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CONTENTS

Volume: 2 Issue: 3 Year: 2024

ORIGINAL ARTICLES

CASE REPORTS

LETTER TO THE EDITOR

The Intercontinental Journal of
Emergency Medicine

Original Article

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Assessment of emergency physicians' awareness and knowledge of hereditary angioedema

Nihal Ertürk[1], Şadan Soyyiğit[2], Gülhan Kurtoğlu Çelik[2], Edip Varan[3]

[1]*Department of Emergency Medicine, Ankara Bilkent City Hospital, Ankara, Turkiye*
[2]*Department of Immunology and Allergy, Faculty of Medicine, Ankara Yıldırım Beyazıt University, Ankara, Turkiye*
[3]*Department of Neurology, Beypazarı State Hospital, Ankara, Turkiye*

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Corresponding Author: Nihal Ertürk, nihalseylan@gmail.com

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ABSTRACT

Aims: Hereditary angioedema can occur with life-threatening attacks of severe laryngeal edema, and epinephrine is insufficient in the treatment of attacks. We sought an answer to the question, 'Do emergency physicians, who frequently encounter angioedema cases that are so important for the emergency department, have sufficient awareness about this issue?'

Methods: In this study, the online questionnaire was conducted among physicians working in adult emergency departments between April and August 2022. The questionnaire form consisted of two parts. The first part contained three questions about medical experience, academic degree, and encounter with hereditary angioedema patients. The second part of the questionnaire contained seven questions about the diagnosis and treatment of hereditary angioedema.

Results: A total of 103 physicians working in emergency departments participated in the survey. The proportion of physicians is as follows: The percentage of physicians with less than 15 years of experience was 92.2%. Research assistants represented the largest group of participants at 51.5%. When asked "What is not a symptom of hereditary angioedema?" Only 40.6% of physicians could answer the question correctly. While 39.8% of physicians thougt that epinephrine and antihistamines were useful in treating these attacks, 53.4% felt that epinephrine and antihistamines were not. While there was a difference in hereditary angioedema awareness between the group with more than 15 years of professional experience and the group with less experience, there was no meaningful difference between research assistants, specialists, and academicians. According to this survey, professional experience was important, but academic title did not make a difference in terms of disease awareness.

Conclusion: It is necessary to increase the awareness of emergency physicians about hereditary angioedema, which can cause fatal attacks and whose diagnosis and treatment are different from other angioedemas.

Keywords: Hereditary angioedema, HAE, survey, emergency

INTRODUCTION

Hereditary angioedema (HAE), which usually results from C1 esterase inhibitor (C1-INH) deficiency, affects the skin, gastrointestinal tract, and upper respiratory tract.[1] Symptoms of angioedema may also affect the face and tongue. The most important clue to HAE is the presence of angioedema that is not accompanied by urticaria and pruritus.[2] It is an autosomal dominant inherited disease.[1] HAE is more severe than allergic angioedema and takes longer to heal.[3,4] HAE symptoms usually do not respond to antihistamines, corticosteroids, or epinephrine.[3] Edema in the gastrointestinal mucosa (GI) is the cause of abdominal symptoms. HAE attacks of abdominal pain, nausea, vomiting, and diarrhea may be confused with acute abdomen and acute gastroenteritis.[5,6] Laboratory tests (C1-INH and C4 levels) are indicated in patients with symptoms. HAE attacks should be treated immediately. Plasma-derived C1-inh concentrates and recombinant C1 inhibitors are administered intravenously or bradykinin B2 receptor antagonist and plasma kallikrein inhibitor are administered subcutaneously.[7]

Early diagnosis and treatment are critical to minimize mortality and morbidity. These patients can not be diagnosed for 1 to 6 years.[8] Sometimes these patients are misdiagnosed or treated incorrectly. Although not very common, emergency physicians are the physician group that encounters these patients most seriously. A significant number of patients experience a laryngeal edema attack at some point in their lives. These attacks can be fatal because they do not benefit from antihistamines and epinephrine. There may be delays and difficulties in managing these attacks in the emergency department. Therefore, it is very important to diagnose this condition in the emergency department, manage such attacks and provide post-treatment care. With this study, we aimed to determine if emergency physicians have sufficient knowledge, experience, and equipment to manage and treat HAE attacks in the emergency department.

METHODS

The study was approved by the Ankara City Hospital Clinical Researches Ethics Committee No. 1 (Date: 29.12.2021, Decision No: E1-21-2282). The study was conducted in accordance with the Principles of the Declaration of Helsinki by informing the participants and obtaining their consent. An online questionnaire was sent to physicians working in emergency departments of all types of hospitals in different cities in Turkey in 2022. 'Google Forms' was used in this study, which indicates that it is confidential and secure, that it does not transfer information to third parties, and that it does not leak information to different channels. Online survey form was sent to 210 physicians. 103 physicians wanted to participate in the survey. The questionnaire form consisted of two parts. It included a total of ten questions. The first part included 3 questions about medical experience and academic degree. The second part included 7 questions related to the diagnosis and treatment of HAE in the emergency department.

Statistical Analysis

First, the descriptive characteristics of the variables (number and percentage) were found. The total scores of the respondents were calculated according to the number of correct answers, assuming that those who answered all seven questions correctly would receive 100 points. The Chi-square test was used to compare categorical variables. When comparing continuous variables, the Mann-Whiney U was used to compare two groups, and the Kruskal-Wallis test was used to compare more than two groups. Risk factors for giving less than 4 correct answers were investigated with logistic regression analysis. First, single logistic regression was performed and those with $p<0.25$ were included in multiple regression analysis. The "Statistical Package for Social Sciences" SPSS 25 (IBM Corp., Armonk, NY, USA) program was used to evaluate the results. $p<0.05$ was accepted as significant.

RESULTS

The percentage of physicians with 15 or more years of professional experience was 7.8%, while the percentage of physicians with less than 15 years of professional experience was 92.2% (Table 1). The highest participation rate was 52% in the group of assistants, followed by emergency medicine specialists with 41.2% (Table 1). The percentage of physicians who reported having already examined a patient with HAE was 58.3% (Table 1). You can also see all the questions and answers in Table 1.

40.6% correctly answered the question "Which finding does not belong to HAE?" with "itchy red lesions (Table 2)." Which is not a factor that triggers HAE?" the answer to the question was 32% correct and 68% incorrect (Table 2). "C1-esterase deficiency is the key factor involved in the etiopathogenesis of HAE" While 83.5% of the respondents answered the question correctly saying they agree, 7.8% gave the wrong answer and 8.7% said they had no idea (Table 1). While 39.8% of the population thought that epinephrine and antihistamines were useful in treating attacks, 53.4% disagreed (Table 1). When asked ''Which agent should not be used in the treatment of HAE attacks?'', 51.5% of those who mentioned epinephrine gave the correct answer, while 48.5% gave the incorrect

Table 1. Analysis of demographic data

Professional experience	**n**	**%**
<15 years	94	92.2
>=15 years	8	7.8
Profesion group		
Assistant	53	52
Specialist	42	41.2
Academician	7	6.9
Have patients with HAE*		
Yes	60	58.3
No	43	41.7
Finding does not belong to HAE*		
Cutaneous swelling in different parts of the body	8	7.9
Stomachache	6	5.9
Diarrhea	39	38.6
Itchy red lesions	41	40.6
Shortness of breath	7	6.9
Not one of the factors triggering HAE*		
Oral contraceptive	5	5
Menstruation	21	21
Trauma	41	41
Danazol	32	32
Infection	1	1
C1-esterase deficiency is involved in the etiopathogenesis of HAE*		
Agree	86	83.5
No opinion	9	8.7
Not agree	8	7.8
Epinephrine and antihistamines are useful in treating attacks		
Agree	41	39.8
No opinion	7	6.8
Not agree	55	53.4
Should not be used in the treatment of HAE* attacks		
C1 esterase inhibitor	5	5
Fresh frozen plasma	21	20.8
Bradykinin	6	5.9
Epinephrine	52	51.5
Kallikrein	17	16.8
Non HAE* features		
Associated with stress	9	8,9
Takes longer to heal from allergic angioedema	9	8,9
Begins at an early age	10	9.9
Associated with food, pollen, and odorsand odors	59	58.4
More severe than allergic angioedema	14	13.9
Not in the differential diagnosis of HAE*		
Acute abdomen	17	16.7
FMF**	6	5.9
Allergic angioedema	3	2.9
AGE***	40	39.2
Urticaria	36	35.3

*HAE: Herediter angioedema, ** FMF: Familial Mediterranean Fever, ***AGE:Acute gastroenteritis n: Number of patients

answer (Table 2). When asked about non-HAE features, we got 41.6% wrong and 58.4% correct answers (Table 2). When asked about the differential diagnosis of HAE, we received 64.7% incorrect answers and 35.3% correct answers (Table 2). The average of correct answers to a total of 7 knowledge questions 3.54+-0.7 and the median score was 4.

