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Original Article
Eurasian Journal of Critical Care

Prospective Analysis of Application Reasons of Alzheimer's Patients Applying to the Emergency Department

Halil İbrahim Çıkrıklar[1], Murat Aslan[1], Vahide Aslıhan Durak[1], Serhat Atmaca[1], Suna Eraybar[1], Hakan Çelebi[1], Erol Armagan[1]
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Abstract

Background: The aim of this study is to analyze the reasons for admission of Alzheimer's patients who applied to the emergency services.

Materials and methods: The study was conducted prospectively on patients with Alzheimer's disease who applied to the emergency departments of Bursa Uludag University Health Application and Research Center, Health Sciences University Bursa Yüksek İhtisas Training and Research Hospital and Bursa City Hospital between 01.07.2021 and 01.07.2022.

Result: A total of 248 patients, 103 male (41.5%) and 145 female (58.5%), were included in the study. It was determined that the three most common diagnoses received by the patients in the emergency department were pneumonia (17.7%), ischemic cerebrovascular disease (10.3%), and urinary system infection (9.3%). It was determined that 42.7% of the patients were hospitalized in clinical and 18.1% in intensive care units.

Conclusion: As a result, it was determined that the most common diagnoses of Alzheimer's patients admitted to the emergency department were pneumonia, ischemic cerebrovascular disease and urinary tract infection, respectively and more than half of all admitted patients had indications for hospitalization.

Keywords: Alzheimer Disease, Emergency Department, Geriatric Patient.

Introduction

Alzheimer's disease (AD) is a neurodegenerative syndrome characterized by global cognitive impairment and neuropsychiatric symptoms[1]. It is the most common type of dementia and accounts for 60% to 70% of all causes of dementia[2]. Alzheimer's disease affects more than 30 million people in worldwide[3].

AD follows a clinically progressive course. It begins with forgetfulness and short-term memory loss. Over time, place, time and person orientation deteriorates. The patient, whose cognitive and motor functions are impaired, becomes immobile and in need of care over time[4]. Currently, there is no treatment that cures AD or stops its progression[5].

Emergency Departments (ED) are units where patients can quickly access medical care when needed[6]. ED applications of elderly patients with serious chronic diseases are increasing day by day[7]. AD has an important place among the patient groups[8-10]. The aim of this study is to investigate the most common reasons for admission and hospitalization processes of patients with AD and admitted to ED.

Material and Methods

An ethics committee report was obtained with the decision dated 02.06.2021 and numbered 2021-7/31 by appealing to Bursa Uludağ University Faculty of Medicine Clinical Research Ethics Committee within the scope of the master thesis. The research was conducted prospectively on patients with AD who applied to ED of Bursa Uludağ University Health Application and Research Center, University of Health Sciences Bursa Yüksek İhtisas Training and Research Hospital and Bursa City Hospital between 01.07.2021 and 01.07.2022.

Patients over the age of 18 who applied to the emergency medicine clinics of the health centers on the specified date and were previously diagnosed with AD were included in the study.The patients included in the study, or their relatives were informed and their consents were obtained. The data obtained were recorded in the patient file by the doctor who examined the patient.

The patients name, surname, date of application to the emergency department, hospital protocol number, age, gender, reason for applying to the emergency department,

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chronic diseases, how many years have been diagnosed with AD, who has been caring for the patient, number of applications to the emergency department in the last year, whether consultation is requested, patient outcome, length of stay in ED were recorded in the patient file. The interventional procedure, examination or drug administration except the routine health care was not applied to the patient.

Descriptive statics for continuous variables from the featured features are expressed as Average Standard Deviation, Minimum and Maximum values while categorical variables are expressed as numbers and percentages. Independent groups t-test was used to compare continuous variables according to categorical variables. Pearson correlation multiples were calculated to determine the relationship between these variables.

Chi-square test was used to determine the relationship between groups and categorical variables.The significance value was determined as $p<0.05$ for all analyses.Data were analyzed using the IBM SPSS (Version 21.0. Armonk, NY: IBM Corp.) program.

Results

248 applicants included in the study were evaluated according to gender in terms of age, duration of AD, duration of stay in ED and the number of ED applications in the last year (Table 1).

It was determined that 103(41.5%) of the applicants were male and 145 (58.5%) were female. The average age of 248 Alzheimer's patients participating in the study was calculated as 79.32±9.44 (Table-1).

The average time from the diagnosis of AD to the day of admission was found as 4.58±. While this period was found as 4.22±3.68 in men, it was found as 4.8±3.66 in females (Table-1).

The patient's average duration of stay in the ED was found as 7.93±5.93 hours. It was determined that female patients stayed longer in ED (Table-1).

125 patients once, 18 patients twice, 16 patients 3 times, 7 patients 4 times, 1 patient 5 times and 1 patient 6 times applied to the ED during the study period. The average number of ED applications made by the patients in the last year was found as 3.90±3.05.When the applications of men and women were compared in the last year, it was found that men applied more frequently, and this was found to be statically significant (p=0.02)(Table-1).

According to the age groups of the patients who applied to ED; they were grouped as 65-74 young old, 76-84 old, 85 and over very old and it was showed in Table-2. The number of young old people was 50(20.1%), the number of old people was 125(50.4%) and the number of very old people was 64(25.8%). It was determined that 9 patients were under 65 years of age. The average of ED admissions in the last year were compared according to the age groups. As seen in Table-2, the frequency of applying to ED was found to increase with increasing age (p=0.05).

Table 1: Analysis of Patient's age, duration of Alzheimer's Disease, duration of staying in the Emergency Department and Emergency Service applications made in the last year according to the gender of the patients.

		Number	Mean	Standard Deviation	Min.	Max	p-Value
Age	Male	102	78.64	6.709	65	93	0.339
	Female	145	79.81	10.960	40	99	
	Total	247	79.32	9.440	40	99	
Duration of AD (year)	Male	103	4.22	3.686	1	15	0.203
	Female	145	4.83	3.665	1	20	
	Total	248	4.58	3.679	1	20	
Duration of stay in ED (hours)	Male	103	7.35	5.866	1	25	0.197
	Female	145	8.34	5.968	1	30	
	Total	248	7.93	5.934	1	30	
Number of ED application in the last year	Male	103	4.43	3.945	0	21	**0.020**
	Female	145	3.52	2.138	0	10	
	Total	248	3.90	3.048	0	21	

Significant *p* valuesarepresented in bold.
AD: Alzheimer's disease, ED: Emergency Departments

Table 2: Average of Patients Over 65 Years of Admission to the Emergency Department in the Last One Year.

	Age Groups	Average application	Standard Deviation	Min.	Max	p
Emergency Service Applications (1 year)	65-74	2.90	1.854	0	7	0.050
	75-84	4.03	2.552	0	13	
	>84	4.16	4.325	0	21	

Table 3: Comorbidities of the Patients and Percentages of Existence.

Comorbidity	Number (n)	Percentage (%)
Hypertension	155	62,5
Diabetes Mellitus	66	26,6
Coronary Artery Disease	51	20,6
Cerebrovaskuler Disease	39	15,7
Chronic Renal Failure	27	10,9
Parkinson	13	5,2
Asthma/Chronic Obstructive Pulmonary Disease	13	5,2
Arrhythtmia	12	4,8
Malignancy	9	3,6
Congestive Heart Failure	9	3,6
Epilepsy	5	2,0
Bipolar Disorder	1	0,4
Hepatic Cirrhosis	1	0,4

When the people who took care of the patients were questioned, it was determined that 185 (74.6%) of them were cared for by their families, 34 patients (13.7%) stayed in s nursing home, 26 (10.5%) stayed at home with a nursemaid and 3 patients lived alone.

The comorbidities and percentages of the patients are given in Table-3. According to the table, the most common comorbidities in patients were hypertension (HT), diabetes, coronary artery disease, cerebro vascular disease and chronic kidney failure (CRF).

The complaints of the patients were examined (Table-4). As seen in Table-4; the most common complaints of patients were found as general condition disorder, dyspnea, fever, falling and asthenia.

The diagnoses received by the patients according to their admission complaints were evaluated as their primary diagnosis and it was showed in Table-5. According to the table, the most

Table 4: Examination of Patients According to the Application Complaints.

Complaint	Number	Percentage (%)
General Condition Disorder	47	18,9
Dsypnea	39	15,7
Fever	35	14,1
Fall	23	9,3
Asthenia	11	4,4
Abdominal pain	9	3,6
Seizure	9	3,6
Cough	8	3,2
Oral Intake Disorder	7	2,8
Speech Disorder	6	2,4
Others	54	22

Table 5: Primary Diagnoses of the Patients.

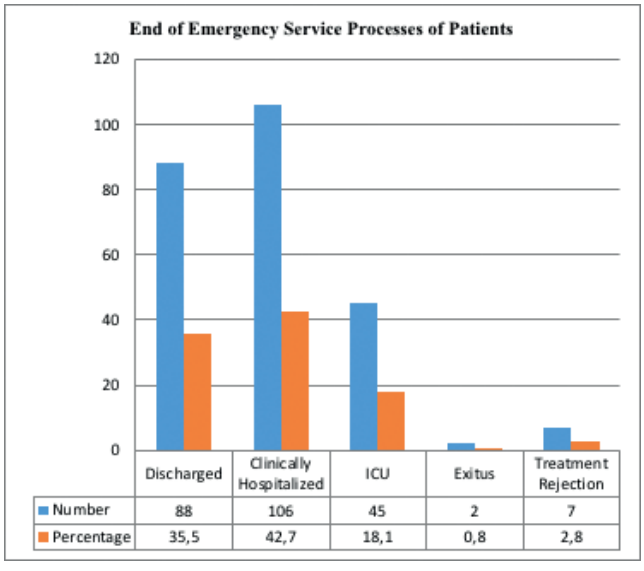
Primary Diagnoses	Number	Percentage (%)
Pneumonia	44	17,7
Ischemic Cerebro Vascular Disease	25	10,3
Urinary Tract Infection	23	9,3
Coronavirus disease 2019	16	6,5
Acute Renal Failure	15	6
Femur Fracture	9	3,6
Pulmonary Embolism	7	2,8
Soft Tissue Trauma	7	2,8
Hypernatremia	6	2,4
Upper Respiratory Infection	6	2,4
Others	90	36,2
Total	248	100

common diagnoses were pneumonia (17.7%), ischemic cerebro vascular disease (10.3%), urinary tract infection (UTI) (9.3%), COVID 19 (6.5%), acute renal failure (ARF) (6%).

Clinics for which consultation was requested were investigated. The rate of patients who requested one or more consultations was 81.5%. The most frequently consulted clinics were Chest Diseases (n=81), Internal Medicine(n=66), Neurology (n=56), Infectious Diseases (n=41), Cardiology (n=27), Anesthesia and Reanimation (n=20), Orthopedics (n=16) and Neurosurgery (n=12).

The termination of ED processes of the patients was examined. According to this, while 42.7% of the patients were hospitalized in clinics, 18.1% were admitted to the intensive care unit. While 35.5% were discharged from the hospital, two patients (0.8%) died while in the ED process. 2.8% left from the ED by signing treatment rejection (Figure 1).

When the patients' hospitalized clinics are compared, the first five places are seen as Chest Diseases, Internal



ICU: Intensive Care Unit

Figure 1: End of Emergency Service Processes of Patients.

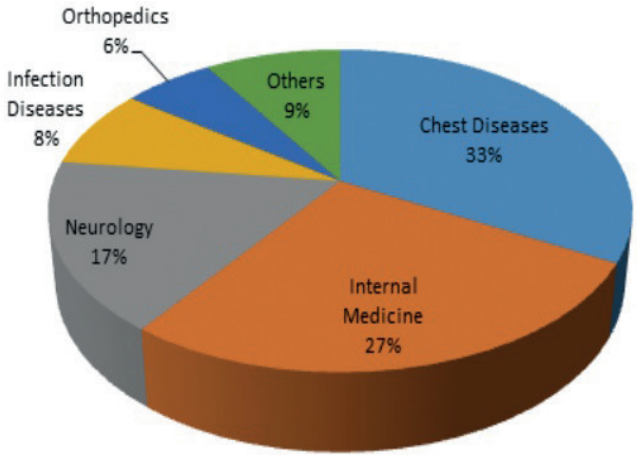


Figure 2: Distribution of Hospitalized Patients According to the Clinics

Medicine, Neurology, Infectious Diseases and Orthopedics clinics. The distribution of hospitalized patients according to clinics is schematized in Figure-2.

Discussion

The number of populations aged 65 and over is increasing globally, and there is an increase in the applications of elderly patients to the ED, which is the gateway to the hospital[9]. Diagnosis and treatment of elderly patients are difficult for ED physicians who do not receive adequate training for this condition[10]. Among the elderly patient groups, AD has a vital place[8]. We examined the causes, and care processes of AD cases admitted to the ED in our study.

In studies conducted on AD, It was seen that the mean age was approximately 81[8]. In our study, AD participants' mean age was 79.32 years, which was consistent with these studies.

Estrogen hormone decreases with menopause in women. It has been shown that the decrease of estrogen hormone, which is thought to reduce the risk of AD, is related to the increased incidence of AD in women[11]. According to several studies, the prevalence of AD is higher in women than in men[12]. In our study, the majority of the application (58.5%) were made by women.

Our country has limited nursing homes for Alzheimer's patients and institutional structures to support caregivers. Due to the culture of the society in which we live, the relatives of the patients consider caring for their patients a family duty[13]. It has been observed that 80-90% of care is provided by families in the United States[14]. On the contrary, patient care was mostly (75%) provided by their families in our study.

The number of chronic diseases increases with advancing age. In a study conducted with 72.815 patients over 64 years of age in Spain, the most common comorbidities in patients with dementia were hypertension and diabetes[15]. In a study performed on 497 patients with dementia in our country, the most common chronic disease was hypertension, followed by cataracts, depression, and diabetes[16]. In our study, the most common comorbid disease was found to be hypertension, while other comorbidities were diabetes, coronary artery disease, cerebro vascular disease and CRF, respectively.

Gülalp et al. examined applications of 2046 patients with ED over 65 years. The authors reported that the most common complaints at presentation were falling, chest pain, dyspnea, chronic extremity pain, abdominal pain, and fever[17]. In another study, the most common reasons for presentation in patients with AD were impaired consciousness, fever, falling, and dyspnea[18]. In our study, the most common complaints were general condition disorder, dyspnea, fever, falling from the same level, and fatigue.

