)	**p<0,001***
	Yes	n (%)	95 (33,6)	188 (66,4)	283 (100)	
Deprivation	No	n (%)	727 (50,6)	709 (49,4)	1436 (100)	p>0,05*
	Yes	n (%)	41 (56,9)	31 (43,1)	72 (100)	
Self-harm	No	n (%)	543 (49,4)	556 (50,6)	1099 (100)	p>0,05*
	Yes	n (%)	225 (55,0)	184 (45,0)	409 (100)	
Delusion	No	n (%)	551 (53,3)	482 (46,7)	1033 (100)	**p<0,05***
	Yes	n (%)	217 (45,7)	258 (54,3)	475 (100)	
Depressive Complaints	No	n (%)	556 (53,3)	488 (46,7)	1044 (100)	**p<0,05***
	Yes	n (%)	212 (45,7)	252 (54,3)	464 (100)	
Total		n (%)	768 (50,9)	740 (49,1)	1508 (100)	

* Chi-square/ Fisher's exact Test

group (Table 6).

No statistically significant difference was found in the Mann-Whitney U test performed to investigate whether there was a difference between the age and length of hospitalization of the patients with the period before and after the pandemic [(p>0.05), (p>0.05)].

DISCUSSION

Psychiatric emergency is a term used to refer to situations that occur in an individual's emotions, thoughts or behaviors, which may harm the individual's health or the people around him/her, requiring emergency assistance. In recent years, the number of psychiatric emergencies and applications to emergency services has been increasing. In studies conducted in our country, it was reported that such admissions represented a rate between 3% and 17% of total admissions [5, 6].

COVID-19 has not only affected the health of many people around the world, but has also had economic and social impacts. Therefore, many countries needed economic and social support to deal with the pandemic. The COVID-19 pandemic has had significant psychological effects on people (2), which has led to emotional reactions such as anxiety, stress and fear in many individuals due to the nature of the pandemic, its high contagiousness, lethality and uncontrolled nature. In a study conducted by Wang *et al*. in 2020, it was reported that people who do not work are more prone to psychiatric disorders due to the stress they experience [7].

The economic crisis and recession during the COVID-19 pandemic triggered the fears of individuals in the society. Social distancing, isolation, and travel restrictions have led to a decrease in labor force and many people have lost their jobs [8]. In the study conducted by Alexis *et al*. in 2020, the percentage of unemployed patient applications was found to be

Table 6. Analysis of Psychiatric Medication and Evaluation Findings by Groups

Variables			Groups		Total	Chi-square/ Fisher's exact Test
			Pre-Pandemic	Post-Pandemic		
Psychiatric Drug Use	No	n (%)	514 (54,0)	437 (46,0)	951 (100)	***p<0,05****
	Yes	n (%)	254 (45,6)	303 (54,4)	557 (100)	
Antidepressant	No	n (%)	554 (51,4)	524 (48,6)	1078 (100)	p>0,05*
	Yes	n (%)	214 (49,8)	216 (50,2)	430 (100)	
Antipsychotic	No	n (%)	589 (51,8)	547 (48,2)	1136 (100)	p>0,05*
	Yes	n (%)	179 (48,1)	193 (51,9)	372 (100)	
Anxiolytic	No	n (%)	753 (51,8)	702 (48,2)	1455 (100)	***p=0,001&***
	Yes	n (%)	15 (28,3)	38 (71,7)	53 (100)	
Emotion-State Regulator	No	n (%)	707 (50,3)	698 (49,7)	1405 (100)	p>0,05*
	Yes	n (%)	61 (59,2)	42 (40,8)	103 (100)	
Presence of Suicidal Thoughts	No	n (%)	595 (50,7)	579 (49,3)	1174 (100)	p>0,05*
	Yes	n (%)	173 (51,8)	161 (48,2)	334 (100)	
Hallucination	No	n (%)	539 (48,8)	566 (51,2)	1105 (100)	***p<0,05****
	Yes	n (%)	229 (56,8)	174 (43,2)	403 (100)	
Aggression Status	No	n (%)	673 (49,6)	683 (50,4)	1356 (100)	***p<0,05****
	Yes	n (%)	95 (62,5)	57 (37,5)	152 (100)	
Openness to Communication	No	n (%)	200 (53,2)	176 (46,8)	376 (100)	p>0,05*
	Yes	n (%)	568 (50,2)	564 (49,8)	1132 (100)	
Treatment Compliance	No	n (%)	378 (51,0)	363 (49,0)	741 (100)	p>0,05*
	Yes	n (%)	390 (50,8)	377 (49,2)	767 (100)	
Presence of Neurological Findings	No	n (%)	700 (51,6)	656 (48,4)	1356 (100)	p>0,05*
	Yes	n (%)	68 (44,7)	84 (55,3)	152 (100)	
Forensic Status	No	n (%)	581 (49,6)	590 (50,4)	1171 (100)	p>0,05*
	Yes	n (%)	187 (55,5)	150 (44,5)	337 (100)	
Other Consultation Request	No	n (%)	642 (52,2)	587 (47,8)	1229 (100)	***p<0,05****
	Yes	n (%)	126 (45,2)	153 (54,8)	279 (100)	
Computerized Brain Tomography	No	n (%)	695 (51,3)	660 (48,7)	1355 (100)	p>0,05*
	Yes	n (%)	73 (47,7)	80 (52,3)	153 (100)	
Cranial Magnetic Resonance Imaging	No	n (%)	703 (50,6)	685 (49,4)	1388 (100)	p>0,05*
	Yes	n (%)	65 (54,2)	55 (45,8)	120 (100)	
Total		n (%)	768 (50,9)	740 (49,1)	1508 (100)	

* Chi-square/ Fisher's exact Test

77.8% in the post-pandemic period [9]. In our study, the unemployment rate among patients was seen to increase from 46.3% to 53.7% in the post-pandemic period. We think that this situation is related to the increase in unemployment caused by the pandemic. In addition to the problems caused by the pandemic, economic concerns caused negative effects on the psychology of patients such as stress, sadness, anxiety, anxiety, and depressive symptoms.

Pandemics have the potential to have a psycho-social impact on the society as well as physical effects [10]. Studies comparing the marital status of people before and after the pandemic have been conducted. In a study on this subject, it was found that there was an increase in divorce rates after COVID-19 [11]. In the study conducted by Wang Y *et al*. in China, which investigated the psychological status during the COVID-19 pandemic and the factors affecting this, it was determined that the percentage of married individuals was lower than the pre-COVID-19 period, while the percentage of single individuals was higher in the period when the COVID-19 pandemic ended. In addition, it was found that there was a limited increase in the percentage of divorced individuals and

there was no statistically significant difference [12]. In our study, the number of single patients was higher than married patients in the post-pandemic period. We think that factors such as the problems caused by the quarantine process, anxiety about illness and death, exposure to more stressors, insufficient socialization, and increased conflicts due to increased time spent with family members increase this situation.

In the COVID-19 pandemic, it was observed that most of the patients admitted to the emergency department had a history of psychiatric illness. During the pandemic, an increase was observed in the prevalence of emergency department visits in patients with a history of psychiatric illness [9]. In a cross-sectional study, it was shown that people with diagnosed mental disorders were significantly more likely to experience anxiety, depression and stress disorders than people without mental disorders [13]. This may be explained by the change in the daily routine of the patients during the quarantine process, disruption of psychiatry follow-up-treatment, and the inability to regularly attend psychiatry outpatient clinic controls in this process [14]. In our study, it was found that patients with a history of psychiatric illness (53.3%) were more common than those without a psychiatric diagnosis in the applications made in the post-pandemic period.

Uncertainty about the future, information pollution about COVID-19, restrictive practices such as quarantine can cause fear, distress, irritability, panic, sadness, helplessness and loneliness. Such symptoms can lead to serious mental distress. In addition to its negative effects on physical health, COVID-19 can also cause serious mental health problems such as stress, insomnia, high anxiety and chronic depression [15]. In a cross-sectional study conducted by Islam *et al*. in 2020, it was shown that 79.6% of people in the community had panic symptoms and 37.6% had depressive symptoms during the pandemic [16]. In the study conducted by Alexis *et al*. it was found that generalized anxiety disorder was significantly increased in emergency department admission diagnoses [9]. In our study, in the post-COVID-19 period, the rate of patients with anxiety disorder, panic disorder, and depressive complaints was found to be higher in patients with psychiatric complaints in the emergency department, which is consistent with the literature.

The COVID-19 pandemic has contributed alcohol consumption due to stress and social isolation [17]. A study conducted in Australia showed that approximately one in five people increased their alcohol use during the COVID-19 pandemic [18]. In March 2020, a study conducted in the USA showed that alcohol sales increased by 54% compared to the same period of the previous year [19]. In our study, the number of patients admitted to the emergency department due to alcohol use decreased compared to the pre-pandemic period. We think that this situation was caused by the decrease in alcohol consumption due to the restriction of people's social environments during the quarantine period, and at the same time, unnecessary presentations to the emergency department due to alcohol use decreased during the pandemic. The restriction in alcohol sales during the lockdown period may also have been a reason.

The incidence of delirium in hospitalized elderly is estimated to be 23% (20). In the first studies conducted during the pandemic period, it was shown that delirium and mental status changes were observed between 20-30% in COVID-19 patients, and this rate was 60-70% in cases of severe disease [20]. During the COVID-19 period, delirium may have been observed in those with neuropsychiatric predisposition or in the elderly due to isolation. In our study, the rate of delirium was found to be significantly higher in the post-pandemic group. The data obtained in the study were consistent with the literature.

The most important limitation was the retrospective nature of the study and that the data searches were performed through patient files and the Hospital Information Management System. In addition, the fact that the study was single centered and some patients were excluded from the study due to missing data were other limitations.

The COVID-19 pandemic is a trauma with physical and psychological effects. These traumatic effects may vary according to the class, socioeconomic and cultural status, and individual characteristics. Knowing and anticipating the situations that cause the emergence of these symptoms and the emotions that are difficult to cope with will make it easier to overcome the mental difficulties and reduce mental damage.

In conclusion, according to the data in our study, in the post-pandemic group, the admission rate of patients with a diagnosis of psychiatric illness, generalized anxiety disorder, panic disorder and delirium, taking psychiatric medication, having agitation, panic, delusions and depressive complaints, being single, unemployed, and requiring consultation other than psychiatry was significantly higher than in the pre-pandemic period.

