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Original Article
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Evaluation of Prognostic Scores in Patients with Head Trauma in the Emergency Department

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Abstract

Background: The aim of this study was to investigate the effectiveness of Glasgow coma scale (GCS), GCS-motor component (mGCS), and FOUR (Full Outline of Un-responsiveness) Scores in predicting the prognosis of patients who presented to the emergency department with head trauma.

Methods: In this prospective cross-sectional study, was obtained to collected data of patients with head trauma, who presented to the emergency department. Participants' demographic data, medical history, GCS, FOUR scores, the duration of emergency department stays, as well as 24-hour, 7-day, and 28-day mortality rates were recorded on the case report forms.

Result: Data from 302 patients were used to develop a risk score for detecting significant brain pathology via computed tomography (CT) scans. The regression model, incorporating total GCS and sex-based variables, explained 22.5% of variance and accurately classified 91.1% of cases. The model's area under the curve for detecting significant pathology via CT was 0.714.

Conclusion: GCS, mGCS, and FOUR scores did not achieve the necessary the diagnostic performance benchmark to be used alone to predict or exclude clinically significant brain injury in patients with head trauma.

Keywords: Glasgow Coma Scale, Head Trauma, Acute Brain Injuries, FOUR score

Introduction

Head trauma is a significant public health problem both economically and sociologically. It accounts for approximately half of all trauma-related mortality and stands as the leading cause of death among individuals aged ≤25 years [1,2]. Rapid diagnosis and early effective treatment were crucial in preventing morbidity and mortality in such patients [3]. Previous studies reported that the widely used and generally accepted Glasgow Coma Scale (GCS) and Full Outline of Un-Responsiveness (FOUR) score, developed as an alternative for the GCS to assessing trauma patients, demonstrated similar effectiveness [4–7]. Furthermore, the motor component of the GCS (mGCS) was reported to be as effective as the GCS and could be used in place it for the prehospitalization assessment of trauma patients [8]. These scores can guide clinicians in defining the clinical status of the patient at the time of admission, predicting primary brain injury in the emergency department, and to implement measures against the occurrence of secondary injuries [9]. The aim of the present study is to investigate the effectiveness of assessing trauma patients using the GCS, FOUR, and mGCS scales at the time of presentation to the emergency department in detecting clinically significant brain injury.

Materıals and Methods

Study Design: The study was initiated following approval from the local ethics committee (Ethics Committee Approval number: 274 / October 3, 2022). It was a prospective cross-sectional study involving patients who presented to the emergency department of a tertiary training and research hospital with an annual average admission of 500,000 patients. The study included patients with head trauma who presented to the emergency department between October 2022 and January 2023. Written consent was obtained from patients who agreed to participate in the study. Those who declined to participate, individuals aged <18 years, pregnant women, and patients under the influence of drugs or alcohol were excluded.

Data Collection: Patients with head trauma, who presented to the emergency department underwent examination by an emergency medicine specialist. Subsequent examinations were conducted as outlined in the Advanced Trauma Life Support Guidelines (ATLS) and treatment was organized accordingly [10]. The CT images of patients considered suitable for neuroimaging by the emergency physician, following the Canadian brain CT guidelines, were assessed alongside the associated reports, and the results were recorded in the case report form [4].

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Patients deemed unsuitable by the emergency physician did not undergo the CT imaging procedure.

Demographic data, medical history, mechanism of trauma, GCS and FOUR scores at admission for participants were meticulously recorded on the case report form. The patients' outcomes, categorized as discharge, ward admission, or intensive care unit (ICU) hospitalization, were also documented on the case report form. Mortality statuses of the patients at 24 hours, 7 days, and 28 days after admission were retrieved from the patient record system and meticulously recorded in the case report form. It's essential to note that no alterations were made to the examination, follow-up, and treatment procedures for the patients included in the study.

Clinically significant brain injury associated with head trauma was defined as any acute brain result on brain computed tomography (CT) that typically required hospitalization and neurosurgical follow-up. All brain injuries were considered clinically important unless the patient remained neurologically intact and exhibited one of the following lesions on CT: solitary contusion of less than 5 mm in diameter, localized subarachnoid blood less than 1 mm thick, smear subdural hematoma less than 4 mm thick or closed depressed skull fracture not extending through the inner table. This definition aligns with the criteria outlined in the "Canadian CT Head Rule" validation study conducted by Stiel IG et al. [11].

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS v.29, IBM Corp., Released 2019. IBM SPSS Statistics for Windows, Version 29.0. Armonk, NY: IBM Corp) was employed for statistical analyses of the data. The normal distribution of continuous data was assessed using the Shapiro–Wilk test. In case where no continuous variable exhibited a normal distribution, the Mann–Whitney-U Test was utilized for intergroup comparisons, and the data were presented as median (25%–75% quartiles). Categorical data were expressed as frequency (%), with Chi-Squared test and Fisher Exact test applied for intergroup comparisons as necessary.

Receiver Operating Characteristics (ROC) analysis was employed to investigate the diagnostic performance, and area under the curve (AUC) was calculated accordingly. Logistic regression was utilized in multivariate analysis. Correlations between variables and variance inflation factor were analyzed to test multicollinearity. The goodness of fit of the model was determined using the Hosmer–Lemeshow test. Statistical significance was denoted by $p < 0.05$ for all analyses conducted in this study.

Results

The present study examined a total of 388 patients with head trauma who presented to the emergency department. Exclusions from the study comprised patients, who declined to participation(43), those under the influence of alcohol or drugs (32), individuals who left the hospital without permission (8), and pregnant women (3) were excluded. The data collected from the remaining 302 patients included in the study were thoroughly assessed. The median age of the patients was 44 years, with 206 (68.2%) male participants and 96 (31.8%) female participants. The most prevalent reason for presentation was "fall from same level" observed in 106 (35.1%) cases. The median GCS and FOUR levels were 15 (15–15) and 16 (16–16), respectively. Clinically significant pathology was confirmed via CT in 33 patients (10.9%), representing the primary endpoint. Among the patients 270 (89.4%) were discharged following the completion of emergency department follow-up, 22 (7.3%) were hospitalized in the relevant ward, and 10 (3.3%) were admitted to the ICU. Two patients (0.7%) succumbed within 28 days (Table 1). Patients enrolled in the study were classified into two groups based on the presence or absence of clinically significant pathology on brain CT, which served as the primary endpoint. The scores from GCS and its components, as well as the FOUR and its components were

Table 1: Baseline descriptive characteristics of patients included in the study

Age	44 (30–67)
Sex (male)	206 (68.2%)
GCS	15 (15–15)
FOUR Score	16 (16–16)
Hypertension	63 (20.9%)
Diabetes Mellitus	32 (10.6%)
CAD	27 (8.9%)
Heart failure	7 (2.3%)
CRF	3 (1%)
Chronic obstructive pulmonary disease	16 (5.3%)
History of ischemic stroke	17 (5.6%)
Active malignancy	5 (1.7%)
Neurodegenerative disease	11 (3.6%)
Epilepsy	13 (4.3%)
Trauma mechanism	
Non-vehicle traffic accident	20 (6.6%)
Vehicular traffic accident	13 (4.3%)
Fall from same level	106 (35.1%)
Battery	69 (22.8%)
Tumbling down the stairs	15 (5%)
Motorcycle accident	46 (15.2%)
Fall from scooter	4 (1.3%)
Hit a hard place	9 (3)
Falling from height	20 (6.6%)
Patients hospitalized in the relevant ward	26 (8.6%)
Length of ward stay (days)	4 (3–7)
Patients admitted to the intensive care unit	14 (4.6%)
Duration of intensive care unit stay (days)	7 (1–40)
Mortality (28 days)	2 (0.7%)
Clinically significant pathology by CT	33 (10.9%)

CT Brain: Computed tomography of the brain, FOUR: Full Outline of Un-Responsiveness, GCS: Glasgow Coma Scale. CAD: Coronary artery disease CRF: Chronic renal failure

significantly lower in the group of patients with pathology on CT scan ($p < 0.001$ for all variables). No significant intergroup differences were observed in terms of other variables (Table 2). The AUC of total GCS, total FOUR score, and their individual components were calculated through ROC analysis. The first four variables with the highest diagnostic performance were total FOUR score, total GCS score, FOUR eye response, and GCS verbal response (AUC = 0.665, 0.664, 0.650, and 0.649, respectively) (Table 3). Analysis was conducted based on the optimal thresholds of the GCS sensitivities. The analyses indicated that the sensitivity of GCS for detecting the occurrence of clinically significant pathology on CT was 33.3% (95%CI = 18–51.8), FOUR score sensitivity was 15.2% (95%CI = 5.1–32) and GCS motor score sensitivity was 27.3% (95%CI = 13.3–45.5). Additionally the specificity of GCS was 99.3% (95%CI = 97.3–99.9), specificity of FOUR score was 99.6% (95%CI = 98–99.9) and specificity of GCS motor score was 99.6% (95%CI = 97.9–99.9). The test performance metrics of the three scores are briefly summarized in Table 4. A logistic regression analysis that includes all variables to identify independent predictors of the occurrence of clinically significant pathology on brain CT could not be performed due to the similarity between the variables, resulting in multicollinearity. However, the aim of this study was to develop a risk score based on the data included in the study in o determine the occurrence of clinically significant pathology via brain CT. The regression model that best suited this purpose included the total GCS and sex variables (Table 5). The model was fitted, predicted the outcome at a statistically significant level, and explained 22.5% of the variance (Hosmer & Lemeshow $p = 1$, $p < 0.001$, Nagelkerke R2 = 0.225, respectively). Through the model, we were able to accurately classify 91.1% of cases. Regarding the performance of the model in detecting the occurrence of clinically significant pathology via CT, the AUC value was 0.714 (95%CI = 0.610–0.817) (Figure 1).

Table 2: Results of univariate analysis of variables

	Without pathology on CT Brain	With pathology on CT Brain	p value
Age	44 (30–67)	50 (28–70)	0.948
Sex (male)	179 (66.5%)	27 (81.8%)	0.075
GCS	15 (15–15)	15 (12–15)	<0.001
Eye response	4 (4–4)	4 (3–4)	<0.001
Verbal response	5 (5–5)	5 (4–5)	<0.001
Motor response	6 (6–6)	6 (5–6)	<0.001
FOUR Score	16 (16–16)	16 (13–16)	<0.001
Brain stem	4 (4–4)	4 (4–4)	<0.001
Respiration	4 (4–4)	4 (4–4)	<0.001
Eye response	4 (4–4)	4 (3–4)	<0.001
Motor response	4 (4–4)	4 (3–4)	<0.001
Hypertension	53 (19.7%)	10 (30.3%)	0.157
Diabetes Mellitus	29 (10.8%)	3 (9.1%)	0.526
CAD	23 (8.6%)	4 (12.1%)	0.339
Heart failure	6 (2.2%)	1 (3%)	0.559
CRF	3 (1.1%)	0 (0%)	0.706
COPD	14 (5.2%)	2 (6.1%)	0.540
CVA	15 (5.6%)	2 (6.1%)	0.575
Active malignancy	5 (1.9%)	0 (0%)	0.558
Neurodegenerative disease	9 (3.3%)	2 (6.1%)	0.343
Epilepsy	11 (4.1%)	2 (6.1%)	0.426

CT Brain: Computed tomography of the brain, FOUR: Full Outline of Un-Responsiveness, GCS: Glasgow Coma Scale, CAD: Coronary artery disease, CRF: Chronic renal failure, COPD: Chronic obstructive pulmonary disease, CVA: Cerebrovascular accident.

Table 3: Analysis of the performance of the scores and their components in detecting the occurrence of clinically significant pathology on CT

	AUC (95%Confidence Interval)
Total FOUR	**0.665 (0.549–0.781)**
Total GCS	**0.664 (0.547–0.780)**
GCS-Motor response	0.635 (0.519–0.751)
GCS Verbal response	**0.649 (0.533–0.765)**
GCS Eye response	0.620 (0.504–0.735)
FOUR Brain stem	0.559 (0.447–0.670)
FOUR Respiration	0.545 (0.435–0.656)
FOUR Eye response	**0.650 (0.534–0.766)**
FOUR Motor response	0.635 (0.519–0.751)

AUC: Area under the curve, CT: Computed tomography, GCS: Glasgow Coma Scale, FOUR: Full Outline of Un-Responsiveness

Discussion

The primary objective of the current study was to assess the effectiveness of GCS, mGCS, and FOUR scores in predicting clinically significant brain injury among patients presenting to the emergency department with head trauma. To achieve this, epidemiologic data, such as age, sex, comorbid diseases, medication use, and the mechanism of trauma at admission, were systematically recorded. The investigation aimed to determine whether these data had any influence on the follow-up and treatment procedures of the patient in

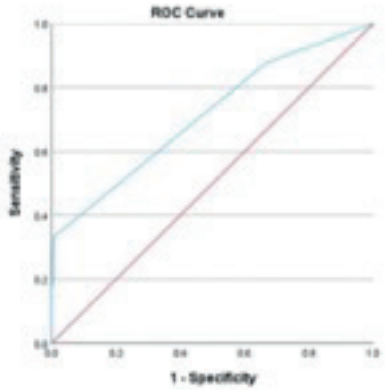

Figure 1: Performance of the regression model to detect the occurrence of clinically significant pathology on CT (ROC: Receiver Operating Characteristics).

Table 4: Diagnostic performance measures of GCS and FOUR scores at the optimal threshold value, for detecting the occurrence of clinically significant pathology on CT Brain

	GCS (Threshold:14)	FOUR Score (Threshold:11)	GCS-motor (Threshold: 5.5)
Sensitivity	33.3% (95%CI = 18–51.8)	15.2% (95%CI = 5.1–32)	27.3% (95%CI = 13.3–45.5)
Specificity	99.3% (95%CI = 97.3–99.9)	99.6% (95%CI = 98–99.9)	99.6% (95%CI = 97.9–99.9)
Positive likelihood ratio	44.8 (95%CI = 10.4–193.5)	40.8 (95%CI = 4.9–338.4)	73.4 (95%CI = 9.6–560.9)
Negative likelihood ratio	0.67 (95%CI = 0.53–0.85)	0.85 (95%CI = 0.74–0.98)	0.7 (95%CI = 0.6–0.9)
Positive predictive value	84.6% (95%CI = 56–96)	83.3% (95%CI = 37.6–97.7)	90% (95%CI = 54.1–98.6)
Negative predictive value	92.4% (95%CI = 90.5–93.9)	90.6% (95%CI = 89.2–91.8)	91.8% (95%CI = 90.1–93.2)
Accuracy	92% (95%CI = 88.4–94.8)	90.4% (95%CI = 86.5–93.5)	91.7% (95%CI = 88–94.6)

CT Brain: Computed tomography of the brain, GCS: Glasgow Coma Scale, FOUR: Full Outline of Un-Responsiveness

Table 5: Summary of the regression model to detect the occurrence of clinically significant pathology on CT.

	Coefficient B	Wald statistic	p value	Odds ratio (95%CI)
GCS	−1.066	9.865	0.002	0.334 (0.177–0.670)
Sex (male)	-1.030	3.299	0.069	0.357 (0.118–1.085)
Constant	13.293	6.990	0.008	

CT Brain: Computed tomography of the brain, GCS: Glasgow Coma Scale

the emergency department and on the overall outcomes. In a prior study, it was noted that the prehospitalization mGCS scores in patients with head trauma, who presented to the emergency department, were equally effective as the overall GCS in detecting clinically significant traumatic brain injury. Moreover, mGCS was suggested as a potential substitute for GCS due to its relative ease of application [8]. However, a study by Chou et al. reported that the total GCS score better predicted whether the patient had clinically significant traumatic brain injury when compared to the mGCS [12]. In another study, it was reported that, unlike the GCS, the FOUR score did not include a verbal component. This characteristic makes it feasible to utilize the FOUR score in limited groups, particularly in tracheostomized, aphasic, ventilator-dependent intubated patients, and unconscious patients presented to the emergency department. Additionally, the components for respiratory and brainstem reflexes were suggested to offer a more comprehensive assessment of patients in coma or vegetative state, particularly during the diagnosis and follow-up stages [13,14]. The findings of the present study indicate that scores from GCS, mGCS, or FOUR, and their respective components did not reach the diagnostic performance threshold to be used in isolation for predicting clinically significant CT pathology in patients presenting to the emergency department with head trauma. Notably, the specificity and negative predictive values of all three scores were quite high. According to the study results, patients with GCS, mGCS, or FOUR scores below the optimal threshold (14 points for GCS, 5.5 points for mGCS, and 11 points for FOUR score) should be considered at high risk for the occurrence of clinically significant pathology on CT. Therefore, due care should be taken in the follow-up of these patients. However, considering the low sensitivity of all three scores, relying solely on a patient's full score on the GCS, mGCS or FOUR scales in insufficient to exclude clinically significant brain injury. Consistent with similar studies in the relevant literature, the majority (68.2%) of the patients presenting to the emergency department with head trauma in the present study were male [15–17]. In conclusion, the inclusion of the sex variable, along with GCS or FOUR scores, contributed toa relative improvement in the performance of the regression model for predicting the occurrence of clinically significant brain injury on CT scans. The use of blood thinners has been reported to result in differences in patient outcomes. Several previous studies have indicated that intracranial incidence and mortality were elevated in cases of comorbid heart diseases and coagulopathy [18–20]. On the other hand, other studies have reported no significant difference in intracranial hemorrhage and mortality between patients with and without blood thinners [21]. According to the results of the present study, there was no increase in the incidence of intracranial hemorrhage in patients who received blood thinners. The findings of this study revealed no significant correlation between the duration of hospital stay and GCS, mGCS, and FOUR scores, as well as their subgroups.. These results align with previous studies in the relevant literature that had larger sample sizes. [7,22].

Limitations

The primary limitation of the current study lies in its single-center nature. Despite being designed as a prospective observational research, patient follow-ups were conducted through records and the hospital information system, potentially introducing bias to the data, albeit in adherence to relevant ethical principles. Additionally, the study faced a limitation in that only two patients died during follow-up, precluding an investigation into the effectiveness of scores in predicting mortality.

Conclusion

According to the findings of the present study, it can be concluded that the GCS, mGCS, and FOUR scores did not exhibit diagnostic performance sufficient to be used in isolation for predicting and excluding clinically significant brain injury in patients with head trauma. The study suggests that patients with GCS, mGCS, or FOUR scores below the optimal threshold (14 points for GCS, 5.5 points for mGCS, 11 points for FOUR score) should be regarded as at high risk for the occurrence of clinically significant pathology on CT. Therefore, careful attention should be given to the follow-up of these patients.

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Original Article
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Relationship Between Glucose, Prealbumin and HbA1c in Hypoglycemic Patients Running Title: Glucose, Prealbumin and HbA1c in Hypoglycemic Patient

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Abstract

Background: To investigate whether there is a relationship between glucose values and prealbumin and HbA1c in hypoglycemic patients and to determine their use as predictive values in minimizing hypoglycemic episodes or determining the measures to be taken..

Material and Methods: The study included 200 patients admitted to the emergency department within 1 year. Age, gender, complaints, presence of chronic disease history, nutritional status, glucose, prealbumin and HbA1c values were recorded.

Results: In our study, no significant difference was found between the mean ages of the case group and the control group ($p>0.05$). Gender distributions were similar. Blood glucose levels were significantly lower and HbA1c levels were significantly higher in the case group ($p<0.05$). No significant difference was found when prealbumin values were compared ($p>0.05$). Patients presenting with hypoglycemic attacks were more likely to have moderate or poor nutritional status ($p<0.05$).

Conclusion: We found that HbA1c value was high and prealbumin value was low in hypoglycemic patients. This shows that nutrition is one of the important criteria as well as drug use in diabetic patients, especially in terms of hypoglycemia risk.

Keywords: Emergency department, HbA1c, hypoglycemia, prealbumin, glucose

Introduction

Hypoglycemia is one of the most common and important causes of endocrine emergency admissions worldwide. In some diseases, disturbances in blood glucose homeostasis cause hypoglycemia. Hypoglycemia causes activation of the brain and sympathetic nervous system and leads to some signs and symptoms (1).