A study conducted in Turkey found that the rate of consultation requested was 4.5% when all ED applications were examined[19]. In a study performed with geriatric patients, this rate was 43.4%[20]. In our study, which included only AD cases, the rate of patients for whom consultation was requested was 81.5%.

Logoğlu et al. examined the patients over the age of 65, and they determined that the departments for which consultation was requested most frequently were Cardiology, Internal Medicine, Chest Diseases, Neurology, and General Surgery[20]. Bozkurt et al. showed that the departments for which consultation was requested most frequently were Cardiology, Internal Medicine, Chest Diseases, Orthopedics, and Neurology[21]. In our study, the most frequently requested clinics for consultation were determined as Chest Diseases, Internal Medicine, Neurology, Infectious Diseases and Orthopedics.

Özşaker et al. reported that geriatric patients required more hospitalization and treatment compared to younger patients, and the duration of stay in the hospital was longer[22]. In a study conducted with patients over the age of 65 in 2018, the hospitalization rate was found to be 15.8%[23]. In a study by Wofford et al. on geriatric patients, the hospitalization rate from ED was between 32% and 46%[24]. In our study, the hospitalization rate of AD cases admitted to ED was 60.8%.

In the study conducted on the geriatric patient group by Bedel at al, it was determined that the departments with the highest number of hospitalizations were Internal Medicine, Cardiology, Chest Diseases and Neurology[23]. In our study, it was seen that the five clinics with the highest number of hospitalizations were Chest Diseases, Internal Medicine, Neurology, Infectious Diseases and Orthopedics clinics respectively.

Limitations

Although our study is multicenter and prospective, the small number of cases is one of the factors limiting our study.

Conclusion

As a result, the most common diagnoses in AD cases applying to ED were pneumonia, ischemic cerebro vascular disease and urinary system infection. Respectively, it has been determined that the frequency of applying to ED increases with age and that more than half of the patients have an indication for hospitalization. It is thought that increasing the geriatrician in hospitals will contribute positively to the diagnosis, treatment, and follow-up process of AD cases among the elderly patient groups. We hope that our study, which we think is one of the few studies in its field, can contribute to the literature. We believe that there is a need for new studies on the subject.

Conflict of Interest

No conflict of interest was declared by the authors.

Financial Disclosure

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Original Article
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Effect Of Covid-19 On Emergency Service Workers

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Abstract

Introduction: Healthcare professionals have been of the fight against the pandemic, continued for more than a year. The anxiety levels of healthcare workers due to increased workload, social isolation, fear of catching COVID-19, etc. have increased significantly. The aim of this study is to determine the anxiety levels of emergency service workers who are always at the forefront of the fighting against the pandemic in Turkey.

Methods: A questionnaire containing demographic information and the questions of 2 different scales (generalized anxiety disorder-7 scale, coronavirus anxiety scale), whose validation and reliability were performed in Turkey, was delivered via the web to the emergency room workers.

Results: Personnel working in the emergency service of a tertiary state hospital, 74% were reached. On the generalized anxiety scale, 53% of the participants received a score of 11 or above (severe anxiety). While the mean values of the generalized anxiety scale in the income and education groups showed a statistically significant correlation, the anxiety mean scores of those with less than 2 years of employment were found to be statistically significantly lower, and the anxiety mean scores of those who had covid-19 during the pandemic were found to be statistically significantly higher. This was found to be related to those with high anxiety and covid-related anxiety scores not wanting to work in the emergency service.

Conclusion: As a result of the study, it was revealed emergency service workers have a high level of anxiety originating from pandemics, regardless of their seniority, age, and gender.

Keywords: Emergency, Coronavirus (COVİD-19), Pandemic, Generalized Anxiety Disorder-7 (GAD-7), Coronavirus Anxiety Scale Short Form (CAS)

Introduction

Coronavirus disease 2019 (Covid-19) emerged in December 2019 as a disease that affects the whole body, especially the lungs, caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)[1]. The World Health Organization (WHO) declared Covid-19 a public health problem of international concern on January 30, 2020[2]. On March 11, 2020, the first case was seen in Turkey[3]. After these processes, it has caused panic due to the rapid spread of the virus and the severe course of the disease, in the world and Turkey[4].

Both the poor prognosis of the disease and the panic in the public increased the admissions to the health institutions, the need for health services, and health expenses such as hospital beds, mechanical ventilators, and intensive care beds. When the obscurities of Covid-19 disease, the burden of disease, the panic it created, and the inability to meet the health needs came together, they have caused the healthcare workers to have too much burden, and the prolongation of this process has caused burnout and ongoing anxiety[5].

Many studies on the cause of this anxiety in healthcare professionals have revealed the following: lack of appropriate personal protective equipment, increased workload, not being able to access sufficient information and inadequate training especially at the beginning of the covid-19 disease, delay in diagnosis and treatment in case of exposure to infection, and therefore, the thought of spreading the disease, the inability to spend quality time with his/her family and his/her environment due to both the workload and the fear of carrying the infection to his/her family, and the symptoms of burnout due to the uncertainty of the process[6,7,8].

The aim of our study, considering all partners around them (hospital, home, family, colleagues, in-house training, media, internet) during the covid-19 pandemic, is to reveal how the psychological states of all staff (doctor, nurse, medical secretary, cleaning or auxiliary staff, etc.) in the emergency service, who feels most of these problems and

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concerns and who works at the front line in Turkey, are affected.

Material and Method

2.1 Ethical approval

Van TRH Clinical Research Ethics Committee approved this study (protocol number: 2021/03)

2.2. Sampling and data collection

The study is a cross-sectional study conducted between the dates of 02.01.2021 and 04.01.2021 among the personnel working in the emergency service of the tertiary hospital. In the sample selection, it was aimed to reach all healthcare professionals working in the Emergency Service. In the center where the study was conducted, the number of patients entering the emergency room daily is approximately 1500. The total number of staff working in the hospital emergency service is 135 people. Among the workers, 100 (74%) healthcare workers were reached.

After obtaining ethical approval for the study, an online questionnaire consisting of 27 questions was prepared to collect data via Google Forms between 02.01.2021 and 04.01.2021. The questionnaire was initially applied to 18 health employee from Akdeniz University Faculty of Medicine emergency service personnel who were health professionals and were not, and it was rearranged according to their feedback. The questionnaire link was sent to all workers via e-mail. The questionnaire time was approximately 3-5 minutes.

The data collected included the sociodemographic characteristics of the participants, the Coronavirus Anxiety Scale Short Form and the Generalized Anxiety Disorder-7 (GAD-7) scale.

Coronavirus Anxiety Scale Short Form (CAS): A brief mental health scan, CAS, was developed by Lee to identify possible causes of dysfunctional anxiety associated with the COVID-19 crisis[9]. The scale, whose validity and reliability study was conducted by Biçer et al., consists of 5 questions and one dimension, and the Cronbach Alpha reliability coefficient of the scale was calculated as 0.832[10]. CAS is a 5-point Likert scale. Scoring of the scale was carried out as "0" "never", "1" "Rare, less than a day or two", "2" "a few days", "3" "more than 7 days" and "4" "almost every day in the last two weeks".

Generalized Anxiety Disorder-7 (GAD-7): The GAD-7 scale, developed by Spitzer et al., 11according to DSM-IV-TR criteria, was translated into Turkish by Konkan et al. and its validity and reliability study was conducted. It is a short self-report scale that evaluates generalized anxiety disorder. It is a 7-item four-point Likert (0=none, 1=many days, 2=more than half of the days, 3=almost every day) pen-and-paper type scale, which evaluates the experiences asked in the scale items in the last 2 weeks. The total scores obtained from the scale are 5, 10, and 15 cut-off points for mild, moderate, and severe anxiety, respectively. The total score Cronbach alpha value of the GAD-7 test was found to be 0.852[12].

In the analyses, specialist physicians, general practitioners, nurses were classified as health professionals occupational group 1, and medical secretary, assistant staff (staff who transport patients to any location, help patients with their basic needs when they want them), and cleaning staff were classified as health professionals occupational group 2, according to their duties in the emergency service. In addition, considering the education they received, they were classified into 2 as associate and postgraduate degree graduates and high school graduates and below. According to the duration of their employment any hospital, those under 2 years are classified as for beginners, and those with 2 years or more as experienced personnel[13].

2.3.Statistical analysis.

IBM® SPSS® Statistics V21 software was used for statistical analysis of the data. After determining whether the data were parametric, the data were expressed as mean ± standard deviation (SD), median (minimum-maximum), and number (%). Kolmogorov-Smirnov test was used to evaluate the conformity of quantitative data distribution to normal distribution. The significance test of the difference between the two means and the ANOVA test was used in the analyzes. Mann-Whitney U test was used to analyze data that did not conform to normal distribution.

Results

The mean age of our participants was 33.7 (sd±6.92), with 70% male and 30% female. Those who have a working period of fewer than 3 years are 30%, those who have 3 years and over are 70%. Other demographic data of the participants are given in Table 1.

The distribution of Hamilton Anxiety Scores is presented in Table 2.

When the distribution of the scores given to the Hamilton anxiety scale was examined, the highest rate was in the group with 11 and above scores with 53%. A moderately significant correlation was found between the total anxiety score and the Covid scale score. (r = .476 p: 0.001)

The reliability of the scales is given in Table 3.

While the reliability coefficient of the anxiety scale was found to be 86.3%, this value was found to be 94.5% in the Covid scale.

The distribution of the mean values obtained from the scales by the variables is given in Table 4. While the Hamilton scale mean values showed a statistically significant correlation in income and education groups, a

Table 1: The demographic data of the participants

	Mean (SD)	N (%)	Range
Age	33.7(st +-6,92)		23-53
Gender			
Female		30	
Male		70	
Education status			
Primary school		2	
Secondary school		3	
High school		21	
Associate Degree		6	
Bachelor's degree		53	
Master		7	
PhD graduate		8	
Profession Group			
Health vocational high school		6	
Medical secretary		13	
Assistant staff		11	
Cleaning staff		9	
Nurse		32	
General Practitioner		17	
Emergency medicine specialist		11	
Income status			
Income less than expenses		43	
Income equal to expense		29	
Income more than expenses		28	

Table 2: Classification of the scores given to the Hamilton anxiety scale

score	**N**	**%**
5 and less	23	23.0
6-10	24	24,0
11 and above	53	53,0

Table 3: Distribution of Coronavirus Anxiety Scale (CAS) and Generalized Anxiety Disorder-7 (GAD-7)of the scales

	Number of questions	Cronbach alfa
Generalized Anxiety Disorder-7 (GAD-7)	7	86,3
Distribution of Coronavirus Anxiety Scale(CAS)	5	94,5

statistically significant correlation was observed between the occupational groups in the Covid scale.

When we look at the anxiety scores of the participants by age, the anxiety level of those under the age of 35 was lower than the others. However, no statistical significance was found. (P=0.09)

Table 4: Distribution of mean values of Coronavirus Anxiety Scale (CAS) and Generalized Anxiety Disorder-7 (GAD-7)

	GAD-7		CAS	
	Mean±SD	P	Mean±SD	P
Gender				
Male	10,98±7,01		2,11±3,89	
Female	12,40±6,47	.347	2,0±4,24	,896
Income status				
Income less than expenses	9,13±6,65		1,97±3,85	
Income equal to expenses	12,62±5,32		1,10±2,05	
Income more than expenses	13,64±7,68	.012*	2,08±3,97	,122
Education				
High school and below	9,1±7,6		2,06±3,55	
Associate degree and above	12,73±5,98	.015	2,14±4,21	.923
Profession group				
1	13,21±6,54		,89±1,83	
2	11,35±6,06	.221	2,68±4,46	.020

Profession group 1; Medical secretary, assistant staff, cleaning staff, group 2; Health vocational high school, nurse, general practitioner, emergency medicine specialist

It is important to spend at least 2 years to fully fit an emergency service system, to be able to work as a full professional in the emergency service. For this reason, we evaluated those who worked less than 2 years as apprentice workers and those with more than 2 years as experienced workers. Of our participants, 30% were apprentice workers and 70% were experienced workers.

Among the participants, the anxiety mean scores of those with less than 2 years of employment and of those who want to work in emergency service were found to be statistically significantly lower, and the anxiety mean scores of those who had Covid-19 during the pandemic were found to be statistically significantly higher (Table 5).

It was revealed that approximately 65% of the participants received up-to-date information about the Covid-19 pandemic from the website of the Ministry of Health. It was seen that social media (56%) followed this. The sources used by the participants in our study to obtain up-to-date information about the covid-19 pandemic are given in Table 6.

To our question "If you were set free, would you like to work in the pandemic emergency service?", 53% have answered positively. The reasons for positive respondents are that they generally like to work in the emergency service and help people, that they are committed to their profession and duty, that they learn a lot in the emergency service during the pandemic, and that they think the risk of covid is the same everywhere. The reasons for those who respond negatively to this question were stated as the higher risk of getting covid-19 in the emergency department, inability to spend free and quality time with his/her family due to

Table 5: Coronavirus Anxiety Scale (CAS) and Generalized Anxiety Disorder-7 (GAD-7) survey results according to working time, catching COVID-19, and willingness to work in the Emergency department.

	N	GAD-7		CAS	
		Mean ±SD	P	**Median**(IQR)	P
Working time					
>= 2	70	12.34±6,72		0 (IQR 2.50)	
< 2	30	9.23±6,76	.037	0 (IQR 1,25)	.239
Catching COVID-19					
No	72	10.25±7,07	.006	0 (IQR 2,00)	
Yes	28	14.39±5,27		0 (IQR 7,50)	.193
Willingness to work in the Emergency department.					
No	47	14.40±6,01		1 (IQR 5,00)	
Yes	53	8.75±6,49	.001	0 (IQR 0,50)	.002

Table 6: Sources where participants get updated information on Covid-19

	N(%)
Articles and publications	45
Ministry of health website	65
Television	44
Social media	56
News web sites	40

fear of infecting his/her family and environment with the covid-19 disease, and that Covid-19 protection measures and protective equipment were not adequately provided in the emergency service and they were left alone in this regard, and that having fatigue in this long process.