It was found that there was a significant difference in the mean of correct answers between those with less than 15 years of experience and those with more than 15 years of experience (Table 3).

There was no significant difference in the mean of correct responses between residents, specialist and academicians (Table 4).

Table 5 evaluated the relationship between the rate of correct answers to information-based questions and demographic data and previous encounters with a HEA patient. While previous encounter with a HAE patient and professional experience were significant, there was no difference between professional groups (Table 5).

Table 2. Accuracy rates of answers to questions about the diagnosis and treatment of the disease

Finding does not belong to HAE*	n	%
Incorrect	60	59.4
Correct	41	40.6
Not one of the factors triggering HAE*		
Incorrect	68	68
Correct	32	32
C1-esterase deficiency is involved in the etiopathogenesis of HAE*		
Incorrect	17	16.5
Correct	86	83.5
Epinephrine and antihistamines are useful in treating attacks		
Incorrect	48	46.6
Correct	55	53.4
Should not be used in the treatment of HAE* attacks		
Incorrect	49	48.5
Correct	52	51.5
Non HAE* features		
Incorrect	42	41.6
Correct	59	58.4
Not in the differential diagnosis of HAE*		
Incorrect	66	64.7
Correct	36	35.3
Number of correct answers	n	P
0	3	2.9
1	22	21.4
2	14	13.6
3	12	11.7
4	16	15.5
5	14	13.6
6	13	12.6
7	9	8.7
Correct answer group		
3 or less correct	50	49.0
4 or more correct	52	51.0
Point **	57.1 (28.6-71.4)	

*HAE: Herediter angioedema, n: Number of patients **Median value (25-75%)

Table 3. Relationship between professional experience and correct answers

	Professional experience				
	<15 years		>=15 years		p value**
	n	%	n	%	
Number of correct answers					0.001
0	3	3.2	0	0	
1	21	22.3	0	0	
2	14	14.9	0	0	
3	12	12.8	0	0	
4	15	16	1	12,5	
5	12	12.8	2	25	
6	11	11.7	2	25	
7	6	6.4	3	37,5	
Number of correct answers					0.006
< =3 Correct	50	53.2	0	0	
>=4 Correct	44	46.8	8	100	
Point*	42.9(14.3-71.4)		85.7(71.4-100.0)		0.001

*Median Value (%25-75) ** p< 0.05 significant, n: Number of patients

Table 4. The relationship of proffesion groups and correct answers

	Assistant		Specialist		p**
Number of correct answers	n	%	n	%	0.168
< =3 Correct	29	54.7	17	40,5	
>=4 Correct	24	45.3	25	59,5	
	Assistant		Academician		p**
Number of correct answers	n	%	n	%	1.000
< =3 Correct	29	54.7	4	57.1	
>=4 Correct	24	45,3	3	42.9	
	Specialist		Academician		p**
Number of correct answers	n	%	n	%	0.443
< =3 Correct	17	40.5	4	57.1	
>=4 Correct	25	59.5	3	42.9	
Point*	42.9 (28.6-71.4)	57,1 (14.3-85.7)	42,9 (42,9-100,0)		0.223

*Median value (%25-75), ** p< 0.05 significant, n: Number of patients

When logistic regression analyses were performed in Table 4, it was observed that having a previous HAE patient was effective in giving the correct answer, while it became clear that professional experience and professional group were insignificant.

DISCUSSION

The survey was sent to 210 physicians online and 103 people responded with a rate of 49%. In Baran's thesis study,[5] 42% of the physicians responded to the survey, while in the study conducted by Riedl et al.[9] 3% of the physicians responded to the survey sent to 6750 physicians via e-mail.Although Baran attributed this difference to the fact that they conducted the survey face-to-face, our survey achieved higher participation

Table 5. The relationship between professional years, groups, having any HAE and number of correct answers

	Number of correct answers				
	<=3 Correct		>=4 Correct		
	n	%	n	%	p*
Professional years					0.006
<15 years	50	100,0	44	84.6	
>=15 years	0	0.0	8	15.4	
Proffesion groups					0.436
Asistant	29	58.0	24	46.2	
Specialist	17	34.0	25	48.1	
Academician	4	8,0	3	5.8	
Have you ever had HAE?					0.037
Yes	24	47.1	36	69.2	
No	27	52.9	16	30.8	

* p< 0.05 significant

Table 6. Logistic regression analysises for risk factors of giving fewer than 4 correct answers

Risk factors for giving fewer than 4 correct answers	Single logistic regression analysis				Multiple logistic regression analysis			
	B	CI (%95)		p*	B	CI (%95)		p*
Professional years (being more than 15 than being less than 15)	0.555			0.999				
Professional group (Being a specialist or a academician compared to being an assistant)	0.620	0.284	1.358	0.232				
HAE patient (have you ever had patient or not)	2.531	1.130	5.666	0.024	2.439	1.086	5.464	0.031

* p< 0.05 significant

despite being online. We can attribute this situation to sending it to all of the addressees one by one via WhatsApp instead of e-mail. Nevertheless, when we look at these rates, survey participation was evaluated as low, and considering that the experiences and opinions of physicians are very valuable, it was concluded that survey participation should be increased.

As a result of this study that awareness and knowledge of HAE, especially attack management in emergency department should be improved. We also concluded that having previously encountered a HAE patient was effective in giving a correct answer, but academic title or length of professional experience did not make a significant difference in terms of disease awareness. Not having a patient with hereditary angioedema increases the risk of less than 4 correct answers by 2.439 times (1.086-5.464) p=0.031).

Although there was a difference in HAE knowledge when physicians with more professional experience were compared to physicians with less professional experience, no significant difference was found when we looked at the logistic regression analysis. Unlike our study, young physicians heard about HAE more frequently than older physicians in Mete Gökmen et al.'s[10] study. We think that this difference may be due to the low rate of physicians with more than 15 years of experience in our study (7.8%) or the comparison of young physicians by age in the other study (35.9±8.2 years vs. 45.7±13.2 years, p=0.04). No significant difference was found between academicians, experts, and residents in terms of the average of correct answers. This shows that there is no difference in the practice of HAE after medical school, specialization training and afterwards. Recently, some faculties have been trying to increase HAE awareness. We would like to emphasize that this disease, which is of particular interest to emergency physicians, should be given more attention during emergency medicine specialization training, as it poses a life-threatening risk to patients due to laryngospasm that may occur during an attack and is treated differently than other angioedemas.

One of the aims of medical education is to provide continuous learning behavior. Continuous professional development, which includes self-learning activities as well as courses, conferences, lectures, is necessary for people to develop their knowledge and skills and their professional lives.[11]

In this study, the rate of physicians who reported that they examined a patient with HAE was 58.3%. In the 2016 dissertation study by M. Baran, the proportion of physicians who had a patient with HAE was 26%. The low rate in this study may be due to the fact that the physicians participating in the study were not only emergency physicians, but also physicians working in other units.[5] Similarly, in another study conducted by Mete et al.[10] with the participation of 155 internal medicine physicians, a significant portion of the physicians (93.5%) reported that they had heard of HAE and 41.9% reported that they followed at least one HAE patient.

The prevalence of the disease is reported to be 1:50,000 to 1:400,000.[1,12] According to the study conducted by Ozdemir et al.[8] the total number of patients diagnosed with HAE in Turkey is believed to be between 500 and 7500. This autosomal-dominant inherited disease is thought to be more common in society than is known, but it is difficult to diagnose. In the study conducted by Ozdemir and his friend

and published in 2017, 60 relatives of 4 diagnosed HAE patients were examined, and 38.2% of them were diagnosed HAE.[8] As awareness of the disease increases among physicians, the number of patients diagnosed with HAE will also increase, and thus awareness of treatment will become more important.