Blood glucose is normally kept within very narrow limits. Many organs can oxidize fatty acids such as glucose and use them as metabolic fuel. For the brain, however, glucose is the only fuel that must be used. The brain cannot synthesize glucose and can only store it as glycogen for various uses. It must therefore constantly receive it through the blood. A decrease in plasma glucose concentration below physiologic limits decreases blood-brain glucose transport, causing the brain to have difficulty in providing energy and threatens life (1-3). The patient's consciousness starts to deteriorate and it is important that the parameters measured at admission have a predictive value in terms of the transformation of this deterioration into mortality (1,4). In the 2021 guidelines of the American Diabetes Association (ADA), the limit of hypoglycemia in patients with diabetes is accepted as plasma glucose below 70 mg/dl (5). Prealbumin is a negative acute phase reactant. It has a shorter half-life compared to albumin and is not affected by hydration status. It is highly affected by inflammatory reactions. It has been reported that it can be used in the evaluation of malnutrition in hospitalized patients (6). At the same time, blood levels decrease as a result of protein-induced malnutrition such as cancer, cirrhosis, protein-losing enteropathy and zinc deficiency, but not in vitamin deficiency. It may increase in progesterone use and acute alcohol intoxication. It is a more reliable and sensitive parameter for monitoring nutritional support program. Since prealbumin synthesis increases above baseline levels within 2 days after protein supplementation, adequate nutritional support may increase prealbumin levels by 2 mg/dL per day and return to normal prealbumin levels within 8 days (7). Among all nutritional parameters, prealbumin is the best predictor of mortality (8). Low prealbumin level is a modifiable risk factor for infection. Other risk factors for infection such as age, body mass index and comorbidities cannot be easily modified. Therefore, prealbumin is particularly important in prognosis.

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and use them as metabolic fuel. For the brain, however, glucose is the only fuel that must be used. The brain cannot synthesize glucose and can only store it as glycogen for various uses. It must therefore constantly receive it through the blood. A decrease in plasma glucose concentration below physiologic limits decreases blood-brain glucose transport, causing the brain to have difficulty in providing energy and threatens life (1-3). The patient's consciousness starts to deteriorate and it is important that the parameters measured at admission have a predictive value in terms of the transformation of this deterioration into mortality (1,4). In the 2021 guidelines of the American Diabetes Association (ADA), the limit of hypoglycemia in patients with diabetes is accepted as plasma glucose below 70 mg/dl (5). Prealbumin is a negative acute phase reactant. It has a shorter half-life compared to albumin and is not affected by hydration status. It is highly affected by inflammatory reactions. It has been reported that it can be used in the evaluation of malnutrition in hospitalized patients (6). At the same time, blood levels decrease as a result of protein-induced malnutrition such as cancer, cirrhosis, protein-losing enteropathy and zinc deficiency, but not in vitamin deficiency. It may increase in progesterone use and acute alcohol intoxication. It is a more reliable and sensitive parameter for monitoring nutritional support program. Since prealbumin synthesis increases above baseline levels within 2 days after protein supplementation, adequate nutritional support may increase prealbumin levels by 2 mg/dL per day and return to normal prealbumin levels within 8 days (7). Among all nutritional parameters, prealbumin is the best predictor of mortality (8). Low prealbumin level is a modifiable risk factor for infection. Other risk factors for infection such as age, body mass index and comorbidities cannot be easily modified. Therefore, prealbumin is particularly important in prognosis.

The amount of HbA1c is directly proportional to the average blood glucose carried by HbA over its 120-day lifespan. However, in the last weeks, HbA1c is more closely related to glucose levels. Glucose levels in the last month account for 50% of HbA1c. The normal value is between 4.5-6.1%. In newly diagnosed diabetic patients, HbA1c levels are quite high until treatment is started (9).

Hypoglycemia is one of the most feared complications in diabetic patients and there is no test to indicate which patients are likely to develop hypoglycemia. The relationship between HbA1c, prealbumin and hypoglycemia remains unclear. While HbA1c gives information about 3-month blood glucose, prealbumin level gives an idea about 3-day nutrition. Measured blood glucose reflects the current value. In this study, we aimed to investigate whether there is a relationship between HbA1c, prealbumin and glucose in hypoglycemic patients. To the best of our knowledge, there is no study investigating the value of serum glucose, prealbumin and HbA1c parameters in hypoglycemia.

Material and Method

The study was performed prospectively in patients who presented to the Emergency Department of the University of Health Sciences Bursa High Specialization Training and Research Hospital within one year and were followed up in the emergency department with a diagnosis of hypoglycemia. In the ADA 2009 guideline, the limit of hypoglycemia for patients with diabetes was accepted as a plasma glucose level below 70 mg/dl and our diagnosis of hypoglycemia was based on this value (10). This hypoglycemia limit was updated as 70 mg/dl in 2021 (5). A total of 200 patients, 100 from the case and control groups, were included in the study. Case group patients were selected consecutively. Patients over the age of 18, non-traumatized and non-pregnant were included in our study. Patients under 18 years of age and patients whose consent could not be obtained were excluded. Written approval was obtained from the clinical research ethics committee of our hospital during the planning phase of our study (2011-KAEK-25 2016/06-06).

Demographic characteristics, complaints, comorbidities, nutritional levels, blood glucose, prealbumin and HbA1c levels were investigated. The data obtained were recorded in the study form.

The study was explained to the patients in detail and informed consent was obtained from the patients or their relatives. After blood samples were taken from the patients, HbA1c was analyzed by HPLC (High Performance Liquid Chromatography) method on an Arkroy Adams device. The value range is between 4% and 6.5%.

For serum prealbumin assessment, samples were centrifuged 20 minutes after collection and then serum was stored at -18°C. Prealbumin was analyzed by turbidimetric immunoassay using a COBAS 6000 automated analyzer (Roche, Basel, Switzerland). The range of values was 17-42 mg/dl.

Glucose values of the patient were studied with Lever Chek TD-4231 glucometer device and after the sample was taken from the patient, it was studied with Olympus AU2700 device by colorimetric and kinetic methods. Treatment was started immediately after sample collection. The results were recorded in the data study form.

In order to determine the nutritional status of the patients, food intake in the last two or three days was obtained by asking the patients or their relatives. If the amount of food intake in the last days was the same as in the previous days, it was considered good. If food intake was less than the previous day and meals were skipped, it was considered moderate. Food intake in the last few days was defined as poor if there was little or no food intake.

Statistical Analysis

The study data were uploaded to the SPSS 22 program (IBM Corporation, Armonk, New York, United States of

America) and the analysis of the variables was performed with the SPSS 22 program. The conformity of the data to normal distribution was evaluated by Shapiro-Wilk test and homogeneity of variances was evaluated by Levene's test. Independent-Samples T test with Bootstrap results and Mann-Whitney U test with Monte Carlo results were used to compare two independent groups according to quantitative data. Pearson Chi-Square Monte Carlo Simulation technique was used to compare categorical variables with each other, while Fisher Exact test was evaluated with Exact results. Odds ratio was used to determine the most important risk factor among categorical significant risk factors. Logistic regression test with the Enter method was used to determine the cause-effect relationship between the categorical response variable and the explanatory variables in dichotomous and multinominal categories. Quantitative variables in the tables are shown as mean±std. (standard deviation) and median range (Maximum-Minimum) and categorical variables are shown as n (%). Variables were analyzed at 95% confidence level and p≤ 0.05 values were considered significant.

Results

57% of the patients in the case group and 56% of the patients in the control group were female. The gender distribution of the case and control groups was homogeneous (p=1).

The mean age of the case group was 59.22±18.30 years and the mean age of the control group was 54.80±14.97 years. There was no statistically significant difference between the groups in terms of age (p>0.05).

When the symptoms of the patients admitted to the emergency department were analyzed, it was seen that 18% were unconscious and 82% were conscious. The most common symptoms were change in consciousness 40%, fatigue 36%, sweating 22%, drowsiness 19%, loss of consciousness/coma 18%, speech disorder 17%, tremor 17%, palpitations 14%.

In the case group, 86% of patients were receiving antidiabetic treatment. Among the patients with diabetes, 46% used only insulin, 24% used oral antidiabetics (OAD) and 16% used insulin and OAD. 14% of the case group did not receive any antidiabetic treatment. 7% of the patients had a chronic disease and did not have diabetes (Figure 1).

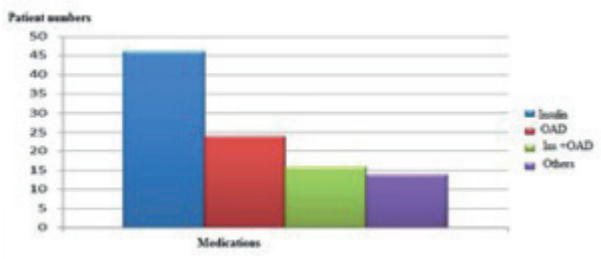

Figure 1: Antidiabetic treatment used in hypoglycemic patients

Only 21% of the patients had diabetes and no other chronic disease. In the case group, 53 patients had hypertension (HT), 26 had chronic renal failure (CRF), 21 had coronary artery disease (CAD) and 7 had congestive heart failure (CHF).

The median blood glucose level was 46 mg/dl in the case group and 99.5 mg/dl in the control group. Blood glucose levels of the case group were significantly lower than those of the control group (p<0.05).

When the nutritional levels were compared, it was determined that the nutritional levels of the case group were worse than the control group (p<0.05). The nutritional levels of the case group were 17.2 times worse than the control group (95% confidence interval, 3.96-74.84).

The mean prealbumin value was 17.90±6.07 mg/dl in the case group and 23.02±6.28 mg/dl in the control group. There was a significant difference between the groups in terms of prealbumin values (p<0.05). When the prealbumin values of the groups were compared, the case group had significantly lower prealbumin values (p<0.05). The probability of prealbumin groups being fair or poor was 6.62% higher in the case group than in the control group (95% confidence interval, 1.87-23.39).

The median HbA1c value was 6.65% in the case group and 5.3% in the control group. The HbA1c value of the case group was significantly higher than the control group (p<0.05). When the HbA1c values of the groups were compared, the HbA1c values of the case group were found to be higher (p<0.05). The probability of high HbA1c values in the case group was 107.25 times higher than in the control group (95% confidence interval, 14.39-799.26) (Table 1).

Independent variables of the case group were re-evaluated by Multiple Logistic Regression method. In this analysis, nutritional levels, clinical outcome and HbA1c values were significant (P<0.001). The probability of moderate or poor nutritional status in the case group was 10.14 times higher than in the control group and was statistically significant (p<0.05) (95% confidence interval, 1.65-62.20). The probability of being hospitalized in the clinic and intensive care unit was 6.26 times higher and statistically significant in the case group compared to the control group (p<0.05) (95% confidence interval, 1.72-22.72).

There was no significant difference in the probability of having moderately or severely low prealbumin levels in the case group compared to the control group (p>0.05). The probability of having high HbA1c levels in the case group was 133.44 times higher than in the control group and statistically significant (p<0.05) (95% confidence interval, 17.54-1015.38). When the predictability rates of these variables were analyzed according to the groups, it was calculated that the case group had a 76% accuracy rate, the control group had a 95% accuracy rate, and the overall accuracy rate was 85.5% (Table 2).

Table 1: Statistical analysis of case and control group

	Patient (n=100) mean ± SD	Control (n=100) mean ± SD	Total (n=200) mean ± SD	P
Age	59.22 ± 18.30	54.80 ± 14.97	57.01 ± 16.82	**0,063**
Prealbumin	17.90 ± 6.07	23.02 ± 6.28	20.46 ± 6.67	**0,001**
	Median (Max. - Min.)	**Median (Max. - Min.)**	**Median (Max. - Min.)**	
Glucose	46 (68 - 23)	99.50 (137 - 78)	73 (137 - 23)	**<0.001**
HbA1C	6.65 (15.60 – 4.20)	5.30 (6,70 – 3.80)	5.60 (15.60 – 3.80)	**<0.001**
	n (%)	n (%)	**N (%)**	
Sex				
Male	43 (43)	44 (44)	87 (43,5)	1
Female	57 (57)	56 (56)	113 (56,5)	
Nutrition status				
Good	74 (74)	98 (98)	172 (86)	**<0.001**
Moderate	20 (20)	2 (2)	22 (11)	
Bad	6 (6)	0 (0)	6 (3)	
Clinical Outcome				
Discharge	71 (71)	96 (96)	167 (83,5)	**<0.001**
Hospitalization-service	24 (24)	4 (4)	28 (14)	
ICU	5 (5)	0 (0)	5 (2,5)	
Prealbumin				
Normal	59 (59)	87 (87)	146 (73)	
Mild low	24 (24)	10 (10)	34 (17)	**<0.001**
Moderate low	14 (14)	3 (3)	17 (8,5)	
Seriously low	3 (3)	0 (0)	3 (1,5)	
HbA1C				
Normal	48 (48)	99 (99)	147 (73,5)	**<0.001**
High	52 (52)	1 (1)	53 (26,5)	107.25 (14.39-799.26)*

Independent t Test (Bootstrap) - Mann-Whitney U Test (Monte Carlo) - Fisher Exact Test(Exact) - Pearson Chi Square Test (Monte Carlo) / SD.: Standard deviation - Max.:Maximum - Min.:Minimum / *Odss Ratio (%95 Confidence Interval)

Table 2: Evaluation of the independent variables of the groups with the Multiple Logistic Regression method.

	B ± SE.	P Value	Odds Ratio	%95 Confidence Interval	
				Lower Limit	Upper Limit
Nutrition (Moderate+Poor)	2.32 ± 0.93	0,012	10,14	1,65	62,2
Clinical Outcome (admission+ICU)	1.83 ± 0.66	0,005	6,26	1,72	22,72
Prealbumin (Moderate + Severe)	0.42 ± 0.99	0,668	1,53	0,22	10,62
HbA1C (High)	-4.89 ± 1.04	<0.001	133,44	17,54	1015,38
Still	3.57 ± 1.01	<0.001	35,69		

Dependent Variable: Groups Predicted Cases=76 Predicted Control=95 Predicted: 85.5 P Model<0.001

Multiple Logistic Regression (Method = Enter) / B: regression coefficients - SE: Standard error

Discussion

In this study, we aimed to investigate whether there is a relationship between plasma glucose, prealbumin and HbA1c values in patients presenting to the emergency department with hypoglycemia attack.

In the study by Kaganski et al. hypoglycemia was observed more frequently in women with a rate of 58% (11). In the study by Kumar et al. hypoglycemia was observed more frequently in males with a rate of 62.9%. The mean age of the patients was 57±14.7 years (12). In the study by Eren et al. the mean age was 59.1±18.6 years and 56.4% were female (13). In our study, 57% of the patients who presented with hypoglycemic attacks were female and the mean age of the patients was 59.2±18.3 years. Our study is similar to other studies in terms of age and gender.

In the study by Kumar et al. 60.63% of diabetic patients with hypoglycemia had confusion, 22.00% had dizziness, 3.54% had sweating/stroke, 1.42% had seizure, 1.06% had

motor deficit/paresthesia, and 11.35% were associated with other/nonspecific symptoms. In the non-DM group, the most common symptom was clouding of consciousness with a rate of 56.33% (12). In our study, blurred consciousness was observed most frequently in 40% of patients, coma in 18%, and lethargy, tremor, palpitations, sweating and other nonspecific symptoms in 42%.

In the study of Eren et al. the lowest plasma glucose level was found to be 10 mg/dl, the highest 49 mg/dl and the mean 34±10.4 mg/dL (14). In our study, the lowest blood glucose level was 23 mg/dl, the highest was 68 mg/dl and the mean was 45.5±12.1 mg/dl. It is possible that the reason why the mean glucose value was found to be high in our study was due to the difference in the plasma glucose value in which ADA is the basis for hypoglycemia. In other studies, the limit value for hypoglycemia was reported to be 50 mg/dl and below (10,14).

Studies have shown that insulin-induced hypoglycemia is the most common cause of hypoglycemia during DM treatment (12-16). In our study, the most common hypoglycemic episode was detected in patients using insulin for DM treatment. Our study is similar to other studies in this respect.

In the study by Nassar et al. it was found that HT was most frequently observed in patients with hypoglycemia (17). In our study, the most common chronic diseases other than DM were HT, CRF and CAD. In the study by Kyle et al. evaluating patients who received enteral nutrition, it was determined that patients who were mechanically ventilated needed more energy and protein than those who were not. It was found that serum albumin, prealbumin and IGF-1 levels decreased and CRP increased as a result of low protein administration (18). In our study, it was observed that 74% of the patients who presented with hypoglycemic attacks were well-nourished, 20% were moderately-nourished and 6% were malnourished. Although malnutrition led to hypoglycemia in our study, skipping meals was found to be the most important cause.

Forga et al. found normal levels of prealbumin in 49.4%, RBP in 48.4%, and retinol in 30.1% of patients with type 1 DM (19). Lee et al. reported that low prealbumin levels were associated with markers of malnutrition including BUN, Cr, albumin and transferrin. Nutritional levels of well-controlled diabetic patients are similar to the normal population. Patients with poor control had lower prealbumin levels than the normal population. It was found that this low prealbumin level may be related with malnutrition (8).

Luis et al. In a study conducted on type 2 DM patients, a significant decrease in HbA1c level was observed; a significant increase was observed in weight, body mass index, fat mass, albumin, prealbumin and transferrin levels (20). Gannon et al. investigated the effect of nutrition in patients with uncontrolled type 2 DM and found that HbA1c and prealbumin values were affected by the diet (21). In our study, the mean prealbumin value was found to be 17.90±6.07 mg/dl in patients presenting with hypoglycemia attack. It was significantly lower compared to the control group. Although similar to other studies, prealbumin values were lower in our study compared to other studies. In our study, prealbumin values were also found to be lower in patients with poor general condition and requiring intensive care follow-up. This suggests that nutrition is the most important factor in preventing hypoglycemia attacks.

In the study by Munshi et al. HbA1c value was found to be <7% in 26%, 7.1-8% in 42%, 8.1-9% in 21% and >9% in 11% of the patients. There was no difference between HbA1c groups in terms of the depth of hypoglycemia (22). In the study by Albrecht et al. the mean HbA1c value was 7.1% and it was found to be <7.0% in 43.5% and <7.5% in 64.6% of the patients. It was reported that these values provided good or acceptable metabolic control (23). Davis et al. reported that high HbA1c value was one of the factors predicting the frequency of severe hypoglycemia (24). Although no significant relationship was found between HbA1c and hypoglycemia in the study by Nassar et al. Intensive glycemic control and HbA1c <7% target are associated with an increased risk of hypoglycemia. It was stated that low HbA1c value was an independent and significant predictor of hypoglycemia (17). Mahmoodpoor et al. reported that the risk of hypoglycemia increased as HbA1c increased (25). However, Yu et al. reported that the prevalence of hypoglycemia increased significantly when HbA1c decreased (26). In our study, the mean HbA1c value was found to be 6.65% in patients presenting with hypoglycemia attack. This suggests that high HbA1c may be a warning for hypoglycemia.

Limitations

Our study was single-center and only patients admitted to the emergency department were included in the study. The study population was not as large as desired because patients who did not meet the study criteria and whose consent could not be obtained were excluded. In addition, nutritional information may not be optimal because it was obtained from patients and/or their relatives.

Conclusion

In our study, we found that HbA1c value was high and prealbumin value was low in hypoglycemic patients. This shows that nutritional compliance is one of the important criteria in diabetic patients, especially in terms of the risk of developing hypoglycemia, in addition to drug use. In addition, high HbA1c value and low prealbumin value may be a guide in the detection of hypoglycemic episodes.

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Original Article
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Assessments at week 2 and 3 in Term Newborns Diagnoses with Prolonged Jaundice

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Abstract

Introduction: Jaundice is one of the most common problems at neonatal period and seen in 60-70% of all newborns at first days of life. Prolonged jaundice is defined as hyperbilirubinemia persisting at the end of week 2 in term newborns.

In this study, we reviewed term newborns diagnosed with prolonged jaundice. It was aimed to demonstrate delaying laboratory evaluations for a week in infants with favorable clinical presentation can prevent unnecessary tests in majority of newborns.

Materials and Methods: The study included full-term newborns who presented after day 14 of life and diagnosed with prolonged jaundice at neonatology outpatient clinic of Health Sciences University, Keçiören Teaching and Research Hospital in 2016. Overall, 336 infants with prolonged jaundice were screened. The infants with congenital anomaly, those with findings of sepsis or severe infection, those with history of intrauterine infection, those with history of acholic stool and those with no available data were excluded. In 180 patients included, clinical evaluations, bilirubin levels and advanced test results were assessed at baseline and weekly follow-up.

Findings: Of the infants included, 51.7% were boys while 48.3% were girls. The most common blood type was A Rh (+). There was ABO incompatibility alone in 24 infants (14.2%), Rh incompatibility alone in 6 infants (3.5%) and ABO plus Rh incompatibility in 3 infants (1.2%). In 130 infants, total bilirubin was studied on both week 2 and 3. At week 3, total bilirubin value was ≥10 mg/dl in only 36 infants (27.7%) while it was decreased below 10 mg/dL in 94 infants (72.3%). Urinary tract infection (UTI) was detected in 7 of 38 infants with available tests at week 2. Two of 6 infants with UTI had other clinical signs of UTI. Mean total bilirubin value was 17.9 mg/dL in 5 infants. A significant correlation was found between UTI and vomiting, breastfeeding and feeding pattern ($p<0.05$). Congenital hypothyroidism was detected in 6 of 38 infants with available tests at week 2. It was seen that 2 infants had suspected congenital hypothyroidism in neonatal heel prick test and underwent further evaluations while mean total bilirubin value was 17.5 mg/dL at week 2 in remaining 4 infants. Given the vast majority of cases are breast milk jaundice, a novel cut-off value was defined for total bilirubin measurement at week 2 to distinguish the cases in which total bilirubin decreases below 10 mg/dL at week 3.