Discussion

The fear caused by the Covid-19 uncertainty and intensive work since the first period of the pandemic has caused anxiety, burnout, insomnia, and fatigue in healthcare professionals who work with willingness and devotion. However, it is observed that these symptoms increase visibly with the prolongation of this period[14]. Many studies have been conducted to find out the reasons for this situation and find solutions. This study was planned and implemented due to a lack of studies in our country that identified these problems, particularly among emergency service workers. This study we conducted is one of the first studies in its field for our country. The results of the study show that the anxiety symptoms of emergency service workers are high.

Two types of scales were used in our study. The rate of participants who got a severe anxiety score (11 and above) according to the generalized anxiety scale-7 (GAD-7), which is one of them, is 53%. In the study conducted by Stojanov et al., the rate of those who got severe anxiety scores on the GAD-7 scale was 38%, while the rate of participants who got severe anxiety scores in the study of Rossi et al was 19.8%[15,16]. According to the study conducted by Rossi et al., the most important reason for it to be very high has been that they do it on all healthcare professionals who want to participate, and in our study, we only included emergency service workers[15]. The study of Stojanov et al. was conducted in healthcare institutions specially allocated for Covid-19. However, as their conditions are better than our hospital in terms of working conditions, workload, and patient density, in our study, there are many more healthcare workers with high anxiety scores[16]. The other coronavirus anxiety scale we used is newly created[17]. The lack of significance of the results is generally thought to be since the healthcare professionals who took part in our study are constantly in direct contact with Covid-19 positive patients, so they are less affected by news about the coronavirus included in the scale, etc.

The strengths of the study are reaching the vast majority of the workers in the emergency service where the study was conducted, the reliability tests performed well, the pilot study implementation beforehand, and the compatibility of open-ended question answers with other answers. In addition, the diversity of our participants' age, educational status, occupational group, receiving/not receiving health education, income status, etc. enabled our questionnaire to be evaluated from a broad perspective. When we looked at the anxiety scores with the responses we received from our participants, it was found that more than half of them showed severe anxiety symptoms. These results show similar characteristics to studies conducted with healthcare workers who encountered COVID-19. Similar to other studies, the risk of getting Covid-19, social isolation, intense work pace, and increased responsibilities are among the reasons for this situation[18,19,20].

It has been observed in many studies that frontline healthcare workers have more intense anxiety than other healthcare workers and non-healthcare workers[21,22,23]. This study was conducted in busy emergency service in a neighboring province, which is the regional hospital position in the application center in the surrounding provinces and districts, the average number of daily patients reaches 500-1000, where there is no system to distinguish Covid-19 patients in practice. The working of our participants at the forefront in the emergency service, having an intense working environment, contact with a patient who is constantly infected with Covid-19, and fear of getting an infection may be the reasons why their anxiety scores are higher than other studies.

When the factors affecting anxiety results are examined, there was no difference between gender and occupational groups in terms of anxiety. This result does not support other studies[5,20]. The reasons for this difference may originate from the fact that the emergency service workers are generally male due to the cultural difference in the region where the hospital is located and therefore there are too many male participants, that the job descriptions in the occupational groups in the emergency service where the study is conducted are not clearly defined and the emergency room conditions include sudden events, so everyone, regardless of gender, is doing similar jobs, that all participants are emergency service workers and therefore they are constantly exposed to the same situations in the same indoor environment.

When the anxiety levels of participants with various educational backgrounds were compared, it was discovered that those who graduated from undergraduate and higher education levels had higher anxiety levels. Similarly, the study conducted in Wuhan draws attention to the findings. 24 As the education level increases, it may be important to have more information about the consequences, mortality, prevention methods, and treatments of viral infections, higher awareness of the precautions and treatments not taken may also be a factor as well. The reason for the increase in anxiety with the increase in income is thought to be related to the increase in the level of income as the level of education increases.

As the working times of the participants increased, their anxiety levels increased. What is expected is a decrease in the amount of anxiety since they are more experienced. However, the anxiety caused by a lack of adequate in-service training and the exhaustion of personnel with more working years due to the difficulties of emergency service conditions were at higher levels. Anxiety by age was not significant and decreased with age. In other studies, a clear result by age and years of seniority could not be reached. While some studies show that anxiety increased with age, some studies have found the opposite[25,26].

Because of the fact that approximately 1500 patients enter the emergency room in which we conducted the study, it is included in the crowded emergency services group.27 Caring for so many patients causes healthcare professionals to have difficulty in taking covid-19 measures to protect themselves. This situation also increases the anxiety in the emergency department.

It is not possible for healthcare professionals to care for patients efficiently with a high level of anxiety. For this reason, it is necessary to reduce the anxiety levels of health workers. In order to reduce anxiety, the number of emergency service applications should be reduced, better triage should be performed, and they should be able to work under conditions where covid-19 measures can be taken.

We found that people who had a Covid-19 infection once had a high level of anxiety. We thought that the reasons for this were: having the disease again; the fear of experiencing the traumas caused by the events such as shortness of breath and fear of death in patients they have encountered in the hospital; fear of infecting family or co-workers, and likewise the fear of seeing them getting worse. It has been clearly shown in the study of Arpacıoğlu et al. that the fear of secondary traumatization increases anxiety too much. 28 In addition, Jiang Du et al. have also emphasized in their study that the thought of his family, himself, and his colleagues being caught with covid-19 infection significantly increased the perception in people[24].

The answers to open-ended questions support our other findings, and the risk of transmitting the COVID-19 during the pandemic period, social isolation due to the fear of infecting the family and the environment, lack of personal protective equipment, extra workload added to emergency working conditions, and increased responsibilities have been stated as increasing factors. Concerning these situations, the majority of the participants stated that they do not want to work in emergency service with their own free will during the pandemic period.

More than half of our participants said that they use the ministry of health website and social media to get up-to-date information on Covid-19. It is thought that they follow the Ministry of Health website as they give their daily number of cases every day and social media for current news. Nekliudov et al. and Clavier et al. have shown in their studies that the use of social media significantly increased anxiety in the Covid-19 period[29,30]. Our participants may also be affected by this situation.

Our study has some limitations; it is not known whether the participants had psychiatric disorders before Covid-19, the correlation of this anxiety state with continuous long-term exposure could not be examined because it was a cross-sectional study, and the effect of geographical differences could not be evaluated because it was a single center study.

In future studies, emergency service workers can be examined on their anxiety states in their exposure to long-term cases of covid-19 and infection.

Conclusion

As a result of the study, it was revealed that emergency service workers have a high level of anxiety originating from pandemics, regardless of their seniority, age, and gender. To adjust this situation, the working conditions, hospital conditions, and social conditions of emergency service workers need to be improved.

Author Contributions

FS: Writing – original draft, Conceptualization (equal), Data curation (lead), Formal analysis
EG: Data curation, Formal analysis
YŞ: Writing – review & editing, Conceptualization (equal), Formal analysis (lead)

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Original Article
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Head Trauma in Refugee Children Under The Age Of 2

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Abstract

Background: It was aimed to determine the rates of head trauma and admission to the emergency department in refugee children under the age of2, and laboratory findings with computed tomography (CT) imaging in the emergency.

Materials and methods: Between 01/08/2018 and 01/08/2021, 71 refugee children under the age of 2 with head trauma who applied to the Elazığ Fethi Sekin City Hospital Emergency Department were analyzed using statistical methods.

Result: 66.2% of the target group admitted to our emergency was male and 33.8% was female. Those with Glasgow Coma Scale (GCS) 15 were 39.4%, those with GCS 14 were 40.8% and those with GCS 13 were 19.7% of those with pathological CT results. Hemoglobin (Hb) levels were significantly higher in those with pathological imaging. Hematocrit (Hct) value was found to be significantly higher in hospitalized patients ($p<0.05$). Blood amylase levels were low in patients with pathology in their imaging ($p<0.05$). Aspartate aminotransferase (AST) was significantly lower in those who were observed and discharged ($p<0.05$).

Conclusion: Refugee children are open to all kinds of health problems. Head trauma also takes an important place in this. As in all head trauma patients, good neurological examination and GCS scoring can be used in refugee children under the age of 2 years. CT is an effective imaging method that should be used on site. Laboratory markers need more scientific publications to provide insight before observation, discharge, and hospitalization.

Keywords: Refugee children, head injury, Glasgow Coma Scale,

Introduction

In our age, the phenomenon of refugees is a serious social problem. Wars, political imbalances and financial problems in different parts of the world have forced large groups of people to become refugees. Legally, refugees are definied as those who have to flee their country of origin for well-founded fear of persecution or serious harm, as stated in the 1951 United Nations Convention (1).

It is a predictable situation for refuguees to encounter various health problems. It is clear that children will be most affected by these problems. Refugee children are at high risk in terms of physical, developmental and behavioral health problems (2). Head trauma is also included in these problems (3).

On the other hand, when the general population is considered, head trauma is one of the most common reasons for children to apply to the emergency department (4). It is one of the most important causes of death and sequelae in the young population and especially in children under the age of 2 (5). Falls take the first place among the causes of head trauma. This is followed by traffic accidents and sports injuries (6). It can also be a part of domestic violence (7).

Diagnosis and follow-up of traumatic brain injury (TBI) due to head trauma can be made with Glasgow Coma Scale (GCS). It is also used in different algorithms in children. Pediatric Emergency Application Network, namely PECARN is one of the most frequently used algorithms (8) (9).

The aim of this study is to detect head trauma exposure in refugee children under the age of 2 who applied to our emergency department and to monitor the clinical process.

Material and Metods

Our study is a retrospective cohort study. Approval was obtained from the non-interventional research ethics committee of Firat University. The medical records of the patients who applied to the emergency department of our hospital between 01/08/2018 and 01/08/2021 were reviewed. Refugee children under the age of 2 who presented with isolated head trauma were included in the

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study. Repeated applications were excluded due to the same trauma. Information on 72 refugee children under the age of 2 who applied with isolated head trauma was obtained. Brain CT results, laboratory findings, observation follow-up forms and existing comorbidities were examined. The disease process of those who were hospitalized was observed. The clinical conditions of the patients, which were determined according to GCS, were examined. It was determined that PECARN algorithm was taken into account in most cases, but the family's request and the physician's clinical preference were also effective when making the CT scan decision. No data could be found about the education and socioeconomic status of the parents.

Statistics

Descriptive statistics of data are expressed as mean and standard deviation (SD). Differences between means were analyzed by independent sample t-test and one way analysis of variance. Tukey test was used to determine the differences between groups for one-way analysis of variance. All statistical analyzes were performed using the SPSS 22 program. Significance level was taken as p<0,005.

Table 1: Descriptive Statistics

	Average	Median	SD
Wbc	14,33	12,30	13,78
Hb	11,39	11,50	1,83
Hct	33,68	33,40	4,74
Urea	22,34	23,00	8,72
Creatinin	0,33	0,27	0,20
AST	47,86	44,00	23,47
ALT	58,97	57,00	42,37
Amylase	24,25	21,00	13,41

According to GCS, those who were discharged from the hospital as a result of observation without CT scan, those who were discharged from the hospital with CT scan, and those with pathological findings, are summarized in Table 2. Pathological results included 2 subdural hematomas, 1 intracerebral hemorrhage, and 7 cranial bone fracture.

Demographic data are also collected in Table 2. Male gender predominates in the patients who apply. The observed patients were followed for at least 6 hours in the emergency room observation area, and no-nausea-vomiting, drowsiness, or a newly developed neurological deficit was observed. The activities and food intake of the patients were observed and they were discharged with recommendations within their current situation.

Table 2: Demographic Information

		n	%
Gender	Male	47	66,2
	Female	24	33,8
Age	1	34	47,9
	2	37	52,1
Hospitalization	+	15	21,1
	-	56	78,9
GCS	13	14	19,7
	14	29	40,8
	15	28	39,4
Mortalite	Exitus	1	1,4
	Discharged	70	98,6
CT Diagnosis	Observation	23	32,4
	Normal	38	53,5
	Pathological	10	14,1

Table 3:

		CT Diagnosis						Hospitalization			
		Observation		Normal		Pathological		+		-	
		n	%	n	%	n	%	n	%	n	%
GCS	13	1	4,3	5	13,5	8	72,7	10	66,7	4	7,1
	14	0	0,0	26	70,3	3	27,3	5	33,3	24	42,9
	15	22	95,7	6	16,2	0	0,0	0	0,0	28	0,0

When Table 4 is examined, Hb,Hct and Ast values showed significant differences according to CT diagnostic groups (p<0,05). When the CT diagnostic groups were compared according to the Tukey test, the Hb values of the groups with pathology as a result of tomography were statistically significantly higher than the Hb values of the group that did not have tomography (p<0,05). On the hand, the Hct values of the group formed by those who did not undergo CT scan were statistically significantly lower than the Hct values of the other groups (p<0.05). Ast values of the group of those who did not undergo CT scan were statistically significantly lower than Ast values of the other groups (p<0.05).

When Table 5 is examined, there was a significant difference between those who were hospitalized and those who did not (p<0.05) for Hct and Amylase values. It is seen that those who are hospitalized have higher Hct values than those who do not and those who are hospitalized are lower than those who do not have Amylase values.

Table 4:

CT Diagnosis	Observation		Normal		Pathological		p value
	Average	SD	Average	SD	Average	SD	
Wbc	17,93	23,18	12,08	4,69	14,36	4,38	,282
Hb	10,62**A**	1,68	11,58**AB**	1,44	12,38**B**	2,70	**,019***
Hct	31,08**A**	4,04	34,28**B**	3,48	37,08**B**	6,94	**,001***
Urea	24,46	10,02	21,09	8,62	22,07	5,22	,350
Creatinin	0,38	0,15	0,32	0,24	0,29	0,13	,359
AST	36,83**A**	17,49	51,62**B**	23,27	58,27**B**	27,96	**,014***
ALT	52,48	42,31	59,38	39,33	71,18	52,87	,489
Amylase	27,83	16,16	23,16	12,76	20,45	6,98	,255

* p<0.05 Horizontally, means that do not share capital letter are significantly different (p<0.05).

Table 5:

Hospitalization	+		-		p value
	Mean	SD	Mean	SD	
Wbc	14,06	4,67	14,40	15,36	,934
Hb	11,98	2,49	11,24	1,61	,165
Hct	36,04	6,45	33,04	4,01	**,029***
Urea	20,74	6,78	22,76	9,17	,430
Creatinin	0,41	0,33	0,31	0,15	,272
AST	50,80	20,12	47,07	24,39	,588
ALT	68,73	47,51	56,35	40,95	,318
Amylase	19,20	4,97	25,61	14,62	**,008***

* p<0.05

Discussion

War and persecution result in massive migrations. Current estimates indicate that there are 23 million refugees in the world (10). This number is increasing day by day. The phenomenon of migration, which is an international problem in today's world, affects children more than adults. Children who have to migrate with their families and sometimes even alone, face various health problems. Along with the migration process, low socioeconomic conditions in the destination country also make children vulnerable to various health problems. Head traumas are also included in these problems.