In our study, the rate of physicians who answered all questions requiring information was determined to be 8.7%. In the study conducted by Lisa Fu et al.[13] in Canada and including 34 physicians, it was determined that all physicians were aware of the HAE guidelines, however, it was stated that members of groups such as the Canadian Hereditary Angioedema Network, the Canadian Society of Clinical Immunology and Allergy, and the Canadian Hematology Association were included in this study. And this result showed that being in contact with various organizations and associations related to HAE increases awareness of the disease.

The awareness of the deficiency of the most important factor, C1-INH, in the etiopathogenesis of HAE was found to be very high 83.5%. In the study conducted by Mete Gökmen et al.[10] in 2014, only 22% of physicians knew the role of C1 inhibitor in HAE, while 38.7% had no idea about the pathogenesis of HAE. We think that the reason why awareness of this issue is so high is because it is a question that has recently been included in the medical specialty exam.

In our study, 39.8% thought that epinephrine and antihistamines could be used during an attack and were beneficial, while 6.8% had no idea and 53.4% gave the correct answer. In the other study 34.8% had no idea what drugs are used to treat HAE attacks, while 54.8% reported that they would treat the patients with drugs that have no effect in HAE, such as adrenaline or antihistamines. More than 80% of the doctors did not know which drugs are used in the prophylactic therapy of HAE.[10] One of the most important mistakes in treating HAE attacks is wasting time by giving antihistamines, steroids, and epinephrine to the patient. HAE is a disease related to the complement system, and replacing the missing C1-INH is the most important treatment regimen. 2 (0.8%) of the physicians who participated in the study by Terzioğlu et al.[14] chose the exact correct answers regarding emergency management**.** In a 2012 study of emergency departments by Jaiganesh et al.[15] it was found that although therapeutic C1-INHs were available in the emergency departments studied in England, there was a significant shortage regarding their use. In recognition of this shortage, a guideline for treatment was developed in the same study.

Another survey conducted in the U.S. published in 2021 shows that diagnostic and treatment patterns of physicians in the U.S. have improved significantly between 2010 and 2019 HAE.[9] Time is very important in this disease because many patients die before they are diagnosed. For this reason it is very important to keep an eye on this disease. It is necessary to increase the awareness of doctors about treatment. We can improve knowledge and awareness through a variety of training interventions like in a survey of pharmacists, e-learning programs were shown to increase knowledge about anaphylaxis, even in the long term.[16]

Another study conducted in Brazil among pediatricians, whether board certified in allergy and immunology or not, found insufficient knowledge about HAE, and attributed the large degree of unawareness among physicians to the fact that HAE is a rare disease. This and many similar studies, in line with our study, argue that physicians' awareness of HAE should be increased.[17]

The strength of the survey is that it is the first survey we know of that measures emergency physicians' awareness of HAE. The survey is reliable. With this survey and its continuation, we can increase awareness, curiosity, and thus knowledge about the disease.

Limitation

This study is limited by the nature of the survey instrument and the fact that the study was conducted via an Internet survey, by the lack of a standard questionnaire, by the high proportion of physicians with less than 15 years of experience, by the unequal number of groups, and by the small number of total academicians participating in the survey. We did not use a standardized and validated questionnaire. In addition, our study is a national study, which affects the generalizability of the results.

CONCLUSION

As a result, HAE should definitely come to mind in patients presenting to the emergency department with angioedema without urticaria; in cases of angioedema that does not respond to treatments such as antihistamines, cortisol, adrenaline; in patients with widespread edema in the intestines; family history should be questioned and the patient should be referred to relevant departments such as internal medicine or allergy immunology for a definitive diagnosis. In this way, we can ensure that patients receive a more rapid diagnosis at a lower cost. Most importantly, In order to avoid catastrophic consequences such as mortality and morbidity due to laryngeal spasm, it is imperative that we increase awareness of this disease, especially its attack treatment, in emergency services.

Training about HAE should be increased. Programs need to be developed for diagnosis and treatment of the disease and for raising awareness. It is possible to increase the level of knowledge of physicians about HAE through regular training. Training can take the form of theoretical and practical courses, e-learning, or a combination of these and support from associations can be made available. These factors may be more meaningful to patients and may better reflect the benefits of treatment.

Although further study is needed, the results of the survey will shed light on the subject in planning what needs to be done to develop sufficient and necessary awareness.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was initiated with the approval of the Ankara City Hospital Clinical Research Ethics Committee No. 1 (Date: 29.12.2021, Decision No: E1-21-2282).

Informed Consent

Written consent was obtained from the patient participating in this study.

Referee Evaluation Process
Externally peer-reviewed.

Conflict of Interest Statement
The authors have no conflicts of interest to declare.

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Author Contributions
All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Original Article

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Analysis of the hemogram and biochemistry parameters of patients with trauma

Fatih Ahmet Kahraman[1], Havva Şahin Kavaklı[1], Ferhat İçme[1], Yavuz Otal[2], Alp Şener[1]

[1]*Department of Emergency Medicine, Ankara Bilkent City Hospital, Ankara, Turkiye*
[2]*Department of Emergency Medicine, Ankara Etlik City Hospital, Ankara, Turkiye*

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Corresponding Author: Fatih Ahmet Kahraman, fahmetkahraman@gmail.com

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ABSTRACT

Aims: Trauma-related deaths remain a significant public health concern, with organ complications in over 30% of multitrauma patients leading to high morbidity and mortality. This study aims to understand the changes and reliability of hemoglobin, hematocrit, AST, and ALT levels in trauma cases and their impact on treatment planning.

Methods: A retrospective analysis was conducted on 259 multitrauma patients admitted to Ankara Atatürk Training and Research Hospital between July and December 2012. Data on demographic details, trauma types, laboratory parameters, physical and tomographic examinations, treatment modalities, and outcomes were analyzed using SPSS software.

Results: The study group predominantly comprised males (74.9%) with a mean age of 42.15 years. Various trauma types were analyzed, including traffic accidents and falls. Significant fluctuations in hemoglobin and hematocrit levels were observed post-fluid resuscitation, regardless of bleeding status. Notably, AST and ALT levels were reliable indicators of hepatic injury. The study also highlighted the effects of fluid hydration volumes on hemoglobin and hematocrit levels.

Conclusion: IThe findings challenge the conventional understanding that drops in hemoglobin and hematocrit levels primarily indicate bleeding in multitrauma patients. Instead, these changes might also result from fluid resuscitation. The study underscores the importance of considering both bleeding and resuscitation efforts when interpreting these laboratory parameters. This study provides new insights into the interpretation of hemoglobin, hematocrit, AST, and ALT levels in trauma patients. It suggests a more nuanced approach in treatment planning, considering the significant impact of fluid resuscitation on these parameters, alongside bleeding.

Keywords: Trauma, emergency service, retrospective study, blood tests, demograph

INTRODUCTION

Trauma-related death cases are still a major public health issue and efforts to reduce its impact are crucial.[1] Serious organ complications occur in a significant proportion (greater than 30%) of multitrauma patients, which lead to a high morbidity and, in some cases, death.[2,3] Traffic accidents (in-vehicle and out-of-vehicle), falls from a height, and battery are the main causes of multitrauma.

While bleeding and monitoring hemorrhagic shock dictates fluid and blood transfusions in trauma patients, hemoglobin and hematocrit levels are the main parameters that are taken into account in clinical practice. However, these laboratory tests are affected both by the endocrinological response to trauma and the resuscitation efforts. In addition, evaluations of the liver, which is frequently injured in abdominal trauma, are mainly driven by physical examination and radiological tests. However, there are several studies indicating that hepatic function tests (AST and ALT are studied in the emergency biochemistry panel) guide management of hepatic injuries.[1-3]

Therefore, we designed the present study to seek the answers to several questions such as how do the parameters like hemoglobin, hematocrit, AST, and ALT change, how reliable are they, and by which situations are they affected in trauma cases. We aimed to make objective recommendations to clinicians by investigating whether these parameters may contribute to treatment planning.

METHODS

This study was produced from the thesis, it prepared at Ankara Research Hospital on 30/07/2013. Institutional approval was obtained. All procedures were carried out in

accordance with the ethical rules and the principles of the Declaration of Helsinki

This study retrospectively analyzed the data of 259 patients who were admitted to the emergency department of Ankara Atatürk Training and Research Hospital after in-vehicle traffic accident, out-of-vehicle traffic accident, motorcycle accident, fall from a height, and battery between 01.07.2012 and 31.12.2012.