Conclusion: Although several disorders that may lead prolonged jaundice at neonatal period have been identified, it is well-known that prolonged jaundice can be seen without any pathological condition in majority of infants fed by breast milk. Delaying laboratory evaluations recommended at week for prolonged jaundice is an approach that may prevent unnecessary testing in most infants.

Keywords: Prolonged jaundice, total bilirubin, newborn

Introduction

Jaundice is one of the most common problems at neonatal period, which is seen in 60% of full-term infants and 80% of preterm infants [1]. In newborns, higher number of red blood cells and shorter lifespan of red blood cells are major reasons for increased bilirubin production. Jaundice develops in most newborns as a results of these physiological alterations [2]. In full-term infants, prolonged jaundice is defined as hyperbilirubinemia lasting more than 14 days of life. Majority of prolonged jaundice cases are breast milk jaundice [3]. The diagnostic workshop for etiology include many blood and urine tests. However, there is no consensus on the priority and value of laboratory tests employed in the evaluation for prolonged jaundice. Congenital hypothyroidism is a rare endocrine disorder. It is a serious but treatable cause of prolonged indirect hyperbilirubinemia (IHB). In congenital hyperthyroidism, early diagnosis and timely treatment are highly important for normal development of intelligence. It is included in the neonatal screening program in Turkey. It was reported that development of intelligence is normal when diagnosed and treated within first 4 weeks of life. In addition, prolonged jaundice may be due to urinary tract infection in newborns [4].

In this study, we reviewed term newborns diagnosed with prolonged jaundice. It was aimed to demonstrate delaying laboratory evaluations for a week in infants with favorable clinical presentation can prevent unnecessary tests in majority of newborns.

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Material and Method

This study was approved by Ethics Committee of Health Sciences University, Keçiören Teaching and Research Hospital (approval#12.04.2017/1394). In the study, we reviewed the files of full-term newborns who presented and diagnosed with prolonged jaundice at neonatology outpatient clinic of Health Sciences University, Keçiören Teaching and Research Hospital. The infants with total bilirubin ≥10 mg/dL were considered as prolonged jaundice. We extracted data regarding history, systemic examination and laboratory evaluations from electronic records of 336 infants who were diagnosed as prolonged jaundice between 01.01.2016 ad 31.12.2016. We excluded 81 infants with gestational age of 37 weeks and 75 infants with no available data. In addition, we intended to exclude infants with congenital anomaly, findings of sepsis or severe infection, history of intrauterine infection or history of acholic stool; however, no infant with such clinical conditions were detected.

In 180 patients included, day of presentation, clinical assessments at presentation and during weekly follow-up, bilirubin levels and results of further examinations for etiology were assessed. For each infant included, research data sheet was completed. In all patients, we recorded data regarding age, mode of delivery, birth weight, feeding and vomiting status, maternal age, gravidity, blood types of mother and baby, history of traumatic delivery, feeding characteristics, smelly urine, treatments given for jaundice, ethnicity, weight gain, height, head circumference, presence of cephalic hematoma or ecchymosis, and total bilirubin measurements during weekly follow-up. In 84 infants underwent evaluations for etiology of hyperbilirubinemia, blood type and results of direct Coombs (DC) test, complete blood count, reticulocyte count, urinalysis, urine culture test, thyroid function tests, G6PD and urine glucose chromatography were extracted. Urinary tract infection was diagnosed by ≥ leukocyte per field in urine microscopy and single microorganism growth (>105 CFU/mL) in urine sample collected in a sterile manner. TSH was studied by Abbott Architect I200R immunoassay analyzer using chemiluminescence method. The patients with TSH>10 µIU/ml who were prescribed thyroid hormone replacement were deemed as congenital hypothyroidism. Throughout study period, transcutaneous bilirubin measurements were performed using JM103 Drager jaundice meter which was set to display average of 3 measurements. In all infants evaluated, total bilirubin and direct bilirubin values from venous samples were studied using Abbott Architect I200R immunoassay analyzer at central laboratory. Complete blood count and reticulocyte count were performed using Cell Dyn 3700 hematology analyzer.

Statistical analysis

All statistical analysis were performed using IBM SPSS version 23.0. Descriptive statistics are presented as count and percent for categorical variables whereas standard deviation, median, and minimum-maximum for continuous variables. The categorical variables were analyzed using Chi-square test. The normal distribution was tested continuous variables and the differences between groups were analyzed using Mann-Whitney U test. ROC analysis was performed too identify a novel cut-off point for total bilirubin measurement in the diagnosis of prolonged jaundice. A p value≤0.05 was considered as statistically significant.

Findings

The study included 180 full-term newborns diagnosed with prolonged jaundice. Mean birth weight was 3260±385.9 g while mean birth height was 49.7±1.9 cm. Mean maternal age was 27.5±5.4 years ranging from 17 to 42 years. Mean age at presentation was 18.2±4.2 days ranging from 14 to 39 days.

Of the infants included, 51.7% were boys while 48.3% were girls. When mode of delivery was assessed, it was found that 57.2% of infants were born via normal spontaneous vaginal delivery while 38.3% was first pregnancy. When blood types were assessed, it was found that the most common blood type A Rh (+) in both mothers and infants while there was ABO incompatibility alone in 24 infants (14.2%), Rh incompatibility alone in 6 infants (3.5%) and ABO plus Rh incompatibility in 3 infants (1.2%). None of the infants had history of traumatic delivery. Table 1 presents demographic characteristics.

It was found that there was poor feeding in 4 infants (2.2%), vomiting in 8 infants (4.4%), failure to gain weight in 13 (7.2%) and foul odor in urine in 1 infant (0.6%). It was seen that 27 of infants (15%) underwent phototherapy.

When distribution of total bilirubin values were assessed, there were 159 infants with total bilirubin≥10 mg/dL in week 2 (day 14-20). The first presentation to hospital was at week 3 or later in remaining 21 infants. OF these, first total bilirubin measurement was performed at week 3 in 13 infants and at week 4 in 8 infants.

In 130 infants, total bilirubin was studied on both week 2 and 3. At week 3, total bilirubin value was ≥10 mg/dl in only 36 infants (27.7%) while it was decreased below 10 mg/dL in 94 infants (72.3%). This result was important since the study aimed to assess whether laboratory tests can be delayed one week by assessing full-term newborns with prolonged jaundice at weeks 2 and 3.

Table 2 presents that there was no significant differences in parameters evaluated between infants with total bilirubin <10 mg/dL and those with total bilirubin >10 mg/dL at week 3 or later (Chi-square test, p>0.05).

Table 1: Presents demographic characteristics

Birth weight (g)	3260.3 ±385.9		3210	(2350-4285)
Maternal age (years)	27.5 ±5.4			27 (17-42)
Age at presentation (days)	18.2 ±4.2			17 (14-39)
Height (cm)	49.75 ±1.9			50 (45-57)
Head circumference (cm)	35.9 ±1.5			36 (33-47)
		n		
Gender	Female	87		48.3
	Malle	93		51.7
Mode of delivery	NSVD	103		57.2
	C/S	77		42.8
Pregnancy order	First pregnancy	69		38.3
	Subsequent pregnancy	111		61.7
Maternal blood type	A+	71		41.5
	A-	3		1.8
	B+	32		18.7
	B-	1		.6
	0+	43		25.1
	0-	8		4.7
	AB+	11		6.4
	AB-	2		1.2
Infant blood type	A+	83		48.3
	A-	4		2.3
	B+	25		14.5
	B-	4		2.3
	0+	40		23.3
	0-	4		2.3
	AB+	10		5.8
	AB-	2		1.2
Incompatibility	Yok	136		80.5
	AB0	24		14.2
	Rh	6		3.5
	ABO+Rh	3		1.2
Ethnicity	Turkey	173		96.1
	Foreign national	7		3.9

Table 2: Comparison of some clinical findings between infants with total bilirubin<10 mg/dL and >10 mg/dL at week 3 or later

		Tbil>10		Tbil<10		
		Count (n)	*Percent (%)*	*Count (n)*	*Percent (%)*	*p value*
Gender	Female	49	52.1	21	42.9	0.293
	Male	45	47.9	28	57.1	
Mode of delivery	SVD	53	56.4	30	61.2	0.578
	C/S	41	43.6	19	38.8	
Feeding	Good	94	100.0	48	98.0	0.343
	Poor	0	0.0	1	2w.0	
Vomiting	No	91	96.8	48	98.0	0.576
	Yes	3	3.2	1	2.0	
Pregnancy	First pregnancy	35	37.2	18	36.7	0.953
order	Subsequent pregnancy	59	62.8	31	63.3	
Incompatibility	No	67	77.0	41	87.2	0.170
	AB0	18	20.7	4	8.5	
	Rh	2	2.3	2	4.3	
Feeding pattern	Breast milk	70	74.5	41	83.7	0.339
	Formula	1	1.1	1	2.0	
	Mixed	23	24.5	7	14.3	
Drugs used	None	26	27.7	14	28.6	0.908
	Vitamin D	68	72.3	35	71.4	
Smell in urine	No	94	100.0	49	100.0	-
	Foul odor	0	0.0	0	0.0	
Weight gain	No	5	5.3	6	12.2	0.140
	Yes	89	94.7	43	87.8	
Phototherapy	No	78	83.0	43	87.8	0.452
	Yes	16	17.0	6	12.2	
Ethinicity	Turkey	88	93.6	48	98.0	0.240
	Foreing national	6	6.4	1	2.0	

Table 3 presents some continuous variables and differences between groups. The continuous variables showed skewed distribution in Kolmogorov-Smirnov test; thus, descriptive statistics are presented as median and minimum-maximum. The groups were compared using Mann Whitney U test. No significant difference was found in parameters evaluated between groups ($p>0.05$).

Table 3: Comparison of some descriptive characteristics between infants with total bilirubin<10 mg/dL and >10 mg/dL at week 3 or later

		Tbil<10		Tbil>10	
	Mean ±Standard deviation	Median (Min-Max.)	Mean. ±Standard deviation	Median (Min-Max)	p value
Birth weight (g)	3275.0 ± 389.1	3265 (2400-4285)	3242.7 ± 369.8	3200 (2470 - 4000)	0.743
Maternal age	27.3 ± 5.6	27 (17 - 40)	27.4 ± 5.4	27 (19 - 42)	0.917
Height (cm)	49.7 ± 1.7	50 (46 - 57)	49.8 ± 1.9	50 (46 - 57)	0.887
Head circumference (cm)	35.9 ± 1.2	36 (33 - 40)	35.8 ± 2.0	36 (33 - 47)	0.456

The prolonged jaundice was diagnosed at the end of week 2 in 88.3% whereas at the end of week 3 in 7.2% and at the end week 4 in 4.4% of infants. In all infants diagnosed on days 21-27 and 28-34, laboratory evaluations were started within same week; however, of the infants diagnosed on days 14-20, laboratory evaluations were started within same week in 23.9% (n=38), on days 21-28 in 11.3% (n=18) and on days 28-35 in 4.4% (n=7).

In our study, it was found that total bilirubin decreased below 10 mg/dL in 94 of 159 infants diagnosed at week 2 while it was above 10 mg/dL in 36 infants. When timing of laboratory evaluations was assessed, it was found that total bilirubin was above 10 mg/dL in 5 of 96 infants without any laboratory evaluation while in 12 of 38 infants who underwent laboratory evaluations at week 2, 17 of 18 infants who underwent laboratory evaluations at week 3 and 2 of 7 infants who underwent laboratory evaluations at week 4.

Regardless of time of diagnosis, feeding was considered as good in all infants who underwent no laboratory evaluation. In 3 infants with vomiting, no laboratory test was performed as they had good feeding and adequate weight gain. UTI was detected in 7 of 38 infants who underwent laboratory evaluations at week 2, 5 of 31 infants who underwent laboratory evaluations at week 3 and 3 of 15 infants who underwent laboratory evaluations at week 4. It was found that there was vomiting in 3 and poor feeding in 2 infants who underwent laboratory evaluations at week 2; all of which were diagnosed with UTI. It was found that there was failure to gain weight in 6 infants who underwent laboratory evaluations at week; UTI was detected in one while congenital hypothyroidism in one of these infants. It was found that there was failure to gain weight in 3 infants who underwent laboratory evaluations at week 3, all of which were diagnosed with UTI. Again, it was found that there was poor feeding in 2 and vomiting in another 2 infants who underwent laboratory evaluations at week 4, all of which were diagnosed with UTI.

It was found that TSH was 5-10 µIU/mL in 1 and >10 µIU/mL in 6 of 38 infants who underwent laboratory evaluations at week 2 while it was >10 µIU/mL in 1 of 31 infants who underwent laboratory evaluations at week 3. It was found that hemoglobin was 15.22 g/dL in infants who underwent laboratory evaluations at week 2 whereas 14.63 g/dL in infants who underwent laboratory evaluations at week 3 and 12.43 g/dL in infants who underwent laboratory evaluations at week 4. Mean reticulocyte count was higher in 15 infants who underwent laboratory evaluations at week 4 when compared to infants who underwent laboratory evaluations earlier. DC test was found to be negative in all infants. Again, urine glucose chromatography and G6PD level were found to be normal in all infants.

In 6 infants with TSH>10 µIU/mL in , mean T4 was 0.85 ng/dL while mean hemoglobin was 16.33 g/dL and mean reticulocyte count was 0.73. In these infants, mean total bilirubin was 14.6 mg/dL (range: 10.0 -19.9 mg/dL) at week 2. It was seen that 2 infants (total bilirubin: 10 mg/dL and 13 mg/dL, respectively) had suspected congenital hypothyroidism in neonatal heel prick test and underwent further evaluations. In remaining 4 infants, mean total bilirubin was 17.5 mg/dL (Range: 16.4-19.9 mg/dL).

In one infant with total bilirubin of 12 mg/dL, control tests were performed as TSH was 5.6 µIU/ml. In the control tests, it was found that TSH decreased below 5.0 µIU/ml; thus, congenital hypothyroidism was excluded.

It was found vomiting was present in 35.7% of infants diagnosed with UTI while no vomiting was observed in infants without UTI. Again, it was found that feeding was good in all infants without UTI, the rate was 71.4% in infants with UTI. When feeding pattern was assessed, it was seen that formula feeding or combined feeding was more common in infants diagnosed with UTI when compared to those without UTI. No significant correlation was detected between UTI and hemoglobin values (Mann Whitney U: 396.500; p=0.452).

Of 38 infants who underwent laboratory evaluations at week, no UTI was detected in 28 while UTI was detected in 7. Mean total bilirubin was 14.3 mg/dL in infants with UTI while it was 16.5 mg/dL in infants without UTI but the difference did not reach statistical significance (p>0.05).

These results provide important data since in our study, it was aimed to reduce test burden, costs and parental anxiety by delaying laboratory evaluations one week in infants without risk factor. In addition, establishing a novel cut-off value will help to distinguish cases with normal laboratory evaluations in which total bilirubin value decrease below 10 mg/dL since majority of the cases have breast milk jaundice.

ROC analysis was performed to determine a novel cut-off value for total bilirubin measurements at week 2. It was aimed to discriminate infants with prolonged jaundice at week 3 more effectively at week 2.

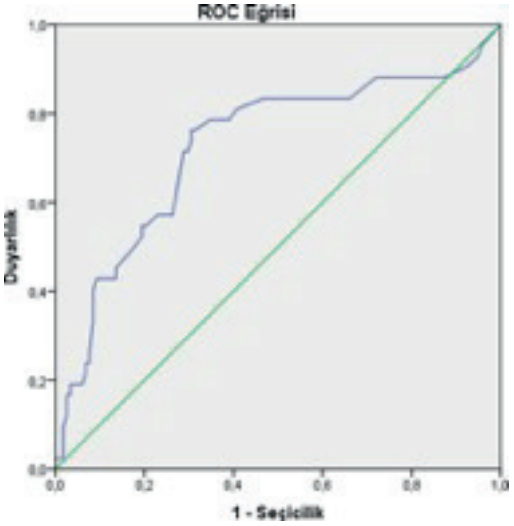

Figure 1: ROC analysis of total bilirubin level on days 14-20. The area under curve (AUC) was estimated as 0.725; the sensitivity and discriminative value were estimated as 0.76 and 0.70, respectively. Diagnostic value was found to be significant for bilirubin (p<0.05).

Discussion

Jaundice is one of the most common problems at neonatal period, which is seen in 60% of full-term infants and 80% of preterm infants [1]. It affect 2-15% of all infants and 40% of breastfed infants [4]. Vast majority of prolonged jaundice are breast milk jaundice. However, the question "Are infants undergoing substantial tests" have been brought in mind in recent years since laboratory evaluations recommended for etiologic evaluation of prolonged jaundice include many blood tests and urinalysis [3].

In this study, we reviewed full-term neonatal infants and aimed to demonstrate delaying laboratory evaluations for a week in infants with favorable clinical presentation can prevent unnecessary tests in majority of newborns.

The finding that, of 130 infants with total bilirubin measurement at both week 2 and 3, total bilirubin value was ≥10 mg/dl in only 36 infants (27.7%) while it was decreased below 10 mg/dL in 94 infants (72.3%) at week 3 is highly supportive for our hypothesis. In a prospective study including 183 full-term infants with prolonged jaundice, Tyrell et al. assessed the infants on day 14 and 21 and found that laboratory evaluations were normal in 79 infants (43.2%) at week 2 and that no infant had jaundice at week 3 [5]. In a study including 154 infants with prolonged jaundice, Hannam et al. found no pathology in 145 infants (95%) [6]. Authors concluded that number of tests can be safely minimized in infants with prolonged jaundice by a comprehensive clinical assessment. However, no further comprehensive study has been performed. In a study including 154 infants with prolonged jaundice, Cetinkaya et al. found that all laboratory evaluations were normal in 81 infants (%53), indicating prolonged jaundice due to breast milk. Authors found that mean bilirubin value was lower in the group with breast milk-associated prolonged jaundice when compared to other groups (due to UTI, hemolytic causes, hypothyroidism) [7].

In a study, Koc et al. evaluated 94 infants with prolonged jaundice. No etiology was detected in 55 infants (56.7%) and total bilirubin value returned normal during follow-up [8]. In a study by Tekinalp et al., breast milk jaundice was identified as the cause of prolonged jaundice in 76.8% of cases [9]. In our study, of 180 infants with prolonged jaundice, UTI was detected in 15 (8.3%) and hypothyroidism in 7 (3.9 while no etiology was detected in 158 infants (87%) and prolonged jaundice was attributed to breast milk jaundice.

In our study, we reviewed 180 infants with prolonged jaundice including 87 girls (48.3%) and 93 boys (51.7%). Male: female ratio was found as 1.1. Several authors have reported that male gender is a risk factor for IHB [10.11]. In the prospective study by Cetinkaya et al., male: female ratio was found as 1.4 in 154 infants with prolonged jaundice [7]. Our results are in agreement with literature.

When age at presentation was assessed, it was found that 88% of infants were diagnosed on days 14-20. This emphasizes the importance of the assessment for prolonged jaundice at week 2. When the infants were assessed by birth weight, mean birth weight was 3260 ±385.9 g (range: 2350-4285 g). Since only infants with gestational age ≥37 weeks, there was no infant with low birth weight. However, Osborn and Frisberg suggested a close association between low birth weight and jaundice [12, 13]. In our study, ABO incompatibility was detected in 14.2% while Rh incompatibility in 3.5%. ABO incompatibility was found in 13.4% by Cetinkaya et al. and 19% by Tuygun et al. [7, 14]. In our study, total rate of Rh incompatibility was detected as 4.7% including 3.5% of cases with Rh incompatibility alone and 1.2% of cases in combination with ABO incompatibility. This rate was reported as 3.8% by Cetinkaya et al. and 3.9% by Tuygun et al. [7, 14]. Our results are consistent with literature.

Congenital hypothyroidism is a rare endocrine disorder (1:3000-1:4000). It is a serious but treatable cause of prolonged indirect hyperbilirubinemia (IHB). In congenital hyperthyroidism, early diagnosis and timely treatment are highly important for normal development of intelligence [1].