Response to trauma and long-term prognosis in head traumas in the pediatric age group differ compared to the adult age group. According to the figures of the United States, approximately 10 out of 100,000 children die from head trauma each year (11). Approaches under 2 year of age and above show differences when evaluating pediatric head trauma. Under 2 years of age, clinical evaluation is more difficult. Babies may be asymptomatic. The type of trauma, clinical findings of the skull or scalp, the infant's wakefulness and the response to stimuli may be indicative (12). However, the gold standard is computed tomography. It is especially important in the early diagnosis pf intracranial hemorrhages (13). However, some studies show that even in a single-shot CT, the risk of death from life-threatening cancers such as brain tumors and leukemia may increase, and that low-dose ionizing radiation that brain is exposed to in infancy may affect cognitive abilities in adulthood (14) (15). The current situation has shown that there is a need for algorithms that take into account age in children with head trauma. The most reliable of all clinical parameters is the GCS score (16).

Head trauma patients with GCS scores between 13 and 15 are included in the mild head trauma group. Since the rate of intracranial lesion detection is high in the patients with a GCS score of 13 in this group, they are included in the moderate head trauma group by some authorities (17). The risk is lower in those with a GCS score of 14, but it is high enough to justify CT scan (18). Dolanbay et al. found similar results in their study and used brain CT as the gold standard (19). There is no consensus among those with a GCS score of 15. It is necessary to determine the correct clinical parameters in patients with GCS 15 and to justify the CT scan (16).

PECARN (Pediatric Emergency Care Applied Research Network) and several other clinical decision rules have been developed. Thus, it was aimed reduce unnecessary CT use and to ensure accurate identification of patients with real head trauma (20).

In our study, GCS was taken into account in refugee children under the age of 2 with head trauma, who came within the targeted time frame, but PECARN clinical decision rules could not be fully applied to all cases.

Here, the wishes of the family and the decision made by the physician according to the clinical situation came to fore. Those with an entry GCS of 15 were in the majority. (95.7%). It showed a high correlation in the detection of pathological conditions with CT scanning. It was concluded that GCS scoring was effective in the decision of CT scan and observation hospitalization process.

The hemogram and some biochemical markers taken in the emergency room of the patients who were observed and the patient groups with or without pathology after CT scan were examined. In some studies, a correlation between low neurological level of head trauma and low hemoglobin has been shown in children (21)

HB levels in our study; subdural hematoma, intracerebral hemorrhage and cranial bone fracture were significantly higher in the pathological group. As a result of the analysis in Table5, hematocrit was found to be high in the same group, that is, in the patients with pathology and hospitalization. On the other hand, the hematocit values of the observation group were significantly low. In general, hemoglobin and hematocrit values decrease in patients with bleeding. However, there are no drastic decrease in bleeding in the intracranial area. We found elevated hemoglobin and hematocrit in the group with intracranial pathology. There may be increased intracranial pressure after trauma. One study claims that perihematomal edema will continueto in crease in the first 7 to 10 days (Staykow at al. 2011). This edema can couse a pressure increase. And cerebral blood flow may be impaired. As a result, we thought that peripheral blood hemoglobin and hematocrit levels might increase in the first admission to the emergency depertment

In addition, AST values were significantly lower in patients who were discharged after the end of observation period. It was determined that the AST value secreted from many tissues, especally the liver, was low. Noted in our work. it was hoped that this finding, which did not make sense in the light of our current analyses, would from the basis for new studies. It was thought that the analysis could be remarkable in the follow-up of the blood parameters of the patients under observation. In some studies, salivary amylase levels were examined in mild head trauma and no significant correlation was found with the severity of the trauma. However, salivary amylase level in patients with isolated head trauma was significantly associated with pathological findings in CT examinations (22). In our study, on the other hand, a significantly low blood amylase level was found in patients who were hospitalized after a pathology was detected. We studied blood amylase levels at the first admission to the emergency department. Therefore, different results may have been obtained. We think that this analytical data needs to be supported by further studies.

It is possible to prevent unnecessary CT scans and reduce mortality and morbidity with detailed examination, good neurological follow-up and evaluation of concurrent laboratory data. Considering the fact that the discharge and hospitalization processes of the patients took place in the light of the determinations made in the first step, the value of the available data is understood.

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Original Article
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Predictors of In-hospital Death in Patients with Stanford Type B Acute Aortic Dissection

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Abstract

Background: Even with immediate surgical intervention, acute aortic dissection (AAD) is a cardiovascular emergency with a high mortality rate. The purpose of this study was to look at the relationship between in-hospital mortality and red cell distribution width (RDW)/lymphocyte ratio (RLR), monocyte/lymphocyte ratio (MLR), and systemic immune inflammation index (SII) in patients with type B acute aortic dissection (BAAD).

Materials and methods: 59 BAAD patients who presented to the emergency room of a tertiary hospital were included in this cross-sectional study. The predictive ability and cut-off value of biomarkers for mortality were evaluated using Receiver Operating Characteristic (ROC) analysis. The variables believed to be connected to in-hospital mortality were subjected to multiple regression analysis, and the odds ratio was calculated.

Results: The study consisted of 59 patients in total, 44 of whom (74.6%) were male. 17 of these patients died in the hospital. In terms of predicting in-hospital mortality in BAAD patients, MLR, and neutrophil/lymphocyte ratio (NLR) have excellent diagnostic power (AUC: 0.826, 0.822, respectively), while platelet/lymphocyte ratio (PLR), RLR, and SII have acceptable diagnostic power (AUC: 0.758-0.786). Increased NLR, PLR, MLR, RLR, and SII were found to be independent predictors of in-hospital mortality in patients with BAAD (odss ratio: 9.16, 7.68, 9.33, 6, 8.57, respectively).

Conclusion: MLR, RLR, and SII are valuable parameters for estimating in-hospital mortality in adult BAAD patients. Increased NLR, PLR, MLR, RLR, and SII in BAAD patients are independent predictors of in-hospital mortality.

Keywords: RDW to lymphocyte ratio, monocyte to lymphocye ratio, acute aortic dissection type B, in-hospital death, systemic immune inflammation index.

Introduction

Even with immediate surgical intervention, acute aortic dissection (AAD) is a cardiovascular emergency with a high mortality rate[1]. According to the Stanford system, aortic dissections are classified as type A or type B depending on whether or not the ascending aorta is involved[2]. Age, hypotension/shock, history of cardiac and renal surgery, and mesenteric or myocardial ischemia are all independent risk factors for AAD mortality, per the International Registry of Acute Aortic Dissection[3]. Furthermore, biomarkers such as inflammation, thrombosis, and vascular injury have been investigated as potential contributors to AAD diagnosis or risk estimation tools[4,5].

Recent research has found that inflammatory indices like and red cel distribution width (RDW) platelet ratio (RPR), neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR), and lymphocyte monocyte ratio (LMR), which can be easily calculated from routine blood tests, can predict mortality[6–9].

There have been no research has looked at the relationship between inflammatory biomarkers like RDW lymphocyte ratio (RLR), monocyte lymphocyte ratio (MLR), and systemic immune inflammation index (SII) and patients with AAD who have a mortal course. The relationship between mortality in Stanford Type B Acute Aortic Dissection (BAAD) patients has not been thoroughly revealed.

The purpose of this study was to look at the relationship between in-hospital mortality and RLR, MLR, and SII in patients with type B acute aortic dissection (BAAD).

Materials and Methods

This cross-sectional study included 59 BAAD patients who presented to a tertiary hospital emergency department between April 18, 2020 and April 18, 2022. The local ethics committee approved the study and waived the requirement for informed consent (protocol code:120, decision no:120, issue:E-48670771-514.99 date:18 April 2022). The current study was carried out in accordance with the Helsinki Declaration.

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Post-study power analysis

According to the cross-sectional study design, the NLR value, which is the main outcome variable, was used to determine the reliability assessment (post-study power) of the number of patients included in the groups. While NLR was 9.37±5.79 in-hospital deaths, it was 5.39±2.78 in survivors. According to the difference in NLR levels between the independent group averages, the post-study power was 94.47%. According to the difference in the secondary outcome variables PLR, MLR, RLR, and SII, the post-study power was above 80%.

Study Protocol

Following ethical committee approval, data from the hospital's data network were analyzed retrospectively. The diagnosis of BAAD was confirmed by aortic angiography with multi-detector computed tomography (CT) scanning. Patients over the age of 18 who were diagnosed with BAAD inside of 24 hours of onset were included in the investigation. Patients who had missing clinical, laboratory, or radiographic data, were pregnant, had peripheral vascular disease, heart failure, hematologic disease, or liver disease, were on anticoagulants or steroids, had other acute or chronic infections, or had a history of aortic dissection were excluded from the study. BAAD patients were split into two groups: those who died in the hospital and those who survived. Demographic data of the groups (gender, age, etc.) and laboratory findings obtained at the first admission to the emergency department were recorded. The cardiovascular surgeons at our hospital determined the patients' treatment approach (the reason for and strategy of surgical techniques).

Laboratory analyses

The complete blood count (CBC) was measured with an automated hematological analyser. Hematological parameters white blood cell (WBC), neutrophil (NEU), lymphocyte (LYM), monocyte (MON), platelet (PLT), RDW, NLR, PLR, MLR, SII, and RLR values were recorded.

Primary purpose

To assess the predictive value of RLR, MLR, and SII in BAAD patients.

Statistical analysis

Parametric tests were used without the normality test due to the compatibility of the Central Limit Theorem10. The mean and standard deviation, as well as the minimum and maximum values of the features, were used in the data analysis while performing continuous data statistics. Categorical variables were defined using frequency and percentage values. The student's t-test was used to compare the means of two independent groups. Chi-square test statistics were used to examine the relationships among categorical variables. The cut-off in diagnostic value measurements was ascertained using Receiver Operating Characteristic (ROC) analysis. The statistics of specificity, sensitivity, positive predictive value (PPV), and negative predictive value (NPV) were used to determine statistical significance. An AUC of 0.5 to 0.6 was interpreted as poor, 0.6 to 0.7 as fair, 0.7 to 0.8 as acceptable, 0.8 to 0.9 as excellent, and greater than 0.9 as outstanding. The variables believed to be linked to in-hospital mortality were subjected to multiple regression analysis, and the odds ratio was calculated. The level of statistical significance of the data is considered $p<0.05$. The www.e-picos.com New York software and the MedCalc statistical package program were used to analyze the data.

Results

A total of 59 patients with type B AAD were included in this study, 44 of whom (74.6) were male. The average age of the patients was 63.2±13.3 years. The in-hospital mortality rate was 29% (17 of 59 patients). Table 1 shows the mean values of all patients' laboratory results in detail. While there was no significant difference in PLT, HGB, HTC, RDW, NEU, and MON group averages ($p>0.05$), there was a significant difference in LYM, NLR, PLR, MLR, SII, and RLR group averages (p0.05) (table 1).

In Table 2, the diagnostic accuracy of prognostic parameters used to predict type B AAD related in-hospital mortality in ROC analysis is given in detail (table 2, figure 1).

In predicting in-hospital mortality in patients with BAAD, MLR and NLR have excellent diagnostic power (AUC: 0.826, 0.822, respectively), while PLR, RLR and SII have acceptable diagnostic power (AUC: 0.758-0.786).

When the probability ratio of the variables thought to be associated with in-hospital mortality was evaluated; Increased NLR, PLR, MLR, RLR and SII were found to be independent predictors of in-hospital mortality in BAD (Odss ratio: 9.16, 7.68, 9.33, 6, 8.57, respectively) ($P<0.05$) (Table 3).

Discussion

Emergency physicians are constantly on the lookout for non-invasive, dependable, and easily accessible tools to detect life-threatening conditions in patients. This study showed that MLR, RLR and SII are valuable parameters in predicting in-hospital mortality in adult patients with BAAD in the emergency department. Furthermore, in-hospital mortality was found to be high in patients with high MLR, RLR, and SII at admission. This is the first study in the literature, as far as we know. These results indicate that MLR, RLR, and SII may be used as biomarkers in future BAAD risk classifications.

BAAD is responsible for roughly one-third of all AAD cases. Predicting the prognosis of each BAAD patient is difficult due to the variety of clinical features of

Table 1: Comparison of clinical characteristics of the study population

		Total (n=59)	Survivors (n=42)	In-hospital death (n=17)	P-value	
Features		**x̄±SD**	**x̄±SD**	**x̄±SD**		
Age		63.2±13.3	63.2±13.8	63.1±12.2	0.97	
PLT (10^3mcL)		328.39±62.08	300±57.93	324.41±73.11	0.76	
HGB (g/L)		12.95±2.29	13.02±2.43	12.8±1.96	0.74	
HTC (%)		39.11±6.31	39.23±6.59	38.8±5.73	0.81	
RDW (fL)		14.39±1.71	14.38±1.79	14.42±1.52	0.95	
NEU (10^3mcL)		8.5±3.42	8.39±3.76	8.77±2.51	0.71	
LYM (10^3mcL)		1.53±0.62	1.71±0.61	1.09±0.39	**<0.001**	
MON (10^3mcL)		0.58±0.19	0.57±0.15	0.61±0.26	0.65	
NLR		6.53±4.25	5.39±2.78	9.37±5.79	**0.01**	
PLR		253.49±133.22	214.17±73.86	350.67±190.44	**0.01**	
MLR		0.43±0.17	0.36±0.12	0.58±0.19	**<0.001**	
RLR		11.79±8.94	9.67±4.06	17.01±14.39	**0.05**	
SII(PLT*NLR)		2106.23±1221.53	1763.14±956.76	2953.85±14.11	**0.004**	
		n(%)	**n(%)**	**n(%)**		
Gender	Female	15 (25.4)	12 (28.6)	3 (17.6)	0.38	-
	Male	44 (74.6)	30 (71.4)	14 (82.4)		

Student's t-test, Chi-Square test (p<0.05 significance)

PLT: Platelets, **HGB:** Hemoglobin, **HCT:** Hematocrit, **RDW:** Red Cell Distribution Width, **NEU:** Neutrophil, **LYM:** lymphocyte, **MON:** monocyte, **NLR:** neutrophil to lymphocyte ratio, **PLR:** platelet to lymphocyte ratio, **MLR:** monocyte to lymphocyte ratio, **RLR:** RDW to lymphocyte ratio,
SII: Systemic immune-inflammation index

BAAD[11]. Recent research has revealed that inflammation plays a prominent role in aortic dissection. Lymphocytes, macrophages, and neutrophils contribute to the apoptosis of smooth muscle cells in the aortic artery and ultimately lead to medial degradation. This is widely accepted as the fundamental mechanism of aortic dissection[5].