The patients' age, sex, trauma type, hemoglobin, hematocrit, AST, and ALT levels at first admission, physical examination findings in the head, thorax, abdomen, and extremities, findings in the tomographic examination, hydration and blood transfusion status and volumes, status of alcohol ingestion before trauma, treatment type (surgical intervention, medical follow-up), length of hospital stay, and outcome (death, intensive care unit admission) were analyzed. Patients who were older than 16 years, who were admitted after a traffic accident (in-vehicle or out-of-vehicle), fall from a height, or battery, whose hemogram (hemoglobin and hematocrit) and biochemistry (AST and ALT) parameters were measured, whose control hemogram (hemoglobin and hematocrit) parameters were measured, and among cases with abdominal injury, those who had solid organ injury (liver, spleen, kidney) were included.

The forensic files and the emergency department follow-up charts of the patients were reviewed, and the physical examination findings, sociodemographic characteristics, trauma type, hemogram and biochemistry results, tomographic findings, treatment type, and outcome of each patient were recorded on the study forms. The patients' hemogram (hemoglobin and hematocrit) and biochemistry parameters (AST and ALT) taken within a 48-hour period after trauma were included in the study whereas blood tests taken later were excluded. Patients with a missing emergency department follow-up chart were also excluded due to possibly missing data.

The findings on abdominal tomography were defined as hepatic injury, renal injury, splenic injury, and pancreatic injury (solid organ injury). The findings on thorax tomography were defined as rib fracture, hemothorax, pneumothorax, and contusion. The findings on limb tomography were defined as lower extremity and upper extremity findings. Bone, joint, soft tissue, and vascular injuries were included in the lower and upper extremity injuries. Alcohol blow test and blood ethanol level were used to detect alcohol ingestion. Blood transfusion and hydration were defined as the treatments that were administered to the patients. Hydration was defined as the administration of crystalloid or colloid fluids at a volume of at least 1000 cc. Blood transfusion was defined as the transfusion of at least 1 unit of erythrocyte suspension or whole blood.

Statistical Analysis

The data obtained from this study were recorded on a computer and analyzed using SPSS (Statistical Package for Social Sciences) Windows 19.0 software.

RESULTS

This study included 259 multitrauma patients who presented to the adult emergency department. The mean age of the patients was 42.15±1.80 years. Seventy-four point nine percent of patients were male and 25.1% were female. Fifty-nine point eight percent of them had an in-vehicle traffic accident (IVTA), 8.5% out-of-vehicle traffic accident (OVTA), 2.3% motorcycle accident, 25.5% fell from a height, and 3.9% were battered. The outcomes of patients included discharge from the emergency department (35.0%), admission to the ward (46.7%), admission to the intensive care unit (11.3%), and death (7.0%) (Table 1).

Table 1. Distribution of the patients by sex, cause of trauma, and patient outcome

Variables		n	%
Sex	Female	65	25.1
	Male	194	74.9
Cause of trauma	IVTA	155	59.8
	OVTA	22	8.5
	Motorcycle accident	6	2.3
	Fall from a height	66	25.5
	Battery	10	3.9
Outcome	Discharge from the emergency department	90	35.0
	Admission to ward	120	46.7
	Intensive care	29	11.3
	Death	18	7.0
Total		259	100

IVTA: In-vehicle traffic accident, OVTA: Out-of-vehicle traffic accident

According to the results of the Wilcoxon Signed Rank Test, there was a significant difference between the admission and control hematocrit levels among patients who did not receive hydration (Z: -2.341, $p<0.05$). According to a hydration volume of 1000 cc, there was a significant difference between the admission and control hemoglobin levels (Z: -6.065, $p<0.05$). According to a hydration volume of 1000 cc, there was a significant difference between the admission and control hematocrit levels (Z:-5.334, $p<0.05$). According to a hydration volume of 1500 cc, there was a significant difference between the admission and control hemoglobin levels (Z: -2.945, $p<0.05$). According to a hydration volume of 1500 cc, there was a significant difference between the admission and control hematocrit levels (Z:-3.041, $p<0.05$). According to a hydration volume of 2000 cc, there was a significant difference between the admission and control hemoglobin levels (Z:-4.336, $p<0.05$). According to a hydration volume of 2000 cc, there was a significant difference between the admission and control hematocrit levels (Z: -4.866, $p<0.05$) (Table 2).

Table 2. Testing the difference between the admission and control levels by the volume of hydration (Wilcoxon Signed Rank Test)

Volume of Hydration	Levels	Median (Min-Max)	Negative Mean Rank	Positive Mean Rank	Wilcoxon	p
0	Hemoglobin	14 (8.1 - 16.9)	47.98	39.92	-1.837	0.066
	Control hemoglobin	13.7 (8.4 - 17)				
	Hematocrit	41.9 (24.1 - 51.2)	43.11	44.23	-2.341	0.055
	Control hematocrit	40.45 (24.1 - 51)				
1000	Hemoglobin	14.1 (8.1 - 18.8)	37.61	48.83	-6.065	0.000
	Control hemoglobin	13.2 (7.1 - 18.3)				
	Hematocrit	41.6 (23.8 - 53.3)	37.77	43.30	-5.334	0.000
	Control hematocrit	38.35 (24 - 49)				
1500	Hemoglobin	13.8 (6.9 - 16)	13.23	15.00	-2.945	0.003
	Control hemoglobin	12.8 (7.7 - 15.8)				
	Hemotokrit	40.3 (20.4 - 47.6)	13.41	14.00	-3.041	0.002
	Control hematocrit	38.2 (23.1 - 45)				
2000	Hemoglobin	13.8 (5.2 - 16.1)	26.20	32.29	-4.336	0.000
	Control hemoglobin	12.2 (2.7 - 16.4)				
	Hematocrit	40.1 (15.6 - 47.7)	27.50	23.71	-4.866	0.000
	Control hematocrit	35.4 (8.4 - 45.8)				

Wilcoxon Signed Rank Test. The correlation is statistically significant at the $p<0.05$ level. Min: Minimum, Max: Maximum

According to the results of the Wilcoxon Signed Rank Test, there was a significant difference between the admission and control hemoglobin levels in patients who had no finding on abdominal tomography (Z: -6.762, $p<0.05$). There was a significant difference between the admission and control hematocrit levels in patients who had no finding on abdominal tomography (Z: -6.621, $p<0.05$). There was a significant difference between the admission and control hemoglobin levels in patients with splenic injury on abdominal tomography (Z: -2.685, $p<0.05$). There was a significant difference between the admission and control hematocrit levels in patients with splenic injury on abdominal tomography (Z: -2.072, $p<0.05$). There was a significant difference between the admission and control AST levels in patients with splenic injury on abdominal tomography (Z: -2.175, $p<0.05$). There was a significant difference between the admission and control hemoglobin levels in patients with hepatic injury on abdominal tomography (Z: -2.395, $p<0.05$). There was a significant difference between the admission and control hematocrit levels in patients with hepatic injury on abdominal tomography (Z: -3.294, $p<0.05$). There was a significant difference between the admission and control AST levels in patients with hepatic + splenic injury on abdominal tomography (Z: -2.505, $p<0.05$) (Table 3).

According to the results of the Wilcoxon Signed Rank Test, there was a significant difference between the admission and control hemoglobin levels in patients with hemothorax (Z: -6.258, $p<0.05$). There was a significant difference between the admission and control hematocrit levels in patients with hemothorax (Z: -5.347, $p<0.05$). There was a significant difference between the admission and control AST levels in patients with hemothorax (Z: -2.153, $p<0.05$). (Table 4)

When the amount of drop in the Hb and Htc levels were analyzed by the volume of fluid hydration in patients who were not considered to have bleeding, statistically significant Hb and Htc drops were found in patients who received fluid replacement with at least 1000 cc fluid volume. According to the results of the Wilcoxon Signed Rank Test, there was a significant difference between the admission and control hemoglobin levels by 1000-cc volume replacement in patients without injury (Z: -4.498, $p<0.05$). There was a significant difference between the admission and control hematocrit levels by 1000 cc volume replacement in patients without injury (Z: -4.388, $p<0.05$). There was a significant difference between the admission and control hemoglobin levels by 1500-cc volume replacement in patients without injury (Z: -3.646, $p<0.05$). There was a significant difference between the admission and control hematocrit levels by 1500-cc volume replacement in patients without injury (Z: -3.634, $p<0.05$). There was a significant difference between the admission and control hemoglobin levels by 2000-cc volume replacement in patients without injury (Z: -3.308, $p<0.05$). There was a significant difference between the admission and control hematocrit levels by 2000-cc volume replacement in patients without injury (Z:-3.308, $p<0.05$) (Table 5).