CONCLUSION

Conflict of Interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical Approval

The protocol of the study was approved by the Medical Ethics Committee of University of Health Sciences, Bursa Yuksek Ihtisas Training and Research Hospital, Bursa, Turkey. (Decision number: 2011 KAEK-25 2021/02-11, date: 17.02.2021).

Authors' Contribution

Study Conception: FBÇ, MOA, MY, HK, Yİ; Study Design: FBÇ, MOA, MY, HK, Yİ; Literature Review: FBÇ, MOA, MY, HK; Critical Review: FBÇ, MOA, MY, HK, Yİ; Data Collection and/or Processing: FBÇ, MOA, MY, Yİ; Analysis and/or Data Interpretation: FBÇ, MOA, MY, HK; Manuscript preparing: FBÇ, MOA, MY, HK, Yİ.

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The importance of second-trimester AFP and preconception TSH levels for predicting the severity of proteinuria in patients with preeclampsia

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ABSTRACT

Objectives: This study aimed to investigate the relationships between preconception thyroid stimulating hormone (TSH) and thyroxine (T4) levels, as well as second-trimester alpha-fetoprotein (AFP) levels, and the severity of proteinuria in 24-hour urine samples from patients with preeclampsia.

Method: This retrospective analysis focused on preeclampsia patients categorized by proteinuria in 24-hour urine. Inclusion criteria involved patients aged 20-44 with singleton pregnancies diagnosed with preeclampsia and delivery after 20 weeks of gestation. Patients were divided into mild (0.3 to <2 g, n = 94), severe (2 to <5 g, n = 38), and massive (≥5 g, n = 11) proteinuria groups. Comparison included second-trimester AFP levels, preconception TSH, and maternal/neonatal outcomes.

Results: Second-trimester AFP levels increased with proteinuria severity (mild: 47.97 ng/ml; severe: 60.52 ng/ml; massive: 65.50 ng/ml [p<0.001]). AFP emerged as a significant independent predictor of severe proteinuria (odds ratio=1.041), while TSH was not predictive (odds ratio=1.098; p=0.463).

Conclusion: AFP proved to be a valuable marker for predicting proteinuria severity in 24-hour urine samples from preeclampsia patients, whereas preconception TSH was a less compelling predictor.

Keyword: AFP, TSH, preeclampsia, proteinuria, pregnancy

Preeclampsia poses significant challenges in obstetrics, contributing to maternal and neonatal mortality and morbidity [1]. Effective treatment involves the removal of the placenta through delivery, particularly in severe cases requiring urgent action. Accurately assessing preeclampsia severity is crucial for identifying high-risk

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pregnant women [2]. Therefore, the accurate determination of the severity of preeclampsia is important for identifying pregnant women at greater risk of complications. Recent publications have shown that severe proteinuria is valuable in the prediction of poor obstetric outcomes in women with preeclampsia [3, 4]. In the past, the amount of proteinuria was important to assess the severity of preeclampsia [5]. However, in 2013, the American College of Obstetricians and Gynecologists removed the amount of proteinuria as a key criterion [6]. If the severity of proteinuria can be predicted at the time of diagnosis of preeclampsia, there may be additional time to prevent preterm labor and other poor obstetric outcomes.

Alpha-fetoprotein (AFP), the major plasma protein of the fetus is synthesized by the yolk sac and fetal liver, and it is presumably the fetal counterpart of serum albumin [7]. Unexpected increases in AFP in the second trimester may increase the risk of complications related to placental insufficiency, such as preeclampsia [8]. Impairments in the structure of placental capillary endothelial cells and the placental barrier in women with preeclampsia may cause elevated levels of AFP in maternal blood. Some studies have found a relationship between maternal serum AFP levels and the development of preeclampsia [9, 11]. Theories have been presented about its development. Faulty placentation, which is responsible for preeclampsia pathogenesis is one theory. For this reason, it has been suggested that AFP can move from the placenta to maternal circulation for many weeks before preeclampsia develops [12].

The increase in estrogen levels during pregnancy and the physiological increase in the half-life of thyroid-binding globulin lead to increased levels of thyroid-binding globulin. Patients with preeclampsia exhibit low estrogen levels, which can reduce the half-life of thyroid-binding globulin and lead to the reduction of serum T3 and T4 levels. It has been suggested that a high thyroid-stimulating hormone (TSH) level and low free Tri-iodothyronine (free T3) and free tetraiodothyronine (free T4) levels may be associated with the development and complication of preeclampsia [13, 14]. Therefore, this study explored the relationships of second-trimester AFP, TSH, and free T4 levels with the severity of proteinuria in 24-h urine samples from patients with preeclampsia. The effect of proteinuria level on maternal/perinatal outcomes in 24-h urine was also evaluated.

METHODS

This retrospective study was conducted in our hospital between January 2017 and October 2019. The study protocol was approved by the hospital's ethics committee. Informed consent was obtained from all participants prior to inclusion in the study.

Patients aged 20-44 years old with a singleton pregnancy who were diagnosed with preeclampsia and delivered after 20 weeks of gestation were included in the study. Pregnant women were excluded if they met the following criteria: delivery of an infant with a birth weight < 500 g; missing preconception TSH or second-trimester AFP data; body mass index (BMI) > 35; multiple pregnancies; gestational hypertension, chronic hypertension, or high blood pressure before the 20th week of pregnancy; known antepartum thyroid disease (e.g., Hashimoto's disease or Graves' disease); use of medication for hypothyroidism or hyperthyroidism; pre-pregnancy nephropathy; and diagnosis of congenital anomalies (e.g., neural tube defect), uterine fibroids, and bleeding during pregnancy. For the patients included in the study relevant data were retrieved from the hospital database.

In the diagnosis of preeclampsia, hypertension was defined as the first occurrence of a systolic blood pressure ≥ 140 mmHg and a diastolic blood pressure ≥ 90 mmHg after the 20th week of pregnancy, measured at least twice at 4-h intervals in the left lateral decubitus position. A pregnant woman with no kidney disease was determined to have < 0.3 g in a 24-h urine sample for protein measurement in the third trimester [4]. All patients diagnosed with preeclampsia were followed up for 12 weeks after birth. Patients with persistent hypertension were excluded from the study because of the possibility of a chronic hypertension diagnosis during pregnancy. Patients who met the diagnostic criteria for preeclampsia and provided 24-h urine samples for protein measurement in the third trimester were divided into three groups based on proteinuria level: (1) mild (0.3 to < 2 g, n = 94), (2) severe (2 to < 5 g, n = 38), and (3) massive (≥ 5 g, n = 11) [15]. We compared the groups demographic characteristics (i.e., maternal age, parity, BMI, secondary diseases, and smoking), laboratory findings (i.e., second-trimester AFP, preconception TSH, and free T4 levels), maternal outcomes (maternal postpartum conditions [i.e., use of magnesium sulfate, intensive care unit requirement, wound infection, placenta abruption, acute

kidney failure, and dialysis]; cesarean section rate; cesarean section indication [e.g., persistent high blood pressure that did not decrease below 160/110 mmHg despite medical treatment, abnormal labor, placenta previa, placenta abruption, eclampsia, breech presentation, fetal distress, and/or previous cesarean history]; and length of stay), and neonatal outcomes (fetal weight, first minute Apgar score, fifth minute Apgar score, small for gestational age, neonatal intensive care unit [NICU], respiratory distress syndrome, intraventricular hemorrhage, necrotizing enterocolitis, neonatal sepsis, neonatal death, and NICU duration). In addition, we evaluated the effects of these factors on severe and massive proteinuria using multivariate and univariate logistic regression analyses.

Abnormal labor included an active-phase arrest in the first or second stage of labor. The arrest of labor in the first stage was defined as ≥ 6 cm of dilation with ruptured membranes and failure to progress despite (a) 4 h of adequate uterine activity or (b) at least 6 h of oxytocin administration with inadequate uterine activity and no cervical change. Arrest of labor in the second stage was diagnosed after at least 2 hour of pushing in multiparous women and at least 3 hour of pushing in nulliparous women. All women with abnormal labor underwent cesarean delivery. Deliveries before 37 weeks were classified as premature. Intrauterine growth restriction was diagnosed if the estimated fetal weight was below the 10th percentile for gestational age. Fetal distress was diagnosed by the International Federation of Gynecology and Obstetrics (16). The second-trimester prenatal screening test was performed between 16 and 20 weeks of gestation for all participants. Maternal serum AFP (ng/ml) was measured in the same laboratory by enzyme-linked immunosorbent assay. TSH (mIU/ml; reference range, 0.27–4.2) and free T4 (ng/dl; reference range, 0.8–1.9) were determined by immunoassay (Immulite