In our study, congenital hypothyroidism was detected in 7 infants; 6 of which was diagnosed at week 2. Of the infants diagnosed at week 2, 2 had suspected screening in neonatal heel prick test. It is striking that remaining 4 infants had high total bilirubin levels ranging from 16.4 to 19.9 mg/dL in the assessment at week 2. In their study, Araz et al. evaluated 80 infants with total bilirubin level >5 mg/dL for congenital hypothyroidism and found hypothyroidism in 5 infants (6.3%) [15]. In a study by Siklar et al. hypothyroidism was detected in 6 (5%) of 110 infants with prolonged jaundice [16]. Our results are in agreement with literature.

In congenital hypothyroidism, early diagnosis and timely

treatment are highly important for normal development of intelligence. It was reported that development of intelligence is normal when diagnosed and treated within first 4 weeks of life. In Turkey, congenital hypothyroidism was added to National Screening Program in 2006, allowing early diagnosis in infants. Although prolonged jaundice is an important clue alarming the clinicians for early diagnosis of congenital hypothyroidism, total bilirubin level was significantly higher in infants diagnosed with congenital hypothyroidism in our study. Given that, we think that delaying laboratory evaluation for one week will not lead delay diagnosis in infants with good clinical presentation.

In newborns, prolonged jaundice can develop due to urinary tract infection. Failure to gain weight, irregular body temperature, difficulties in feeding, irritability, vomiting, abdominal distention and foul odor in urine are alarming for UTI [17].

In a study, Tuygun et al. assessed 231 full-term infant with prolonged jaundice and found UTI in 17 infants (7.4%). It was found that there were one or more clinical signs of UTI (fever, vomiting, irritability, anemia etc.) 11 infants with UTI [14]. Littlewood reviewed 66 infants with UTI for jaundice and noted that other clinical signs of UTI were present in all cases with jaundice [18].

In our study, UTI was detected in 15 (8.3%) of 180 infants diagnosed with prolonged jaundice. When 7 infants diagnosed at week 2 were assessed, the presence of failure to gain weight and vomiting in two infants with total bilirubin of 12 mg/dL was alarming for UTI. The presence of vomiting, poor feeding and formula feeding or mixed feeding pattern showed significant difference between infants with and without UTI. It was found that mean total bilirubin was 15.5 mg/dl in 4 infants without any symptom other than jaundice. In a study including 121 infants with prolonged jaundice, Okten et al. found that all infants with UTI were in the group with total bilirubin level of 12 mg/dL [19]. All findings suggest that infants with UTI can be selected among infants diagnosed with prolonged jaundice at week 2 by a detailed clinical assessment including questioning UTI symptoms, weight gain and total bilirubin measurement; proposing an appropriate approach to prevent performing laboratory evaluations in all infants with prolonged jaundice.

In a prospective study including 121 infants with prolonged jaundice, Okten et al. assigned infants into two groups: infants with total bilirubin<12 mg/dL and those with total bilirubin>12 mg/dL. A potential cause of jaundice was detected in 79% of infants with total bilirubin>12 mg/dL and in 32% of infants with total bilirubin<12 mg/dL, indicating a significant difference. It was shown that there was prematurity and/or low birth weight in 45%, ABO incompatibility in 30%, Rh incompatibility in 3.7%, and subgroup incompatibility in 22% of the infants with low total bilirubin level. In this group, no infant was diagnosed with UTI, congenital hypothyroidism or sepsis. No etiology was detected in 67.1% of infants and jaundice was attributed to breast milk [19]. The findings reported by Okten et al. support reliability of cut-off value determined in our study.

In our study, it was found that infants with total bilirubin >15 mg/dL who were diagnosed with prolonged jaundice at week 2 can have UTI and hypothyroidism; thus, laboratory evaluations can be performed at week 2 by questioning in details regarding UTI and hypothyroidism. Although several disorders that may lead prolonged jaundice at neonatal period have been identified, it is well-known that prolonged jaundice can be seen without any pathological condition in majority of infants fed by breast milk [20]. It was found that total bilirubin was >12.65 mg/dL at week 2 in infants in which total bilirubin level persisted above 10 mg/dL at week 3. It may be an appropriate approach to perform laboratory evaluations for prolonged jaundice in infants with total bilirubin>12.65 mg/dL.

In conclusion, Although several disorders that may lead prolonged jaundice at neonatal period have been identified, it is well-known that prolonged jaundice can be seen without any pathological condition in majority of infants fed by breast milk. In newborns, prolonged jaundice can be due to a severe underlying etiology including urinary tract infection, congenital hypothyroidism or biliary atresia; however, this approach does not delay diagnosis or treatment. Delaying laboratory evaluations recommended at week for prolonged jaundice in infants considered as well clinically is an approach that may prevent unnecessary testing in most infants.

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Original Article
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Comparison of Characteristics and Performances of Emergency Medicine Journals Published in Turkey: Where Do We Stand?

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Abstract

Background: To our knowledge, the performances of Emergency Medicine (EM) journals have not been investigated in terms of contribution to scientific literature. This study, Aimed to reveal the characteristics of EM journals and compare them in terms of their qualitative and quantitative features.

Material and Method: Conducteda hand-searching on the websites of 8 EM journals. Also categorized the articles published in these journals into subgroups in terms of relevance to trauma and disaster medicine, cardiovascular and cardiology emergencies, pulmonary emergencies, toxicology, COVID-19, surgical emergencies, internal medicine/gastroenterological emergencies, medical treatment and marker studies, resuscitation and airway management, infectious diseases, sedation and analgesia, imaging, neurological emergencies, forensic medicine, epidemiological and statistical studies, hospital and emergency department management, intensive care and mechanical ventilation, prehospital care, experimental studies, elective surgery and surgical complications. The journals were also compared according to their contribution to COVID-19 literature.

Result: Among 8 journals, only Ulus Travma Acil Cerrahi Derg is indexed in SCI-E. The top 3 journals according to the number of published articles and citations were as follows: Ulus Travma (1792 articles, 7834 citations), EAJEM (784 articles, 822 citations) and TJEM (646 articles, 3146 citations). Mean citation per article was the highest in TJEM (n=4.87) followed by Ulus Travma Acil Cerrahi Derg (n=4.37) and EAJEM (n=1,05). Ulus Travma Acil Cerrahi Derg has the highest H index (n=25).

Conclusion: Academic development of EM is strongly linked to the performance of EM journals. The quality, amount and number of grant-supported research should increase in EM.

Keywords: Emergency Medicine Journals, publications, citations, COVID-19.

Introduction

Governments, funding agencies and promotion committees, and academic institutions are increasingly interested in measuring the research quality and productivity of individual scientists as an indication of their scholarly excellence. Citation rating using data from the Institute for Scientific Information (ISI), owned by the Thomson Corporation of Toronto, is now a popular method to evaluate the impact on the scientific community of individual scientists and research institutions. The argument is that the greater the value of the article, the more times it will be cited, and that the citation number is thus viewed as a direct measure of the recognition that this publication has had in its scientific field (1). Although there is obviously considerable debate regarding the value of citation rates, the analysis of citation rates may give an encyclopedic review of citation frequency and key areas of scientific interest. Emergency Medicine (EM) has undergone substantial developments in the past few decades and is now evolving at a rapid pace. However, a systemic analysis of top-cited articles in the field of EM is not yet available (2).

Emergency medicine (EM) is a relatively young but rapidly developing field. Emergency Medicine journals play a significant role in the increase in the number of EM scientific studies. In order to achieve this goal, academic performance and the growing impact of these journals must enhance. In concordance, the quality and quantity of EM scientific studies have increased substantially in the past (2).

The Emergency Medicine Residency Programme was first initiated at Cincinnati University in 1972 (1). In Turkey, with the efforts of Prof Dr Namık Çevik, who was the rector of 9 Eylül University, Emergency Medicine took its place as a separate discipline in the speciality charter on April 30th, 1993. Subsequently, in 1994, Emergency Medicine Department was founded at 9 Eylül University and began to receive its first students (2).

The Emergency Medicine Association of Turkey was established by Dr John Fowler in 1995. In 2001, the Turkish Journal of Emergency Medicine started its publication life

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(1). In this article, our aim was to evaluate and compare the quality and scientific performance of 8 journals associated with EM published in Turkey.

Materials and Methods

For this study, have reviewed emergency medicine journals published in Turkey since 1995. Emergency Medicine Journals published in Turkey were selected from the official site of Scopus© and the official sites of Emergency Medicine Associations. A total of 8 journals were determined. These journals were the Turkish Journal of Emergency Medicine (TJEM), Eurasian Journal of Emergency Medicine (EAJEM), Journal of Emergency Medicine Case Reports (J Emerg Med Case Rep), Anatolian Journal of Emergency Medicine (Anatolian J Emerg Med), Eurasian Journal of Critical Care (Eurasian J Crit Care), Eurasian Journal of Toxicology (Eurasian J Tox), Global Emergency and Critical Care (Glob Emerg Crit Care) and Turkish Journal of Trauma and Emergency Surgery (Ulus Travma Acil Cerrahi Derg). The information about the journals, (foundation date, publication frequency, language, publication type, affiliated international publisher, indexing and abstracting, cite score, publication policy, etc..) was obtained from their official sites. Categorized the articles published in these journals into subgroups in terms of relevance to trauma and disaster medicine, cardiovascular emergencies, pulmonary emergencies, toxicology, COVID-19, cardiology emergencies, surgical emergencies, internal medicine/gastroenterological emergencies, medical treatment and marker studies, resuscitation and airway management, infectious diseases, sedation and analgesia, imaging, neurological emergencies, forensic medicine, epidemiological and statistical studies, hospital and emergency department management, intensive care and mechanical ventilation, prehospital care, experimental studies, elective surgery and surgical complications. The journals were compared according to the subjects of the articles.

Also separately investigated articles on COVID-19 in Turkey and made a comparison with the Emergency Medicine Journals in the World in order to reveal where we stand regarding contribution to COVID-19 literature.

All data were entered into Excel© Programme and given as numbers and percentages. Ethical approval was not required due to the nature of the study.

Results

According to self-findings, the first published journal in Turkey was Ulus Travma Acil Cerrahi Derg (1995) followed by TJEM (first issue in 2000) and EAJEM (published in 2003 as Academic Emergency Medicine Journal). When the number of published articles and citation numbers in Web of Science were investigated, it was determined that Ulus Travma Acil Cerrahi Derg has published 1792 articles with a citation count of 7834 and EAJEM has published 784 articles with a citation count of 822. While 646 articles were published in TJEM, the citation count number was 3146. Mean citation per article was the highest in TJEM (n=4.87) followed by Ulus Travma Acil Cerrahi Derg (n=4.37) and EAJEM (n=1,05). Ulus Travma Acil Cerrahi Derg has the highest H index (n=25). Nevertheless, TJEM has the highest cites core (n=7) and JCI (n=0.93). While Ulus Travma Acil Cerrahi Derg was the only journal indexed in Science Citation Index Expanded (SCI-E), TJEM, EAJEM and JEMCR were indexed in Emerging Source Citation Index (ESCI). Characteristics of the journals are summarized in Table 1.

When articles published in the journals were investigated according to subjects, it was determined that the greatest proportion of articles published in TJEM was related to toxicology (n=21, 11.1%), in EACEM to trauma (n=25, 12.7%), in J Emerg Med Case Rep to surgical emergencies (n=29, 17.8%), in Anatolian J Emerg Med to Hospital and Emergency Department Management (n=21, 16.3%), in Eurasian J Crit Care to surgical emergencies (n=18, 16.8%), in Eurasian J Tox to toxicology (n=66, 93%), in Glob Emerg Crit Care to COVID-19 (n=4, 33.3%) and in Ulus Travma Acil Cerrahi Derg to trauma and disaster medicine (n=279, 38.9%). The most popular topics were trauma, toxicology and surgical emergencies. The distribution of the subjects of the articles in each journal is summarized in Table 2.

When journals were investigated in terms of COVID-19 publications, it was determined that Ulus Travma Acil Cerrahi Derg has published the greatest number of COVID-19 articles when compared to other journals (n=33), followed by EAJEM (n=16). When COVID-19 proportion to other articles in each journal was investigated, Glob Emerg Crit Care was on top of the list (33.3%). The proportion of COVID-19 articles is presented in Table 3.

Discussion

Citation is described as a reference to a published or unpublished source. Citation analysis is the examination of the frequency, patterns, and graphs of citations in articles and other text. It is a fact that scientifically important articles are cited more frequently. The impact of an article on its scientific field is generally measured by the number of citations since it is the only quantifiable parameter (3,4). When number of publications in Web of Science and citefactors of the articles published in EM journals in Turkey were determined, Ulus Travma Acil Cerrahi Derg had the highest number of publications in Web of Science. The reason why researchers prefer Ulus Travma Acil Cerrahi Derg is that it is indexed in SCI-E and Pubmed. In addition, new metric systems such

Table 1: Characteristics of the Emergency Medicine journal published in Turkey

	Ulus Travma Acil Cerrahi Derg	***TJEM***	***EAJEM***	***J Emerg Med Case Rep***	***Anatolian J Emerg Medicine***	***Eurasian J Crit Care***	***Eurasian J Tox***	***Glob Emerg Crit Care***
First Publication Year	1995	2000	2003	2010	2018	2019	2019	2022
Affiliation	TATES	EMAT	EPAT	EPAT	EMAT	EPAT	EPAT	TEMF
Publication Frequency Per Year	12	4	4	4	4	3	3	3
Publisher	Kare Yayıncılık	Wolters Kluwer - Medknow Publications Wolters Kluwer India Pvt. Ltd	Glenos Yayınevi	DergiPark	DergiPark	DergiPark	DergiPark	Glenos Yayınevi
Indexing and Abstracting	SCI-E, PubMed, Euro PMC, Scopus, ProQuest, EMBASE, CINAHL, TRDizin, Journal Citation Reports, Index Medicus	ESCI, Scopus, PubMed, EBSO, SCImago, TRDizin, Google Scholer, DOAJ, Science Direct, Türkiye Atıf Dizini	ESCI, EBSO, Index Copernicus, Gale, J-Gate, DOAJ, TRDizin, DRJI, HINARI, ProQuest, AGORA, Türkiye Atıf Dizini	ESCI	Google Scholer, ASOS Index, Türkiye Atıf Dizini, SIS, TRDizin, EuroPub	EuroPub, SIS, DRJI, Türkiye Atıf Dizini, ASOS Index	SIS, DRJI, EuroPub, Google Scholer, ASOS Index	J-Gate, Gale
CiteScore (SCOPUS)	1.40	7.00	-	-	-	-	-	-
Journal Impact Factor(2021)	0,929	-	-	-	-	-	-	-
Journal Citation Indicator (2021)	0,40	0,93	0,07	0,01	-	-	-	-
CiteScore Category Rank (Emergency Medicine)(2021)	44 (90)	5 (90)	-	-	-	-	-	-
Publication (Web of Science)	1792	646	784	524	0	0	0	0
Citing Articles (Web of Science)	7834	3146	822	178	0	0	0	0
Without Self-Citations (Web of Science)	7249	3076	736	155	0	0	0	0
Average Citation Per Article (Web of Science)	4.37	4.87	1.05	0.34	0	0	0	0
H-Index (Web of Science)	25	16	10	4	-	-	-	-
Time to Final Decision (week)	3.20	-	-	-	-	-	-	-

Ulus Travma Acil Cerrahi Derg: Turkish Journal of Trauma and Emergency Surgery TJEM: Turkish Journal of Emergency Medicine, **EAJEM:** Eurasian Journal of Emergency Medicine, **J Emerg Med Case Rep:** Journal of Emergency Medicine Case Reports, **Anatolian J Emerg Medicine:** Anatolian Journal of Emergency Medicine, **Eurasian J Crit Care:** Eurasian Journal of Critical Care, **Eurasian J Tox:** Eurasian Journal of Toxicology, **Glob Emerg Crit Care:** Global Emergency and Critical Care **TATES:** Turkish Association of Trauma and Emergency Surgery **EMAT:** Emergency Medicine Assosiation of Turkey **EPAT:** Emergency Medicine Physicians Association of Turkey **TEMF:** Turkish Emergency Medicine Foundation **SCI-E:** Science Citation Index Expended EURO PMC: Euro PubMed Central **EMBASE:** Excerpta Medica Database **CINAHL:** Cumulative Index to Nursing and Allied Health Literature ESCI: Emerging Science Citation Index **DOAJ:** Directory of Open Access Journals **DRJI:** The Directory of Research Journal Indexing **HINARI:** Health Inter-Network Access to Research Initiative **ASOS Index:** Akademik Sosyal Bilimler indeksi **SIS:** Science Indexing Service

as Almetric have emerged as an alternative to traditional citation systems in recent years (5). These systems are also used by Elsevier, including platforms such as Scopus and Mendeley (6). These metric systems aim to demonstrate the scientific implications of published papers. (7). TJEM had the highest Journal Citation Indicator among these journals (n=0.93). Although TJEM is not indexed as SCI, one of the reasons why it has the highest citation index may be that it is indexed on platforms such as Scopus.

Yang Liang et al. In a study that examined the Impact Factors of emergency medicine journals between 2005 and 2014, we see that only Ulus Travma Acil Cerrahi Derg from

Table 2: Distribution of main topics in journals

	Ulus Travma Acil Cerrahi Derg	*TJEM*	*EAJEM*	*J Emerg Med Case Rep*	*Anatolian J Emerg Medicine*	*Eurasian J Crit Care*	*Eurasian J Tox*	*Glob Emerg Crit Care*
Trauma and Disaster Medicine (n, %)	**279 (38.9)**	11 (5.7)	**25 (12.7)**	28 (17.1)	14 (10.9)	14 (15.9)		1 (8.3)
Cardiology and Cardiovascular Emergencies (n, %)	3 (0.4)	15 (7.9)	15 (7.6)	14 (8.6)	12 (9.3)	6 (5.6)	1 (1.4)	1 (8.3)
Pulmonary Emergencies (n, %)		9 (4.7)	8 (4.1)	8 (4.9)	10 (7.8)	12 (11.2)		
Toxicology (n, %)		**21 (11.1)**	12 (6.1)	28 (17.1)	15 (11.6)	8 (7.5)	66 (93.0)	2 (16.7)
COVİD-19 (n, %)	33 (4.6)	10 (5.2)	16 (8.1)	11 (6.7)	8 (6.2)	9 (8.4)		4 (33.3)
Surgical Emergencies (n, %)	164 (22.8)	16 (8.4)	12 (6.1)	**29 (17.8)**	13 (10.1)	**18 (16.8)**		1 (8.3)
İnternal Medicine / Gastroenterological Emergencies (n, %)	22 (3.1)	8 (4.2)	11 (5.6)	17 (10.4)	10 (7.8)	13 (12.1)	1 (1.4)	
Medical Treatment and Marker Studies (n, %)		9 (4.7)	17 (8.6)	1 (0.6)	3 (2.3)	3 (2.8)		1 (8.3)
Resuscitation and Airway Management (n, %)	4 (0.6)	20 (10.5)	9 (4.6)	2 (1.2)		4 (3.7)		1 (8.3)
İnfectious Diseases (n, %)		11 (5.8)	10 (5.1)	6 (3.7)	1 (0.8)	3 (2.8)		1 (8.3)
Sedation and Analgesia (n, %)		10 (5.3)	5 (2.5)					
İmaging (n, %)	11 (1.5)	15 (7.9)	15 (7.6)	6 (3.7)	6 (4.7)	2 (1.9)		
Neurological Emergencies (n, %)		12 (6.3)	9 (4.6)	13 (8.0)	8 (6.2)	11 (10.3)	1 (1.4)	
Forensic Medicine (n, %)	1 (0.1)	1 (0.5)	2 (1.0)					
Epidemiological And Statistical Studies (n, %)	9 (1.3)	6 (3.2)	1 (0.5)		2 (1.6)			
Hospital and Emergency Depertment Management (n, %)		9 (4.7)	24 (12.2)		**21 (16.3)**	2 (1.9)	1 (1.4)	
Intensive Care and Mechanical Ventilation (n, %)	7 (1.0)	6 (3.2)	1 (0.5)			1 (0.9)		
Prehospital Care (n, %)	3 (0.4)	1 (0.5)	4 (2.0)		6 (4.7)			
Experimental Studies (n, %)	98 (13.6)		1 (0.5)			1 (0.9)	1 (1.4)	
Elective surgery and surgical Complications (n, %)	84 (11.7)							
Total	718	190	197	163	129	107	71	12

Ulus Travma Acil Cerrahi Derg: Turkish Journal of trauma and Emergency Surgery **TJEM:** Turkish Journal of Emergency Medicine, **EAJEM:** Eurasian Journal of Emergency Medicine, **J Emerg Med Case Rep:** Journal of Emergency Medicine Case Reports, **Anatolian J Emerg Medicine:** Anatolian Journal of Emergency Medicine, **Eurasian J Crit Care:** Eurasian Journal of Critical Care, **Eurasian J Tox:** Eurasian Journal of Toxicology, **Glob Emerg Crit Care:** Global Emergency and Critical Care

Turkey could be included in this review (8). Despite the lapse of time, the only emergency medicine journal in Turkey still published as SCI-E is Ulus Travma Acil Cerrahi Derg.