In patients considered to have bleeding, on the other hand, there was a significant drop in the hematocrit level in the group that did not receive hydration. There was a drop in the hemoglobin level, albeit statistically insignificant. In patients who were hydrated with a fluid volume of at least 1000 cc, on the other hand, both the hemoglobin and hematocrit levels significantly dropped. According to the results of the Wilcoxon Signed Rank Test, there was a significant difference between the admission and control hematocrit levels by 0-cc volume replacement in patients with injury (Z: -2.325, $p<0.05$). There was a significant difference between the admission and control hemoglobin levels by 1000-cc volume replacement in patients with injury (Z: -4.103, $p<0.05$). There was a significant difference between the admission and control hematocrit levels by 1000-cc volume replacement in patients with injury (Z: -3.114, $p<0.05$). There was a significant difference between the admission and control hemoglobin levels by 1500-cc volume replacement in patients with injury (Z: -2.011 $p<0.05$). There was a significant difference between the admission and control hematocrit levels by 1500-cc volume replacement in patients with injury (Z: -2.011 $p<0.05$). There was a significant difference between the admission and control hemoglobin levels by 2000-cc volume of replacement

Table 3. Testing the difference between the admission and control levels by the results of abdominal CT (Wilcoxon Signed Rank Test)

Abdominal CT	Levels	Median (Min-Max)	Negative Mean Rank	Positive Mean Rank	Wilcoxon	p
No finding	Hemoglobin	13.9 (8.1 - 18.8)	81.79	59.44	-6.762	0.000
	Control hemoglobin	12.75 (2.7 - 17.7)				
	Hematocrit	41.25 (24.1 - 53.3)	77.89	66.69	-6.621	0.000
	Control hematocrit	38.2 (8.4 - 51)				
	AST	32 (6 - 321)	17.63	22.42	-1.721	0.085
	Control AST	49.5 (14 - 232)				
	ALT	24 (2 - 816)	19.96	21.50	-1.470	0.142
	Control ALT	37.5 (11 - 95)				
Splenic injury	Hemoglobin	14.5 (5.2 - 16.4)	12.77	17.50	-2.685	0.007
	Control hemoglobin	13.1 (9.3 - 15.5)				
	Hematocrit	41.8 (15.6 - 47)	11.68	23.50	-2.072	0.038
	Control hematocrit	37.9 (29.1 - 44.7)				
	AST	45 (19 - 308)	6.50	9.17	-2.175	0.030
	Control AST	97 (57 - 340)				
	ALT	28 (12 - 188)	7.00	10.00	-0.623	0.533
	Control ALT	68 (29 - 177)				
Hepatic injury	Hemoglobin	15.1 (8.9 - 16.8)	17.73	18.78	-2.395	0.017
	Control hemoglobin	14 (8.3 - 18.3)				
	Hematocrit	42.8 (25.4 - 47.5)	18.43	16.29	-3.294	0.001
	Control hematocrit	40.2 (23.5 - 49)				
	AST	111 (15 - 691)	8.83	12.00	-0.443	0.658
	Control AST	109 (17 - 187)				
	ALT	86 (13 - 571)	7.70	12.56	-0.725	0.468
	Control ALT	96 (10 - 161)				
Hepatic + splenic injury	Hemoglobin	11.6 (8.1 - 14.4)	6.10	8.50	-1.741	0.082
	Control hemoglobin	11.5 (7.1 - 13.5)				
	Hematocrit	34.2 (23.8 - 41.1)	7.00	5.50	-1.337	0.181
	Control hematocrit	34.1 (24 - 39)				
	AST	186 (45 - 309)	1.50	6.50	-2.505	0.012
	Control AST	204 (77 - 413)				
	ALT	85 (27 - 261)	4.50	6.17	-0.971	0.331
	Control ALT	81 (58 - 401)				
Intraabdominal free fluid	Hemoglobin	13.55 (6.9 - 15)	8.67	8.00	-1.867	0.062
	Control hemoglobin	12.4 (7.7 - 14.7)				
	Hematocrit	39.25 (20.4 - 43)	8.50	8.50	-1.760	0.078
	Control hematocrit	37.1 (23.1 - 42.5)				
	AST	56 (14 - 136)	3.50	8.50	-0.665	0.506
	Control AST	75 (11 - 92)				
	ALT	33 (6 - 84)	5.50	5.50	-1.687	0.092
	Control ALT	19 (5 - 61)				

Wilcoxon Signed Rank Test
The correlation is statistically significant at the p<0.05 level.
Min: Minimum, Max: Maximum, AST: Aspartat aminotransferase, ALT: Alanin aminotransferase

Table 4. Tesing the difference between the admission and control levels by the results of the thorax CT (Wilcoxon Signed Rank Test)

Thorax CT	Levels	Median (Min-Max)	Negative Mean Rank	Positive Mean Rank	Wilcoxon	p
Patients with hemothorax	Hemoglobin	13.8 (6.9 - 16.6)	55.45	40.10	-6.258	0.000
	Control hemoglobin	12.5 (2.7 - 16.9)				
	Hematocrit	40.05 (20.4 - 47)	52.85	46.59	-5.347	0.000
	Control hematocrit	36.8 (8.4 - 49.3)				
	AST	63 (6 - 691)	14.90	17.23	-2.153	0.031
	Control AST	77 (33 - 340)				
	ALT	44 (2 - 571)	13.50	19.50	-0.899	0.368
	Control ALT	58 (28 - 177)				

Wilcoxon Signed Rank Test
The correlation is statistically significant at the p<0.05 level
CT: Computed tomography, Min: Minimum, Max: Maximum, AST: Aspartat aminotransferase, ALT: Alanin aminotransferase

Table 5. Testing the difference between the injury status wih respect to admission and control levels by the volume of hydration (Wilcoxon Signed Rank Test)

Injury	Volume of hydration	Levels	Median (Min-Max)	Negative Mean Rank	Positive Mean Rank	Wilcoxon	p
Absent	0	Hemoglobin	13.6 (8.1 - 16.9)	32.36	28.22	-1.128	0.259
		Control hemoglobin	13.4 (8.4 - 17)				
		Hematocrit	41.8 (24.1 -51.2)	29.06	30.17	-1.251	0.211
		Control hematocrit	40.6 (24.1 - 51)				
	1000	Hemoglobin	14.1 (8.3 - 18.8)	21.00	21.00	-4.498	0.000
		Control hemoglobin	12.7 (9.3 - 17.7)				
		Hematocrit	41.1 (24.7 -53.3)	20.78	23.00	-4.388	0.000
		Control hematocrit	38.2 (27.9 - 49)				
	1500	Hemoglobin	14.3 (10.5 - 16)	9.00	0.00	-3.646	0.000
		Control hemoglobin	12.8 (10.4 -15.8)				
		Hematocrit	41.2 (37.6 -47.6)	9.00	0.00	-3.634	0.000
		Control hematocrit	38.2 (33.3 - 45)				
	2000	Hemoglobin	13.9 (10.1 -15.9)	7.50	0.00	-3.308	0.001
		Control hemoglobin	11.8 (2.7 - 13.1)				
		Hematocrit	41.2 (29.5 -47.7)	7.50	0.00	-3.308	0.001
		Control hematocrit	34.1 (8.4 - 37.9)				
Present	0	Hemoglobin	14.5 (10.8 - 16)	16.47	11.45	-1.755	0.079
		Control hemoglobin	13.9 (11.5 -16.9)				
		Hematocrit	42.3 (33.3 -45.9)	14.52	14.43	-2.325	0.020
		Control hematocrit	40.3 (34.7 -49.3)				
	1000	Hemoglobin	14.3 (8.1 - 16.8)	17.12	32.50	-4.103	0.000
		Control hemoglobin	13.5 (7.1 - 18.3)				
		Hematocrit	41.9 (23.8 - 47.5)	17.41	20.83	-3.114	0.002
		Control hematocrit	39.4 (24 - 49)				
	1500	Hemoglobin	13.8 (6.9 - 15.7)	6.20	3.50	-2.011	0.032
		Control hemoglobin	12.5 (7.7 - 14.4)				
		Hematocrit	38.7 (20.4 - 46.5)	6.20	3.50	-2.011	0.002
		Control hematocrit	36.5 (23.1 -42.9)				
	2000	Hemoglobin	13.45 (5.2 - 16.1)	18.75	25.71	-2.934	0.003
		Control hemoglobin	12.6 (8.3 - 16.4)				
		Hematocrit	40 (15.6 - 46.1)	20.06	19.71	-3.518	0.000
		Control hematocrit	36.7 (23.5 -45.8)				

Wilcoxon Signed Rank Test
The correlation is statistically significant at the p<0.05 level.

in patients with injury (Z: -2.934, p<0.05). There was a significant difference between the admission and control hematocrit levels by 2000-cc volume replacement in patients with injury (Z: -3.518, p<0.05) (Table 5).