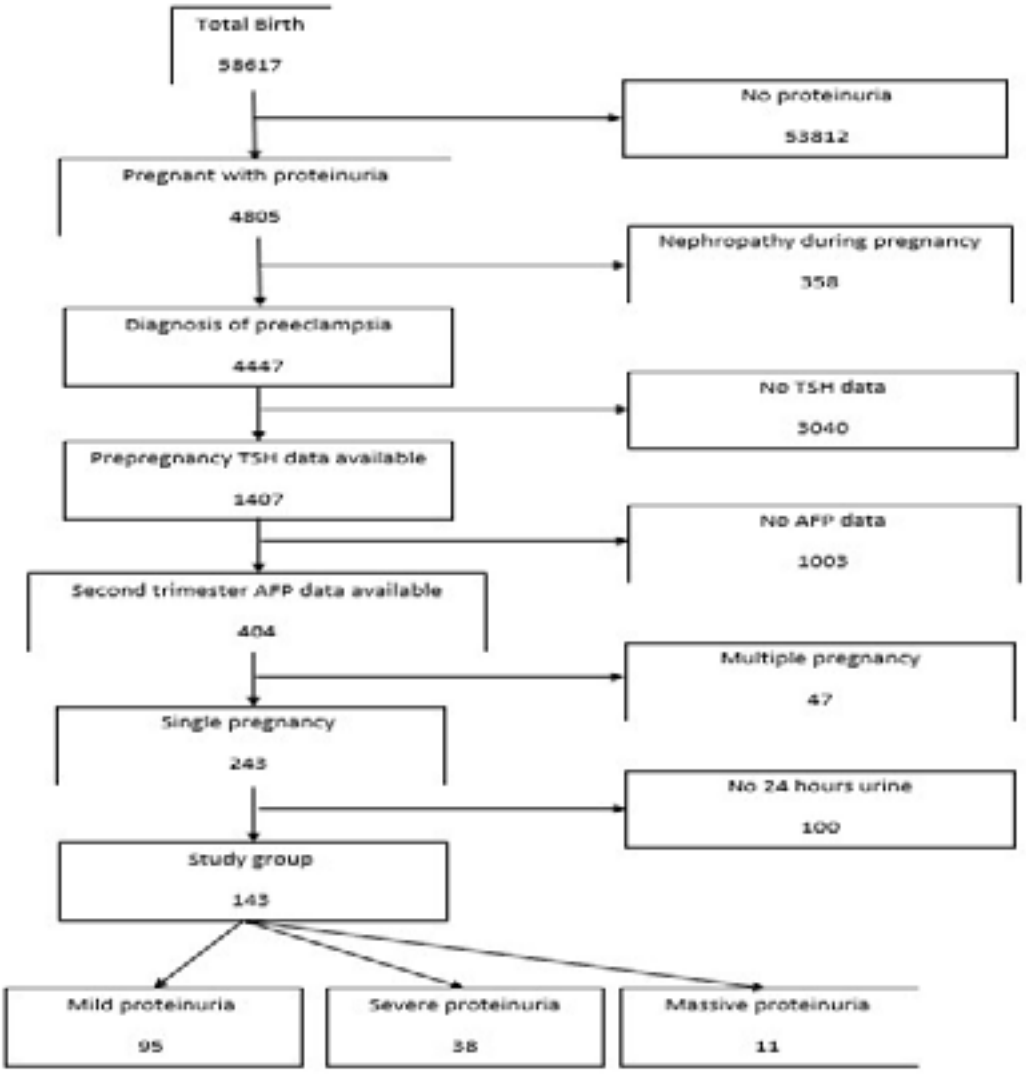

Figure 1. Flow chart.

2000, USA). The TSH values in the three months before pregnancy were taken.

The primary outcomes were the ability of preconception second-trimester AFP, TSH, and free T4 levels to predict the severity of proteinuria in 24-h urine samples from patients with preeclampsia. The secondary outcomes were the effects of proteinuria levels on maternal and neonatal outcomes in patients with preeclampsia.

Statistical Analysis

The statistical package program SPSS 20 (IBM SPSS Statistics for Windows version 20.0, IBM Corp., Armonk, NY, USA) was used to evaluate the data. Data were expressed as the mean ± SD and in percentages. Continuous variables were investigated using visual (histograms, probability plots) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilks test) to determine whether they were normally distributed. If the numerical data were non-parametric, the Kruskal-Wallis test would be conducted; if they were parametric, a one-way ANOVA test would be performed. The Bonferroni correction was used for the post-hoc assessment. The relationships between categorical variables were analyzed by the chi-square test. The bivariate correlations were investigated by Spearman's correlation analysis. For the multivariate analysis, the possible factors identified using univariate analyses were further entered into the logistic regression analysis to determine independent predictors of proteinuria. A p-value < 0.05 was considered statistically significant.

RESULTS

A total of 58,617 deliveries were recorded in our hospital between January 2017 and October 2019. Among them, 358 patients were excluded because they had been diagnosed with nephropathy during pregnancy. Among the remaining patients, 4,447 had been diagnosed with preeclampsia after the 20th week of pregnancy. Pre-pregnancy TSH data were only available for 1,407 pregnant women with preeclampsia. Second-trimester AFP data were available for 404 of these patients. After the exclusion of 47 patients with multiple pregnancies and 100 patients diagnosed with preeclampsia without a urine protein/creatinine ratio, 143 patients with preeclampsia remained and were included in the study. The flow charts of the study are shown in Figure 1. Among these patients, 94 had mild proteinuria (0.3 to <2 g), 38 had severe proteinuria (2 to <5 g), and 11 had massive proteinuria (≥5 g).

Table 1 presents the demographic characteristics and laboratory findings of patients with preeclampsia, stratified by severity of proteinuria. BMI (mild: 29.91±2.5 kg/m2; severe: 28.98 ±2.78 kg/m2; massive: 27.85±1.53 kg/m2 [p=0.017]), parity (mild: 0.66±0.48; severe: 0.53±0.51; massive: 0.27±0.47 [p=0.029]), and a gestational week at birth (mild: 35.53±3.11; severe: 34.45±3.22; massive: 33.55±3.42 [p=0.027]) were significantly lower in the massive proteinuria group. Patients with higher protein levels in the 24-h urine samples had an earlier gestational week at birth and exhibited lower parity. In addition, the second-trimester AFP levels increased with the

Table 1. Demographic characteristics and laboratory findings of preeclamptic patients classified according to the severity of proteinuria.

Variables	Mild proteinuria group (n:94)	Severe proteinuria group (n:38)	Massive proteinuria group (n:11)	*p*
Maternal age(n)*	30.19±5.7	30.26±7.89	27.73±8.61	0.461 γ
BMI (kg/m2) *	29.91±2.5[c]	28.98±2.78	27.85±1.53	0.017&
Parity (n)*	0.66±0.48[c]	0.53±0.51	0.27±0.47	0,029 γ
Gestational week at birth*	35.53±3.11[c]	34.45± .22	33.55±3.42	**0.027** γ
DM	3 (3.1)	1 (2.6)	-	0.697 γ
Smoking**	20 (21.3)	8 (21.1)	2 (18.2)	0.972 δ
TSH (mIU/ml)*	1.91±1.55[c]	2.61±1.77	2.92±1.71	**0.012** γ
Free T4 (ng/dl)*	1.07±0.44	6.89±2.51	0.97±0.17	0.492 γ
AFP (ng / ml)*	47.97±16.33[b,c]	60.52±15.01	65.5±26.52	**<0.001** γ

γKruskal Wallis test, & One-way ANOVA test, δChi-square test. Values were presented as *mean±SD or ** n (%). p-value <0.05 statistically significant. SD: Standard deviation; BMI: body mass index; DM: diabetes mellitus; TSH: Thyroid Stimulating Hormone; AFP: Alpha-fetoprotein; T4: thyroxine.

[b]There was a significant difference with the compared Severe proteinuria group in post-hoc comparison. [c]There was a significant difference with compared Massive proteinuria group in post-hoc comparison.

Table 2. Maternal and neonatal outcomes of preeclamptic patients classified according to the severity of proteinuria

Variables	Mild proteinuria group (n:94)	Severe proteinuria group (n:38)	Massive proteinuria group (n:11)	*p*
Cesarean section ratio, n (%)	74 (78.7)	33 (86.8)	11 (100.0)	0.153 [δ]
Cesarean section indication, n (%)				0.334 [δ]
Persistent high blood pressure	11 (14.9)	11 (33.3)	2 (18.2)	
Abnormal labor	8 (10.8)	-	1 (9.1)	
Placenta previa	2 (2.7)	-	-	
Placenta abruption	3 (4.1)	2 (6.1)	1 (9.1)	
Previous cesarean	11 (14.9)	6 (18.2)	1 (9.1)	
Fetal distress	34 (45.9)	10 (30.3)	4 (36.4)	
Eclampsia	3 (4.1)	4 (12.1)	2 (18.2)	
Breech presentation	2 (2.7)	-	-	
Fetal weight (gr) (± SD)	2554.3 (802.8)	2226.1 (688.3)	1835.5 (678.6)[b]	0.005 [γ]
IUGR	10 (10.6)	14 (36.8)	9 (81.8)	<0.001 [δ]
1st minute Apgar score ± SD	7.06 ± 1.50	6.63 ± 1.48	6.27 ± 1.85	0.058 [γ]
5th minute Apgar score ± SD	8.18 ± 1.29	7.97 ± 1.28	7.73 ± 1.35	0.247 [γ]
Neonatal complications, n (%)				0.001 [δ]
RDS	10 (10.6)	5 (13.2)	3 (27.4)	
IVH	-	1 (2.6)	2 (18.1)	
NEC	1 (1.1)	1 (2.6)	2 (18.1)	
Neonatal sepsis	-	1 (2.6)	1 (9.0)	
Neonatal death	1 (1.1)	-	1 (9.0)	
Composite adverse neonatal outcome	12 (12.8)	8 (21)	9 (81.8)	< 0.001 [δ]
Use of magnesium sulfate	30 (31.9)[b]	20 (52.6)	10 (90.9)	< 0.001 [δ]
ICU requirement	3 (3.2)[b]	5 (13.1)	8 (72.7)	< 0.001 [δ]
Wound infection	6 (6.4)	3 (7.9)	1 (9.0)	0.915 [δ]
Placenta abruption	3 (4.1)	2 (6.1)	1 (9.1)	0.607 [δ]
Acute kidney failure and dialysis	1 (1.0)[b]	1 (2.6)	3 (27.4)	< 0.001 [δ]
Length of hospital stay (days) ± SD	6.27 ± 3.74[b]	7.05 ± 3.00	8.18 ± 2.09	0.007 [γ]

[γ]Kruskal Wallis test, [δ]Chi-square test. Values were presented as mean ± SD or numbers and percent (%). *p* value < 0.05 statistically significant. SD: Standard deviation; IUGR: Intrauterine growth restriction; NICU: neonatal intensive care unit; RDS: respiratory distress syndrome; IVH: intraventricular hemorrhage; NEC: necrotizing enterocolitis; ICU: Intensivecare unit. [b]There was a significant difference with compared Massive proteinuria group in post-hoc comparison.

severity of proteinuria (mild: 47.97 ng/ml; severe: 60.52 ng/ml; massive: 65.50 ng/ml [p<0.001]). In addition, there was a significant relationship between preconception TSH levels and severity of proteinuria (p=0.012). Conversely, no significant relationship was found between preconception free T4 levels and severity of proteinuria (p=0.492).

The maternal and neonatal outcomes are shown in Table 2. All neonatal outcomes and composite adverse neonatal outcomes differed significantly among groups. The cesarean rates were high in all three groups (mild proteinuria group, 78.7%; severe proteinuria group, 86.8%; massive proteinuria group, 100%). The length of hospital stay was the longest in the massive proteinuria group (mild: 6.27±3.74 days; severe: 7.05±3.00 days; massive: 8.18±2.09 days [p=0.007]). Postpartum maternal complications were the most common in the massive proteinuria group. The use of magnesium sulfate, intensive care unit requirement, acute kidney failure, and dialysis were more common among women with preeclampsia who had massive proteinuria (p values <0.001, <0.001, <0.001, respec-

Table 3. Factors affecting patients with proteinuria greater than 2 g were evaluated by multivariate and univariate logistic regression analysis.