Nunez et al. discovered a link between lower lymphocyte counts and higher monocyte counts and poorer cardiovascular outcomes[12]. Lin et al. found that LMR with a cut-off value of 1.43 (around 0.7 AUC) in patients with type A AAD (AAAD) could predict in-hospital mortality[4]. Chen et al. found an AUC of 0.575 and a cut-off value of 1.435 for LMR in predicting 30-day mortality (sensitivity 49%, specificity 64%)[13]. Our study found that an equivalent of LMR, MLR, is an independent predictor of mortality.

Variability in circulating erythrocyte size, as measured by red cell distribution width (RDW), is a risk factor for cardiovascular mortality. RDW indicates an underlying inflammatory condition leading to impaired erythrocyte maturation[14]. RLR is a new biomarker. Wu et al. demonstrated high sensitivity and specificity of RLR in predicting hepatic impairment in patients with hepatitis E virüs[15]. Moreover, RLR was shown to have acceptable diagnostic power in the detection of acute appendicitis in pediatric patients[16]. RLR

Table 2: Diagnostic accuracy of prognostic parameters to predict type B AAD related in-hospital mortality with the best predictive cut-offs.

	AUC	Cut-off	Sensitivity %	Specificity%	AUC 95% CI	P	PPV %	NPV%
NLR	0.82	>6.32	76.47	78.57	0.70-0.91	<0.001	59.1	89.2
PLR	0.77	>241.38	70.6	78.6	0.65-0.87	<0.001	57.1	86.8
MLR	0.83	>0.44	82.35	73.81	0.71-0.91	<0.001	56	91.2
RLR	0.76	>10.72	70.59	71.43	0.63-0.86	<0.001	50	85.7
SII(PLT*NLR)	0.78	>2579.85	58.82	88.10	0.65-0.87	<0.001	64.3	82.2

AUC, Area under curve; SE, Standard error; PPV, positive predictive value; NPV, negative predictive value; CI, confidence interval;

NLR: neutrophil to lymphocyte ratio, **PLR:** platelet to lymphocyte ratio, **RDW:** Red Cell Distribution Width, **RLR:** RDW to lymphocyte ratio,
MLR: monocyte to lymphocyte ratio, **PLT:** Platelet, **SII:** Systemic immune-inflammation index

Table 3: Multiple regression analysis of risk factors affecting in-hospital mortality associated with type B AAD

Variables	Odds ratio	95% CI	P-value
NLR	9.16	2.46-34.11	0.001
PLR	7.68	2.17-7.13	0.002
MLR	9.33	2.3-37.94	0.002
RLR	6	1.74-20.73	0.005
SII(PLT*NLR)	8.57	2.35-31.33	0.001

CI: confidence interval, **NLR:** neutrophil to lymphocyte ratio, **PLR:** platelet to lymphocyte ratio, **MLR:** monocyte to lymphocyte ratio, **RLR:** Red Cell Distribution Width (RDW) to lymphocyte ratio, **SII:** Systemic immune-inflammation index, **PLT:** Platelet

was found to be an independent predictor of mortality in BAAD patients in our study.

SII is a new inflammatory index that comprehensively reflects the host immune and inflammatory state balance[17]. It has even been proposed that SII is more useful than NLR and PLR alone in predicting inflammatory status and prognosis in a variety of clinical scenarios[18]. A high SII score has been linked to poor outcomes in cancer patients, heart failure, and coronary artery disease[19]. Therefore, we thought that patients with BAAD might show a similarly poor prognosis. In the light of our study results, we can conclude that SII is a new predictor of mortality in BAAD.

In cases of increased inflammation, the neutrophil count increases rapidly, while the lymphocyte count decreases, thus significantly increasing NLR. In patients with AAAD, Karakoyun et al. showed a specificity of 74%, and a sensitivity of 77% for the prediction of in-hospital mortality with an NLR value >8.51 (AUC: 0.829)[20]. Bedel et al. observed that a cut-off point of 9.74 (AUC 0.746) accurately predicted in-hospital mortality in type A AAD with 70.6 percent sensitivity and 76.8 percent specificity in AAAD[21]. When compared to the AAAD literature, NLR had a higher predictive power of mortality (AUC: 0.822) in BAAD, with a lower cut-off value (6.32).

PLR has been linked to the magnitude of inflammation in recent studies[22]. In the study of Du et al. in patients with BAAD, both elevated and decreased PLRs were independently associated with in-hospital mortality[23]. Contrary to this study, in the logistic regression analysis performed by Li et al in patients with BAAD, PLR was an independent predictor of all-cause mortality (hazard ratio 6.14, 95% CI:1.401-26.895, P: 0.02). PLR 9.16 (CI: 2.46-34.11, P: 0.001) predicted mortality with odds ratio in our study.

Limitations

Our study has several limitations. This is a single-center retrospective study. We used the laboratory results of the first application for analysis and could not include follow-up values. Serial follow-up of these indices we studied can also predict mortality. Therefore, our findings cannot be generalized but may be informative and supportive for future studies for more reliable and conclusive results.

Conclusion

MLR, RLR, and SII are valuable parameters in predicting in-hospital mortality in adult patients with BAAD. In patients with BAAD, increased NLR, PLR, MLR, RLR, and SII are independent predictors of in-hospital mortality.

Ethics Committee Approval: *The local ethics committee approved the study and waived the requirement for informed consent (protocol code:120, decision no: 120, issue: E-48670771-514.99 date: 18 April 2022). The current study was carried out in accordance with the Helsinki Declaration.*

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Original Article
Eurasian Journal of Critical Care

Is it Possible to Predict High-Risk Patients in Acute Pulmonary Embolism with Systemic Immune-Inflammation Index?

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Abstract

Background: Acute pulmonary embolism (APE) is a cardiovascular emergency that has a high morbidity and mortality probability. The aim of this study is to investigate the clinical value of SII in predicting high-risk patients admitted to the emergency department with a diagnosis of Acute pulmonary embolism (APE)

Materials and methods: This clinical study, which was conducted according to a cross-sectional study design, included 193 patients diagnosed with APE who presented to the emergency department of a tertiary hospital. According to the guideline, patients with Pulmonary Embolism Severity Index (PESI) class III–V or sPESI ≥I were identified as high risk. ROC (Area Under the Curve) analysis was used to determine the cut-off in predicting high-risk APE.

Result: In our research, 71 of the patients had high-risk APE. In detecting high-risk APE, the systemic immune inflammation index (SII) was found to have excellent diagnostic power (AUC: 0.84), while neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), and monocyte to lymphocyte (MLR) were found to have acceptable diagnostic power (AUC: 0.76-0.78), red cell distribution width (RDW) to lymphocyte (RLR) was of fair diagnostic power (AUC: 0.68).

Conclusion: We have shown that SII can be a valuable and useful potential biomarker to identify high-risk patients in patients with APE. We also found that MLR and RLR are biomarkers that can be used to predict severe APE.

Keywords: Acute pulmonary embolism, the severity of pulmonary embolism, systemic immune inflammation index, monocyte to lymphocyte ratio, RDW to lymphocyte ratio.

Introduction

Acute pulmonary embolism (APE) is a cardiovascular emergency that has a high morbidity and mortality probability[1,2]. Early detection, accurate diagnosis, and treatment are crucial for reducing the high mortality rate in these patients. Many diagnostic tests and risk scoring are used for this purpose[1,3]. Blood pressure, biomarker evidence of right ventricular (RV) ischemia, lower extremity venous doppler ultrasonography, echocardiographic evidence of RV overload, computed tomography pulmonary angiography, pulmonary embolism severity index (PESI), and the simplified form of PESI (sPESI) are typically used to risk classifying patients[1,4–6]. But these remain both costly and cumbersome for quick decision making[7].

The pathogenesis of venous thromboembolism has been linked to inflammation markers like IL-6, IL-8, and monocyte chemotactic protein, according to a meta-analysis[8]. APE exhibits elevated levels of pro-inflammatory and pro-coagulant factors produced by platelets and leukocytes[9]. Platelet activation and neutrophil count rise as a result of this acute inflammatory response[10]. However, as the disease develops, the lymphocyte count decreases in response to the release of adrenaline and glucocorticoids by a sympathetic response[11]. Studies have demonstrated the importance of inflammatory indices in predicting prognosis in pulmonary embolism, including neutrophil to lymphocyte ratio (NLR), lymphocyte to monocyte ratio (LMR), platelet to lymphocyte ratio (PLR), mean platelet volume to platelet ratio (MPR), red cell distribution width (RDW) to platelet ratio (RPR), and RDW[12–15].

A new systemic inflammatory index relying on neutrophil, platelet, and lymphocyte counts, the systemic immune inflammation index (SII) (PLT*NLR), has been widely used to predict clinical outcomes in cancer patients[16–18].

The relationship between SII and pulmonary embolism severity in APE patients has not been fully elucidated. The purpose of this study is to look into the clinical utility of SII in predicting high-risk patients presented to the emergency department with APE.

Materials and Methods

This clinical study, which was conducted according to a cross-sectional study design, included 193 patients diagnosed with APE who presented to the emergency department of

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a tertiary hospital between April 18, 2020, and April 18, 2022. The study was approved by Local Ethics Commission (protocol code:121, decision no:121, issue: E-48670771-514.99 date: 18 April 2022). The institutional review board waived informed consent to conduct this retrospective study. The current study was carried out in accordance with the Helsinki Declaration.

Post-study power analysis

According to the cross-sectional study design, the NLR value, which is the main outcome variable, was used to determine the reliability assessment (post-study power) of the number of patients included in the groups. While NLR was 9.58±7.24 high-risk APE, it was 5.12±3.04 in non-high-risk APE. According to the difference in NLR levels between the independent group averages, the post-study power was 99.85%. According to the difference in the secondary outcome variables PLR, MLR, RLR, and SII, the post-study power was above 80%.

Study Protocol

After obtaining ethics committee approval, the data were retrospectively analyzed from the hospital's data network. In the study, patients upwards of 18 years old with an APE diagnosis confirmed by multidetector computed tomography (CT) pulmonary angiography scanning were enrolled. Patients with missing clinical, laboratory, or radiographic data, pregnant patients, patients with peripheral vascular disease, malignancy, heart failure, hematological disease or liver disease, using anticoagulants or steroids, using immunosuppressive drugs, patients with other acute or chronic infections, and patients underneath the age of 18 were all excluded from the study. Venous peripheral blood samples were obtained from each patient at the time of attendance to the emergency department in order to measure SII and other common laboratory parameters. According to the guideline, patients with PESI class III–V or sPESI ≥I were identified as high risk[1].

Laboratory analyses

The complete blood count (CBC) was measured with an automated hematological analyser. Hematological parameters WBC, NEU (neutrophil), LYM (lymphocyte), MON (monocyte), platelet (PLT), RDW, NLR, PLR, monocyte to lymphocyte (MLR), red cell distribution width (RDW) to lymphocyte (RLR), and SII (PLT×NLR) values were recorded.

Primary Purpose

To assess SII's usefulness in predicting high-risk APE.

Statistical analysis

Parametric tests were used without the normality test due to compliance with the Central Limit Theorem[19]. In the assessing the data, while the mean and standard deviation are used while making the data statistics in the continuous variables; frequency and percentage values were used to define categorical variables. The student's t-test was used to compare the means of two independent groups. Chi-square test statistics were used to examine the relationships among categorical variables. ROC (Area Under the Curve) analysis was used to determine the cut-off in predicting high-risk APE. The statistics of specificity, sensitivity, positive predictive value , and negative predictive value were used to determine statistical significance. An AUC of 0.5 to 0.6 was interpreted as poor, 0.6 to 0.7 as fair, 0.7 to 0.8 as acceptable, 0.8 to 0.9 as excellent, and greater than 0.9 as outstanding. The level of statistical significance of the data is considered $p<0.05$. The www.e-picos.com New York software and the MedCalc statistical package program were used to analyze the data.

Results

A total of 195 patients, 71 of whom were high-risk APE, were enrolled in this clinical study. 121 (62.7%) of the patients were male. Table 1 shows the mean and standard deviation values of the studied biomarkers, gender, age, and mortality status. There was a significant difference between the groups in terms of age, PLT, NEU, LYM, MON, NLR, PLR, MLR, RLR, SII, Troponin T, D-Dimer, gender, and mortality ($p<0.05$). HGB, There was no significant difference between the groups regarding the mean of HCT and RDW values ($p>0.05$) (table 1).

In Table 2, the diagnostic accuracy of biomarkers that are important in detecting high-risk APE patients in ROC analysis is given in detail (table 2, figure 1). In detecting high-risk APE, the SII was found to have excellent diagnostic power (AUC: 0.84), while NLR, PLR, and MLR were found to have acceptable diagnostic power (AUC: 0.76-0.78). RLR was of fair diagnostic power (AUC: 0.68).

Discussion

Emergency physicians are always looking for a non-invasive, reliable and easily accessible tool to detect life-threatening conditions in patients. In this study, we investigated the value of SII in predicting high-risk patients in APE in patients with APE. We discovered that SII, a simple, inexpensive, easily accessible, and immediately calculated parameter, has excellent diagnostic power in detecting high-risk patients in APE patients, with an optimal cut-off value of >1235.35. Moreover, this is the first research to suggest that MLR and RLR can be used as biomarkers to detect high-risk individuals in APE patients.