DISCUSSION

Hemoglobin and hematocrit levels, as well as ALT and AST levels, are commonly used in the follow-up of trauma patients.[4] A drop in the hemoglobin and hematocrit levels are important for monitoring bleeding while elevated AST and ALT levels are important because that they indicate hepatic injury.[5]

In our study, the drop in both the hemoglobin and hematocrit levels was statistically significant in patients who were administered only fluids. In addition, when we analyzed the hemoglobin and hematocrit levels by examining patients with hemorrhagic, we still observed a significant drop in both parameters. Hence, it will be more prudent to consider the drop in the Hb and Htc levels as a sign of primarily bleeding in multi-trauma patients. Our study also shows that AST and ALT levels are useful for indicating hepatic injury in multitrauma patients.

In patients admitted to the emergency department, the administration of 1-2 liters of isotonic crystalloid solution is considered the standard treatment. Vital signs and hemoglobin level are used to detect bleeding during patient monitoring.[6] Studies in the literature that demonstrated the amount of hemoglobin drop resulting from the infusion of 1-2 liters of isotonic saline have been conducted in small patient groups. Grathwohl et al.[7] examined the effect of IV volume loading on blood count parameters in healthy volunteers; they reported no significant difference in the leukocyte and thrombocyte series but significant drops in the hemoglobin and hematocrit levels. However, they reported that those levels returned to baseline over time. In

a study conducted by Lobo et al.[8], the subjects were given 2 L isotonic saline or 2 L 5% Dextrose within a hour, and the their body weight, hemoglobin, serum albumin, serum and urine biochemistry, and bioelectrical impedance were measured on an hourly basis for 6 hours before and after the infusion. In patients who were administered isotonic saline, the hematocrit and hemoglobin levels dropped by 7.5%. The same study also drew attention to a Hb drop of about 12% after fluid replacement, and advocated that a sudden increase in intravascular volume was the main reason for the Hb drop. Lobo et al.[9] also compared volume loading with 2000 cc 5% dextrose and isotonic saline; the authors reported that the Hb level significantly dropped in both groups within an hour (Hct 7.5%), and the levels tended to re-surge after the infusion was stopped. Karaaslan et al.[10] reported that isotonic saline replacement after 2 Units of blood was drawn caused Hb and Hct levels to drop.

Thoraon et al.[11] reported that the changes in Htc were the single most reliable test demonstrating blood loss in trauma patients undergoing fluid replacement. In that study, it was found that a Hct change of 6 or greater was highly suspicious of blood loss while smaller Hct changes may be a warning sign. Studies on this subject have shown that the Hb and Hct levels that dropped after fluid treatment were stabilized or even slightly increased after some time. Our study included no evaluation or test that would corroborate this finding.

Our study revealed a significant drop in both the Hb and Hct levels in patients who were administered 1000 cc or larger fluid volumes. Our study evaluated hydration volumes separately and found similar results in all of those groups. It was found that the liquid volumes in previous studies are generally constant.[9,10]

Here, the potential hemorrhagic conditions of these patients will naturally lead to a drop in those levels, which ultimately cause a question mark. Thus, when we separately evaluated patients without hemorrhagic injuries and looked at their hemoglobin and hematocrit levels, we still observed a significant drop in their levels. Here, that question mark cannot be eliminated. While the hemoglobin level dropped by an average of 10% in the group without injury, that 6% drop occurred in the group having injury. Theoretically, the opposite of this calls to mind. To our opinion, this contradiction can be explained by the changes in the fluid-electrolyte balance. In this case, interpreting Hb and Hct drops in multitrauma patients as a sign of bleeding would be more prudent.[12]

In the systematic evaluation conducted by Quispe-Cornejo and colleagues,[13] they found that there was a decrease in hemoglobin values with fluid administration and they had difficulty in determining the reason for this. Across 63 studies suitable for meta-analysis, the Hb decreased significantly by a mean of 1.33 g/dl after fluid administration: in non-acutely ill subjects, the mean decrease was 1.56 g/dl, and in acutely ill patients 0.84 g/dl.

In our study, the patients who had injuries on tomographic imaging but did not receive fluid replacement between Hb and Hct controls had a mean Hb drop of 4.1% and a mean Htc drop of 4.7%. While even such decreases lead to injury outcomes, we believe that it would not be safe to give an average level for these Hb and Htc drops.

Our study demonstrated a male predominance in the patient population. This is in line with general trauma data in the previous studies.[3]

Tan et al.[14] showed a relationship between hepatic injury and increased hepatic transminase levels after blunt abdominal trauma. They reported that AST and ALT levels that were elevated to two times of the upper limit of normal indicate major hepatic injury and recommended that the case should be managed accordingly. Sola et al.[15] in a study on pediatric trauma patients, reported that AST and ALT measurements proved to be useful markers of intraabdominal injury in blunt abdominal trauma. They also stated that pediatric patients with a negative FAST and liver trasaminases below 100 IU/L could be conservatively managed instead of being sent to tomography that pose radiation risks. Hennes et al.[16] studied pediatric patients with hemodynamically stable blunt abdominal trauma and found that an AST level greater than 450 IU/L and an ALT level greater than 250 IU/L had a sensitivity of 100% and a specificity of 92.8% for hepatic injury. They opined that patients with hepatic enzymes above those levels should be evaluated with tomography.

Kumar et al.[17] found that routine use of amylase and lipase levels alone in blunt trauma to reveal extrapancreatic injury is not appropriate regarding the cost/benefit ratio, but may be useful when used in conjunction with hepatic enzymes. In that study, the urinary lipase level was significant on the first day and the use of the urinary lipase/amylase ratio in conjunction with AST, ALT, and ALP on the first, third, and fifth days was significant in patients with hepatic injury. In splenic injury, on the other hand, it was shown that serum amylase, AST, ALT, Hb, and Hct levels on the first day were significant. In a study, Tian et al.[18] investigated whether AST, ALT, GGT, and LDH levels indicated the presence and the severity of hepatic injury in blunt abdominal trauma. They concluded that ALT >57 U/L and AST >113 U/L strongly indicated hepatic injury although a link between those levels and the severity of hepatic injury could not be established. A study by Bevan et al.[19] studied ALT alone; it reported that ALT was a useful marker for assessing the presence or absence of hepatic injury. It was also stated that hemodynamically stable pediatric patients with an ALT level less than 104 IU/L can be monitored without tomography to avoid unnecessary radiation exposure.

In the study by Da-wei Zhao and colleagues,[20] they evaluated liver function tests in trauma patients, the aspartate aminotransferase and lactate dehydrogenase concentrations and the aspartate aminotransferase/alanine aminotransferase ratio were positively correlated with the grade of liver injury and serum liver enzyme measurement exhibited high consistency with CE-MDCT for both detection and grading of intraparenchymal lesions in blunt liver trauma. The results they found are similar to our study. In the study by Bilgiç and her colleagues,[21] significant increases in AST, ALT and LDH values were detected in patients with liver trauma.

In parallel with the aforementioned studies, our study demonstrated that AST and ALT levels are useful for indicating hepatic injury in multitrauma patients. When we correlated the elevation of any of ALT or AST with the signs of hepatic injury on abdominal tomography, we found that the combined use of AST and ALT had a sensitivity of 91.5% and a specificity of 45.6%. The reason for a low specificity

may be that these tests may be elevated in many other organ injuries. Possible examples include AST elevation in cardiac trauma cases,[22,23] and the elevation of these markers in splenic injury.[17] We did not statistically evaluate AST and ALT individually because both were above the upper limit or both were below the lower limit in all patients. According to the literature data, ALT reflects hepatic injury more sensitively.[24] In our study, AST was found to accompany ALT in all patients. These data may imply that AST is as valuable as ALT as a marker of hepatic injury.