	Multivariate					Univariate				
	B	**S.E.**	***p***	**OR**	**95% C.I.**	**B**	**S.E.**	***p***	**OR**	**95% C.I.**
Maternal age	0,126	0,054	0,021	1,134	1,020- 1.262	-0,012	0,027	0,666	0,988	0,938- 1.042
BMI	-0,200	0,111	0,073	0,819	0,658- 1.018	-0,191	0,075	0,011	0,826	0,713 – 0.957
Parity	-1,513	0,692	0,029	0,220	0,057- 0.854	-0,784	0,360	0,029	0,457	0,226 – 0.924
TSH	0,094	0,128	0,463	1,098	0,855- 1.411	0,281	0,111	0,012	1,324	1,065 – 1.647
AFP	0,040	0,012	0,001	1,041	1,016- 1.066	0,045	0,011	<0,001	1,046	1,023 – 1.069

B: Standardized regression coefficient SE: Standard error. OR: odds ratio. CI: confidence interval. p values with statistical significance ($p < 0.05$) are shown in bold. BMI: body mass index; TSH: Thyroid Stimulating Hormone; AFP: Alpha-fetoprotein.

tively). With the severity of proteinuria, birth weight decreased (mild: 2,554.3 (802.8) g; severe: 2,226.1 (688.3) g; massive: 1,835.5 (678.6) g [p=0.005]), and the frequency of IUGR increased (mild: 10 (10.6); severe: 14 (36.8); massive: 9 (81.8) [p<0.001]).

The factors affecting the outcomes of patients with proteinuria >2 g (Table 3) were examined using multivariate and univariate logistic regression analysis. AFP was identified as the most important independent predictor of severe proteinuria with an odds ratio of 1.041 (p<0.001). TSH was not predictive of severe proteinuria (odds ratio =0.463; p=1.098). Correlation analysis showed that increased proteinuria was associated with significant increases in AFP and TSH levels and with significant reductions in age, BMI, and parity (Table 4). The strongest association was found between AFP and proteinuria as shown in Figure 2. The correlation of TSH with proteinuria was showned in Figure 3.

DISCUSSION

AFP and preconception TSH were found to be valuable markers for predicting the severity of proteinuria in 24-h urine samples from patients with preeclampsia. As AFP and preconception TSH increased, the severity of proteinuria increased. Higher levels of proteinuria were associated with composite adverse maternal and neonatal outcomes.

Li and colleagues [17] found that maternal age and BMI were negatively correlated with increased 24-h proteinuria levels and that gestational age at delivery became noticeably younger as the level of proteinuria increased. By contrast, Tanacan and colleagues [3] found no significant relationships between proteinuria and each of the following factors: maternal age, BMI and parity. In our study, maternal age, BMI, and parity significantly decreased as the severity of proteinuria increased. Moreover, the incidences of early birth and preterm labor increased with the severity of proteinuria. These findings show that severity of proteinuria is a valuable predictor of preterm labor. Preterm labor, which occurs in 10%–12% of pregnancies, is the leading cause of neonatal mortality and morbidity [18]. Therefore, the accurate prediction of severe proteinuria in patients with preeclampsia can improve maternal and neonatal outcomes.

The cesarean rates in our study were high consistent with the published literature [2]. Although we did

Table 4. Correlation of some values with proteinuria.

	Proteinuria	
	r	**P**
AFP	0.418	< 0.001
TSH	0.282	0.001
Maternal age	-0.101	0.231
BMI	-0.237	0.004
Parity	-0.175	0.036

Spearman's correlation analysis was used. p values with statistical significance ($p < 0.05$) are shown in bold. r: correlation coefficient; BMI: body mass index; TSH: Thyroid Stimulating Hormone; AFP: Alphafetoprotein.

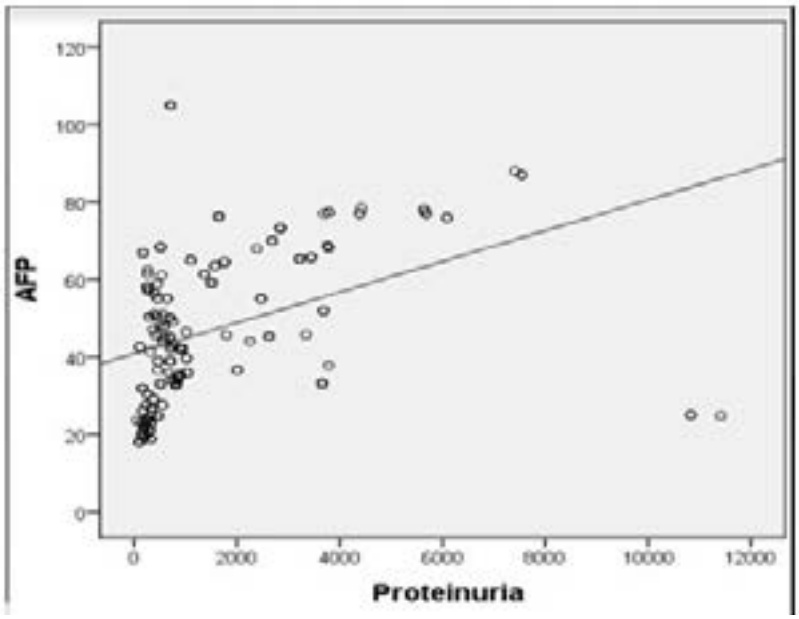

Figure 1. The correlation of AFP with proteinuria.

not stratify the symptoms according to the severity of preeclampsia. This study results suggest a meaningful association between the severity of preeclampsia and the severity of proteinuria. The diagnosis of the patients in the group with massive proteinuria was made earlier in the gestational weeks and the neonatal complication rates in this group were high in the study, consistent with other studies [3, 15, 19, 20]. The rates for the usage of magnesium sulfate, admission to ICU, acute kidney failure and dialysis, and length of hospital stay were higher in the severe and massive proteinuria groups. Similarly, IUGR and preterm delivery rates were higher in the massive proteinuria group. These results are compatible with the literature [3, 15, 19, 20]. Whereas retrospective studies found a significant relationship between severity of proteinuria and negative maternal/neonatal outcomes, this relationship was not found in prospective studies. However, the severity of proteinuria should not be used alone to determine the time of birth in preeclampsia [21].

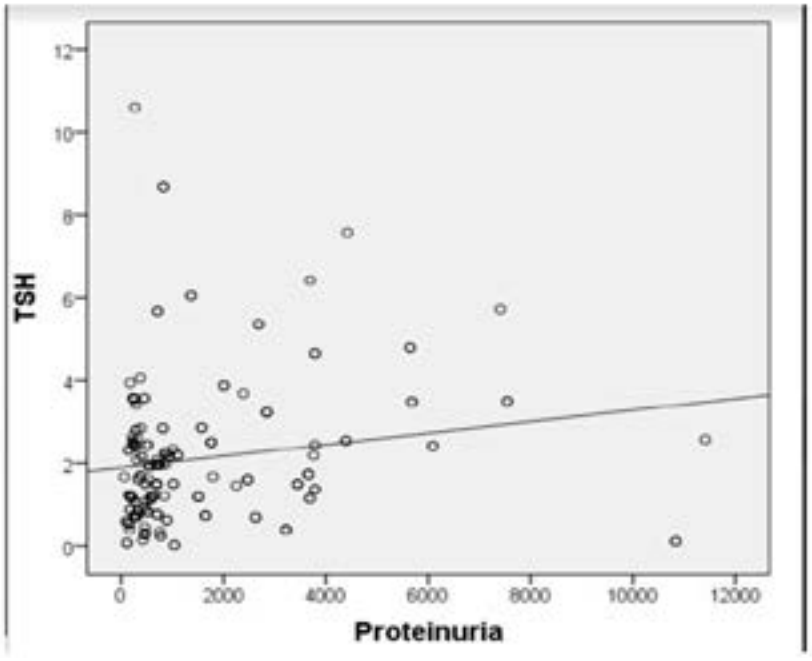

Figure 1. The correlation of TSH with proteinuria.

In Yadav *et al*.'s study [22], the second-trimester AFP levels were 151.04±7.2 ng/ml in women with severe preeclampsia and 52.50±15.52 ng/ml in healthy pregnant women; thus, unexplained high levels of maternal serum AFP were presumably associated with preeclampsia. In another study that stratified patients into healthy, non-severe preeclampsia and severe preeclampsia groups, the only significant differences among the groups were observed in maternal serum AFP and AFP multiples of the median values [23]. The average AFP level for pregnant women with severe preeclampsia, including those with progressive renal insufficiency, was 50.11±33.81 U/ml; conversely, the average AFP level in the non-severe preeclampsia group was 42.47±15.46 U/ml. We identified AFP as the most important independent predictor of severe proteinuria, with an odds ratio of 1.041. AFP multiples of the median values were not included in our study, but we found that a linear increase in maternal serum AFP level corresponded to the severity of proteinuria. A study that calculated AFP levels, adjusted for maternal age and BMI, revealed a linear relationship with severity of proteinuria [23]. The study performed multivariate regression analysis to ensure that the interactions among these factors did not result in bias.

Deshpande *et al*. [24] showed that serum albumin was positively correlated with T3 and T4 levels but was negatively correlated with serum TSH levels in women with preeclampsia. Some studies have shown a statistically significant positive relationship between thyroid hypofunction and preeclampsia [25]. However, Arbib and colleagues [25] found that firsttrimester TSH levels were not a significant predictor of preeclampsia. They conducted a regression analysis and determined that subclinical hypothyroidism approximately doubled the risk of preterm birth. Our study found a significant relationship between preconception TSH levels and proteinuria levels in pregnant women with preeclampsia but not between preconception free T4 levels. TSH levels tended to increase as proteinuria increased and their association was statistically significant. This result may be related to the collection of these data three months prior to conception. Perhaps if investigators had collected first-trimester data, as in other studies, might have found a strong association similar to that between AFP and proteinuria.

Limitations

The main limitation of this study is its retrospective nature. In addition, this study hospital's birth rates were particularly high during the study period. These factors may have limited the accessibility of patient data. Moreover, this study is limited by the patients not stratified according to severity of preeclampsia. The study did not analyze the symptoms and laboratory findings associated with severe preeclampsia. As clinical results not only depend on the severity of proteinuria, this might have caused bias. Another limitation is the relatively small sample size and the singlecenter experience.