The systemic immune-inflammation index (SII), a brand-new inflammatory index, fully illustrates the balance between the host's immune and inflammatory states. The following definition was given for it: platelet count ×neutrophil count/ lymphocyte count[20]. Recent studies have shown that SII is

Table 1: Comparison of basic and laboratory characteristics of high-risk APE and non-high-risk APE

		Total (n=193)	Non-high-risk APE (n=122)	High-risk APE (n=71)	
Features		**x̄±SD**	**x̄±SD**	**x̄±SD**	**p-value**
Age		63.1±**16.**7	59.6±16.5	69.1±15.5	<0.001
PLT (10^3mcL)		256.32±74.21	234.69±63.28	293.48±77.26	<0.001
HGB (g/L)		12.51±1.62	12.51±1.53	12.52±1.76	0.99
HCT (%)		37.15±5.37	36.85±4.82	37.66±6.2	0.34
RDW (fL)		15.02±9.16	14.25±1.4	16.33±14.96	0.25
NEU (10^3mcL)		9.19±3.2	8.09±2.75	11.07±3.07	<0.001
LYM (10^3mcL)		1.72±0.71	1.89±0.76	1.43±0.49	<0.001
MON (10^3mcL)		0.71±0.34	0.63±0.26	0.85±0.41	<0.001
NLR		6.76±5.44	5.12±3.04	9.58±7.24	<0.001
PLR		183.49±152.33	142.99±65.61	253.07±220.08	<0.001
MLR		0.51±0.45	0.37±0.2	0.75±0.68	<0.001
RLR		10.91±9.2	8.86±3.81	14.43±10.51	0.03
SII(PLT*NLR)		1799.99±1615.72	1194.69±803.88	2840.08±2287.97	<0.001
Troponin		26.64±19.91	18.29±16.84	40.98±34.01	<0.001
D-Dimer		2.94±1.8	2.68±1.57	3.39±2.08	0.01
		n(%)	n(%)	n(%)	
Gender	Female	72(37.3)	55(45.1)	17(23.9)	0.002
	Male	121(62.7)	67(54.9)	54(76.1)	
Mortality	No	184(95.3)	122(100)	62(87.3)	<0.001
	Yes	9(4.7)	-	9(4.7)	

Student's t-test / Chi-Square test (p<0.05 significance)

APE: acute pulmonary embolism, **PLT:** platelets, **HGB:** hemoglobin, **HCT:** hematocrit, **RDW:** red cell distribution width, **NEU:** neutrophil, **LYM:** lymphocyte, **MON:** monocyte, **NLR:** neutrophil to lymphocyte ratio, **PLR:** platelet to lymphocyte ratio, **RLR:** RDW to lymphocyte ratio, **MLR:** monocyte to lymphocyte ratio, **SII:** systemic immune inflammation index.

notable for both the diagnosis and prognosis of mortality in VTE[21]. Peng et al. found SII as an independent predictor of VTE after hip fracture in elderly patients[22]. Gok et al classified 442 patients with APE as massive, submassive, and non-massive. They revealed that SII was a strong independent predictor of massive APE, with a cut-off value of >1161[23]. Since according our results obtained, SII can predict high-risk APE with a cut-off of >1235.35. (AUC:0.84).

Neutrophil-to-lymphocyte ratio (NLR) is a biomarker reflecting the balance between systemic inflammation and immunity[24]. Telo et al. found increased PLR and NLR in high-risk patients with APE[25]. Ateş et al. examined the diagnostic differentiation of independent predictors of massive APE compared to the submassive group and found that NLR had 0.893 ± 0.013 AUC[13]. Throughout line with the literature, we discovered that NLR was useful in determining severe APE in our study.

PLR and the CT pulmonary artery obstruction index were found to be positively correlated in one study, which suggests that a higher PLR is linked to a higher thrombus

Table 2: Diagnostic accuracy of inflammatory parameters for differentiation of high-risk APE from non-high-risk APE

High-risk APE (n:71) Non-high-risk APE (122)	AUC	Cut-off	Sensitivity %	Specificity%	AUC 95% CI	P-value	PPV %	NPV%
NLR	0.78	>5.71	74.65	72.13	0.71-0.83	<0.001	60.9	83
PLR	0.77	>154.38	76.06	66.39	0.70-0.83	<0.001	56.8	82.7
MLR	0.76	>0.41	74.65	70.49	0.69-0.82	<0.001	59.6	82.7
RLR	0.68	>8	80.28	50	0.61-0.75	<0.001	48.3	81.3
SII(PLT*NLR)	0.84	>1235.35	87.32	68.85	0.78-0.89	<0.001	62	90.3

AUC, Area under curve; SE, Standard error; PPV, positive predictive value; NPV, negative predictive value; CI, confidence interval;

NLR: neutrophil to lymphocyte ratio, **PLR:** platelet to lymphocyte ratio, **MLR:** monocyte to lymphocyte ratio, **RLR:** RDW to lymphocyte ratio, **SII:** systemic immune inflammation index.

load[26]. PLR was significantly higher in patients with massive pulmonary embolism (PE) proportion of patients with submassive or low-risk PE, according to research by Ateş et al[13]. In the study by Phan et al., PLR was statistically significantly lower in patients with massive PE (90.3 (50.4-164)), while it was higher in patients with low-risk PE (173 (109-145))[15]. Kundi et al. discovered that PLR could predict patients with sPESI 1 (high-risk) APE with 149 cut-off, 76.3% specificity, and 77.1% sensitivity, in their study (AUC: 0.860)[27]. Similarly, PLR was able to predict high-risk APE in our study.

LMR has been demonstrated to be a marker of the systemic inflammatory response and a potential prognostic factor in a number of cancers[28]. Duyan et al found that MLR is a valuable parameter in the diagnosis of acute appendicitis in children[29]. LMR levels were substantially lower in survivors after APE than in those who died after APE, according to Ertem et al.[30]. LMR was found to be related to prognosis in patients with intermediate-low and low-risk PE by Köse et al.[12]. Our study found that MLR, an equivalent of LMR, was higher in patients with high-risk APE (AUC: 0.76). According to the literature review, our study was a first in this respect.

Red blood cell distribution width (RDW) is a quantitative measure of the variability in the size of circulating red blood cells. A study concluded that high RDW level is an independent predictor of short-term mortality in PE[31]. RLR is a new biomarker. Wu et al. demonstrated high sensitivity and specificity of RLR in predicting hepatic impairment in patients with hepatitis E virus[32]. Furthermore, it was revealed that RLR has acceptable diagnostic power in the determination of acute appendicitis in pediatric patients[29]. However, this is the first study to show that RLR can predict the severity of APE patients. Our study contributed to the literature in terms of the fair diagnostic power of RLR in predicting high-risk patients with APE.

Limitations

The most important limitations of our study are that it is a single-center and retrospective study. Although the completeness of our dataset is satisfactory, the small number of patients is also one of the limitations. Therefore, our findings cannot be generalized but may be informative and supportive for future studies for more reliable and conclusive results.

Conclusion

As a result, we found that SII is valuable and stronger than other markers in predicting high-risk patients with APE diagnosed in the emergency department. In addition, as a contribution to the literature, we determined that MLR and RLR are biomarkers that can be used to predict severe APE.

Ethics Committee Approval: *The study was approved by Local Ethics Commission (protocol code:121, decision no:121, issue: E-48670771-514.99 date: 18 April 2022). The institutional review board waived informed consent to conduct this retrospective study. The current study was carried out in accordance with the Helsinki Declaration.*

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Original Article
Eurasian Journal of Critical Care

Investigation of HBV, HCV, and HIV Seropositivity in Healthcare Workers of Reproductive Age

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Abstract

Background: Hepatitis B virus (HBV), hepatitis C virus (HCV), and Human Immunodeficiency Virus (HIV) infections are health problems that threaten human health. This study aimed to investigate HBV, HCV, and HIV seropositivity in female healthcare workers of childbearing age in our hospital.

Materials and Methods: 1224 women working in our hospital, who were of childbearing age, were included in the study. The HBsAg, Anti-HBc total, Anti-HBs, Anti-HCV, and anti-HIV results of the patients were analyzed using the hospital database.

Results: Seven (0.5%) reproductive-age female healthcare workers were positive for HBsAg. While anti-HB positivity was detected in 1128 (93.6%) of 1224 healthcare workers, anti-HBs and anti-HBc were positive in 80 (6.53%) patients. Both anti-HBs and anti-HBc were negative in 16 (1.3%) subjects (neither vaccinated nor exposed to HBV).

Conclusion: Healthcare workers are at high risk for viral hepatitis and other infectious diseases. The fact that the frequency of HBV, HCV, and HIV among healthcare professionals of reproductive age is relatively low in our region shows that the training for healthcare professionals has been quite successful in recent years, both in our country and in our area.
Due to the high contagiousness of viral hepatitis B in our country, not only healthcare professionals of reproductive age but all healthcare personnel should be meticulously vaccinated. It is essential to implement standard infection control programs for HBV, HCV, and HIV and to increase compliance with national and international programs.

Keywords: Seroprevalence, healthcare professionals, hepatitis B virus, hepatitis C virus, HIV

Introduction

Blood-borne diseases are among the most common risks that healthcare workers are exposed to.1 According to the World Health Organization (WHO) data, more than 80 million healthcare workers worldwide are infected with contaminated medical devices.2 Infections caused by hepatitis B (HBV) and hepatitis C (HCV) viruses and human immunodeficiency virus (HIV) have become significant health problems due to the increase in the number of patients all over the world. Hepatitis B virus (HBV) infection can lead to chronic hepatitis, cirrhosis, and hepatocellular carcinoma over time, which may threaten life.3-4-5 The Prevalence of HBV is 3.5-4% in the general population. It has been reported that this rate is 1.5-2 times higher in healthcare personnel.4 The prevalence of HCV is lower than HBV (0.2%-2%). However, it causes chronic hepatitis and cirrhosis more frequently compared to HBV. It is known that approximately 71 million people in the world are infected with HCV.6 The frequency of HCV in Turkey varies between 0.3-1.8% in the general population.7 Health workers may become infected with this virus during interventional procedures, surgical interventions, and dressings.8 It is essential to investigate risky diseases such as HBV, HCV, and HIV in female healthcare workers. These infections pose a danger to both the mother and the fetus and negatively affect both health. Our research is significant because it is the first study conducted on female workers of reproductive age in our country.

This study aimed to investigate HBV, HCV, and HIV seropositivity in female healthcare workers of childbearing age working in our hospital.

Material and Method

The study included 1224 female health personnel of reproductive age, aged between 19-50 years, working in the Education and Research Hospital of our University between

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January 01, 2020, and December 31, 2021. Ninety-three people whose data could not be reached or whose data were missing were excluded from the study. Ethics committee approval was obtained for this study. The international Declaration of Helsinki carried out the study. Demographic information about the patients, their departments, and their occupations were recorded in the forms. They were grouped according to their occupations, age groups, and years of employment. Obtained laboratory results were compared with these groups. The patients were divided into groups according to their professions as doctors, nurses, laboratory workers, technicians, and other staff of our hospital. In terms of working time, they were divided into groups of one, five, ten years, and more than ten years.

Laboratory Analysis

Serum samples HBsAg, anti-HBc total, anti-HBs, anti-HCV, and anti-HIV were measured by the ELISA method based on chemiluminescence in an E170 modular (Roche, USA) device. The examinations were carried out by the manufacturer's instructions. Anti-HCV was studied with third-generation testing systems (Abbott AXSYM system, HCV version 3.0, Hepatitis C virus Encoded Antigen (Recombinant HCr43, c200, c100-3, NS5). All samples above the minimum positive value were considered reactive.

Statistical analysis: The obtained data were evaluated using number and percentage calculations. In evaluating HBsAg and Anti-HBs, HCV, and HIV positivity, the age comparison calculated with the odds ratio univariate was compared within itself. The Chi-square test and Fisher exact Chi-square test were applied when necessary. The relationship between age (19-25, 26-35, 36-45 and over 45 years old) and working time (<1, 2-5, 6-10, >11 years) was analyzed by using a multiple logistic regression model. A similar application was made for hepatitis C and HIV, and $p<0.05$ was considered statistically significant. Statistical Package for the Social Sciences (SPSS) 22.0 (SPSS, Inc., Chicago, IL, USA) program was used for statistical evaluation of the data.

Results

This study was carried out on 1224 female healthcare workers of reproductive age working in our university's training and research hospital.

The age range of employees of childbearing age is between 19-50, and the average age is 30.02 ± 5.42 years. Of our staff, 211 (17.2%) are doctors, 750 nurses (61.2%), 57 (4.6%) are anesthesia technicians, 20 (1.6%) are in the dialysis unit, 60 are laboratory professionals 4.8), six people (0.49%) were emergency medical technicians, 80 cleaning personnel (6.5%) and 40 people (3.2%) were x-ray technicians.

In our study, we found the HBsAg seroprevalence of women of childbearing age to be 0.57% (Table 1). While 1128 (93.6%) isolated anti-HBs positivity of 1224 healthcare workers were detected, anti-HBs + anti-HBc total positivity was found in 80 (6.64%) individuals (Table 1).

In the comparison made between the task groups, no statistically significant difference was found between the hepatitis B risk and the duty performed by the health personnel in the hospital ($p>0.05$). The odds ratio value between nurses and doctors was calculated as 2.54.

Isolated anti-HBs were investigated in healthcare professionals, and an average of 93.6% in the whole group, 96.6% in doctors, 93.3% in nurses, 92.9% in anesthesia technicians, 90% in dialysis workers, 86.6% in laboratory workers, 100% in emergency technicians, 75% in cleaning personnel, 87.5% in x-ray technicians. Found. The difference between the groups was not statistically significant ($p>0.05$). When compared in terms of anti-HBs + antiHBc total ratios of healthcare workers, it was found 22.5% in cleaning personnel, 10% in laboratory and dialysis technicians, 3.3% in doctors, and 5.4% in nurses, and the difference between the groups was not statistically significant ($p>0.05$) (Table 1).