It is obvious that when EM journals are not included in SCI-E, the development of EM may be underestimated (9). Since most of the EM journals in Turkey are not included in SCI-E, the contribution of these journals to the literature remains low.

The progress in the academic performance of EM journals has rarely been studied in the past decade. An objective and multiperspective evaluation of the academic performance of EM journals might provide a more complete understanding of the recent evolution of EM scientific studies (9). In a study by Yi-Lun Tsai et el., the primary focus of study in EM was found to be Toxicology, traumatology, resuscitation medicine, and cardiovascular medicine. Additionally, the median citation number for these top-cited articles was 102 (4). In this pioneering study on EM journals in Turkey, in concordance with the literature, we determined that journals particularly focused on trauma, toxicology and surgical emergencies topics.

In a study, the last 30 original studies were investigated in top EM journals. While the US made the greatest contribution (n=158, 47.9%), Australia was in the second row (n=36, 10.9%) and Canada was in the third row (n=17, 6.1%) (10). The success of Turkey in the academic EM field is highly related to the development of EM journals.

Another parameter compared in studies was the contribution of Turkish EM journals to COVID-19 literature.

Table 3: COVID-19 articles in journals

Journal	*Total Articles*	*Total COVID-19 Articles*	*Total COVID-19 Articles/Total Articles*
Ulus Travma Acil Cerrahi Derg	511	33	0,06
TJEM	112	10	0,08
EAJEM	130	16	0,12
J Emerg Med Case Rep	109	11	0,1
Anatolian J Emerg Medicine	82	8	0,09
Eurasian J Crit Care	77	9	0,11
Eurasian J Tox	48	0	0
Glob Emerg Crit Care	12	4	0,33

Ulus Travma Acil Cerrahi Derg: Turkish Journal of trauma and Emergency Surgery **TJEM:** Turkish Journal of Emergency Medicine, **EAJEM:** Eurasian Journal of Emergency Medicine, **J Emerg Med Case Rep:** Journal of Emergency Medicine Case Reports, **Anatolian J Emerg Medicine:** Anatolian Journal of Emergency Medicine, **Eurasian J Crit Care:** Eurasian Journal of Critical Care, **Eurasian J Tox:** Eurasian Journal of Toxicology, **Glob Emerg Crit Care:** Global Emergency and Critical Care

It is known that since the beginning of the COVID-19 outbreak in December 2019, a substantial amount of COVID-19 medical literature has been generated. The publication of research on COVID-19 helped physicians to share knowledge and experience. In a study investigating COVID-19 publications in top EM journals by Erenler et al., The American Journal of Emergency Medicine published the greatest proportion of articles. World Journal of Emergency Surgery had the greatest number of citations per COVID-19 article.

In the mentioned article, Turkey took place in the 15th row in terms of the number of COVID-19 publications (11).

Similarly, in a study that included the most influential COVID-19 articles, Turkey was not among the top 10 countries (12). According to our results, the highest proportion of COVID-19 articles was published in EAJEM. However, the contribution of Turkey to the literature in terms of COVID-19 publications is insufficient. The main reason is already overcrowded Emergency departments in Turkey had challenges dealing with the pandemic and physicians had to focus mainly on patient care instead of scientific research (13).

Conclusion

This study is the pioneering analysis of journals related to EM in Turkey. It was reported that when compared with the US, Europe has a fragmented system and low scientific competition. Also, in Europe, grants are limited and most of the universities need to be modernised. The quality, amount and number of grant-supported research should increase in EM in order to rival academic medicine. The protection of academic time for faculty is needed for the scholarly activity to be successful. Emergency medicine research centres of excellence must continue to develop (10). Our results revealed that Turkey could not get the place it deserved in terms of academic performance in Emergency Medicine. The EM journals published in Turkey focus on the same topics that international journals focus on. However, the demand for publishing their research in SCI-E journals affects the behaviours of EM physicians and hinders the development of EM journals in Turkey.

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Original Article
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Impact of Omalizumab Treatment on Quality of Life and Activity of Chronic Spontaneous Urticaria

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Abstract

Background: Omalizumab treatment has shown promise in managing Chronic spontaneous urticaria (CSU). This study focuses on evaluating its effect on improving the quality of life and reducing CSU activity and severity in patients of different age groups.

Material and Method: Conducted at Derince Training and Research Hospital, this observational study involved 50 CSU patients, categorized into adolescents (≤18years, n=15) and adults (>18years, n=35). Data were collected through clinical and demographic assessments, including Urticaria Activity Score (UAS), Urticaria Control Test (UCT), and Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL) questionnaires, at the beginning and the third month of Omalizumab treatment.

Result: Significant improvements were observed in UAS, UCT, and CU-Q2oL scores post-Omalizumab treatment, indicating reduced symptom severity and enhanced quality of life. The median UAS at the start was 35 (28-35); at the third month, 7 (0-7); median UCT at the start was 2 (1.25-3), at the third month 16 (13-16); median CU-Q2oL at the start was 70.5 (66-74), at the third month 23 (23-28); ($p<0.001$, $p<0.001$, and $p<0.001$, respectively). In adult patients, levels of anti-TPO and anti-TG were significantly higher compared to adolescents with CSU (anti-TPO 28 (0.92-47.4) IU/mL vs. 1.73 (0.79-27.1) IU/mL, $p=0.066$; anti-TG 12.6 (1.4-31.5) IU/mL vs. 1.08 (0.74-9.66) IU/mL, $p=0.007$).

Conclusion: Omalizumab treatment improves the quality of life and reduces disease activity in CSU, demonstrating its efficacy as a therapeutic option for those resistant to antihistamines across all age groups. Further research is warranted to explore the long-term effects of Omalizumab and its potential in personalized CSU management strategies.

Keywords: Omalizumab, Chronic spontaneous urticaria, Urticaria Activity Score, Urticaria Control Test, Chronic Urticaria Quality of Life Questionnaire

Introduction

Chronic spontaneous urticaria (CSU) is a skin condition characterized by recurring, itchy skin lesions and edemas, persisting for at least six weeks. The pathophysiology of CSU still needs to be fully understood, involving a combination of immunological interactions, genetic factors, and environmental triggers.[1,2] Approximately 30-50% of cases are attributed to autoimmune causes. The most common formation of urticaria involves autoantibodies against the alpha chain of the high-affinity IgE receptor (FCεR1α) on the surface of basophils and mast cells. The second and rarer one is the anti-IgE autoantibody against the IgE antibody itself. These IgG-type autoantibodies lead to the activation of basophils and mast cells by binding to FCεR1α or IgE.[2-4]

The Urticaria Activity Score (UAS) is a widely used scoring system for assessing the severity of urticaria symptoms. UAS is based on the intensity of urticaria lesions and itchiness. UAS provides reliable information for both patients and physicians in determining the severity of the disease and assessing the response to treatment. The Urticaria Control Test (UCT) evaluates whether the condition affects the patient's daily activities.[3-7] Improving the quality of life in CSU patients is one of the goals of treatment. Therefore, the Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL) has been translated into Turkish. Using this quality-of-life questionnaire is beneficial in assessing the clinic's effectiveness and treatment efficacy.[8]

Despite treatment options, including antihistamines, corticosteroids, and other immunomodulatory agents, the problem of insufficient symptom control and the emergence of side effects persists in many patients.[9,10] Omalizumab has marked significant progress in managing CSU among monoclonal antibody therapies in recent years. Omalizumab is a monoclonal anti-IgE antibody that exhibits its effect by binding to IgE, reducing the level of IgE, and consequently decreasing the receptors and expressions of IgE on mast

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cells and basophils. Various studies have provided positive findings that Omalizumab reduces symptoms of CSU and enhances quality of life.[11,12] A study by Chang et al. observed a significant reduction in UAS following Omalizumab treatment.[11] Moreover, Tharp et al.'s research examined the impact of Omalizumab on UCT scores, determining that the treatment positively influenced daily life activities.[13] However, some studies have suggested that the impact of Omalizumab on CSU symptoms could vary among patients.[14,15] Further research is needed to determine the specific effects of Omalizumab treatment on UAS and UCT.

This study aims to identify the effects of Omalizumab treatment on urticaria activity, severity, and quality of life in adolescent and adult patients with CSU who are resistant to antihistamine therapy and have started Omalizumab treatment. We evaluated our patients with CSU regarding clinical characteristics and laboratory parameters and analyzed factors affecting antihistamine resistance in these patients. This evaluation provides a more comprehensive understanding of the treatment's clinical efficacy and targets improving the patient's quality of life. Understanding the impact of Omalizumab on UAS and UCT could contribute to developing more effective CSU management strategies.

Material and Methods

This research was conducted at Derince Training and Research Hospital after receiving approval from the local institutional review board (IRB). The study included 50 CSU patients. They were evaluated in two separate groups: 15 adolescents (≤18 years old) and 35 adults (>18 years old). Clinical and demographic data were collected from their medical records. These records included clinical history, urticaria possible etiologic/aggravating factors, Skin Prick Tests (SPT), laboratory tests, and questionnaire assessments (UAS, UCT, and CU-Q2oL) of each patient at the beginning and the third month of Omalizumab treatment. Detailed demographic and clinical features of all CSU patients are shown in **Table 1.**

Statistical analysis: Continuous variables were presented as mean±standard deviation (SD) or median with their 25th-75th percentile. Categorical variables were expressed as numbers and percentages (n, %). We used the Chi-square or Fisher's exact test to compare categorical variables. Non-normal distributed variables were compared with the Mann-Whitney U test. The difference between the two measurements of a dependent group was tested using the Wilcoxon signed-rank test. P-values of less than 0.05 were considered significant. Statistics and visualizations were done with R version 4.3.1 (A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. https://www.R-project.org/.)

Table 1: The demographic and clinical data of CSU patients

Parameters; Mean (SD)	CSU patients (N-50)
Age	38.8 (16.7)
Female/ Male	36 (72.0%)/14 (28.0%)
Clinical follow-up (m)	19.2 (11.6)
Urticaria duration (m)	55.0 (91.5)
Attack frequency	
Every day	39 (78.0%)
Every week	10 (20.0%)
Monthly	1 (2.00%)
ED visit	
Yes	39 (78.0%)
No	11 (22.0%)
Follow-up ED visit	
Yes	10 (20.0%)
No	40 (80.0%)
Lesion disappearance time	
<1 hour	2 (4.00%)
1-24 hours	46 (92.0%)
>24 hours	2 (4.00%)
Angioedema	
Yes	42 (84.0%)
No	8 (16.0%)
Drug - Food	
Yes	23 (46.0%)
No	27 (54.0%)
Stress	
Yes	44 (88.0%)
No	6 (12.0%)
Infection	
Yes	6 (12.0%)
No	44 (88.0%)
Comorbidity	
Yes	14 (28.0%)
No	36 (72.0%)
Additional medication	
Yes	14 (28.0%)
No	36 (72.0%)
Smoking	
Yes	22 (44.0%)
No	28 (56.0%)
SPT result:	
None	28 (56.0%)
HDM positive	8 (16.0%)
Pollen positive	3 (6.00%)
Pollen+HDM positive	1 (2.00%)
Dermographism	4 (8.00%)
Negative	6 (12.0%)

Abbreviations: *CSU: Chronic spontaneous urticaria, M: month, ED: emergency department, SPT: skin prick test, HDM: house dust mite*

Results

The study included a total of 50 patients and assessed them in two separate groups: adolescents (n=15, ≤18 years) and adults (n=35, >18 years). The adolescent group consisted of 73% females and 27% males, with a median age of 18 (17-18 years); the adult group consisted of 71% females and 29%

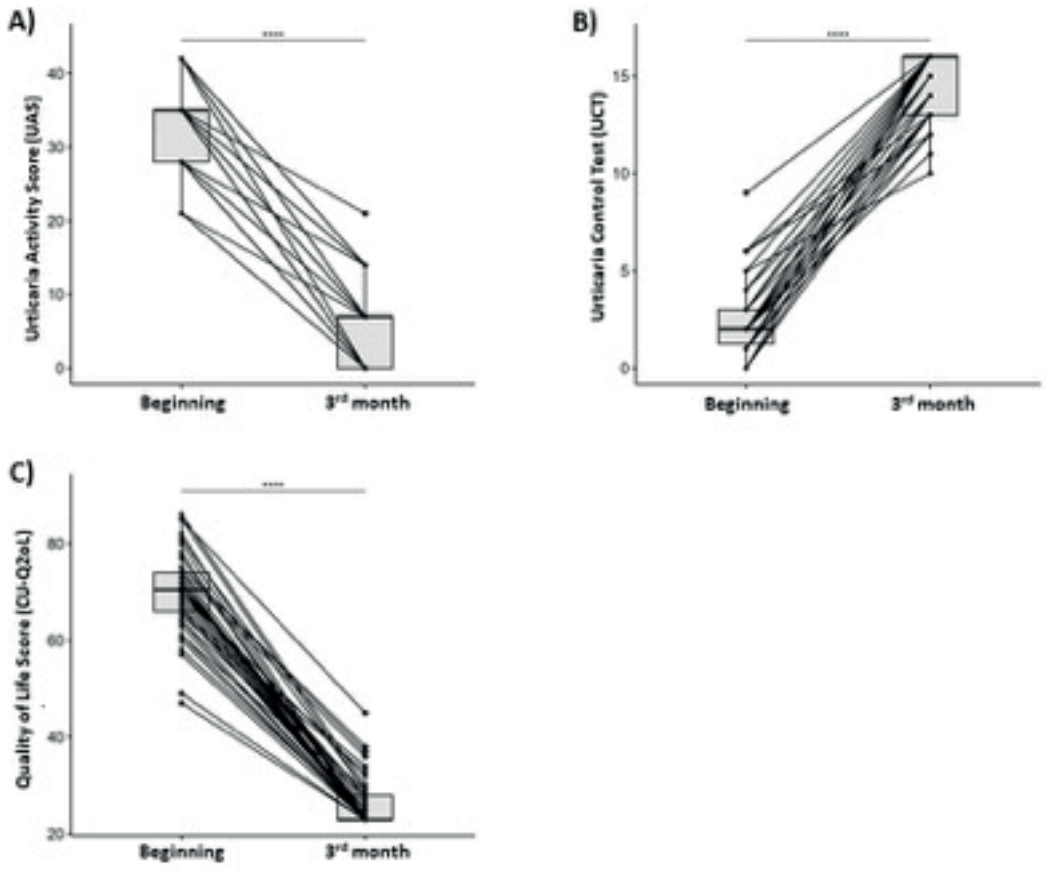

Figure 1: Patients were administered UAS, UCT, and CU-Q2oL questionnaires at the initiation of Omalizumab treatment and the third month of the treatment

males, with a median age of 48 (39.5-57 years). The average clinical follow-up period (19.2±11.6 months, p=0.695) and the duration of urticaria (55±91.5 months, p=0.655) were similar among all patients. The mean duration of Omalizumab treatment for all patients was 12 (±8.6) months **(Table 1).**

Patients were administered UAS, UCT, and CU-Q2oL questionnaires at the initiation of Omalizumab treatment and the third month of the treatment **(Figure 1).** Pre-treatment UAS questionnaire results indicated that 94% of patients had severe urticaria, and 6% had moderate urticaria. Initial UCT questionnaire results showed that all individuals in both groups had poorly controlled disease activity. According to the quality of life questionnaire, 40% were mild to moderately affected, and 60% were severely affected; it was observed that adolescents were more likely to be mild to moderate, while adults were more severely affected (p=0.345). The median UAS at the start was 35 (28-35); at the third month 7 (0-7); the median UCT at the start was 2 (1.25-3); at the third month 16 (13-16); median CU-Q2oL at the start was 70.5 (66-74), at the third month 23 (23-28); ($p<0.001$, $p<0.001$, and $p<0.001$, respectively).

Adult patients had a higher frequency of attacks before Omalizumab treatment compared to adolescents (n=28, 71.8% daily; n=6, 60% weekly vs. n=11, 28.2% daily; n=4, 40% weekly, respectively, p=0.629), but this was not statistically significant. Adults constituted 70% of emergency department visits. The number of pre-treatment emergency department visits (adults median n=4 (3-10), adolescents median n=5 (3-10), p=0.730) decreased during the follow-up (adults average n=3 (1.5-3), adolescents average n=1 (1-3), p=0.721) in both groups, but was not statistically significant. Most patients experienced lesion disappearance within 1-24 hours (p=1.000). It was found that 71.4% of patients with accompanying angioedema were adults, and 28.6% were adolescents (p=0.683) **(Table 2).**

Most patients associated with triggers were adults (n=18, 78.3% adults vs. n=5, 21.7% adolescents; p=0.386). NSAIDs were predominant in adults (n=11, 78.6% adults, n=3, 21.4% adolescents), but no significance was found (p=0.911). Relationships with stress, infection, presence of additional illness, additional medication usage, and smoking were insignificant (p=0.654, p=0.348, p=0.179, p=0.179, p=0.576, and p=0.275, respectively). A skin prick test (SPT) was conducted on 44% of the patients. Of these, 16% tested positive for house dust mites, 6% for pollen, 2% for both pollen and house dust mites, 8% was dermographism, and 12% was negative. No significant correlation was found with the SPT results (p=0.275).

Table 2: Comparison of clinical parameters between adolescent CSU and adult CSU patients

	Adolescents (<18 y) N=15	Adults (>18 y) N=35	P Overall
Age	18.0 [17.0 - 18.0]	48.0 [39.5 - 57.0]	<0.001
Female/Male	11 (30.6%)/4 (28.6%)	25 (69.4%)/10 (71.4%)	1.000
Clinical follow-up (m)	17.0 [11.5 - 28.5]	14.0 [9.00 - 30.0]	0.695
Urticaria duration (m)	15.0 [7.0 - 42.0]	18.0 [7.50 - 73.0]	0.655
Attack frequency			0.629
Every day	11 (28.2%)	28 (71.8%)	
Every week	4 (40.0%)	6 (60.0%)	
Monthly	0 (0.00%)	1 (100%)	
ED visit			0.468
Yes	13 (33.3%)	26 (66.7%)	
No	2 (18.2%)	9 (81.8%)	
Follow-up ED visit			1.000
Yes	3 (30.0%)	7 (70.0%)	
No	12 (30.0%)	28 (70.0%)	
Lesion disappearance time			1.000
<1 hour	0 (0.00%)	2 (100%)	
1-24 hours	15 (32.6%)	31 (67.4%)	
>24 hours	0 (0.00%)	2 (100%)	
Angioedema:			0.683
Yes	12 (28.6%)	30 (71.4%)	
No	3 (37.5%)	5 (62.5%)	
Drug - Food			0.386
Yes	5 (21.7%)	18 (78.3%)	
No	10 (37.0%)	17 (63.0%)	
Stress :			0.654
Yes	14 (31.8%)	30 (68.2%)	
No	1 (16.7%)	5 (83.3%)	
Infection			0.348
Yes	3 (50.0%)	3 (50.0%)	
No	12 (27.3%)	32 (72.7%)	
Comorbidity			0.179
Yes	2 (14.3%)	12 (85.7%)	
No	13 (36.1%)	23 (63.9%)	
Smoking			0.576
Yes	8 (36.4%)	14 (63.6%)	
No	7 (25.0%)	21 (75.0%)	
SPT result:			0.275
None	7 (25.0%)	21 (75.0%)	
HDM positive	1 (12.5%)	7 (87.5%)	
Pollen positive	1 (33.3%)	2 (66.7%)	
Pollen+HDM positive	1 (100%)	0 (0.00%)	
Dermographism	2 (50.0%)	2 (50.0%)	
Negative	3 (50.0%)	3 (50.0%)	

Abbreviations: *CSU: Chronic spontaneous urticaria, y: years, m: month, ED: emergency department, SPT: skin prick test, HDM: house dust mite*

In adult patients diagnosed with CSU, levels of anti-TPO and anti-TG were significantly higher compared to adolescents with CSU (anti-TPO 28 (0.92-47.4) IU/mL vs. 1.73 (0.79-27.1) IU/mL, p=0.066; anti-TG 12.6 (1.4-31.5) IU/mL vs. 1.08 (0.74-9.66) IU/mL, p=0.007). No significance was found in the other laboratory parameters examined **(Table 3).**

Discussion

This study rigorously evaluates the impact of Omalizumab on quality of life and urticaria activity levels in patients with CSU, characterized by morbidity and challenging management barriers. The findings are consistent with and extend the existing literature; It shows significant improvements in UAS and UCT following Omalizumab treatment. These improvements indicate a reduction in the physical symptoms of CSU and an increase in quality of life, as noted by the CU-Q2oL Questionnaire.[15,16] The importance of these results cannot be overstated, given the debilitating impact that CSU exerts on patients' daily lives, underscoring the need for effective management strategies.