The strength of our study is that the frequent application of TSH and free T4 screening in the preconceptional period in our country increased the number of patients containing this data. Especially, it assessed the AFP and TSH levels in patients with preeclampsia stratified according to severity of proteinuria. Moreover, the observance of differences in maternal and neonatal outcomes among these groups demonstrated the usefulness of proteinuria levels in assessing the severity of preeclampsia.

CONCLUSION

The second-trimester serum AFP level may be a valuable predictor in predicting the severity of proteinuria in 24 hour urine samples in patients with preeclampsia. This study findings suggest that second-trimester AFP levels can assist providers in preparing for adverse obstetric outcomes. Maternal and neonatal outcomes can be improved by incorporating earlier preparations for obstetric complications. Given that AFP may be a valuable predictor of complications, it may be advisable to measure second-trimester AFP levels in maternal blood, regardless of the ability to perform a triple test. A similar situation was observed between high TSH levels seen in the preconceptional period and massive proteinuria. In addition, the presence of higher levels (> 5 g) of 24-h urinary protein was closely related to adverse maternal/neonatal outcomes. Multicenter observational cohort studies involving more patients are required for stronger results.

Conflict of Interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Approval

The protocol of the study was approved by the Medical Ethics Committee of Harran University, Urfa,

Turkey. (Decision number: 07, date: 16.12.2019).

Authors' Contribution

Study Conception: NNY; Study Design: EB; Literature Review: NB; Critical Review: FE; Data Collection and/or Processing: SK; Analysis and/or Data Interpretation: EB; Manuscript preparing: SK.

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The Knowledge of Students at Bursa Faculty of Medicine towards Artificial Intelligence: A Survey Study

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ABSTRACT

Objectives: Artificial intelligence (AI) is being increasingly widely employed in medicine. Various artificial intelligence software solutions will most certainly be available to medical students when they begin their jobs after completing school. The goal of this study was to assess medical faculty students' knowledge and attitudes about AI in medicine.

Methods: In 2020-2021, students at the University of Health Sciences, Bursa Training and Research Hospital participated in an online survey using Google Forms. The survey included sections assessing demographic features and attitudes toward AI in medicine.

Results: The questionnaire was completed by 85 students (57 females and 28 males). 50 medical school students and 35 pediatric medical specialty students completed the questionnaire. The mean time spent on the internet per day was 7.5400 ± 3.67123 hours in MS and 3.1143 ± 2.0547 hours in MA ($p < 0.001$). All of the participants had heard AI before ($p = 0.500$). 62% of MS and 65.7% of MA worried about AI doing many things today; no statistically significant difference was found between the two groups ($p = 0.453$). 56.5% of participants felt "curiosity", 16.4% felt "excited", 11.8% felt "look positive", 15.3% felt "frightened" about the increased use of artificial intelligence in our lives. 24% of the MS and 37.1% of the MA knew AI applications used in medicine; there was no statistically significant difference between the two groups ($p = 0.191$). The most commonly known applications of AI in medicine were in the fields of robotic surgery (10.5%) and radiology (3.6%). While 8% of the MS participated in the project / study related to AI; none of the MA participated, there was a statistically significant difference between the two groups ($p = 0.036$). On the contrary, the use of AI in medicine was 5.7% in MA; it was never possible in MS, there was no statistically significant difference between the two groups ($p = 0.057$). 91.8% of the participants would like to use AI in their future careers as physicians. 68% of MS and 94.3% of MA thought AI could not replace doctors in the future; there was a statistically significant difference between the two groups ($p = 0.004$).

Conclusion: Medical students, who will be the physicians of the future, regarded AI applications positively, and they wanted to gain education and experience in this subject with deep curiosity. Since the knowledge level of future physicians in this field is not sufficient, it is important to provide more AI training in medicine, to participate in more

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projects in this field, and to increase the use of AI by medical students in the field of medicine.
Keywords: artificial intelligence, education, medicine, medical students

Machines and systems use artificial intelligence (AI) to solve complicated problems and resemble the intelligence of humans. In 1955, Mc Carthy developed the term AI to define the technology and science of developing computers with intelligence [1]. The aim of these algorithms is to be willing to analyze data from a big database and simulate human choices following a particular set of directions. Medical Sciences, as a complicated scientific discipline, is frequently faced with the difficulties of collecting, analyzing, and using enormous quantities of information [2]. The use with the implementation of large-scale data generation techniques in the field of medicine has become essential. There are also continuing expectations to enhance patient availability of services, reduce operational expenses, and improve outcomes during treatment.

AI in medical treatments has a chance to improve numerous facets of healthcare. The responsibility of adapting the process to ever-changing standards and recommendations increases medical professionals' dissatisfaction and requires highly qualified individuals to work extra time on documents rather than concentrating on caring for patients [3]. Operations are almost impossible for humans to do, such as monitoring patients 24 hours a day, can also be performed safely by AI systems. It can reduce the number of erroneous errors in clinical practice and the differences in judgment among medical professionals. New models discovered by AI through analysis of big data from clinical practice could enable the development of new biomarkers for diagnosis and treatment.

AI tools for medicine often play the role of a virtual assistant for doctors and healthcare systems, helping them provide more accurate and efficient patient care. AI can be designed and used as a virtual assistant for patients and the public in common chronic diseases or primary health care [4]. Counseling on simple health problems or rewriting of chronic drug prescriptions may be possible. If simple but time-consuming work processes are taken care of by AI, it significantly reduces the fatigue of healthcare providers. Doctors can take more care of patients and spend more time concentrating on more complex medical tasks.

As current medical students begin their careers as medical professionals, various AI software tools are likely to be used in clinical practice. When it concerns using AI technology to patients, healthcare providers should be in the driver's position, not in the back seat [5, 6]. The aim of this study was to determine the knowledge and attitudes of medical students and medical specialty education students at the University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital, towards AI in medicine.

METHODS

This cross-sectional, self-administered, survey-based study was conducted by distributing a web-based questionnaire prepared using Google Forms. A web-based questionnaire sent online to 80 students of medicine (MS) and 45 students of medical specialty education studying in the field of pediatrics (MA) at the University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital between 2020 and 2021. Participation in the survey is completely optional and the permission of participants has been obtained. The questionnaire was completed by 50 MS and 35 MA. The literature was used to create the questionnaire. The first 15 questions of the questionnaire evaluated the students' demographic characteristics, technology-related attitudes, and skills. The final section of the questionnaire, which included 15 questions, was designed to assess their knowledge, experience, and attitudes toward AI in medicine. Data was analyzed using the Statistical Package for Social Sciences (SPSS) version 27.0 (released 2020; IBM Corp., Armonk, New York, United States). Descriptive statistics are presented in percentages. Chi-square test and Kruskal–Wallis one-way analysis of variance test was used to examine differences between groups. P-values of < 0.05 were considered statistically significant. Ethical approval was obtained from the ethics committee of University of Health and Science, Bursa Faculty of Medicine (2011-KAEK-25 2021/02-25)

RESULTS

The questionnaire was filled out by 50 MS and 35 MA. 67% of participants were female. While the gen-

Table1. Medical students and medical specialty students' demographic characteristics, technology-related attitudes, and skills. The final section of the questionnaire, which included 15 questions, was designed to assess their knowledge, experience, and attitudes toward AI in medicine.

	Groups **Medical Students (MS)** (n = 50)	**Medical specialty education students (MA)** (n = 35)	**Total** (n = 85)	***p***
Gender				
Female	26 (52%)	31 (88.6%)	57 (67%)	**< 0.001**
Male	24 (48%)	4 (11.4%)	28 (33%)	
Age				
18-25 years	49 (98%)	8 (22.9%)	57 (67%)	**< 0.001**
26-30 years	0 (%0)	22 (62.9%)	22 (25%)	
>30 years	1 (2%)	5 (14.3%)	6 (7%)	
Year in the medical school/speciality education				
First year	34 (68%)	10 (28.6%)	44 (51.7%)	
Second year	3 (6%)	17 (48.6%)	20 (23.5%)	**< 0.001**
Third year	1 (2%)	3 (8.6%)	4 (4.7%)	
Fourth year	12 (24%)	5 (14.3%)	17 (2%)	
Maritial				
Single	50 (100%)	20 (57.1%)	70 (82.4%)	**< 0.001**
Married	0 (0%)	15 (42.9%)	15 (17.6%)	
Family				
Nuclear	42 (84%)	32 (91.4%)	74 (87%)	0.422
Extended	7 (14%)	3 (8.6%)	10 (11,8%)	
Distrubuted	1 (2%)	0 (0%)	1 (1.2%)	
Family income				
High	14 (28%)	14 (40%)	28 (33%)	0.440
Medium	34 (68%)	19 (54.3%)	53 (62.3%)	
Low	2 (%4)	2 (5.7%)	4 (4.7%)	
Mother's education				
Illiterate	2 (4%)	0 (%0)	2 (2.3%)	0.307
Primary education	14 (28%)	7 (20%)	21 (24.7%)	
High school	14 (28%)	9 (25.7%)	37 (43.5%)	
University	20 (40%)	19 (54.3%)	59 (69.5%)	
Father's education				
Illiterate	1 (2%)	0 (0%)	1 (1.2%)	0.451
Primary education	10 (20%)	5 (14.3%)	15 (17.7 %)	
High school	12 (24%)	6 (17.1%)	18 (21.1%)	
University	27 (54%)	24 (68.6%)	51 (60%)	
Mother's work				
Yes	19 (38%)	14 (40%)	33 (38.9%)	0.852
No	31 (62%)	21 (60%)	52 (61.1%)	
Father's work				
Yes	37 (74%)	26 (74.3%)	63 (74%)	0.976
No	13 (26%)	9 (25.7%)	22 (26%)	
Living place				
With family	41 (82%)	8 (22.9%)	49 (57.6%)	**< 0.001**
Own home	7 (14%	27 (77.1%)	34 (40%)	
Dorm	2 (4%)	0 (0%)	2 (2.4%)	
Access to internet				
Yes	49 (98%)	34 (97.1%)	83 (97.6%)	< 0.798
No	1 (2%)	1 (2.9%)	2 (2.4%)	
Time spent on the internet per day (mean ± SD)	7.5400 ± 3.67123	3.1143 ± 2.0547	5.7176 ± 3.791	**< 0.001**
Computer knowledge level				
Bad	3 (6%)	1 (2.9%)	4 (4.7%)	0.557
Little	4 (8%)	7 (20%)	11(12.9%)	
Moderate	22 (44%)	13 (37.1%)	35 (41.1%)	
Good	16 (32%)	11 (31.4%)	27 (31.8%)	
Excellent	5 (10%)	3 (8.6)	8 (9.5%)	
Computer-related training				
Yes	7 (14%)	6 (17.1)	13 (15.3%)	0.459
No	43 (86%)	29 (82.9%)	72 (84.7%)	