Table 1: HBV, HCV, HIV Infection Seropositivity Distribution

Persons	n (%)	HBsAg	Anti-HBs	Anti-HBs+Anti-HBc total	Anti-HCV	Anti-HIV
Doctor	211 (17.2)	0 (0)	204 (96.6)	7 (3.3)	0 (0)	0 (09
Nurse	750 (61.2)	2 (0.2)	700 (93.3)	41 (5.4)	0 (0)	0 (0)
Anesthesiologist	57 (4.6)	1 (1.7)	53 (92.9)	3 (5.2)	0 (0)	0 (0)
Dialysis	20 (1.6)	0 (0)	18 (90)	2 (10)	0 (0)	0 (0)
Lab technician	60 (4.8)	2 (3.3)	52 (86.6)	6 (10)	1 (0.08)	0 (0)
EMT	6 (0.4)	0 (0)	6 (100)	0 (0)	0 (0)	0 (0)
Cleaning staff	80 (6.5)	2 (2.5)	60 (75)	18 (22.5)	0 (0)	0 (0)
Radiology technician	40 (3.2)	0 (0)	35 (87.5)	3 (7.5)	0 (0)	0 (0)
Total	1224 (100)	7 (0.5)	1128 (93.6)	80 (6.53)	1 (0.08)	0 (0)

n (%): Number (percent) EMT: Emergency medicine technician

Table 2: Working time and HBsAg positivity

Working time Year	Total number n (%)	HBsAg positive n (%)
0-1	150 (12.2)	0 (0)
2-5	280 (22.8)	0 (0)
6-10	600 (49)	1 (0.16)
>10	194 (15.89)	6 (3.0)

Healthcare workers were divided into groups regarding their working time and hepatitis B risk, and the ratios between these groups were compared. The difference was not statistically significant (p>0.05). The odds ratio value between the personnel working in the clinic for 11 years or more and the personnel working for one year or less was calculated as 2.45. Since HBsAg positivity was not detected in those who worked less than one year and between 2 and 5 years, it was found positive in 1 (0.01%) of 600 people who worked for 6-10 years, and 6 (0.03%) of 194 people who worked for more than 11 years. The difference was not statistically significant (p>0.05). (Table 2). HBsAg was not positive in 80 people aged 19-25 and 280 people aged 26-35. HBsAg was positive in 1 (0.01%) of 544 patients whose age range was 36-45 and 6 (0.02%) of 220 employees aged 45-50 years. When healthcare professionals were divided into age groups and compared within themselves, no statistically significant difference was found between the age groups (p>0.05) (Table 3). Health professionals were divided into three groups according to their branches: surgery, internal branches, and personnel working in different hospital units separate from these branches. HBsAg was found positive in 3 (0.06%) of 500 people working in surgical departments, 3 (0.06%) of 450 people working in internal branches, and 1 (0.03%) of 274 people working in other units. In healthcare professionals, these three groups were compared among themselves in terms of hepatitis B risk, and no statistically significant difference was found between the groups (p>0.05) (Table 4).

Table 3: Age groups and HBsAg

Age groups	Total n (%)	HBsAg positive n (%)
19-25	180 (14.7)	0 (0)
26-35	280 (22.8)	0 (0)
36-45	544 (44.4)	1 (0.18)
45-50	220 (17.9)	6 (2.7)

Table 4: Department and HBsAg positivity

Department	Total n (%)	HBsAg positive n (%)
Surgical	500 (40.89	3 (0.60)
Internal	450 (36.7)	3 (0.66)
Other	274 (22.3)	1 (0.36)

Discussion

There have been many studies investigating the seroprevalence of HBsAg all over the world. David et al. found this rate to be 0.1% nine among healthcare workers in the United States and 5% in a study conducted in India.10 According to studies, the HBV carrier rate in Turkey is between 1.5-7% 11-12-13. We found the frequency of HBsAg to be 0.5% among healthcare workers of childbearing age in our hospital. This difference can be explained by the fact that healthcare personnel attach importance to preventive measures, investigate the serological indicators of hepatitis B and hepatitis C in patients who will undergo invasive procedures, and the effective use of vaccination. Comparisons were made regarding age groups among healthcare professionals in various centers. Leblebicioglu et al. 11 did not find a significant difference, while Özsoy et al.14 found an important relationship between the 26-35 age group and HBsAg seroprevalence. In our study, healthcare professionals were divided into four groups in terms of age: 19-25, 26-35, 36-45, and 45-50 years old. In our study, no statistically significant difference was found between age groups and HBsAg positivity (p>0.05) (Table 3).

In studies investigating a relationship between occupational groups and hepatitis B infection risk in various centers, Köse et al. 15 found no significant difference, while Otkun et al. 12, Ulusoy et al. 13, Kutlu et al. 16, and Özsoy et al. 11 found a meaningful relationship in favor of nurses. Unlike these, Berktas et al. 17 found this rate high in favor of doctors and attributed this to the fact that most of the nurses included in the study had just started their profession. In our study, no significant difference was found between occupational groups in terms of HBsAg positivity (p>0.05) (Table 1). In our research, HBsAg seroprevalence was determined as 0.0% (0) in doctors, 0.2% (2) in nurses, 3.3% (2) in laboratory workers, 2.5% (2) in cleaning personnel, and 1.7% (1) in anesthesia technicians when we divided female healthcare professionals of childbearing age into groups according to their occupations. Found. In the comparison made between occupational groups, no significant relationship was found between the health personnel in terms of hepatitis B risk and the duty they performed in the hospital (p>0.05) (Table 1).

However, when the nurses and doctors were compared, the odds ratio value was found to be 2.54. This value shows that the risk of encountering hepatitis B infection among nurses is approximately 2.5 times higher than that of doctors. This may be due to reasons such as nurses' invasive procedures, such as vascular access, and patients' exposure to body benefits and secretions more than doctors. On the other hand, because of their active participation in patient care during their school years, nurses probably encounter HBV earlier than doctors. In our country, unlike western countries, the Prevalence of HCV is lower than HBV. Still, it is essential for both the average

population and healthcare professionals in terms of its more chronicity. In the studies performed, Öksüz et al. 18 found anti-HCV positivity of 0.2%, İnci et al. 19 0.34%, and Aşkar et al. 20 reported it as 0.15%.

In our study, the rate of anti-HCV among healthcare workers of childbearing age was found to be 0.08%. In our study, the frequency of HCV among healthcare workers of childbearing age was found to be positive in only one person (0.008%), and our result was found to be lower than other results in our country. In particular, developments in viral hepatitis C (HCV) have occurred at a dizzying pace. Permanent viral response rates have increased from 15-20% with treatments for one year or a half years in the 2000s to 99-100% with one tablet per day treatment today. The world health cover (WHO) talks about the complete eradication of HCV in the 2030s.

According to WHO's 2022 data, an average of 40 million people worldwide are infected with HIV. The risk of transmission of the human immunodeficiency virus (HIV) is between 0.2-0.5%. 21 In studies reported from our country, anti-HIV positivity was not reported in healthcare personnel. 19-21 In our study, HIV was not detected in any patient among the healthcare professionals of childbearing age, which shows that healthcare professionals have received adequate training and precautions.

Conclusion

As it is known, healthcare workers are at high risk for viral hepatitis and other infectious viral diseases. The fact that the values in our study were lower than the results of previous years in the literature indicates that the training and vaccinations given to female employees of childbearing age are pretty successful. Only people aged 45-50 who worked for more than 11 years had a higher HBsAg value than others due to more prolonged exposure. Due to the high contagiousness of viral hepatitis B in the eastern Anatolia region, where we are located, it is very important to meticulously vaccinate not only healthcare workers of reproductive age, but also all healthcare personnel to implement standard infection control programs for HBV, HCV, and HIV, and to increase compliance with national and international programs.

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Case Report
Eurasian Journal of Critical Care

Kounis Syndrome or Adrenalin Side-Effect?

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Introduction

Kounis syndrome, defined by the concurrence of allergic reaction and acute coronary syndrome, was identified by Kounis and Zavras in 1991[1]. The pathophysiology of the disease has been described as a complex process with mast cell-mediated progressive coronary vasospasm, intimal erosion or rupture. One study described, even an intact tunica intima may be damaged through this mechanism[2]. Although there are studies that have shown that arteries of various locations may be affected, coronary arteries (especially LAD) are impacted most[3]. In this article, we present a case of myocardial infarction following a bee sting, which we think was worsened by the anti-allergy treatment.

Case Report

A 66-year-old male, stung in the lower lip by a bee, was brought to our emergency room with sudden onset of vomiting, syncope, and hypotension. The diagnosis of anaphylaxis had been made and 0,5 mg of adrenaline was administered intramuscularly by the paramedics during the transfer. On examination in the ER, he was confused and had diffuse body erythema with lower lip and bilateral upper-eyelid angioedema. His vital signs were as follows: blood pressure, 90/60 mm Hg; pulse, 75 beats/minute; arterial oxygen saturation 96% on room air; and respiratory rate 12-15/minute. He was started on pheniramine 45.5 mg and methylprednisolone 80 mg intravenously. The ECG (electrocardiography) findings included (showed that) ST-segment depression in the anterior and lateral leads (D1-aVL-V1-V6), and ST-segment elevation in the inferior leads (D2-D3-aVF) (Figure 1). Based on these findings, acute ST-elevation myocardial infarction was diagnosed. The patient was given 300 mg of acetylsalicylic acid and 180 mg of ticagrelor orally, and 5000 IU heparin intravenously.

Following the improvement of the anaphylaxis symptoms, the patient underwent coronary angiography. While the 60-70% stenosis in the proximal left ascending artery (LAD) was planned to be electively evaluated through the fractional flow reserve (FFR) technique; stents were placed for the hazy lesion with an 80% stenosis in the proximal right coronary artery (RCA), and for another lesion with 90% stenosis in the later (distal) part of the RCA (Figure 2). ECG findings resolved upon the intervention (Figure 3). The ejection fraction was within normal limits on discharge from the hospital. Additionally, left ventricular hypertrophy and stage II diastolic dysfunction were noted. He was followed up in coronary intensive care unit for four days and was discharged on valsartan-hydrochlorothiazide, benidipine hydrochloride, atorvastatin calcium trihydrate, acetylsalicylic acid, clopidogrel and nebivolol.

Discussion

In the literature, three variants of Kounis syndrome have been described. While type 1 is seen in patients with no risk factors for ischemic heart disease, type 2 is mostly encountered in patients with the pre-existing atheromatous disease. Type 3, on the other hand, involves stent thrombosis following platelet activation. According to this classification, the reaction our patient had corresponded to type 2, due to his predisposing risk factors for coronary artery disease.

Kounis syndrome may develop secondary to various allergens such as medications and insect poison. Atopic people are thought to be more vulnerable to the syndrome4. On further questioning, we have learnt our patient didn't have any known allergies, and it was his first time exposed to bee poison.

Adrenaline plays a vital role in the management of anaphylactic shock caused by Hymenoptera (insects' family) poisoning. The tryptase enzyme secreted by mast cells is shown to cause hypotension and plaque erosion[5,6]. Additionally, it can be extrapolated from the rise in adrenaline

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levels in myocardial infarction that anti-allergy treatment may worsen an underlying coronary heart disease[7]. Likewise, we believe, adrenaline may have aggravated the ongoing myocardial infarction in our patient.

In light of the above, close cardiac monitoring is highly recommended in patients who develop severe allergic reactions, regardless of chest pain. It's worth noting that clinicians must pay even closer attention to patients with underlying cardiac comorbidities.

Conclusion

In this study, we tried to explain the cardiac consequences of severe allergic reactions and anti-allergy treatment. It is not obvious which of these two plays a bigger part in the development of the acute coronary syndrome. However, given the high risk of dire outcomes, close cardiac monitoring and immediate intervention are instrumental in timely diagnosis.

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Case Report
Eurasian Journal of Critical Care

Primary Spontaneous Hemopneumothorax: A Case Report

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Abstract

Spontaneous hemopneumothorax is a rare condition. Bleeding occurs in 0.5% to 12% of patients with spontaneous pneumothorax. Early diagnosis with appropriate imaging methods is important. In order to prevent possible complications of pneumothorax in patients who present to the emergency department with a complaint of shortness of breath. Clinically, if a patient with a pneumothorax suddenly develops unexplained symptoms of shock, SHP should be considered and treated as a life-threatening emergency.

Keywords: Spontaneous hemopneumothorax, pneumothorax, emergency medicine

Introduction

Pneumothorax is defined as the presence of air in the pleural space (1). Primary pneumothorax; is a type of pneumothorax that develops spontaneously. The rate of spontaneous hemopneumothorax (SHP) is 0.5-11.6% in patients with primary pneumothorax (2,3). Hemopneumothorax is the condition whichpresence of air and blood in the pleural space. It usually develops as a result of an injury of the vessels which is located between the leaves of the visceral and parietal pleura during the development of pneumothorax (4). Other causes include the rupture of well-vascularized bullae. The emergency intervention depends on the hemodynamic status, severity of symptoms, and degree of the pneumothorax. In patients presenting to the emergency department (ED) with the complaint of dyspnea, early diagnosis with appropriate imaging methods is important to prevent possible complications of pneumothorax (1).

Case Report

A 33-year-old male was admitted to the ED with a sudden dyspnea that started while walking. He had chest pain for two days and the pain increased this morning. There was no distinctive feature in his medical history except smoking 20 packs/year. His body temperature was 37.1, blood pressure was 137/94 mmHg, heart rate was 110 beats/min, respiratory rate was 18/min, SpO2 was 95% and Glasgow Coma Scale was 15 points. On physical examination, the respiratory sounds were decreased at the left lung. Other system examinations were normal. In the laboratory; the white blood cell count was 13.03 /µL, the hemoglobin value was 14.1 g/dl, and the platelet count was 303 /uL. Prothrombin time was 11.1 sec and the INR value was 0.97. The posteroanterior chest X-ray showed pneumothorax in the upper zone of the left lung and pleural effusion in the basal left lung (Figure 1). Thorax computed tomography showed bilateral pneumothorax, which was more prominent on the left, with bilateral diffuse bullae and left basal air-fluid level (Figure 2). A 28F tube thoracostomy was performed via the sixth intercostal space anterior axillary line of the patient by the thoracic surgeon. During tube thoracostomy, air outflow and approximately 150 cc of hemorrhagic fluid drainage were observed. Control X-ray showed normal ventilation of the lungs (Figure 3). During the follow-up in the thoracic surgery ward, the hemorrhage continued, and the patient underwent video-assisted thoracoscopic surgery for exploration. The patient was discharged on the fourth day with full recovery.

Discussion

Hemopneumothorax is a combination of two medical conditions: pneumothorax and hemothorax. Spontaneous hemopneumothorax (SPH) is a rare condition and bleeding

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occurs in 0.5% to 12% of patients with spontaneous pneumothorax (SP). The most common cause of the disease; rupture of well-vascularized bullae (3,4). SPH is a medical emergency, so it's important to recognize its symptoms right away.