Our study's cohort, including adolescents and adults, is well characterized, and dual assessment via UAS, UCT, and CU-Q2oL questionnaires before and after Omalizumab treatment reflects a robust design to capture objective

Table 3: Comparison of clinical parameters between adolescent CSU and adult CSU patients

	Adolescents (<18 y) N=15	Adults (>18 y) N=35	P Overall
Anti_TPO (IU/mL)	1.73 [0.79;27.1]	28.0 [0.92;47.4]	0.066
Anti_TG (IU/mL)	1.08 [0.74;9.66]	12.6 [1.40;31.5]	0.007
D-dimer (µg/L)	0.38 [0.35;0.45]	0.65 [0.34;1.48]	0.125
CRP (mg/L)	3.03 [2.00;7.44]	5.00 [3.03;11.8]	0.198
Lymphocyte (/µl)	2200 [1700;2845]	2100 [1784;2495]	0.368
Neutrophil (/µl)	4000 [3770;5850]	5000 [3320;6310]	0.695
Eosinophil (/µl)	200 [100;230]	200 [100;200]	0.514
Hgb (gr/dL)	14.1 [13.0;14.6]	13.4 [12.5;14.8]	0.518
Platelet (/µl)	292000 [247500;319000]	273000 [246500;337500]	0.727
Total IgE (IU/mL)	83.4 [61.3;232]	130 [37.2;211]	0.922
ANA			0.652
Positive	1 (16.7%)	5 (83.3%)	
Negative	14 (32.6%)	29 (67.4%)	

Abbreviations: *CSU: Chronic spontaneous urticaria, y: Years, Anti-TPO: Anti-Thyroid Peroxidase antibodies, Anti-TG: Anti-Thyroglobulin antibodies, CRP: C reactive protein, Hgb: Hemoglobin, ANA: Antinuclear Antibody*

and subjective treatment measures. It supports the role of Omalizumab in improving patients' quality of life.[11] The distinction between adolescents and adults regarding attack frequency, emergency department visits, and precipitating relationship is a nuanced contribution to the existing literature. A comprehensive evaluation of potential confounding factors such as medication or food triggers, stress, infection, and comorbidities adds depth to the study's results.

Despite advances in understanding the pathophysiology of CSU, treatment remains complex, and many patients respond poorly to conventional treatments such as antihistamines.[17,18] In this context, Omalizumab, a monoclonal anti-IgE antibody, is emerging as a promising alternative that potentially alters the course of the disease for those resistant to standard treatments.[7,19] Interestingly, our analysis revealed no significant difference in treatment response between adolescents and adults, demonstrating Omalizumab's broad effectiveness across age groups. This observation is particularly noteworthy given the limited number of studies focusing on pediatric and adolescent populations with CSU.[20] Additionally, the study illuminates the subtle interaction between CSU and various demographic and clinical factors, such as gender, age, and autoimmune markers, which may affect the course of the disease and treatment outcomes. The higher prevalence of anti-TPO and anti-TG in adult patients suggests a link between thyroid autoimmunity and CSU severity in adults; considering the significance found in anti-TG levels, this correlation deserves further investigation. This relationship is consistent with existing studies suggesting a higher prevalence of autoimmunity in adult CSU patients.[9,10,21] This correlation not only enriches our understanding of the etiological complexity of CSU but also points to further research on the potential therapeutic effects of targeting autoimmune pathways in managing CSU. Although the study is limited due to sample size and the inherent variability of CSU delivery, it adds valuable information to the management of CSU. The relatively small sample size and short follow-up period may limit our findings' generalizability and interpretative depth. Additionally, the observational design of the study precludes causal inferences. It necessitates randomized controlled studies to prove Omalizumab's efficacy further and investigate its effect's mechanistic basis in CSU.[6,22] Omalizumab is emerging as a valid treatment option, particularly for antihistamine-refractory cases, and the study's findings support its inclusion in CSU treatment protocols, especially given the significant improvement in quality of life.

In summary, our study strengthens the therapeutic potential of Omalizumab to improve quality of life and alleviate disease activity in CSU patients resistant to antihistamines. It also paves the way for personalized treatment approaches by shedding light on the complex network of factors that affect the treatment response and the disease's emergence. The study's findings support its inclusion in CSU treatment protocols, especially given the significant improvement in quality of life.

In conclusion, the study supports the use of Omalizumab in patients refractory to CSU treatment and underlines the importance of personalized treatment strategies. More longitudinal studies with larger groups are needed to elucidate the long-term effects and safety profile of Omalizumab, the mechanistic basis of its efficacy, and identify biomarkers predictive of treatment response. This will ultimately promote a more nuanced and compelling management paradigm for CSU. Additionally, investigating the connections between autoimmune markers and CSU may unlock new avenues for therapeutic intervention.

Author contributions

NK, CO conceptualized and wrote the manuscript. NK, CO followed up with the patients, collected the clinical and laboratory data, and provided samples. NK, CO made an intellectual contribution to the discussion.

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Original Article
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Investigation of The Factors Affecting the Vaccine Preferences of Pre-Hospital Emergency Healthcare Professionals

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Abstract

Background: The aim of this study was to examine the factors affecting the vaccine preferences of prehospital emergency health workers and the status of vaccine opposition.

Materials and Methods: This study was planned as a descriptive study to examine the factors affecting the vaccine preferences of prehospital emergency health care workers working in 112 emergency health services stations and command and control centers affiliated to the Ministry of Health in Aydın province between April 2022 and January 2023, their anti-vaccine status and their attitudes towards Covid-19 vaccine. The population of the study consisted of physicians, emergency medical technicians/technicians (ATT/Paramedics) and ambulance drivers (drivers) working in 112 emergency health services stations and command control centers affiliated to the Ministry of Health in Aydın province (N: 577).

Results: The population of the study was 577 people. 89.7% (n:427) people participated in our study. 51.5% (n:220) of the participants were female. 48.9% (n:209) were found to have Covid-19 infection. 95.8% (n:427) of the participants were vaccinated. Among the vaccinated participants, 70.4% (n:288) received Biontech, 70.4% (n:288) received Sinovac and 5.1% (n:21) received Turkovac vaccine types. When the scores of the attitudes towards Covid-19 vaccine scale and its dimensions were compared according to the descriptive characteristics of the participants, it was found that the positive attitude dimension scores of male participants (3.81) were higher than those of female participants (3.51). It was determined that the positive attitude dimension scores of the participants with chronic diseases and the participants who were vaccinated, and the positive attitude dimension scores of the participants whose vaccine type was Biontech, Sinovac and Turkovak were higher than those of the participants who were not vaccinated. It was determined that the positive attitude dimension and attitudes towards Covid-19 vaccine scale scores of the participants whose vaccine dose was three doses and more were higher than the participants whose vaccine dose was one dose and two doses, and the positive attitude dimension and attitudes towards Covid-19 vaccine scale scores of the participants who had a death due to Covid-19 infection in the family or close environment were higher than those of the participants who did not. According to the findings of our study, the view that there is no vaccine protection in those with chronic diseases has a higher score. Participants who did not have Covid-19 infection, who were not vaccinated, and who had no death loss in their close environment had higher scores on the anti-vaccination scale.

Conclusion: In this study, which examined the hesitancy of prehospital emergency healthcare workers about Covid-19 vaccination, it was found that Covid-19 vaccines were administered at a very high rate. However, it was also found that 4.2% of the employees had high hesitation about vaccines and were not vaccinated. Pre-hospital emergency healthcare workers have an important role and responsibility in the acceptance of Covid-19 vaccine by the public and other healthcare professionals, as in other disaster situations. In a pandemic, vaccination of all members of the society is necessary for the control of the pandemic. For this reason, scientific studies should be conducted for emergency healthcare workers who are not vaccinated and who are hesitant about vaccines, including basic concerns about vaccines and examining potential side effects of vaccines. Training programs should be organized to ensure that healthcare workers are vaccinated with existing Covid-19 vaccines.

Introduction

Emergency health systems are a system that includes health services that respond quickly and effectively to unexpected health situations. In this system, emergency medical interventions are carried out according to the urgency of the patient's health condition. The main characteristics of emergency health systems include speed, accessibility, coordination and quality. Speed emphasizes that time is of critical importance in the system, and it is aimed to reach the scene and the patient as soon as the emergency call is received. Accessibility means that emergency health services should be easily accessible to everyone, emergency health services should be readily available, appropriate vehicles and equipment should be available and all segments of society should be served equally. Coordination states that emergency health services should be coordinated between various health services and emergency responders, which means that appropriate structures should be established and utilized for the planning, management, evaluation and improvement of emergency medical interventions. Finally, quality means that emergency health services are effective, safe and meet the satisfaction of the parties at a high level

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(1). Pre-hospital emergency health systems in our country first started to provide services in 1995 and have been serving throughout the country since then. 112 Emergency Healthcare services have shown significant developments in recent years and are now provided by well-equipped and trained healthcare teams serving full-time (2). Compared to other sectors, healthcare workers are exposed to many risks due to their work. Among the occupational groups in the health sector, pre-hospital emergency health workers are in the most dangerous risk group. These professionals face many biological, ergonomic, physical and environmental risks. When prehospital healthcare workers do not take precautions against the problems that may be caused by biological agents, the risk that may arise is the danger of infection and the most effective method against these dangers is vaccines (3). Vaccines are an important tool used to protect the human body against infections (4). In 2009, many emergency workers encountered the Covid-19 infective agent, which was declared as a pandemic all over the world. The declaration of Covid-19 disease as a pandemic reemphasized the importance of vaccines (5). Having information about the benefits and side effects of vaccines before deciding to be vaccinated increases confidence in the vaccine. Vaccine hesitancy may occur due to misinformation, beliefs, rumors or anti-vaccine propaganda about the safety and efficacy of vaccines. This can pose a serious risk to public health. Because of vaccine hesitancy, these people may refuse to vaccinate themselves and their children, which can lead to the re-emergence of serious infectious diseases. Vaccine hesitancy can affect the success of vaccination programs and make it difficult to control infectious diseases (6). Another concept that causes disruption in vaccination programs is anti-vaccination. Vaccine opposition is a term that refers to people's resistance to vaccines. Opponents are concerned about the potential side effects of vaccines and have doubts about the necessity and effectiveness of vaccines. Some believe that vaccination can adversely affect children's development, while others are generally skeptical about the benefits of vaccines. Anti-vaccination sentiment has become a major public health issue in certain communities and localities, and when vaccination rates are low, it can lead to outbreaks of infectious diseases in the community. Anti-vaccination movements have been strengthened by factors such as information pollution and social media and have become widespread in many countries around the world (7). Vaccine ambivalence and opposition among Emergency Health Services workers in Turkey has gained importance with the pandemic process. Pre-hospital healthcare workers are in direct contact with patients during emergency interventions and the risk of infection transmission in this area is quite high. Therefore, in the prevention and control of the risk of infection transmission, the acceptance of vaccines by employees is also an important issue in terms of public health (8). It has been published that some healthcare workers have the idea of anti-vaccination (9).This situation is worrying for healthcare workers to fulfill their professional obligations and may have an effect that may lead to anti-vaccination in the society (10). It has also been reported that the anti-vaccine attitudes of healthcare professionals may occur when they do not have accurate information about the safety and efficacy of vaccines, may be concerned about fulfilling their professional obligations, and have concerns about the long-term effects of vaccines (11It has been reported that the anti-vaccine attitudes of healthcare workers make it difficult for vaccines to be accepted in the society and cause the spread of epidemics in the society (12). Therefore, it is extremely important to raise awareness and provide accurate information about anti-vaccination attitudes among healthcare workers. Prehospital emergency healthcare workers are responsible for providing fast and effective healthcare services in emergencies, and their health status is important for both themselves and the community. Taking the necessary precautions to protect workers from infection is a vital issue. Although "vaccination" seems to be the most important key in infection prevention, it is also very important to conduct research examining the attitudes and thoughts of employees towards vaccination, vaccine ambivalence and opposition (13). Based on this idea, this study was conducted to examine the factors affecting the vaccine preferences of pre-hospital emergency health workers and the status of vaccine opposition.

Materials and Methods

1. Type of Research: Our research was planned in descriptive design.
2. Place and Time of the Study: This study was conducted between April 2022 and January 2023 among pre-hospital emergency health personnel working at emergency health services stations and command and control centers within the borders of Aydın province within the Ministry of Health.
3. Population and Sample of the Study: Our study consisted of physicians, emergency medical technicians (paramedics), emergency medical technicians (EMTs), and ambulance drivers (drivers) working in 112 A.S.H.İ. and K.K.M. affiliated to the Ministry of Health in Aydın region (n:577). The sample size of the known population was found to be 231. No sample selection method was used and it was aimed to reach the whole population.

Selection and Inclusion Criteria of the Health Workers Participating in the Study. In this study, the employees working in 112 A.S.H.İ. and K.K.M. (command and control center) affiliated to the Ministry of Health in Aydın province were evaluated and the participants who accepted the research were included in the study on a voluntary basis. Exclusion Criteria for the Health Workers Participating in the Study. Employees who did not want to participate in

the study, or who were on maternity leave or unpaid annual leave were not included in the evaluation. Criteria for the Exclusion or Disqualification of the Healthcare Workers Participating in the Study. The purpose of the study was explained to those who participated in the study, and the Informed Consent Form was presented to them, stating that participation in the study was voluntary and that they could decide to withdraw at any part of the study. The e-mail address and telephone number of the principal investigator were given and it was stated that they could call to withdraw from the study at any time. The reason for this was written on the diagnostic form and stated in the study. Participants who encountered problems in a certain part of the study such as the questionnaire were excluded from our study

7. Data Collection Methods and Materials Used: Sociodemographic Data Form, Opposition to Vaccination Scale, Attitudes Towards Covid-19 Vaccine Scale were used to collect the data. The sample selection method was not used and it was aimed to reach the whole population. Data were collected by transmitting online survey forms to social media groups. The questionnaire form was sent to the employees via google survey form and they were asked to fill out the form. The information obtained was recorded electronically.

7.1. Sociodemographic Data Form: The form, which was prepared as a result of literature research, consists of 12 (twelve) questions including socio-demographic characteristics such as age, gender, and educational status.

7.2. Vaccine Opposition Scale: Kılınçarslan et al. developed this scale in 2020. Reliability and validity studies were conducted. This scale has a short and long form. This scale has 4 subscales. These are; Solutions for not getting vaccinated dimension, Vaccine opposition dimension, Vaccine benefit and protective value dimension and Legitimization of vaccine hesitancy dimension. The long form of the scale was used in our study. The long form of the scale has 4 sub-dimensions. It consists of 21 items and a 5-point Likert-type scoring system (1. Strongly disagree and Strongly agree). The items of the vaccine benefit and protective value subscale are reverse scored. The scale has no calculated cut-off value. The higher the score, the more vaccine opposition-anxiety increases(Kılınçarslan et al.2020). Permission to use the scale: 09.04.2022

7.3. Attitudes Towards Covid-19 Vaccine Scale: The 5-point Likert scale was developed by Geniş et al. in 2020 in Turkey. The scale has two sub-dimensions. The scale, which has positive attitude and negative attitude dimensions, consists of 9 questions. High scores from the positive attitude sub-dimension indicate that the attitude towards Covid-19 vaccine is positive. In negative attitude, the items are reversed and then calculated. A high score indicates that negative attitudes towards Covid-19 vaccine are lower (Geniş et al. 2020). Permission to use the scale. 08.04.2022

Data Collection Process: Data were collected by sharing online questionnaire forms on social media groups. The questionnaire form sent to the participants included a voluntary consent form that provided information about the purpose and scope of the data collection tool. The employees who agreed to complete the questionnaire answered the questionnaire questions after selecting the option "I agree to participate in the study" before answering the questionnaire questions. As a result, consent was obtained from the participants online. Doctors, emergency medical technicians and emergency medical technicians who participated in the study participated in the study by answering the questions in the digital environment. The data collection form was entered only once and the application was provided by taking the necessary precautions to be answered. The study was determined as 8-10 minutes maximum for the participants.

Data Evaluation and Statistical Analysis: In our study, SPSS (Statistical Package for Social Sciences) for Windows 25.0 program was used for statistical analysis. Descriptive statistical methods (number, percentage, min-max values, mean, standard deviation) were used to evaluate the data. The data used in the questionnaire were tested for conformity to normal distribution. Compliance with the normal distribution can be examined with Q-Q plot drawing (Chan, 2003:280-285). In order for the data used in this method to show normal distribution, skewness and kurtosis values should be between ±3. When comparing normally distributed quantitative data, t-test was used to find the difference between two independent groups, and one-way analysis of variance was used for comparisons of more than two groups. In cases where a difference was detected, Bonferroni was used to identify the group that made a difference. Pearson correlation was used to determine the relationship between numerical variables. Multiple regression analysis was used to determine the effect of independent variables on the dependent variable. Ethical Disclosures: Our study was conducted in accordance with the principles of the Declaration of Helsinki. Before starting the study, an application was made to Ege University Medical Research Ethics Committee and permission was obtained (decision dated 10.06.2022). Then, permission was obtained from the Ethics Committee of Aydın Provincial Health Directorate (decision dated 06.07.2022). For the scales to be used in our study (permission to use the anti-vaccine scale: 09.04.2022, permission to use the attitudes towards Covid-19 vaccine scale: 08.04.2022), permission was obtained from the scale owners. Informed consent was obtained from all participants before data collection. The study was initiated in line with the permissions obtained.

Results

The population of the study was 577 people. 89.7% (n:427) people participated in our study. 51.5% (n:220) of the participants were female. 48.9% (n:209) were found to

have Covid-19 infection. 95.8% (n:427) of the participants were vaccinated. Among the vaccinated participants, 70.4% (n:288) received Biontech, 70.4% (n:288) received Sinovac and 5.1% (n:21) received Turkovac vaccine types. When the scores of the attitudes towards Covid-19 vaccine scale and its dimensions were compared according to the descriptive characteristics of the participants, it was found that the positive attitude dimension scores of male participants (3.81) were higher than those of female participants (3.51). It was determined that the positive attitude dimension scores of the participants with chronic diseases and the participants who were vaccinated, and the positive attitude dimension scores of the participants whose vaccine type was Biontech, Sinovac and Turkovak were higher than those of the participants who were not vaccinated. It was determined that the positive attitude dimension and attitudes towards Covid-19 vaccine scale scores of the participants whose vaccine dose was three doses and more were higher than the participants whose vaccine dose was one dose and two doses, and the positive attitude dimension and attitudes towards Covid-19 vaccine scale scores of the participants who had a death due to Covid-19 infection in the family or close environment were higher than those of the participants who did not. According to the findings of our study, the view that there is no vaccine protection in those with chronic diseases has a higher score. Participants who did not have Covid-19 infection, who were not vaccinated, and who had no death loss in their close environment had higher scores on the anti-vaccination scale.