Table2. Medical students and medical specialty students' knowledge, experience, and attitudes toward AI in medicine

	Groups Medical Students (MS) (n = 50)	Medical Specialty Students (MA) (n = 35)	Total (n = 85)	*p*
Do you worry about robots entering our lives and communicate with humans?				
Yes	17 (34%)	15 (42.9%)	31 (37.6 %)	0.407
No	33 (66%)	20 (57.1%)	53 (62.4%)	
Have you heard of artificial intelligence before?				
Yes	50 (100%)	35 (100%)	85 (100%)	0.500
No	0 (0%)	0 (100%)	0 (0%)	
Does it worry you that artificial intelligence is doing so many things today?				
Yes	19 (38%)	12 (34.3%)	31(36.4%)	0.453
No	31 (62%)	23 (65.7%)	54 (63.6%)	
How do you feel about the increased use of artificial intelligence in our lives?				
Arouse curiosity	29 (58%)	19 (54.3%)	48 (56.5%)	
Excite	11 (22%)	3 (8.6%)	14(16.4%)	**0.031**
Look positive	2 (4%)	8 (22.9%)	10 (11.8%)	
Frightened	8 (16%)	5 (14.3%)	13 (15.3%)	
Do you know about artificial intelligence applications used in medicine?				
Yes	12 (24%)	13 (37.1%)	25 (29.4%)	0.191
No	38 (76%)	22 (62.9%)	60 (70.6%)	
What are the areas you know about the use of artificial intelligence in medicine?				
• Robotic surgery	4 (8%)	5 (14.2%)	9 (10.5%)	0.379
• Neuralink project for paralyzed patients	1 (2%)	0 (0%)	1 (1.2%)	
• Radiology	3 (6%)	0 (0%)	3 (3.6%)	
• Da Vinci robots	2 (4%)	0 (0%)	2 (2%)	
• X-ray analysis and ECG interpretation for diagnosis	1 (2%)	1 (2.9%)	2 (2%)	
• Pathology	0 (0%)	1 (2.9%)	1 (1.2%)	
• Medical education through patient simulations	0 (0%)	1 (2.9%)	1 (1.2%)	
• None	39 (78%)	27 (77.1%)	66 (77.5%)	
Have you participated in the project regarding AI in medicine?				
Yes	4 (8%)	0 (0%)	4 (4.7%)	**0.036**
No	46 (92%)	35 (100%)	96 (95.3%)	
Have you ever used AI in medicine?				
Yes	0 (0%)	2 (5.7%)	2 (2.3%)	0.057
No	50 (100%)	33 (94.3%)	83 (97.7%)	
Would you like to use AI in your future career as a physician?				
Yes	46 (92%)	32 (91.4%)	78 (91.8%)	0.925
No	4 (8%)	3 (8.6%)	7 (8.2%	
Are hospitals using AI have more advantages in diagnosis?				
Yes	44 (88%)	29 (82.9%)	73 (85.9%)	0.506
No	6 (12%)	6 (17.1%)	12 (14.1%)	
Are hospitals using AI have more advantages in treatment?				
Yes	46 (92%)	28 (80%)	74 (87%)	0.108
No	4 (8%)	7 (0%)	11 (13%)	
Should AI education be provided in medical education?				
Yes	47 (94%)	31 (88.6%)	78 (91.7%)	0.375
No	3 (6%)	4 (11.4)	7 (8.3%)	
Would you like to have AI applications in medical school?				
Yes	49 (98%)	33 (94.3%)	82 (96.5%)	0.365
No	1 (2%)	2 (5.7%)	3 (3.5%)	
Should AI applications be used more in medicine?				
Yes	42 (84%)	32 (91.4%)	74 (87%)	0.305
No	8 (16%)	3 (8.6%)	11 (13%)	
Do you find AI applications used in medicine reliable?				
Yes	37 (74%)	25 (71.4%)	26 (30.6%)	
No	13 (26%)	10 (28.6%)	59 (69.4%)	0.793
Could AI replace doctors in the future?				
Yes	16 (32%)	2 (5.7%)	18 (21.5%)	**0.004**
No	34 (68%)	33 (94.3%)	69 (78.5%)	

der distribution of MS is uniform, 88.6% of MA is female ($p < 0.001$). Although the majority of MS were between the ages of 18 and 25 (98%), the majority of MA was between the ages of 26 and 30 (62.9%) ($p < 0.001$). 68% of MS were in their first year of medical school, 48.6% of MS were second year of specialty education ($p < 0.001$). All of the participants in MS were single while 42.9% of MA was married ($p < 0.001$). 87% of families were nuclear and no statistically significant difference was found between the two groups ($p = 0.422$). Both groups' family income levels were moderate (62.3%) and most parents had university education, no statistically significant difference was found between the two groups ($p>0.05$). 38.9% of the mothers and 74% of fathers were working and no significant difference was found between the two groups ($p >0.05$). While 57.6% of the participants were living with their families, 4% of MS were living in dorm, 77.1% of MA stayed in their own house ($p < 0.001$). 97.6% of the participants had internet access wherever they lived, there was no statistically significant difference was found between the two groups ($p < 0.798$). The mean time spent on the internet per day was 7.5400 ± 3.67123 hours in MS and 3.1143 ± 2.0547 hours in MA ($p < 0.001$). 41.1% of all participants had a moderate level of computer education, and there was no statistically significant difference between the two groups ($p = 0.557$). Computer-related training was received by 86% of MS and 82.9% of MA, there was no statistically significant difference between the two groups ($p = 0.459$) (Table 1).

34% of MS and 42.9% of MA were worried about robots entering our lives and communicate with humans, there was no statistically significant difference between the two groups ($p = 0.407$). All of the participants heard AI before ($p=0.500$). 62% of MS and 65.7% of MA worried about AI doing many things today, no statistically significant difference was found between the two groups ($p = 0.453$). 56.5% of participants felt "curiosity", 16.4% felt "excited", 11.8% felt "look positive", 15.3% felt "frightened" about the increased use of AI in our lives. 58% of MS felt "curiosity" while 54.3% of MA, 22% of MS felt "excited" while 8.6% of MA, 4% of MS felt "look positive" while 22.9% of MA,16% of MS felt "frightened" while 14% of MA, respectively and there was statistically significant difference between the two groups ($p = 0.03$). 24% of the MS and 37.1% of MA were knew AI applications used in medicine, there was no statistically significant difference between the two groups ($p = 0.191$). The mostly known applications of AI in medicine were in the fields of robotic surgery (10.5%), radiology (3.6%), the others were, da Vinci robots (2%), X-ray analysis and ECG interpretation for diagnosis (2%), neuralink project for paralyzed patients (1.2%), pathology (1.2%), and medical education (1.2%) through patient simulations. There was no statistically significant difference between the two groups ($p = 0.379$). While 8% of the MS participated in the project / study related to AI; none of the MA participated, there was a statistically significant difference between the two groups ($p = 0.036$). On the contrary, the use of AI in medicine was 5.7% in the MA it was never possible in MS, there was no statistically significant difference between the two groups ($p = 0.057$). 91.8% of the participants would like to use AI in their future career as a physician, there was no statistically significant difference between the two groups ($p = 0.925$). Although almost all of both groups think that hospitals using AI was more advantageous in diagnosis and treatment; there was no statistically significant difference between the two groups ($p > 0.05$). 91.7% of the participants thought AI education should be provided in medical education, there was no statistically significant difference between the two groups ($p = 0.375$). 96.5% of the participants would like to have AI applications in medical school, there was no statistically significant difference between the two groups ($p = 0.365$). 87% of the participants thought AI applications should be used more in medicine, there was no statistically significant difference between the two groups ($p = 0.793$). 69.4% of the participants not found reliable AI applications used in medicine, there was no statistically significant difference between the two groups ($p= 0.793$). 68% of MS and 94.3 % of MA thought AI could not replace doctors in the future; there was a statistically significant difference between the two groups ($p = 0.004$) (Table2).

DISCUSSION

The purpose of this study was to investigate medical students' knowledge, perceptions, and attitudes toward the integration of AI in the medicine. In our study, we found that the majority of participants had heard of the terms "artificial intelligence" while most of them were even aware that it was recently being discussed in medicine. These findings indicate that students have a basic understanding of AI but require deeper comprehension its use in medicine. a similar pattern was observed in other studies conducted from

different countries [7-12].

The majority of students agreed that AI should be part of medical training and most wanted more teaching focusing on AI in medicine. Medical students appeared optimistic regarding the role of AI in medicine, with most agreeing with the statement that AI will improve medicine in general. The majority of medical students were not concerned about the impact of AI on their job security as a doctor. Our research similar with other research conducted before. However student thought that AI could replace doctors in the future were higher in MS than MA [10-14].

In a study conducted in Australia students selected radiology (72.6%), pathology (58.2%), and medical administration (44.8%) as the specialties most likely to be impacted by AI, and psychiatry (61.2%), palliative care (48.5%), and obstetrics and gynecology (41.0%) as the specialties least likely to be impacted by AI. In our study the mostly known applications of AI in medicine were in the fields of robotic surgery (10.5%), radiology (3.6%), the others were, da Vinci robots (2%), X-ray analysis and ECG interpretation for diagnosis (2%), neuralink project for paralyzed patients (1.2%), pathology (1.2%), and medical education (1.2%) through patient simulations [13].

In our study the time spend on the internet were found to be significantly higher in MS. 8% of MS participated in the project regarding AI in medicine while none of MA did. Male and early age participants were much more in MS however the average age was higher and most of them were women in MA. As a result of these differences, the state of interest in AI in medicine may be higher in MS than in MA. This might be attributed to the recent initiation of studies in this newly developing field or to the fact that MS were more open to technology due to their age.