Limitations

Our study has some limitations. Some of them are the short study period, retrospective study design, and the exclusion of 28 patients with missing data. Other limitations are the inclusion of solely multitrauma patients but no other trauma patients, exclusion of patients admitted with cardiac arrest, and the evaluation of solid organ injuries as present/absent, without staging them. There is a need for prospective, multi-center studies on this subject.

CONCLUSION

In the present study on multitrauma patients admitted to the emergency department, a significant drop in the hemoglobin and hematocrit levels was recorded as a result of fluid resuscitation of 1000 cc or above; even if the patients without bleeding were analyzed separately, a statistically significant drop was still apparent. No correlation could be established for these hemoglobin and hematocrit changes between patients with and without injury. These data suggest that a drop in the hemoglobin and hematocrit levels in multitrauma patients may not result from bleeding alone, but also fluid resuscitation. To our opinion, it would be more accurate to approach such patients as if they have bleeding.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study was produced from the thesis, it prepared at Ankara Research Hospital on 30/07/2013. Institutional approval was obtained.

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Case Report

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Don't miss it as anxiety, ARDS!

Salih Fettahoğlu[1], Süreyya Tuba Fettahoğlu[1], Tuğçe Türkalp[2], Efe Demir Bala[1], Ramiz Yazıcı[1], Serkan Doğan[1]

[1]*Department of Emergency Medicine, Kanuni Sultan Süleyman Training and Research Hospital, İstanbul, Turkiye*
[2]*Department of Emergency Medicine, Reyhanlı State Hospital, Hatay, Turkiye*

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Corresponding Author: Salih Fettahoğlu, salihfettahoglu52@gmail.com

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ABSTRACT

Acute respiratory distress syndrome (ARDS) is a critical condition which compromises with the respiratory functions. Aim of this study is to present the management of ARDS case in the emergency department. This is a case report of a patient who was admitted to an emergency department. We did not apply any statistical methods. A 41-year-old female patient with no medical history was admitted to the emergency department as an outpatient with complaints of shortness of breath and palpitations. After a physical examination, it was first though that the patient was simply experiencing an anxiety episode. However, oxygen saturation was measured as 35 % and further investigation of the patient revealed ARDS as the cause of these symptoms. Patient was admitted to the ICU unit. Even though anxiety can be common, it can be dangerous to dismiss other clinical and potentially lethal pathologies when searching for the cause of respiratory distress. Physical examination and vital signs should be evaluated together to reach a potential diagnosis.

Keywords: Acute respiratory distress syndrome, anxiety, saturation

INTRODUCTION

Acute respiratory distress syndrome (ARDS) is a potentially critical condition which is characterized by non-cardiogenic diffuse bilateral infiltration. ARDS is often caused by a trigger event which can include, sepsis, trauma, drug toxicities and smoke inhalations. Clinically, tachypnea, dyspnea and cyanosis are present, and ventilation/perfusion imbalance has been shown to be an integral part of the pathophysiology of ARDS. ARDS mortality remains quite high, usually above 50%. This high mortality rate is primarily due to complications of multiple organ failures caused by both the trigger events and the ARDS itself.[1,2]

Here, we presented a patient who was admitted to our emergency department with symptoms of respiratory distress, tachypnea and tachycardia, and was diagnosed with ARDS as a result of ongoing examination findings and tests, which at first glance was thought to be a panic attack-anxiety disorder, along with literature information.

CASE

A 41-year-old female patient with no medical history was admitted to the emergency department as an outpatient with complaints of shortness of breath and palpitations. Consciousness was evaluated as clear, oriented-cooperative, GCS: 15. Upon further investigation and anamnesis, it was understood that respiratory distress started suddenly and woke her up from sleep. The patient communicated easily and as a result of this fact it was first thought that the patient was having a panic attack-anxiety disorder. This notion was supported by the fact that the patient did not have any previous medical history and was not an active or former smoker. However, following the measurement of her vitals, the saturation value was detected 30-35% by pulse oximetry. Upon this revelation, she was quickly taken to the resuscitation area. After a careful physical examination, it was detected that the patient had bilateral rales and the dyspnea became apparent with the intercostal muscles joining in to support the respiratory effort. With these findings and extremely low oxygen saturation detected by pulse oximetry alongside a progressing cyanosis with no response to initial oxygen therapy, the decision was made to intubate the patient in order to prevent a pending respiratory arrest. With these processes being completed, what at first glance looked like an panic attack-anxiety disorder, became a potentially life threatening condition. At this point, clinicians had a few diffential diagnosis at hand, which included pneumonia, pulmonary emboli and ARDS. In order to narrow down the list of potential diagnosis, bloodwork and imaging studies were initiated after the patient was intubated and stabilized. ECG was evaluated as Normal Sinus Rhythm. In bloodwork, pH was 7.35 mmHg (normal range 7.35mmHg -7.45 mmHg)

and a pCO_2(partial pressure of carbon dioxide) of 35 mmHg (normal range 22 mmHg-29 mmHg) was detected alongside a PaO_2 (Partial arterial pressure of oxygen) of 23 mmHg. Leukocyte count of 18 10^3/µl (normal range 3.8 10^3/µl -10 10^3/µl was found in the blood results. Further tests showed CRP (C-Reactive Protein) as 6 mg/L (<5 mg/L), D-dimer as 2.2 mg/L (<0.5 mg/L) and troponin T as 7.43 ng/L (<14 ng/L). There was bilateral infiltration and a ground glass appearance in the lungs on thorax computed tomography (CT) (Figure 1,2). With D-dimer being detected above the normal threshold a pulmonary artery CT angiogram was performed in order to exclude the possibility of a pulmonary emboli, which came back negative. Further bloodwork was conducted in order to eliminate the possibility of a cardiogenic edema, and with Pro-BNP being detected <125 pg/ml, we excluded the possibility of a left ventricular dysfunction. Finally with other possibilities being excluded, we proceeded to evaluate the patient for ARDS. With the abrupt onset within hours, a CT scan which reveals bilateral ground glass opacities alongside a low Pro-BNP and a PaO_2 to FiO_2 ratio of 92, which, according to the Berlin Criteria for ARDS, corresponds to a severe ARDS. After the diagnostic processes and the initial treatments were completed, the patient was transferred to the ICU with the preliminary diagnosis of severe ARDS.

DISCUSSION

ARDS should be suspected in patients with symptoms of progressive dyspnea, increased oxygen requirements, and alveolar infiltrates on chest imaging within 6 to 72 hours of a precipitating event. When severe, acute confusion, respiratory distress, cyanosis, and sweating may be evident. Cough, chest pain, wheezing, hemoptysis and fever are inconsistent and mostly depend on the underlying etiology.[3] Clinical findings related to the underlying etiology may also be present at the time of admission, but no certain etiology was found in our case, however with the elevated lymphocyte count a viral infection could be a potential trigger event. Clinical diagnosis of ARDS is made by Berlin criteria.[3,4] Our case also meets most of the Berlin criteria, with respiratory distress starting within hours, bilateral widespread opacity on lung imaging, young age, and lack of any cardiac history based on clinical history and a low PaO_2 to FiO_2 ratio . Because the international consensus definition of ARDS does not specify any criteria for underlying etiology, some uncertainty remains about which conditions should or should not be included in the ARDS diagnostic umbrella. These include disorders that are generally known to cause widespread alveolar damage and have the potential to resolve over time.[5] ARDS mortality remains very high, usually above 50%. This high mortality rate develops due to the complications of multisystem organ failure caused by the pathologies that primarily cause ARDS, rather than ARDS itself. Thanks to modern ventilation protocols, only about 15% of cases with ARDS result in mortality due to the inability of the lungs to oxygenate the blood.[6,7]

CONCLUSION

ARDS is a syndrome with a high mortality rate that is diagnosed with high awareness and requires various clinical findings along with laboratory tests and imaging. Our case report aims to help evaluate ARDS in the Emergency Department and to draw attention to the importance of evaluating patients' general condition, physical examination, laboratory tests, imaging and vitals as a whole for emergency physicians. This case report is presented in order to ensure that panic attack-anxiety disorders should be considered after organic pathologies are excluded, and that such patients are not overlooked in the busy emergency department.