Discussion

According to the data obtained from the participants, the dimension of positive and negative attitude towards Covid-19 vaccine, anti-vaccination and vaccine ambivalence were questioned. The reasons for this and the behaviors chosen by the participants as a result are discussed in the findings section of this study. In our study, it was observed that female participants experienced more ambivalence about vaccination than male participants. In the study conducted by Yıldız and Gencer, it was determined that women had insecure feelings towards the Covid-19 vaccines developed and therefore did not exhibit positive attitudes towards the vaccine (14).In the study conducted by Salmon et al. in 2021, it was determined that the rate of men who never thought of getting the vaccine was lower than the rate of women. In the study by Salali and Uysal (2020) in Turkey, it was determined that the likelihood of accepting the Covid-19 vaccine was higher in men than in women. Covid-19 pandemic poses a great risk for those with chronic diseases such as diabetes, obesity, hypertension, etc. Strizova et al. 2021 reported that in the study conducted by Bish et al. in Italy, it was stated that more than half of the healthcare workers have a chronic disease that is important in their family or close environment and this situation positively affects their willingness to be vaccinated. Since existing chronic diseases may contribute to comorbidity, there are studies showing that attitudes towards vaccines produced against the Covid-19 outbreak are affected

(15). In our study, it was determined that healthcare workers with chronic diseases had positive attitudes towards Covid-19 vaccines. In our study, it was found that the positive attitude dimension and attitudes towards Covid-19 vaccine of the participants who were vaccinated were higher than the employees who were not vaccinated. A similar result was found in a study conducted by Başkaya and Kaya (16). The level of positive attitude towards the vaccine was found to be higher in those who had Covid-19 vaccine and were willing to get Covid-19 vaccine. This result of our study is similar to the results of other studies in the literature (17); Durduran et al. 2022). It is seen that the negative attitude dimension scores of the participants who were vaccinated were lower than the participants who were not vaccinated. Among the participants who received the Biontech, Sinovac and Turkovac vaccines, positive attitude scales were higher than those who did not receive the vaccine. However, their confidence in the protection of the vaccine is also evident, especially in the Biontech vaccine. In the study conducted by Civelek et al. (2021), it was determined that offering options for vaccines to people in Covid-19 vaccination studies positively affected the thoughts about vaccination. Therefore, providing vaccine diversity can be shown as one of the positive methods to get better results in vaccination studies. In Çakal›s study conducted with the critical discourse analysis method, more positive expressions and attitudes towards the Biontech vaccine were found against the Türkovac vaccine. People clearly expressed their opinions on vaccines with clear statements such as “I do not want to be vaccinated with Türkovac” and “I prefer the German vaccine”. This study shows that social media networks, which are widely used, can have great effects among individuals (18). Among the health workers who participated in the study, the positive attitude dimension scores of those who experienced death due to Covid-19 in the family and close environment are seen at higher levels. This finding seems to be related to the survival orientation of people when they encounter or witness a disaster, instinctively showing the behavior of turning towards disaster-preventive measures (19). A similar protective reflex regarding the protection of the vaccine shows that it developed for the participants who saw the Covid-19 destruction closely. The increase in the positive perspective on the Covid-19 vaccine at this point with the literature of this study is consistent with the similarity of the reaction of the participants who saw the disaster closely (seeing the disease through relatives or witnessing the death) (20). This harmony shows that the approach to vaccination can be shaped by psychological conditions. According to

the findings of our study, the view that there is no vaccine protection in patients with chronic diseases has a higher score. In the study conducted by Durduran et al., vaccine hesitancy and refusal of people who did not have a chronic disease were found to be statistically significantly higher than those with a chronic disease (21). Many studies show that having a chronic disease increases vaccine acceptance (22). It is seen that participants who did not have Covid-19 disease were hesitant about getting vaccinated and looked for solutions not to get vaccinated. Anti-vaccination effects are seen in almost all infectious diseases. In the study conducted by Düzel and Doğan (2022), mothers with children stated that they had their childhood vaccinations without interruption and that some of them also received the flu vaccine, and explained that they did not have an attitude that rejected vaccines other than Covid-19 vaccines. In their publication, Erkekoğlu et al. (2020) wrote that misinformation sources cause vaccine hesitation. Untrue news about the Covid-19 virus is spread through social media tools. In order for people to distinguish inaccurate information from false information, they need to have information on the subject, even at the maximum level. While updating their information status, individuals may consume news that is likely to be false, and this news may cause people to experience anxiety and fear (23). This may lead people to seek alternative solutions instead of vaccination. In our study, it was found that participants who were not vaccinated had higher scores on the vaccine benefit and protective value dimension and the anti-vaccination scale than those who were vaccinated. Among the participants, those who had positive attitudes towards vaccination were more likely to be anti-vaccine, vaccine hesitant and in search of solutions to avoid vaccination. Among the participants with negative attitudes, it is seen that they have more negative thoughts than the participants who are anti-vaccine and vaccine hesitant. Thoughts that vaccines are not safe and side effects are the most common reasons for refusal and hesitation about Covid-19 vaccines (24). In our study, it was observed that participants who did not receive Biontech, Sinovac and Türkovac vaccines had higher scores in the dimension of solutions for not being vaccinated, the dimension of legitimization of vaccine hesitancy and the scale of anti-vaccination than the participants who received Biontech, Sinovac and Türkovac vaccines. Therefore, it is very important to build trust in vaccines. Due to the high mortality and infection rate, individuals have naturally experienced anxiety and fear about Covid-19 disease (25). In our study, it was determined that participants who did not have Covid-19 disease in their family or circle of friends and who did not have any loss due to Covid-19 infection in their family or friends were in search of solutions not to be vaccinated. As in all infective epidemics, healthcare workers worked selflessly in the Covid-19 pandemic and were the most affected professional group. In the study conducted by Karaman et al. (26,27), it was reported that 85.4% of intern nurses experienced fear during the pandemic and 83.3% did not want to have Covid-19 vaccines. Considering that the impact of Covid-19 is striking all over the world; we think that pre-hospital emergency healthcare workers are positively affected by the experience of an increase in the number of cases, hospitalizations and deaths, seeing this disease as more important and severe, and their vaccine preferences are positively affected. According to the findings of our study, the rate of healthcare workers willing to vaccinate is higher than the rate of healthcare workers who are against vaccination. The findings show that the participants in our study have a higher perception of Covid-19 risk, concerns about Covid-19 vaccine safety, and preference for Covid-19 vaccine alternatives. It also showed that participants scored lower on the perceived benefits of the Covid-19 vaccine, suggesting that social factors such as family and friends also have an impact on the intention to receive the Covid-19 vaccine. Pre-hospital workers are the groups closest to contracting and transmitting diseases. Therefore, they have to know pre-transmission protection methods. However, given that there is still no certainty about the benefits and side effects of Covid-19 vaccine over time, other Covid-19 prevention methods may have been preferred instead of vaccination.

The low intention of prehospital healthcare workers to receive Covid-19 vaccine over time shows the need for education and provision of valid scientific information about Covid-19 disease, the effects and possible side effects of the vaccine, such as "concerns about Covid-19 vaccine safety and hesitation" and "preference for Covid-19 vaccine alternatives" in our study. Vaccines are one of the most effective inventions in the fight against infectious diseases in the world. In addition to direct immunity and disease prevention in vaccinated individuals, it has been shown to protect unvaccinated individuals with herd immunity when the majority of the population is immune. The Emergency Health Services team has a special importance before the hospital. They are the medical units that first intervene in life-threatening cases at the scene, apply basic and advanced life support, and ensure the safe transportation of patients. In addition to the first intervention, Emergency Health Services also includes the people who are the first contact for the emergency service needs of the society. In Turkey, the vaccine preferences and attitudes of employees on the road from 112 Emergency Call Center employees to the hospital are considered important. According to the results of our study, emergency healthcare workers have a positive attitude towards vaccines. Personal perception of influenza risk, misconceptions about the contagiousness and severity of the disease, and concerns about safety and efficacy are often the reasons for not getting vaccinated. In the study on influenza vaccination and the need for vaccination, the most common reasons for refusing vaccination were the belief that vaccination was not necessary and the search for alternative

Table 1: Distribution of employees according to their descriptive characteristics

Variables		n	%
Age (±SS, 33.59±7.98) 18.0	24 years and younger	47	11.0
	25-29	100	23.5
	30-34	77	18.0
	35-39	114	26.7
	40 years and over	89	20.8
Gender	Female	220	51.5
	Male	207	48.5
Marital status	Married	235	55.0
	Single	192	45.0
Education Status	High school and below	48	11.2
	University	350	82.0
	Graduate	29	6.8
Occupation	Doctor	13	3.0
	Paramedic/A.T.T.	373	87.4
	Driver	41	9.6
Presence of chronic disease	Yes	76	17.8
	No	351	82.2
Covid-19 infection status	Yes	209	48.9
	No	218	51.1
Vaccination status	Yes	409	95.8
	No	18	4.2
Total		**427**	**100.0**
Type of vaccine received Biontech	Yes	288	70.4
	No	121	29.6
Sinovac	Yes	288	70.4
	No	121	29.6
Turkovac	Yes	21	5.1
	No	388	94.9
Completeness of vaccination	One dose	12	2.9
	Two doses	129	31.6
	Three or more	268	65.5
Total		**409**	**100.0**
Family history of Covid-19 infection	Yes	320	74.9
	No	107	25.1
Death due to Covid-19 infection in the family and close environment	Yes	163	38.2
	No	264	61.8
Total		**427**	**100.0**

and safe methods. Vaccination is the most successful preventive health intervention and is important for public health. Vaccines prevent the development and spread of many diseases with direct and indirect effects. Vaccines are very reliable biological products. It should be kept in mind that the likelihood of getting the flu in people who have not been vaccinated against the flu, as well as the morbidity and mortality associated with the disease, are too high to be compared with the possible side effects of the vaccine. As in the world, the number of anti-vaccinationists is increasing day by day in our country. Healthcare professionals have an important role in ensuring that patients who refuse vaccination are vaccinated. Doctors who do not vaccinate themselves or their children do not recommend vaccination to their patients. In order to ensure the successful operation of vaccination programs throughout the country, it is important to raise awareness among healthcare professionals and to increase the number of vaccinations by raising awareness. For this purpose, it is first necessary to identify the factors that lead to opposition to vaccination and develop strategies to change them. Pre-hospital healthcare workers played an important role in the pandemic. Most of the patients affected by the outbreak first and directly encountered prehospital emergency health workers. This group personally provided emergency care and intervention to infected patients. Therefore, prehospital workers have priority in vaccination to protect them from epidemics. Although prehospital workers are expected to prefer vaccination very often, the vaccination rate is not at the desired level. Just like in the society, it has been observed that healthcare workers hesitate to make decisions due to impure information. Vaccination ambivalence persists despite global tragedies related to inadequate immunization. Parents' concerns are many, but educational efforts cannot solve these problems. Health workers and patients need to know the value of advice about vaccination, and stronger advice in hypothetical language effectively increases vaccination rates. Hypothetical language implies that one is seeking advice from the health professional and is willing to follow it. Pre-hospital health workers are a key population in the study of vaccine safety and behavior, as their recommendations influence patient acceptance. In addition, personal vaccination behavior influences the prevention and control of infectious diseases in health care settings. In our study, some of the prehospital health workers reported vaccine hesitancy. Healthcare workers are positively influenced by close friends and colleagues who believe that vaccination against Covid-19 is important, which can support communication between units and roles to improve vaccination. Therefore, certain populations, such as non-physicians or those concerned about adverse reactions, are less likely to be vaccinated against the Covid-19 virus. Work with specific units and roles should be planned to improve this population's knowledge about vaccines against Covid-19. As healthcare workers have more scientific knowledge about how vaccines are made and produced, such as their side effects and potential risks, they are naturally more concerned than other groups of people and may therefore be hesitant to use vaccines. The public mostly obtains information about Covid-19 vaccines and the disease from healthcare professionals and the internet/ social media. Therefore, it is predicted that the government organizing trainings on Covid-19 vaccine such as on-line, question-and-answer sessions for healthcare professionals will be effective in getting more successful results from the public about vaccines. Most health workers have a strong belief in the benefits and safety of vaccines and trust other health professionals. However, low confidence in vaccination

among many health workers has also been observed. The results of our study showed that health workers who perceived vaccines as less beneficial and safe were less likely to accept vaccination for themselves and their children and less willing to recommend vaccination to patients who did not want to be vaccinated. Trust in health workers appears to be directly related to their own vaccination decisions or willingness to recommend vaccination. Trust in evidence-based information about vaccines was found to be associated with the level of education of health workers, so that trust increased as education increased. This is particularly true for claims that require knowledge about specific vaccines or diseases. Further research should investigate whether vaccine adherence can be increased by increasing vaccine education or training. As lay people cite health worker trust as a key factor in health worker vaccination decisions, ensuring that health workers are vaccinated may be important to maintain high vaccine use in the population. We believe that providing trainings on the effects and possible side effects of vaccines and updating the knowledge of healthcare workers with current valid scientific information will lead to more effective and efficient results in vaccination studies.

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Review Article
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CRP/Albumin Ratio and NLR in Recognizing Critically Ill Patients

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Abstract

The blurring of consciousness is one of the common causes of admission to emergency departments. While evaluating an unconscious patient, all system examinations should be done more carefully and thoroughly since the unconscious patients cannot express themself adequately a patient with non-traumatic hemorrhagic cerebrovascular accident & spontaneous pneumothorax is a rare condition. In this case we aim to present, life-threatening severe clinical conditions could be occur, if the intervention is delayed.

Introduction

The management of critically ill patients in the emergency department is a multifaceted process that requires prompt recognition, swift intervention, and ongoing monitoring. Critically ill patients are those whose conditions threaten life or organ function, necessitating immediate medical attention to prevent further deterioration or death. This article aims to outline the essential components of managing critically ill patients, including initial assessment, resuscitation, stabilization, and ongoing care[1,2].

Management

Critically ill patients encompass a broad spectrum of conditions, ranging from severe trauma and acute respiratory distress syndrome to septic shock and cardiac arrest. They typically present with abnormal vital signs, altered mental status, or signs of organ dysfunction. Early recognition of critical illness is paramount, often relying on clinical judgment supported by objective parameters such as vital signs, laboratory tests, and imaging studies[3].

The initial assessment of critically ill patients begins with the ABCDE approach: Airway, Breathing, Circulation, Disability, and Exposure. This systematic approach ensures that immediate life-threatening conditions are identified and addressed promptly. Airway management is prioritized to ensure adequate oxygenation and ventilation, followed by interventions to stabilize breathing and circulation. Disability assessment involves evaluating neurological function, while exposure entails a thorough physical examination to identify injuries or sources of infection[4].

Once life-threatening issues are addressed, resuscitation and stabilization efforts focus on restoring perfusion and oxygenation to vital organs. This may involve fluid resuscitation, vasopressor therapy, and mechanical ventilation to optimize hemodynamics and oxygen delivery. Hemodynamic monitoring with invasive or non-invasive techniques helps guide fluid and vasopressor administration, ensuring appropriate perfusion pressure and tissue oxygenation[5,6].

Critical care extends beyond the initial resuscitation phase, requiring vigilant monitoring and ongoing interventions to prevent complications and optimize outcomes. Continuous assessment of vital signs, laboratory parameters, and organ function guides therapeutic interventions and informs decisions regarding escalation or de-escalation of care. Multidisciplinary collaboration is essential, involving intensivists, nurses, respiratory therapists, and other allied health professionals to deliver comprehensive care tailored to the patient's needs[7,8].

Laboratory parameters

Laboratory parameters play a crucial role in the evaluation of critical patients in the emergency department. Routine laboratory tests such as complete blood count, electrolyte levels, liver and kidney function tests provide critical insights into the patient's overall health status[9]. Additionally,

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inflammatory markers like C-reactive protein (CRP), white blood cell count, and neutrophil-to-lymphocyte ratio can assist in assessing the presence and severity of infections[10]. These aid in determining the urgency of the patient's condition and formulating appropriate treatment plans, supporting clinical decisions. Laboratory results are also regularly monitored to track the patient's condition and assess response to treatment. Therefore, careful evaluation and interpretation of laboratory parameters in the emergency department are of paramount importance[11].

In the management of critical patients in the emergency department, the ratio of CRP and albumin levels can provide important insights into the patient's inflammatory status and overall health condition[12-22]. Here are some key points highlighting the importance of this ratio:

Assessment of Inflammatory Status: CRP levels serve as an indicator of inflammation in the body. Elevated CRP levels may indicate the presence of acute inflammation, infection, or tissue damage. Conversely, albumin levels are generally inversely proportional to inflammation; as inflammation increases, albumin levels decrease. Therefore, the CRP to albumin ratio can help assess the patient's inflammatory status more comprehensively[12,13].

Identification of Infections: An increase in CRP levels can indicate the presence of acute infections. However, diagnosing infections based solely on CRP levels can be challenging. In such cases, comparing CRP levels to albumin levels can provide a clearer view of the severity of infection and the patient's overall health condition[12,14-19].

Assessment of Sepsis: Conditions such as sepsis are critical and require prompt intervention. In these cases, the CRP to albumin ratio can be used as a tool to determine the patient's sepsis risk and assess its severity. A patient with high CRP levels and low albumin levels may indicate a higher risk of sepsis[20,21].

Monitoring Response to Treatment: Monitoring the response to treatment in critical patients is important. Changes in the CRP to albumin ratio after initiating treatment can be used to evaluate the patient's response. For example, a decrease in CRP levels and an increase in albumin levels as a response to treatment may indicate that the patient is improving[15,21].

Prediction of Clinical Outcomes: The CRP to albumin ratio can be used to predict clinical outcomes in patients. Particularly, a high CRP/albumin ratio may increase the likelihood of a poor clinical course for the patient and therefore may require more intensive treatment[12,17-22].

Therefore, the evaluation of the CRP to albumin ratio in the management of critical patients in the emergency department can provide important information about the patient's inflammatory status, infection risk, and response to treatment[23-32]. This ratio plays a critical role in the assessment of the patient and the formulation of the treatment plan.

In the management of critical patients in the emergency department, the neutrophil-to-lymphocyte ratio (NLR) plays a significant role as a prognostic marker and indicator of systemic inflammation. Here are some key points highlighting the role of NLR and how it can be utilized:

Prognostic Marker: NLR serves as a prognostic marker for various acute conditions, including sepsis, trauma, and cardiovascular emergencies. Elevated NLR levels are associated with worse clinical outcomes, such as increased mortality rates and longer hospital stays. Therefore, NLR can help emergency physicians quickly identify patients at higher risk and prioritize their care accordingly[22-27].

Indicator of Systemic Inflammation: NLR reflects the balance between the body's innate immune response (neutrophils) and adaptive immune response (lymphocytes). An elevated NLR indicates a predominance of neutrophils, suggesting an exaggerated inflammatory response. This systemic inflammation may be indicative of underlying infection, tissue injury, or other critical conditions requiring immediate intervention[28,29].

Risk Stratification: NLR can assist in risk stratification of critical patients by predicting the severity of their condition and likelihood of complications. Higher NLR levels are associated with increased severity of illness and higher rates of organ dysfunction. Emergency physicians can use NLR as part of their initial assessment to triage patients effectively and allocate resources appropriately[28,31].

Monitoring Response to Treatment: Changes in NLR levels over time can provide valuable information about the patient's response to treatment. A decreasing NLR may indicate a positive response to therapy, while a persistently elevated NLR may suggest treatment failure or ongoing inflammatory processes requiring further intervention. Regular monitoring of NLR during the patient's hospital stay allows clinicians to adjust treatment strategies accordingly[29,32].

Predictor of Complications: Elevated NLR levels have been linked to an increased risk of various complications, including septic shock, acute kidney injury, and respiratory failure. By monitoring NLR, emergency physicians can identify patients at higher risk of developing complications early in their course of illness and implement preventive measures or escalate care as needed[23,27,30-32].

Lastly, the neutrophil-to-lymphocyte ratio (NLR) serves as a valuable adjunctive tool in the management of critical patients in the emergency department. By providing insights into the patient's inflammatory status, predicting clinical outcomes, and guiding treatment decisions, NLR enhances the ability of emergency physicians to deliver timely and effective care to those most in need.

Conclusion

The management of critically ill patients in the emergency department demands a systematic and coordinated approach to ensure timely and effective interventions. Early

recognition, prompt resuscitation, and ongoing monitoring are critical to optimizing outcomes and reducing mortality in this high-risk population. By adhering to established protocols and leveraging advanced technologies, healthcare providers can deliver high-quality care to critically ill patients and improve survival rates in the emergency setting.

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Review Article
Eurasian Journal of Critical Care

Concurent Cardio-Cerebral infarction: definition, diagnosis, causes and treatment

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Abstract

Acute ischemic stroke and acute coronary syndrome are the major conditions causes of death worldwide. The prevalence of coronary artery disease has been reported in one fifth of stroke patients. The concurent cardio-cerebral infarction defiend if this two conditions occures at the same time or one after the other within several hours. In this review we describe the definition, causes and treatment of the concurent cardio-cerebral infarction

Keywords: Concurent cardio-cerebral infarction, definition, causes, treatment

Introduction

The incidence of acute ischemic stroke (AIS) after acute myocardial infarction (AMI) during the hospital stay ranges from 0.7% to 2.2% [1-3]. Acute ischemic stroke occurred more frequently in the first days after AMI, but incidence progressively decreased over time [4-5]. Brandi Witt et al, suggested that during hospitalization for the acute myocardial infarction (MI), 11.1 ischemic strokes occurred per 1000 MI compared with 12.2 at 30 days and 21.4 at one ear. Positive predictors of stroke after MI included: advanced age, diabetes, hypertension, history of prior stroke, anterior location of index MI, prior MI, atrial fibrillation, and heart failure [6]. The incidence of AMI after acute ischemic stroke was relatively low and unexpectedly highest during the first year after stroke. The 5-year cumulative incidence of AMI was 2.0%. The annual risk was highest in the first year after the index event (1.1%), followed by a much lower annual risk in the second to fifth years (between 0.16% and 0.27%). Coronary heart disease was the most substantial risk factor for AMI after stroke and conferred an approximate 5-fold greater risk [7]. Both AIS and acute myocardial infarction are medical emergency conditions, which require timely diagnosis and management. The incidence of patients who diagnosed acute ischemic stroke about 0.009% [8]. In this article we describe the definitionş causes and treatment options of the concurent cardio-cerebral infarction. Definition of concurent cardio-cerebral infarction: Concurent Cardio-cerebral infarction can generally be defined as primary disorders of heart or brain often result in secondary infarction/injury to the both organs either at the same time or one after the other within 12 hours.