The appearance of the air-fluid line in radiological examinations, the presence of hemorrhagic effusion, and the development of shock findings in the patient may indicate spontaneous hemopneumothorax. The diagnosis of SHP depends on the recognition of sudden chest pain, shortness of breath, shock, and localized clinical signs in the chest. There are no prepared guidelines for the management of patients with SHP. The goals of treatment include resuscitation, hemostasis, and re-expansion of the lung. Initial treatment after prompt diagnosis of patients is adequate fluid replacement and drainage of the pleural space. Therefore, early diagnosis and treatment are important (5).

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Letter to Editor
Eurasian Journal of Critical Care

Complications of SARS-CoV-2 Infection in Geriatrics

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Dear editor,

SARS-CoV-2 was declared a pandemic by the World Health Organization on March 11, 2020, when the first case was seen in Turkey. Since this date, there have been significant changes in the organization of the health system and the health behavior of the society (1). Particularly, the compliance of the elderly from risky groups to vaccination and pandemic measures has been at a high level. Advanced age has been reported as an important risk factor for mortality and poor outcome in SARS-CoV-2 infected patients in the literature (2). In various studies, it has been reported that the symptoms of SARS-CoV-2 infection, especially fever, can be masked in elderly patients, and patients can apply with atypical signs and symptoms (3). This may cause delay in the diagnosis process and the spread of nosocomial disease. SARS-CoV-2 infection generally progresses with a mild clinical picture in people who are not of advanced age and do not have comorbid diseases. However, elderly patients and patients with comorbid diseases have a high risk of progressing with a moderate or severe clinical picture, and these people usually need to be hospitalized in the hospital for diagnosis and treatment processes. Studies have shown that in vitro activities of antiviral drugs such as chloroquine, favipravir and remdesivir, that have been used since the beginning of the pandemic are not as successful as predicted in preventing hospitalizations, intensive care admissions or mortality. Therefore, specific antiviral treatments for SARS-CoV-2, continue to be investigated (4). The data obtained in the treatment of SARS-CoV-2 infection support the importance of the supportive treatments applied and that it is the main treatment approach. Especially in the elderly or those with comorbid diseases, the importance of supportive treatments in the management of clinical conditions and complications increases and has positive effects on survival rates (5).

Many studies show that SARS-CoV-2 infection can progress with complications and mortality rates increase in elderly people and those with comorbid diseases (6,7). Complications in advanced patients were investigated in a study in the literature. In the study of Ramos-Rincon et al., the most common complication was ARDS (43%), followed by acute renal failure (24.6%). Other complications were reported as pneumonia (14.2%), acute heart failure (13.9%), multi-organ failure (10.8%) and sepsis (9.3%). Less common complications were reported as arrhythmia, acute coronary syndrome, venous thromboembolism, myocarditis, intravascular coagulation, seizure, and stroke. Ramos-Rincon et al. reported ARDS and multi-organ failure as cardinal causes regarding mortality and poor outcome in geriatric SARS-CoV-2 infected patients (7). In another study conducted by Zerah et al, it was shown that pulmonary and systemic inflammation findings resulting in multi-organ failure occur more frequently in elderly people infected with SARS-CoV-2 and increase mortality rates (8). The most important complications in this study were ARDS, acute kidney injury, delirium, heart failure, liver dysfunction and lymphopenia. Thrombotic diseases affecting both arterial and venous circulation are reported to develop more frequently in elderly patients with SARS-CoV-2 infection. Zerah et al. reported a higher incidence of advanced inflammation, platelet activation, endothelial dysfunction, stasis, and thrombotic events in older patients as a plausible explanation for complications (8). On the other hand, it was reported that age was not a risk factor for long-term effects in a study in which the six-month effects of SARS-CoV-2 infection were investigated (9).

Infections initiate a complex systemic inflammatory response as part of innate immunity. It activates coagulation following activation of host defense systems. In sepsis, this complex interaction of immune response and coagulation is called thrombo-inflammation or immune-thrombosis. Polyphosphates originating from microorganisms, mast cells, complement system, neutrophil extracellular traps (neutrophil extracellular traps), free DNA, histones are

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the main components that affect thrombin formation in sepsis. Cytokines that emerge in the inflammatory process also activate vascular endothelial cells and create a prothrombotic state by creating endothelial damage. In addition, the fibrinolytic system is also affected, for example PAI-1 activity increases (10). Since it was determined that a different picture developed in SARS-CoV-2 infection from DIC or sepsis-related DIC, this picture was started to be named as SARS-CoV-2 infection-associated coagulopathy. Coagulopathy seems to be related to the severity of the disease, its pathogenesis is not yet known, but it is thought to occur as a result of a "thrombo-inflammation" picture as described above. Its main features can be listed as follows: Coagulopathy becomes evident with an increase in D-dimer and fibrinogen levels, minimal changes in prothrombin time, activated partial thromboplastin time, and platelet count (11). High D-dimer level at admission is associated with increased mortality (10). The continuation of the D-dimer increase after hospitalization is a harbinger of multiorgan failure and the development of overt DIC. In patients who died, the increase is evident from the 4th day of hospitalization. Bleeding findings are not common despite coagulopathy. geriatric patients are at increased risk for thrombo-inflammation (11).

In conclusion, although the mortality rate of SARS-CoV-2 infection has decreased with new variants, age is still among the most known risk factors. Clinicians should be alert for complications in the management of SARS-CoV-2 infected geriatric patients.

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Review article
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Molnupiravir, a New Antiviral Drug for the Treatment of COVID-19

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Abstract

The coronavirus disease first appeared in Wuhan, China in late December 2019 and spread very quickly to many countries around the world. A lot of antiviral drugs have been involved in treating COVID-19. Molnupiravir was the first oral antiviral drug and is a drug with anti-RNA polymerase effect and is still used today as an option in the treatment of patients with coronavirus disease 2019 (COVID-19).. In this review, we aimed to discuss the mechanism of action, safety, efficacy and clinical studies of molnupiravir in the treatment of patients with coronavirus disease.

Keywords: Pandemic, SARS-CoV-2, COVID-19, Molnupiravir

ABSTRACT

There is currently no definitive effective antiviral treatment for COVID-19, but many antiviral drugs have been studied since the first day of the pandemic and administered to patients for the treatment of Coronavirus, despite preliminary or conflicting results from clinical trials. In December 2021, based on the positive results of the MOVe-OUT trial, which was recently published in the New England Journal, it provided a license for molnupiravir, which has been approved and launched in many countries for use in groups of seriously ill patients at high risk of coronavirus disease 2019. Molnupiravir, a new oral antiviral drug, has recently received emergency use authorization (EUA) in the US, UK and India. Molnupiravir, administered orally; A major phase 3 clinical trial for coronavirus disease 2019 patients has delivered significant clinical benefits. (1) It was also the first oral antiviral agent approved for the treatment of coronavirus. We aimed to review and summarize current information about Molnupiravir, the new antiviral drug for COVID-19.

Pathophysiology of Covid 19

Coronaviruses have four main structural proteins, including spike, membrane, envelope, and nucleocapsid proteins. Coronaviruses invade the host cell through interaction between the spike protein and host cell receptors such as angiotensin-converting enzyme 2 and CD147. (2,3) RdRp is involved in Coronavirus replication in host cells and causes the production of Coronavirus with high mutagenicity and diversity. (4) After the first exposure, the immune system is triggered by cytotoxic cells, antibodies and interferons. In the later stages of the coronavirus, alveolar infiltration of T cells, neutrophils and macrophages causes the formation of cytokines such as interleukin (IL)-1, IL-6 and tumor necrosis factor-alpha. Cytokine storming leads to acute respiratory distress syndrome (ARDS) and multiple organ dysfunction. (4) Hyperinflammatory is also associated with the hypercoagulable state through overexpression of the tissue factor in the clotting cascade.

The mechanism of action of molnupiravir in COVID-19

In plasma, molnupyravir is converted by host esterases to the active nucleoside analogue (EIDD-1931). EIDD-1931 has been noted to inhibit a number of viruses, including Chikungunya virus, Venezuelan equine Encephalitis virus, Respiratory Syncytial virus, Norovirus, Influenza A and B viruses, Ebola virus and human Coronaviruses. EIDD-1931 spreads through several tissues and converts into the form of triphosphate. RdRp uses NHC triphosphate as the substrate instead of citidine-triphosphate and urine-triphosphate, which leads to the production of a mutated RNA. Molnupiravir is a more desirable electron donor, which

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changes the mandatory conditions for infectiousness. EIDD-1931 appears to affect the mitochondrial function of viruses, but in vitro studies have not shown a significant toxicity effect on mitochondrial function. (5) Molnupiravir inhibits the RdRp enzyme of SARS-CoV-2 and causes various errors in RNA virus replication. (6) In other words, molnupiravir-like remdesivir may reduce the pathogenesis and replication of coronaviruses. The results of the placement study showed that the limited mutation zone in the drug structure can cause inhibitory effects on the appearance of mutations associated with drug resistance of molnupiravir. Therefore, molnupiravir may be effective in treating remdesivir-resistant patients. (7)

It leads to the fact that viruses turn to molnupiravir instead of cytidine, leading to an error in the formation of RNA chains. Viruses with faulty RNA cannot infect cells (4). Molnupiravir is an analogue of a natural nucleoside molecule called cytidine. In hamster studies, the combination of molnupiravir with favipiravir has been shown to give superior results than its use alone in COVID-19-infected animals (4). The purpose of this article is to update our recent systematic review of molnupiravir and to give some practical tips and tricks regarding the use of molnupiravir for COVID-19 patients. Molnupiravir, which has also been used since October 15, 2021; We also examined its effectiveness compared to other drugs for the Coronavirus.

Clinical Studies

Phase 1 and phase 2 studies with molnupiravir have been concluded. Phase 3 studies are ongoing in different countries. The Phase 1 study was conducted in sixty-five healthy volunteers and there were no problems with absorption and distribution in the body, and side effects of headaches and diarrhea were seen in a very small group of participants. It is better tolerated than placebo (4). In the Phase 2 study, doses of 200, 400, 600, and 800 mg were given over 5.5 days. The rate of patients with virus positivity on day 3 was 20% in molnupiravir, 28% in the placebo group, 0% in the drug group on day 5 and 24% in the placebo group. In addition, all doses of the molnupiravir virus became negative on the 5th day. These results suggest that molnupiravir will rapidly reduce viral load in outpatients. (4). Phase 3 studies are ongoing in many countries. The results are expected to be announced in a few months. (4).

Application Method

Molnupiravir can be prescribed only by doctors to groups of mild to moderate patients. the recommended dose for those over 18 years of age is to take an 800 mg capsule of molnupiravir twice a day for 5 days, with or without food. Covid Tell patients that if they forget to take a dose of molnupiravir and the dose is usually within 10 hours of being taken, the patient should take this dose as soon as possible and continue the normal dosing schedule. If a patient misses a dose for more than 10 hours, the patient should not take the missed dose and instead compensate for the next dose at the regularly scheduled time. The patient is advised not to give two doses to compensate for a missed dose (8,9).

Side effect

Molnupiravir has been observed to cause cell death, mutations, does not cause serious side effects in liver cell lines and in animal studies. (4). The most common adverse reactions (incidence ≥ 1%) were nausea, vomiting, enteritis and dizziness, but similar to placebo. (8.9).

Table 1: Effects of the antiviral drug Molnupiravir

Alternative names	Lagevrio; EIDD-2801; MK-4482
Class	Antivirals; esters; hydroxylamines; pyrimidinones; ribonucleosides; small molecules
Mechanism of action	Viral replication inhibitors
Route of administration	Oral
Pharmacodynamics	Molnupiravir is hydrolysed to N-hydroxycytidine (NHC) which is phosphorylated to pharmacologically active N-hydroxycytidine triphosphate. Inhibits SARS-CoV-2 replication via viral error induction; robust in vitro and in vivo activity against SARS-CoV-2 retains activity against SARS-CoV-2 variants
Pharmacokinetics of NHC	t_{max} 1.5 h; a high-fat meal reduces C_{max} by 35%; does not bind to plasma proteins $t_{1/2}$ 3.3 h; gender, race, age, and kidney and liver impairment have no clinically relevant effect
Most frequent adverse events	Diarrhoea, nausea, dizziness, headache
ATC codes	
WHO ATC code	J05A-X (other antivirals)
EphMRA ATC code	J5B9 (antivirals, others)
Chemical name	[(2R, 3S, 4R, 5R)-3,4-dihydroxy-5-[4-(hydroxyamino)-2-oxopyrimidin-1-yl]oxolan-2-yl]methyl 2-methylpropanoate

High risk group:

1. Over sixty years of age,
2. Patients with active malignancy ,
3. Recipients of Kcell transplantation, patients withecological diseases
4. Patients with chronic kidney disease,
5. Patients with chronic liver disease,
6. Patients with immune-mediated inflammatory disorders (HIV/AIDS, organ transplant patients)
7. Some rare neurological conditions,
8. All patients with Down syndrome, sickle cell anemia,
9. Patients with obesity body mass index [BMI] ≥30 kg/m^2, It is contraindicated to patients who develop an allergy to the 10th drug due to the high risk.

Mild-to-moderate risk group: (10)

1. Fever, shortness of breath or hypoxia without upper respiratory symptoms
2. Patients with shortness of breath who have an exertion seizure, a respiratory rate of 20-≥30 beats per minute and/or a heart rate of <90-≥125 beats/minute <,
3. SpO_2 or additional oxygen >93% in room air
4. Patients without shortness of breath, respiratory failure, shock or multiple organ dysfunction/insufficiency at rest constitute the mild-to-moderate group.

Can we use Molnupiravir in pregnancy and nursing mothers?

Molnupiravir is not recommended for use during pregnancy. When considering molnupiravir for a pregnant individual, the health care provider who prescribes it should tell the pregnant individual about the known and potential benefits and potential risks of using molnupiravir during pregnancy. Breastfeeding during treatment with molnupiravir and for 4 days after the last dose is contraindicated. A breastfeeding individual may consider interrupting breastfeeding and expressing breast milk during treatment and for 4 days after the last dose of molnupiravir. (8)

The end:

Collectively, based on the evidence currently available, molnupiravir appears to be a highly effective agent in reducing the composition of death and hospitalization or death in high-risk adult patients with COVID-19 at a relatively low cost. The role of molnupiravirin is available orally at a lower cost, especially in outpatient settings. Well-designed randomized clinical trials are needed to confirm the therapeutic effects of molnupiravir in patients with Coronavirus in the future.

Application

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