ETHICAL DECLARATIONS

Informed Consent

The patients signed the free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declared that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Case Report

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A side effect that should be considered in patients using metformin: lactic acidosis

Gözde Yılmaz, Fatma Hançer Çelik, Rukiye Aytekin, Haticenur Yıldırım, Necmi Baykan

Department of Emergency Medicine, Kayseri City Hospital, Kayseri, Turkiye

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Corresponding Author: Gözde Yılmaz, beau_gozde@hotmail.com

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ABSTRACT

The most serious and life-threatening side effect seen in patients using metformin is metabolic acidosis. If there is a history of diabetes in patients with high anion gap metabolic acidosis who present to the emergency department, metformin use should be questioned. In our case, metformin-related lactic acidosis was detected in a 67-year-old female patient who applied to the emergency department with a complaint of palpitations. The patient's kidney function tests were within normal range and he did not describe excessive drug intake. Despite the treatments administered in the emergency room, the patient's blood gas lactate level continued to increase and his acidosis deepened. After other causes of lactic acidosis were excluded, the patient was consulted with internal medicine and transferred to the intensive care unit. With this case report, we tried to draw attention to the fact that the patient group for which metformin will be used in the treatment should be carefully selected and that lactic acidosis, which is a fatal side effect, should be considered in the differential diagnosis and treatment should be started in those using this drug.

Keywords: Lactic acidosis, metformin, side effect

INTRODUCTION

Metformin is a drug that reduces insulin resistance and is used to lower blood sugar in patients with type 2 diabetes.[1] The most serious and life-threatening side effect seen in patients is metabolic acidosis. Kidney failure is often the cause of this lactic acidosis. Metformin is not a suitable treatment option for patients with creatinine levels above 1.4 mg/dl. If there is a history of diabetes in patients with high anion gap metabolic acidosis who present to the emergency department, metformin use should be questioned. Our case, a 67-year-old female patient, applied to the emergency department with a complaint of palpitations. His examinations revealed metabolic and lactic acidosis due to metformin. In metformin poisoning, the risk of rapid progression of acidosis and leading to death despite optimal treatment is high.[2] Therefore, caution should be exercised in the use of metformin in people with weakened kidney function and the dose should be adjusted according to GFR.[3]

CASE

A 67-year-old female patient, who had a medical history of high blood pressure, diabetes and cardiovascular occlusion, applied to the emergency room with a feeling of palpitations. He did not mention chest pain, back pain and abdominal pain in his anamnesis. There was no decrease in the patient's oral intake. On physical examination, the pulse was 106\min, SpO_2 was %98, there was bilateral pretibial edema, and no other pathological findings were detected. It was learned that the drugs he used were apixaban, verapamil hydrochloride and metformin. The ECG was in atrial fibrillation rhythm. Blood parameters, including troponin, were requested. In the first blood gas, pH: 7.48 and lactate: 4.7 mmol/L were detected. No other pathology was detected in blood parameters. The patient was hydrated. Control blood gas and troponin were taken. There was no dynamic change in the control ECG. In the control blood gas, pH:7.45 lactate: 5.5 mmol/L was detected. The patient's kidney function tests and infective parameters were within normal limits. CT angiography was performed to rule out pulmonary embolism and mesenteric ischemia, and no pathology was detected. Control troponin result was found to be negative. He was consulted with cardiology because he complained of palpitations and high lactate. As a result of echocardiography performed by the cardiologist, ejection fraction was found to be 60% and wall movements were normal. Acute cardiac pathology was not considered. Blood gas was taken again, pH:7.28, lactate: 10.8 mmol/L, HCO_3: 15 mmol\L. Since the patient's lactic acidosis continued despite hydration and the medications, he used were Mato fin (oral antidiabetic with the active ingredient

metformin), lactic acidosis due to metformin use was considered and internal medicine was consulted. The patient was transferred to the intensive care unit with a diagnosis of lactic acidosis due to metformin use.

DISCUSSION

Metformin, one of the biguanide class of oral antidiabetic agents, is one of the first drugs chosen in the initial diagnosis of the majority of patients with type 2 diabetes mellitus, unless there is a contraindication to its use, since it acts by different mechanisms. Metformin's mechanisms of action include decreasing glucose production in the liver, increasing glucose utilization in insulin-sensitive tissues such as muscle and adipose tissue, decreasing appetite and calorie intake, and decreasing intestinal glucose absorption.[4] Side effects include non-specific symptoms, confusion, nausea, vomiting and pain in the upper abdomen, as well as life-threatening symptoms including moderate renal failure, hypotension, hypothermia, respiratory failure and cardiac rhythm abnormalities may develop.[5] Metformin is a drug commonly used in the treatment of type 2 diabetes and has a safe profile in the right patients. A review of 347 studies in the literature, including 70,490 patients, found no evidence that metformin causes metabolic acidosis.[6] Our patient presented with palpitations, which is a relatively rare symptom. She did not describe any additional symptoms. Although metformin-induced lactic acidosis is expected to be more common in patients with reduced GFR, metformin may rarely cause lactic acidosis even in patients with normal renal function.[3] Our patient had no signs of renal failure and renal function tests were within normal range. Despite this, there was a rapidly deepening lactic acidosis during follow-up. Drug interactions between metformin and other medications used by patients must be evaluated. In our case, the patient was consulted with internal medicine and hydration therapy, frequent venous blood gas measurements and follow-up in the intensive care unit were recommended. The patient with deepening lactic acidosis despite hydration was admitted to intensive care unit. There is no direct antidote for the treatment of metformin-induced lactic acidosis. Parenteral $NaHCO_3$, continuous Ven venous hemodiafiltration and intermittent hemodialysis are used to correct lactic acidosis and alleviate symptoms. Hemodialysis helps to improve acidosis and also removes metformin.[4]

CONCLUSION

With this case report, we tried to draw attention to the fact that the patient group to be treated with metformin should be carefully selected and lactic acidosis, which is a fatal side effect, should be considered in the differential diagnosis and treatment should be started.

ETHICAL DECLARATIONS

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Letter to the Editor

Botulinum toxin-related blepharoptosis in emergency department admissions

Demet Acar

Department of Emergency Medicine, Konya City Hospital, University of Health Sciences, Konya, Turkiye

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Corresponding Author: Demet Acar, dr_demetacar@hotmail.com

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Dear Editor,

I have been following your journal with great interest for a long time. Your emphasis on practical applications, clinical observations, and field experiences, as well as the meticulous selection of your publications, serves as a guide for many researchers and academics, including myself. Based on my clinical observations and firsthand field experiences, I would like to share with you a patient portfolio that we have recently encountered frequently in the green zone of the emergency department.

The use of botulinum toxin A (BoNT-A) is now prevalent not only for therapeutic purposes but also extensively for cosmetic reasons. Compared to surgical methods, its less invasive nature and seemingly easy application have made BoNT-A a popular choice among physicians of all specialties and even among auxiliary healthcare workers. This trend has led to widespread cosmetic BoNT-A administration within family circles and among friends.

With the increase in family or friend-to-friend BoNT-A applications among healthcare workers, there has recently been a noticeable rise in unilateral blepharoptosis cases presenting to the green zone of emergency departments. Blepharoptosis arises due to the weakness of the levator palpebrae superioris muscle. On average, the onset occurs 3-14 days after the initial injection and typically resolves spontaneously once the paralytic effect of BoNT-A diminishes.[1] Improper dosage adjustment of BoNT-A and a lack of detailed knowledge of facial anatomy can lead to complications, as can anatomical variations of the supraorbital foramen or neurovascular pedicle.[2] Even when blepharoptosis develops in individuals who have received cosmetic BoNT-A applications at a legal center by trained and experienced physicians, experts in the field can partially reverse the eyelid ptosis. They do this by administering medications such as oxymetazoline hydrochloride or apraclonidine hydrochloride eye drops, anticholinesterase agents, or transdermal BoNT-A injections.[3]

However, the aforementioned group of healthcare workers who administer BoNT-A among family or friends, and the resulting blepharoptosis cases, are patients we have been encountering more frequently in the green zone of emergency departments. The number of such cases is increasing daily. When considering the gender of patients presenting to the emergency department's green zone with blepharoptosis resulting from BoNT-A application, we observe that the number of men is not significantly lower than that of women.

The application of BoNT-A for the reduction of facial wrinkles may appear simple for a healthcare professional; however, it is crucial to understand the anatomy and be knowledgeable about the causes and treatments of blepharoptosis. Detailed anatomical knowledge of the supraorbital area and orbital roof is essential to prevent incorrect injections into the "danger zones" that increase the risk of eyelid ptosis.

ETHICAL DECLARATIONS

Referee Evaluation Process

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The authors have no conflicts of interest to declare.

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Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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