Almost all of our participants stated that they were aware of the benefits of using AI in the field of medicine while they thought that hospitals using AI would be more successful in diagnosis and treatment. Most of them said that they want to use AI much more in their future medical lives. The rate of those who wanted AI training in medicine was found to be very high in both groups. These findings were found to be compatible with current studies [16, 17].

Although modern AI technologies such as deep learning are known to have high accuracy in finding patterns compared to past technologies, they have a strong dependence on training data. The accuracy of their algorithms cannot go beyond the information specific to the datasets they are trained in and cannot avoid errors in their data. This strong data dependency poses a particular concern in the medical field [18, 19]. In our study, most of the participants found AI safe in the medical field and found AI applications used in medicine reliable. Although the general opinion was that the robots cannot replace physicians, the younger generation believed much more that this might happen.

CONCLUSION

As a result; medical students, who will be the physicians of the future, regarded AI applications positively and they wanted to gain education and experience in this subject with deep curiosity. AI will open completely different doors in medical education and medical applications; future physicians will also be the supporter and practitioner of this technology. Since the knowledge level of future physicians in this field is not sufficient, it is important to provide more AI training in medicine, to participate in more projects in this field, and to increase the use of AI by medical students in the field of medicine.

Conflict of Interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Approval

The protocol of the study was approved by the Medical Ethics Committee of University of Health and Science, Bursa Faculty of Medicine, Bursa, Turkey. (2011-KAEK-25 2021/02-25)

Authors' Contribution

Study Conception: EGKI; Study Design: EGK, DG; Literature Review: DG; Critical Review: EGK; Data Collection and/or Processing: LS, EÜ,; Analysis and/or Data Interpretation: DG; Manuscript preparing: DG.

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An Interesting Case of Posterior Reversible Encephalopathy Syndrome

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ABSTRACT

Posterior Reversible Encephalopathy Syndrome (PRES) is a special type of cerebrovascular disease defined by clinical and imaging findings. The onset of PRES typically includes acute or subacute headaches, visual impairment, seizures, focal neurological defects and nonspecific symptoms such as nausea and vomiting. The purpose of this case report is to present thecharacteristics of these diseases in a pregnant patient with both preeclampsia and PRES, and to contribute to the literature by discussing the differential diagnosis.

Keywords: Posterior Reversible Encephalopathy Syndrome

Posterior reversible encephalopathy syndrome (PRES) is a neurological disorder with an acute onset characterized by several neurological symptoms, such as headache, visual impairment, visual field defects, impaired consciousness, confusion, seizures, and focal neurological defects [1]. PRES is a clinical syndrome that describes a condition that causes reversible subcortical vasogenic brain edema driven by endothelial dysfunction that mainly affects the bilateral parieto-occipital regions [2]. PRES can be triggered by unregulated blood pressure, eclampsia, autoimmune disease, transplantation, kidney failure, or immunosuppressive or cytotoxic medications. Although the exact etiology is undetermined, endothelial dysfunction is probably suspected [3]. There is no specific therapy for PRES; instead, the syndrome is treated by addressing its underlying cause. In situations with pregnancy-related Pre, treatment includes rapid delivery of the fetus. Magnesium sulfate is indicated in pregnant women with PRES and preeclampsia to avoid seizures [4]. The prognosis of PRES depends on the underlying condition, neurologic symptoms are reversible in most individuals, but neurological sequelae may persist if significant complications accompany PRES. Preeclampsia is an obstetric disorder affecting 3 to 8 percent of pregnant women and remains the primary cause of short- and long- term neonatal and maternal mortality [5]. Worldwide, approximately 4 million women are diagnosed with preeclampsia yearly, and an estimated 70,000 women and 500,000 babies die annually [6]. Preeclampsia is a complex multisystemic disorder characterized by abrupt onset hypertension (>20 weeks of gestation) and proteinuria, as well as dysfunction of maternal organs or uteroplacental dysfunction [7]. The etiology of preeclampsia is

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unknown; however, studies suggest that it is caused by uteroplacental pathology. Proteinuria, acute kidney injury, liver dysfunction, hemolysis, thrombocytopenia, seizures, stroke, and mortality can result from preeclampsia-related end-organ damage [8]. B Major risk factors include chronic hypertension, pregestational diabetes mellitus, antiphospholipid syndrome, and a history of obesity. Other risk factors include advanced maternal age, nulliparity, assisted reproductive treatments, chronic kidney disease, and genetic factors [8, 9]. Delivery is the only definitive therapy, and low-dose aspirin is recommended for high-risk pregnant women as a prophylaxis [10].

CASE PRESENTATION

A 26-year-old primigravida 30-week pregnant patient applied to our emergency department complaining of vomiting and hitting her head against the wall due to fainting while standing up. It was found that the pregnancy follow-up was conducted at an external center, there was no issue with the follow-up, and there was no chronic disease.

Her general condition was moderate; her consciousness was confused and disoriented, and her cooperation was limited. Pupils were isochoric, light reflex +/+. Verbal output was normal, there was no motor-sensory loss, and there was no neck stiffness. Other system examinations did not reveal any pathologic findings or trauma-related lesions. The temperature was 36.2 °C, blood pressure was 180/100 mmHg, heart rate was 100 beats per minute, and SpO2 was 98%. Laboratory values were WBC:19830/ml, Hgb:12.6 g/dl, PLT:112000 mcl, BUN 19 mg/dl, creatinine 1.13, ALT 59 U/L, AST 55 U/L, proteinuria 3+ in the urine. In the brain diffusion MRI, which was hyperintense in the ADC and T2 sequences, diffusion was restricted in both basal ganglia and the left occipital lobe (Figure 1).

Betamethasone, nifedipine, and MgSO4 were administered to the patient. Neurology and obstetrics consultation requests were made simultaneously. In the obstetric examination, the fetal heart rate (+) was compatible with the fetus at 30 weeks, and the amniotic fluid was adequate. Posterior Reversible Encephalopathy Syndrome (PRES) was considered in the patient who was evaluated by neurology. The patient underwent an emergency cesarean section due to severe preeclampsia and was hospitalized in the post-operative intensive care unit and discharged on the thirteenth day after recovering.

DISCUSSION

Posterior reversible encephalopathy syndrome (PRES), also called reversible posterior leukoencephalopathy syndrome (RPLS), is a special kind of cerebrovascular syndrome characterized by clinical and imaging features. The onset of PRES typically includes acute or subacute headaches, vision changes, seizures, impaired consciousness, focal neurological changes, and nonspecific symptoms such as nausea and vomiting. The gold standard for diagnosing and assessing PRES is magnetic resonance imaging

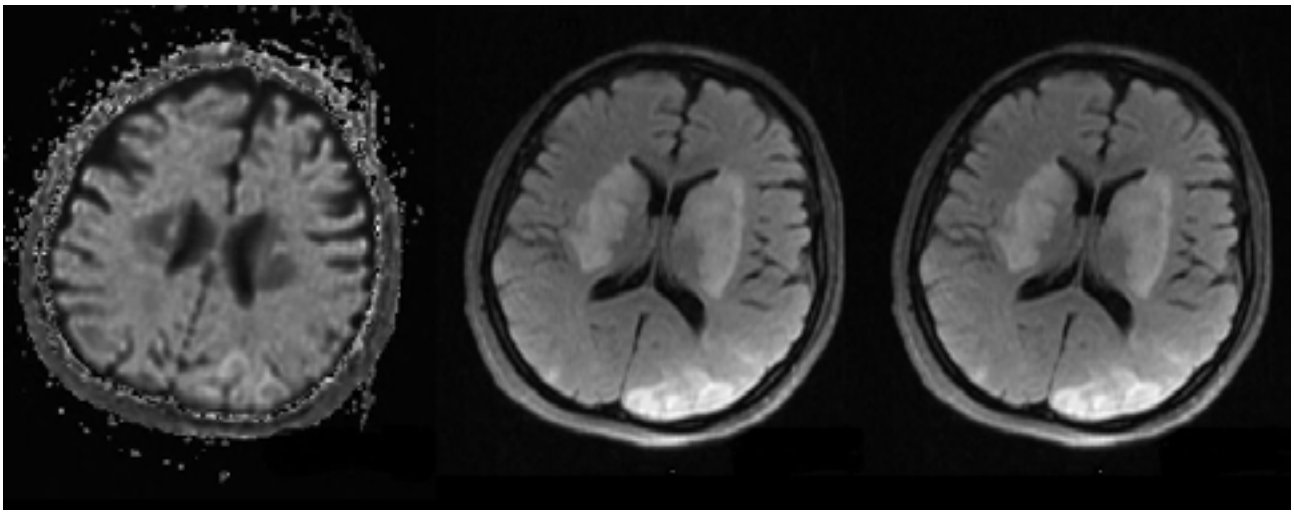

Figure 1. The brain diffusion MRI,hyperintense in the ADC and T2 sequences, diffusion was restricted in both basal ganglia and the left occipital lobe

(MRI). This syndrome's imaging features include vasogenic edema of the subcortical white matter in most patients and possible cytotoxic edema in some patients [11].

Vascular diseases include cerebral venous sinus thrombosis, toxic or metabolic leukoencephalopathy, hereditary leukodystrophy, demyelinating disease of the central nervous system, lymphoma and tumors, and reversible vasoconstriction syndromes should be considered in the differential diagnosis. Many ideas of pathophysiological mechanisms have been presented, even though the actual etiopathogenesis of PRES still needs to be understood entirely. The most prevalent theory is that abruptly elevating blood pressure surpasses the top limit of cerebral blood flow autoregulation, resulting in hyperperfusion, disruption of the blood- brain barrier, and vasogenic edema. Nevertheless, 20% to 50% of PRES patient cases were normotensive or hypotensive [12].

Acute management of PRES is supportive and focused on eradicating the underlying cause. There have been no randomized trials of the various interventions used to treat PRES, and treatment guidelines are generally consensus-based. Patients should be hydrated, and electrolyte imbalances must be addressed. Blood pressure should be steadily lowered by 20- 25% within the first few hours to prevent cerebral, coronary, and renal ischemia in individuals with acute hypertension. Patients with cerebral edema who experience elevated intracranial pressure may require neurosurgical intervention. The prognosis is typically favorable, although more severely afflicted individuals may require critical care support and neurologic sequelae [13].