Diagnosis of concurent cardio-cerebral infarction:

1. AIS (a sudden onset of focal neurological deficit caused by an acute focal injury to the central nervous system due to a vascular narrowing cause)
2. AMI (acute elevation cardiac enzyme plus ischemic electrocardiogram and/or symptoms).
3. The two conditions at the same time or one after the other within 12 hours.

Pathophysiology of concurent cardio-cerebral infarction:
The pathophysiology of simultaneous cardio-cerebral infarction can be classified into three categories:

(1) Cardiac conditions Type 1A: There are several conditions that lead to simultaneous acute cerebral and coronary infarction. The most of these is atrial fibrillation has been reported as a cause of simultaneous cardio-cerebral infarction due to common source of both cerebral and coronary embolism [9]. Type-I acute aortic dissection with dissection flap extending to coronary and common carotid arteries origin had been reported to

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cause concurrent acute myocardial infarction and acute ischemic stroke [10]. In addition, concurrent coronary and cerebral vasospasm due to electrical injury have been reported as an uncommon cause of simultaneous cardio-cerebral infarction [11].Pre-existing intracardiac thrombus from left ventricular tumour or prosthetic valve thrombosis or impaired left ventricular ejection fraction can also lead to simultaneous coronary and cerebral vascular occlusion [12]. The thrombus formed in the right ventricle in acute right ventricular infarction with right ventricular dysfunction in combination with patent foramen ovale can embolize to both vascular territories. Severe hypotension or cardiogenic shock following AMI can also lead to hemodynamic stroke [13].

(2) Brain causes (Brain–heart axis) Type 1B: Brain–heart axis dysregulation might be an alternative pathophysiology of simultaneous cardio-cerebral infarction syndrome. It has been shown that the insular cortex plays a critical role in central autonomic system regulation [14]. Patients with AIS in the parietoinsular region were found to have higher risk of developing arrythmias such as atrial fibrillation [15]. An abnormal electrocardiogram, including ST-segment elevation myocardial infarction, was found to be related to ischemic stroke in the insular cortex [16]. In addition to electrocardiographic abnormalities, myocardial damage determined by elevated serum cardiac troponin T was shown to be associated with acute cerebral infarction in specific brain regions including the right insular and right inferior parietal lobule [17]. Cardiac sympathetic overactivity from an insular cortex lesion can provoke diffuse myocardial damage, "myocytolysis," which leads to elevation of cardiac enzyme [18]. Results from human studies showed that the stimulation of different sides of the insular cortex resulted to different cardiac autonomic responses. And the right-side stimulation of insular cortex resulted in a predominant sympathetic effect, whereas the left-side stimulation resulted in a predominant parasympathetic effect [18]. (3) Non cardiac and non-brain causes: Type 1C: Coronavirus disease 2019 (COVID-19) infection and Type I cardio-cerebral infarction syndrome: Recent studies suggested that coronavirus disease 2019 (COVID-19) infection can be increased the risk of AIS and AMI. However, the evidence base is limited mainly to case reports and two cohort studies. The evidence that COVID-19 may increase the risk of acute ischemic cardiovascular events. the underlying mechanisms may cytokine-mediated hypercoagulability and plaque destabilization [19]. Severe hypotension can be causes infarction in brain and myocardial infarction. Table 1 suggested the causes of concurent cardiocerbral infarction [20]. The causes of concurent cardio-cerebral infarction: multiple causes of cardio-cerebral infarction erer reported, the most common is atrial fibrilation and left ventricle thrombus, other causes such as aortic dissection, COVID 19 infection, Polycythemia, malignancy and patent foramen ovale were reported (Table 1)

Table 1: The causes of concurent cardio-cerebral infarction

Causes	Examples
Left heart thrombus	Atrial fibrilation, left ventricle thrombus, left atrial myxoma, infective endocarditis.
Atherosclerotic	Uncontrolled hypertension, smoking, diabetes mellitus and previous coronary arterydisease
Hyper coagulant states	COVID 19 infection, Polycythemia, malignancy and patent foramen ovale
Hypotensive	cardiogenic shock and severe heart failure.
Mechanical complication	aortic dissection

Treatment: According to the 2018 scientific statement guideline from the American Heart Association/ American Stroke Association (AHA/ASA), For patients presenting with synchronous AIS and AMI, treatment with intravenous alteplase at the dose appropriate for acute ischemic stroke, followed by the percutaneous coronary intervention (PCI) and stenting if indicated, is reasonable [21]. The new recommendation according to 2021 guidelines of the European Stroke Organization (ESO) on intravenous thrombolysis for acute ischemic stroke suggested that [22]: Contraindication of alteplase for patients with acute ischemic stroke of < 4.5 hours duration and with history of subacute (> 6 h) ST-segment elevation myocardial infarction during the last seven days. The intravenous alteplase also has contraindications in patients with acute ST elevation myocardial infarction with recent acute ischemic stroke if the stroke duration is more than 4.5 hours from the onset of symptoms . So that if AIS after 6 hours from STEMI onset, or STEMI after 4.5 hours from AIS intravenous alteplase is a contraindication. In these conditions, we recommended intervention treatment with percuataneous coronary intervention (PCI) ans mechanical thrombectomy (MTE). (Figure 1)

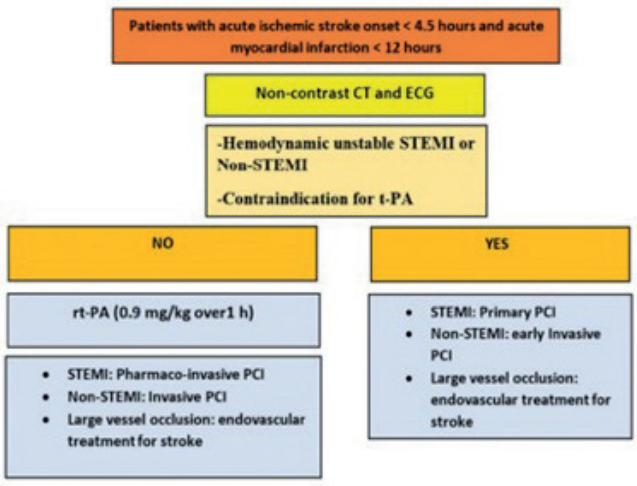

Figure 1: Treatment of concurent cardio-cerebral infarction syndrome.

First presentation AMI or AIS ; Habib et al, suggested that 53% of patients presented with acute ischemic stroke symptoms followed by acute myocardial infarction symptoms. In this patient, the most common MI type was inferior MI. Acute myocardial infarction symptoms followed by acute ischemic stroke symptoms were reported in 20 % of the patients. In this group, the most common stroke type was anterior circulation with the right middle cerebral artery or right internal carotid artery occlusion. At the same time presentation of myocardial infarction and acute ischemic stroke symptoms was occurred in 27% patients. [20]. For alteplase medication, only 44% of patients were treated with intravenous alteplase, percutaneous coronary intervention (PCI) was used to treat 31% of patients Mechanical thrombectomy of cerebral vessels in were administrated in 25% of the patients. Only 22% of the patients were treated in combination with both PCI and Mechanical thrombectomy of cerebral vessels. [20].

Discussion

The causes of concurrent cardiocerebral infarction reported into five types: 1. Embolic (left ventricle thrombus in patients with previous myocardial infarction or dilated cardiomyopathy, left atrial appendage thrombus in patients with atrial 6ibrillation). 2. Hypotensive (patients with cardiogenic shock and heart failure). 3. Atherosclerotic (patient with hypertension, smoking, diabetes mellitus and previous coronary arterydisease). 4. Hyper coagulant states (COVID 19 infection, Polycythemia, malignancy and patent foramen ovale) 5. Mechanical complication (aortic dissection). The left ventricular systolic dysfunction and atrial fibrillation are increasing the likelihood of embolic stroke due to thrombus formation in the left ventricle and left atrial appendage. These two phenomena have been commonly reported in this analysis.

The main concerns about giving alteplase to patients with AIS and a history of recent MI are (Beyond the bleeding): 1. Thrombolysis-induced myocardial hemorrhage predisposing to myocardial wall rupture. 2. Possible ventricular thrombus that could be embolized because of thrombolysis. 3. Post-myocardial -infarction pericarditis may become hemopericardium.

The mortality rate showed that concurrent cardiocerebral infarction had a high during hospital admision 33 % and after three months mortality rate was 49 %. The in-hospital mortality rate was higher in males (35%) than in females (18.9%) and 78% of death related to cardiovascular causes. [20].In metanalysis of 44 patients, ten patients died (23%) and nine (90%) of those were due to cardiac causes [23].

Conclusion

The occurrence of concurrent cardio cerebral infarction is rare with high risk of mortality rate especially in female patients. The rate medical treatment with thrombolytics and percutaenous intervention treatment with PCI and MTE was low. Further studies will need to examine the optimum treatment strategies

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Case Report
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Clinical Case Report of Acute Heart Injury And Acute Rhabdomyolysis Due To Cyanua Poisoning

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Abstract

Cyanide poisoning is one of the most dangerous poisonings, it can be absorbed into the body through the mouth, inhalation and through the skin. A 32-year-old female patient was admitted to our poison control center because of high fever, severe vomiting, and seizures. Physical examination found that the patient was drowsy, had a high fever of 40 degrees Celsius, pulse of 140 beats/minute, and increased tendon and bone reflexes. Exploiting the patient's information, it was discovered that the patient bought Cyanide to drink with the intention of committing suicide. The patient was quickly treated with gastric lavage and activated charcoal. Echocardiography recorded EF: 35%, reduced movement of the entire myocardium. CK blood test: 4562 U/L. The patient's condition rapidly deteriorated and the patient was made ECMO, IHD and CVVHDF. After 3 days of treatment, the patient's condition did not improve, so the family asked for the patient to go home. This article aims to describe the rapidly progressing and severe damage to the heart and muscles of patients with cyanide poisoning.

Keywords: Cyanide poisoning, Acute Heart Injury, Acute Rhabdomyolysis

Introduction

Cyanide is one of the fastest-acting and the most toxic poisons. They can be absorbed into the body through the mouth, inhalation and through the skin. Oral poisoning occurs when patients drink cyanide themselves or eat foods containing a lot of cyanide such as cassava, apricot kernels, cherry tree seeds and leaves, apple cores, plums, and peaches. Cyanide can be in the form of compounds such as potassiumcyanide, sodiumcyanide, hydrocyanide, zinc cyanide, silver cyanide... In this report, we having a 32-year-old female patient admitted to the hospital for cyanide poisoning at the 4th hour. She was taken to the hospital with high fever, convulsions, decreased consciousness and rhabdomyolysis. CK: 4562 U/L, reduced movement of entire the myocardium with EF 35%.

Case Report

32-year-old female patient's history: Untreated depression, intended suicide once with sleeping pills. Entered the poison control center with high fever, convulsions, and decreased consciousness. It is known that on the afternoon of the same day, the patient was found by his family in a state of irritability, vomiting a lot, vomiting white fluid, then She reported self- drinking cyanide purchased online. She was taken to the hospital by her family members with coma Glasgow: 12 points, breathing rate 55l/min, fever 40 degrees Celsius. Then there were many whole body convulsions, each lasting 30 seconds. During the convulsions, the patient could not be awared around, after the convulsions the patient wakes up slowly.

Clinical examination: Patient weighs 54kg, height 152cm, BMI: 23.3. Pulse 140 beats/min, blood pressure: 90/60 mmHg. The patient is agitated and screaming. Called and asked but no response. Pupils on both sides are 3mm, still reflect light, fever is 39 degrees Celsius. Negative stiff neck, negative meningeal stripe. Rapid breathing, respiratory rate: 50-55 L/min. The lungs are ventilated equally on both sides. Spasticity, increased muscle tone in the limbs, increased tendon reflexes. Other agencies have not detected anything unusual.

The patient was tested for gastric fluid and urine with the following results: Cyanide was positive with a concentration of 0.525 mg/L in gastric fluid.

Blood count and coagulation tests were within normal limits. Cre test: 84 µmol/l, CK increased from 4562->54532 U/L within 1 day. Troponin Ths increased 497->772 in 1 day. Lactac: 7.0. Echocardiography EF: 35%, uniformly reduced movement in many areas of the myocardium. The patient received gastric lavage and a dose of activated charcoal (1g/kg). The patient's condition then worsened very quickly with pulse rapidly increasing to 200 beats/

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min, blood pressure dropping very quickly to 50/30 mmHg, consciousness rapidly decreasing from 12 down 8 points. Patients were given vasopressors including: Dobutamine: 20mcg/kg/minute. Noadrenalin: 1.5mcg/kg/min, Adrenalin: 1.5mcg/kg/min, endotracheal tube, mechanical ventilation. Then ECMO was performed to support the heart. 2 days after ECMO, the patient's condition did not improve, the patient's heart appeared in continuous ventricular fibrillation and was electroshocked. IHD and CVVHDF dialysis. However, the condition was not improved, the family asked for the patient to go home.

Discussion

Cyanide is one of the most deadly poisons known. Cyanide is known as sodium cyanide and potassium cyanide. In its gaseous form it is usually hydrocyanide. The mechanism of toxicity is Cyanide binds tightly to the iron ion (Fe3+) of cytochrome oxidase a3, inhibiting this final enzyme in the cytochrome complex of mitochondria. When the activity of this enzyme is blocked, oxidative phosphorylation ceases. Therefore, the cell must switch to anaerobic metabolism with glucose to produce ATP. This leads to increased blood lactase and increased oxygen toxicity in venous blood because cells cannot use oxygen. The heart, muscles and central nervous system are the organs most affected by cyanide poisoning. Cardiovascular disorders occurring after cyanide ingestion may include rapid, shallow pulse, tachycardia, congestive heart failure, increased Troponin Ths, and hypotension. Rhabdomyolysis and increased serum creatine kinase levels are also signs of cyanide poisoning. Metabolic acidosis is seen in 67% of patients with acute oral cyanide poisoning. Headache, loss of consciousness, convulsions, positive Babinsky sign, hemiplegia, difficulty speaking, Parkinson's syndrome, coma, and death may occur due to the effects of nervous system damage after cyanide ingestion. . Additionally, a strong almond odor to the breath and multiple clear pink patches on the skin may be seen on physical examination. Cardiovascular complications in our report included Tachycardia, uniform regional hypokinesia of myocardial regions with reduced ejection fraction EF of 35%. Our patient was intubated and mechanically ventilated using vasopressors, IHD dialysis and CVVHDF and also received ECMO.

Figure 1: Image of a patient's cyanide poisoning test

Conclusion

In our patient, the patient's signs and symptoms manifested in cyanide-sensitive organs including the brain, heart, and muscles. Identifying patients with cyanide poisoning is through medical inquiries and toxicology tests. Once again we want to emphasize that cyanide poisoning is one of the severe poisonings with a high mortality rate. Early identification of toxins and close monitoring of the patient's clinical and paraclinical condition can help the patient have a higher chance of being saved.

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Letter to Editor
Eurasian Journal of Critical Care

Intensive Care: Turkey's First Subspecialty for Emergency Medicine

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Abstract

Diabetes mellitus is a disease that affects millions around the globe. It also comes with a major complication, diabetic foot ulcers. Lower extremities having little to no vascularity in diabetic people leads to wounds that are unable to heal on their own. These wounds later become infected and cause osteomyelitis, a condition in which the infection in soft tissues of the lower extremities spread to the bones of the foot. Charcot arthropathy is one of the more serious foot issues that can arise from diabetic neuropathy. The soft tissues, joints, and bones of the foot or ankle are all impacted by Charcot. The joints in the foot or ankle might dislocate when the bones deteriorate and become brittle. Diabetes patients who have their soft tissues and bones infected might even have to get their extremities amputated if not managed right on time. We describe the case of a 66-year-old man with type 1 diabetes mellitus who presented to the emergency department with increasing pain in the right foot. There was a hyperemic discharge coming out of his wound which increased gradually over time. The patient's been using Lantus and Novorapid and his blood glucose measurement at the time of admission was 466. Our patient said that he was hospitalized in the intensive care unit due to diabetic ketoacidosis 20 days before he applied to our emergency department, and his wounds, discharge, pain, and redness increased after this incident. We requested his anteroposterior and lateral radiographs of the right foot and a lower extremity CT. The scans were examined carefully and at last, amputation was recommended for the patient. The patient did decline our offer and wanted to go home with a dressing. Ampicillin/sulbactam and ciprofloxacin were started. We also recommended he see infectious diseases and plastic surgery consultants in the following days.

Keywords: Charcot arthropathy, Osteomyelitis, Diabetes

To the Editor,

Approximately 30 years after the acceptance of emergency medicine as a new and independent medical specialty in our country in 1993, we are now welcoming with great satisfaction, excitement, and happiness the establishment of the first sub-specialty of intensive care within the main branch of emergency medicine. "Intensive Care," the first subspecialty for emergency medicine, was approved by the Turkish Grand National Assembly on February 15, 2024, and the law was published in the Official Gazette on Friday, March 1, 2024, under the number 32476, officially coming into force (1).

In this significant achievement for our specialty, the Emergency Medicine Specialists Association (EPAT) has played a significant role, contributing through intensive care congresses with broad international content, translated and original intensive care literature provided to Turkish medicine, as well as intensive care, critical care, mechanical ventilator, and advanced cardiac and trauma life support courses and modules held in almost every city across the country. For many years, in some emergency departments of our country, intensive care services have been primarily provided to our patients by emergency medicine professionals, either as an independent department or within units with names such as "critical care," "emergency critical care," or "emergency critical intensive care" (2). As members of the intensive care working group of EPAT and as emergency medicine specialists who have been treating patients in two independent emergency intensive care units (totaling 13 beds) for emergency and critical patients in the emergency department of a tertiary-level training and research hospital in our capital city for about 10 years, we are both pleased and proud of this development. We recognize that the words "emergency," "urgent," or "acute" have become blurred and intertwined in critical patients or injuries (3). Both emergency medicine and critical/intensive care are influenced by similar dynamics in three important pillars: acute deterioration, quality resuscitation, and rapid, effective, and holistic approaches to multi-system dysfunction. The commonalities between them are more than we can imagine. It would be contrary to the natural progression of things if these two intertwined disciplines did not intersect one day. If we define intensive care as a discipline that utilizes all kinds of devices and advanced technology, especially artificial respiration, 24 hours a day to support the impaired functions

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of the body due to the temporary failure of one or more organs until the main cause is eliminated and to keep the patient alive, we can see how much it shares common goals with emergency medicine. Moreover, approximately one-fourth of the patients admitted to emergency departments require critical care, and this common patient population has become the most important reason for defining intensive care as a sub-specialty of emergency medicine in countries such as the USA, Canada, and Japan (2). To such an extent that even the concept of "Emergency Medicine" is now often referred to as "Emergency Medicine and Critical Care" in many places. Since any patient admitted to the emergency department is a potential candidate for critical care or intensive care, and since both emergency medicine specialists and intensivists do not have the chance to limit themselves to a single "organ," the importance and interrelationship of the two disciplines become clearer. Of course, the major difference between the two disciplines is that emergency medicine specialists also deal with minor diseases or injuries, whereas intensivists have almost no contact with this patient group (4).

As with any kind of development, progress, or change, various objections have arisen within the national medical community. The main arguments of these objections revolve around concerns such as the excessive number of specialties available to medical students, which may complicate the standardization of intensive care subspecialty education and quality, the potential decrease in preference for or interest in the intensive care subspecialty, the fear that emergency medicine specialists will transition to becoming intensive care subspecialists, and the concern that emergency departments across the country will be left empty, with emergency departments being provided solely by general practitioners. Many of these objections were found to be unwarranted, hastily made, and lacking in evidence, such as claims that interventional procedures in emergency medicine and intensive care are inherently different, or that intensive care can only be subdivided into categories like internal, surgical, or neurological, with emergency medicine falling outside of this framework. Additionally, some argued that our country's medical system, particularly specialty training, is more aligned with Europe than with the USA.While these objections could be addressed satisfactorily, demonstrating the reality of the situation and concepts, this article does not aim to do so due to space constraints and the intended focus.

The purpose of this article is to convey the satisfaction, happiness, and pride felt by emergency medicine specialists who have been delivering critical and intensive care services in emergency departments for nearly a decade, following a significant development outlined briefly above. We wish to share this sentiment with you, esteemed editor, and thereby with the esteemed readership of the journal.

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