In our case, the neurological symptoms of a 30-week pregnant patient, along with elevated blood pressure and proteinuria, led to the diagnosis of preeclampsia, and MRI findings of hyperintense lesions in the basal ganglia and occipital lobe supported PRES. The patient's blood pressure and neurological symptoms improved after terminating the pregnancy.

In this case report, we emphasized that PRES should also be considered in the differential diagnosis of patients presenting to the emergency department with neurological complaints, with preeclampsia and emergency department management being the most common causes.

Conflict of Interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Authors' Contribution

Study Conception: FBÇ, MY, AK, MOA, UO, HK; Study Design: FBÇ, AK, MY; Literature Review: FBÇ, MY, UO, HK; Critical Review: FBÇ, MY, AK, HK; Data Collection and/or Processing: FBÇ, MY, MOA, HK,; Analysis and/or Data Interpretation: FBÇ, MY, MOA, HK; Manuscript preparing: FBÇ, MY, AK.

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Anesthesia management in a patient with osteogenesis imperfecta

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ABSTRACT

Osteogenesis imperfecta is a rare autosomal dominant collagen tissue disease that primarily affects the bones. It is a condition that requires to be carefully managed during the preoperative period and when administering anesthesia. In this case report, we aimed to present our experience with supraclavicular nerve block in a patient with osteogenesis imperfecta who underwent intervention for left humeral shaft fracture since it is a relatively simple and safe technique to perform.

Keywords: ultrasonography, osteogenesis imperfecta, supraclavicular nerve block

Osteogenesis imperfecta (OI), is one of the rare diseases with autosomal dominant transition and defective collagen maturation is which primarily affects bones. The main issue is that Type I collagen's structure, which is crucial for bone and other structural strength requirements, has been affected by a genetic mutation (disease) [1, 2]. OI's Clinical signs and symptoms include congenital heart disease, valvular heart disease, thin skin, blue sclera, hearing loss from otosclerosis, hyperthermia, hyperhidrosis, dental structural defects, platelet dysfunction, and cor pulmonale [3]. OI also raises the risk of hemorrhage and in patients with brittle OI, taking a blood pressure reading with a cuff every three to five minutes during receiving anesthesia may result in an iatrogenic fracture [4].

Administering general anesthetic presents a number of challenges, including difficult ventilation, difficult intubation, fractures to the teeth and jaw, risk of cervical injury, and difficulty in positioning. In addition, problems that need to be considered include the possibility of both malignant and non-malignant hyperthermia, respiratory failure caused by kyphoscoliosis, and regulation of cardiac anesthetic settings [5].

In this case report, we aim to discuss the perioperative anesthetic management of an adult patient with osteogenesis imperfecta who had a fracture to the left humeral shaft.

A 24-year-old, 44 kg female patient was taken into surgery due to a fracture to the left humerus shaft. The patient had old fractures in both right radius and left tibia. Surgery for scoliosis had previously performed. Physical examination findings during the preoperative evaluation included kyphoscoliosis, short neck (thyromental distance <6 cm), growth retardation, short stature, deformity, and shortness in both lower and upper extremities. The patient's echocardiogram, lung x-ray, and routine blood tests revealed no additional pathology. The operating room was prepared considering the potential complications in account.For the difficult airway device, arrangements were set up.

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Procedures related to the risk of developing Malignant Hyperthermia (MH), which has been reported to have a higher incidence in comparison to the general population, were additionally noted. The inhalation agent vaporizers were removed from the room. The anesthetic device's carbon dioxide absorber has been changed. Previously unappropiated anesthesia circuit was removed and the device was cleaned with 15 L min-1 fresh gas for 30 minutes.

At this point, the pharmacist provided Dantrolen, which was continually accessible in the operating room. The patient was taken to the operating room once the anesthetic consent was received and the patient was informed of any potential complications.

A continuous infusion of 0.9% NaCl was commenced at a rate of 10 mL/kg/hour after an intravenous 20G cannula was inserted into the contralateral arm. The patient was monitored with standard anesthetic motorization (ECG, blood pressure, pulse oximetry). The initial vital signs were 97 beats per minute, 138/95 mmHg for blood pressure, and 95% for oxygen saturation.The patient was positioned in a supine position and given 0.5 mcg/kg of fentanyl and 0.01-0.1 mg/kg of midazolam intravenously for sedoanalgesia. With povidone iodine, the left shoulder area that intended to be blocked was sanitized. A 22G 100mm long needle (Stimuplex Ultra®, Braun, Melsungen, Germany) was used.Next to the injection site, the ultrasonography probe (GE ML6-15-D Matrix Linear) was positioned 1 cm above the clavicle. The subclavian artery and brachial plexus were visible in the transverse sectional view of the patient when the ultrasonography probe was positioned in the supraclavicular fossa in the coronal oblique plane with the head tilted 45° to the contralateral side. The patient was resting supine at the time (Figure 1). The hypoechoic nodule cluster referred to as the brachial plexus was frequently observed lateral to the hypoechoic subclavian artery, which lay on top of the hyperechoic first rib and pulsed firmly (Figure 2). It allowed for real-time observation of the needle's movement. A nerve stimulator (Stimuplex) was activated after the needle reached the brachial plexus cluster. It initiated at 0.5 mA and increased to a maximum of 1.5 mA to trigger a muscle twitch. Using the in-plane approach, 15 cc of 0.5% bupivacaine and 10 cc of 2% lidocaine combination were administered after the localization of the plexus brachialis was determined. Diffusion across the truncus was observed during the injection of local anesthetic (Figure 3). Sensorial block at the 20th minute, motor block at the 30th minute (Essam scale: 2) (normal muscle strength normal hand gripping, wrist and elbow flexion (3), muscle strength decreased but wrist and elbow flexion protected (2), muscle strength decreased, only elbow flexion protected (1), no muscle strength, wrist and elbow flexion absent (0) was observed) (6). During the 60-minute procedure, no additional analgesics were required.After 30 minutes of postoperative anesthetic care unit monitoring, the patient was transferred to the service with a modified aldrate score of 10, showing no block-related complications.

Figure 1. Patient resting at the supine position

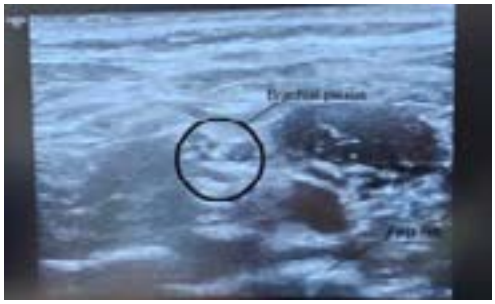

Figure 2. The hypoechoic nodule cluster referred to as the brachial plexus

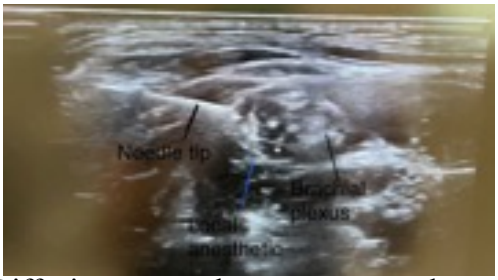

Figure 3. Diffusion across the truncus was observed during the injection of local anesthetic

The ultrasound image of the supraclavicular brachial plexus at the level of the first rib.

DISCUSSION

OI is also called "brittle bone disease" since the fractures can occur following a slight or no trauma. According to a previous study, OI affects approximately 6-7 persons out of every 100,000 and is present in about 1 in 20,000 infants [7].The disorder is caused by a defect in type I collagen synthesis, secondary to a gene mutation. Type I collagen is the principal type in bone, skin, sclera, dentine, and other tissues; therefore, lesions in these areas are more visible [8].

In addition, recurrent pharyngeal collapse and even apnea may occur during sleep due to abnormalities in pharyngeal anatomy, upper airway dilatation and ventilatory regulations [9]. Consequently, managing anesthesia during surgery in individuals with these diseases presents serious difficulties. Patients with OI need to be carefully managed under general anesthesia to minimize the risk of malignant hyperthermia and mandibular bone fractures during tracheal intubation.

During the perioperative period, kyphoscoliosis-related issues or neck movement restrictions may result in difficult airway management and dental injuries. However, the literature also has a large number of cases of successful laryngeal mask use and intubation [10, 11].

The development of MH is definitely the most feared complication, apart from the difficult airway. The syndrome known as MH develops from a hereditary deficiency in the skeletal muscles and is characterized by the emergence of a hypermetabolic reaction following exposure to a trigger, such as depolarizing neuromuscular blockers or volatile anesthetics. Increased carbon dioxide, hyperthermia, tachypnea, tachycardia, muscle rigidity, acidosis, hyperkalemia, and rhabdomyolysis are among the symptoms. This condition develops rapidly and has a high death rate; early diagnosis and treatment are crucial. Remember that cardiac symptoms related to hyperkalemia may also appear [12]. A standard clinical rating score was developed by Laranch and colleagues in 1994, which can be used in the diagnostic approach and is accepted by the international consensus. According to this scoring system, the probability of MH development can be estimated/calculated proportionally [13]. Removal of the triggering substance should be the first action taken once there is clinical doubt.Symptomatic treatment should be applied afterwards.Dantrolene sodium is the only medication that known to stop the MH cascade. After the introduction of the drug, the mortality rate due to MH decreased from 80% to 10%.Though the exact mechanism of action of this drug is unknown, it is believed to be related to ryanodine receptor inhibition-induced blockage of calcium release from the sarcoplasmic reticulum [14]. Total intravenous anesthesia (TIVA) administration is an optimal anesthetic maintenance technique that may be applied to patients at risk for MH. As they are easier to use and less hazardous than general anesthesia, peripheral blocks are utilized more often than general anesthesia [15].

OI is a severe disease with a number of complications. For patients who need surgery, it's important to assess the severity of the state of affairs, practice a comprehensive preoperative evaluation, and create a personalized anesthetic management strategy. Anesthesia safety and smoothness are enhanced by early identification of risk factors and optimizing the preoperative health status of patients with OI.

In our case, we aimed to minimize the risks that may occur during intubation by preferring supraclavicular block.

We believe that peripheral block can be used as an easier, safer and less hazardous method compared to general anesthesia.

Conflict of Interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Authors' Contribution

Study Conception: EU, EÇ; Study Design: EU, EÇ; Literature Review: EU, EÇ; Critical Review: EU, EÇ; Data Collection and/or Processing: EU, EÇ; Analysis and/or Data Interpretation: EU, EÇ; Manuscript preparing: EU, EÇ.

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