



# EURASIAN JOURNAL of CRITICAL CARE



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Emergency Physicians Association of Turkey

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# Eurasian Journal of Critical Care

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**August 2025- Volume: 7 Issue: 2**

**Publisher**

Published by the Emergency Medicine Physicians' Association of Turkey (EPAT).

**Country of Publication**

Turkey

**Frequency of Publication**

Published 3 times a year: in April, August, and December.

**Publication Model**

Open access. All content is freely available without charge. No processing or publication fees are requested.

**Target Audience**

The target audience includes healthcare professionals working in the field of critical care such as emergency medicine and intensive care specialists; specialists in pulmonology, cardiology, surgery, pediatrics, and anesthesiology; clinical researchers, academics; resident physicians, general practitioners, pharmacists and pharmacologists, and other professionals working in the healthcare sector.

**Language of Publication**

English

**Fee Policy**

No fees are charged to authors for evaluation, publication, or article processing. The entire process is free of charge.

**Peer Review Type**

Double-blind peer review system is applied. Authors and reviewers are unaware of each other's identities.

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# Editorial

Dear Readers,

We are delighted to present the first issue of the seventh volume of the *Eurasian Journal of Critical Care*. This edition features timely, interdisciplinary, and clinically impactful studies that contribute directly to the evolving landscape of emergency and critical care medicine. We extend our sincere appreciation to our editors, reviewers, and editorial board members, whose dedication and expertise continue to uphold the scientific integrity of our journal. We also congratulate and thank all contributing authors for their hard work and commitment to advancing the field.

## **Acknowledgment to Reviewers**

We would like to express our deepest gratitude to the dedicated scientists who have served as reviewers for the *Eurasian Journal of Critical Care*. Their insightful evaluations and tireless efforts are crucial to maintaining the quality, objectivity, and credibility of our publication. We truly value their partnership and look forward to their continued support in future issues.

As the pace of medical information accelerates and decision-support tools evolve, we remain committed to guiding clinical practice through the lens of evidence-based medicine.

Sincerely,

## **Başar Cander**

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### Evaluation of Female Patients of Childbearing Age Who Applied to the Emergency Medicine Department with Abdominal Pain

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#### Abstract

**Objective:** Abdominal pain, which has etiological diversity, is associated with an increasing number of patients in emergency departments. Early recognition of its life-threatening causes is important. This study aims to evaluate the diagnoses of female patients of reproductive age who presented with non-traumatic abdominal pain.

**Material and Methods:** A prospective, cross-sectional study was conducted by including demographic and clinical information of women aged 18-50 years who presented to the emergency department of a tertiary hospital between March and September 2020 with non-traumatic abdominal pain.

**Results:** A total of 167 women with non-traumatic abdominal pain were included in the study. The most common presenting complaint was nausea-vomiting (41.3%), and the average duration of symptoms was 24 hours. Physical examination revealed abdominal tenderness in 74.9% of patients. During diagnosis, blood, urine, and stool tests were requested for 95.2% of patients, and imaging tests such as erect abdominal radiograph, ultrasound, magnetic resonance, or computed tomography were requested for 61.7% of patients. The most common diagnosis was urinary tract infection, accounting for 24% of cases.

**Conclusion:** In addition to identifying the pathological condition causing abdominal pain, accompanying comorbidities and history of previous surgery must be investigated. Imaging tests play a crucial role in reaching the correct diagnosis. However, they also seen as a means of reducing emergency department overcrowding, hospitalization, and the need for surgical treatment.

**Keywords:** Childbearing Age, Emergency Medicine, Non-Traumatic Abdominal Pain, Women

#### Introduction

Abdominal pain is one of the most important symptoms that compel patients to seek hospital care in all populations. It has a broad etiological spectrum (1). A comprehensive approach based on demographic data such as age and gender, along with patient history, physical examination, and diagnostic tests, is required to determine the underlying pathological condition (2). Abdominal pain is a common condition in women of childbearing age, and determining the underlying cause is often challenging. However, the location and characteristics of the pain can serve as a starting point for initial diagnosis in the emergency department.

Therefore, advanced diagnostic tests and examinations, conducted by the recommendations of the American College of Radiology after patient stabilization, enable us to reach a diagnosis (3). This will help in the early diagnosis of diseases with high mortality and morbidity rates, as well as in determining the appropriate diagnosis and treatment methods. Despite technological advances, patient management remains one of the most important clinical problems in emergency departments. In particular, patients with non-specific abdominal pain, for whom a definitive diagnosis cannot be made despite the use of all diagnostic methods, continue to constitute a significant proportion (35-40%) of cases (4). This study aims to evaluate the diagnosis and

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**Received:** 05.06.2025 • **Revision:** 22.07.2025 • **Accepted:** 05.08.2025

**DOI:** 10.55994/ejcc.1715030

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Available online at <https://dergipark.org.tr/pub/ejcc>

**Cite this article as:** Enes Guler, Ozlem Bilir, Gokhan Ersunan, Ismail Atas. Evaluation of Female Patients of Childbearing Age Who Applied to the Emergency Medicine Department with Abdominal Pain. Eurasian Journal of Critical Care. 2025;7(2): 1-6

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follow-up process of women of childbearing age who presented to the emergency department of a tertiary hospital with non-traumatic abdominal pain.

## Material And Methods

**Study design:** This study was conducted at a tertiary hospital with approximately 150,000 emergency department visits per year. Women aged 18–50 years of reproductive age who presented to the emergency department between March and September 2020 with non-traumatic abdominal pain were included in the study after obtaining informed consent. The study was approved by the local ethics committee (Date: 11.03.2020, No: 2020/38) and conducted by the principles outlined in Helsinki Declaration. Emergency residents (ER) managed women patients presenting with abdominal pain in the emergency department, categorized during triage, and evaluated by the attending physician. They stabilized after determining their acute care and resuscitation needs. ER transferred them to the appropriate area for further care.

**Study data:** The data of the patients included in the study (age, gender, complaints, family history, vital

signs, and physical examination findings), their clinical conditions, blood and imaging tests, preliminary and final diagnoses, follow-up areas, outcomes, and treatments (medical or surgical) applied according to their diagnoses were recorded in a pre-established study form. Patients whose clinical condition was unstable at the time of admission or during emergency department follow-up were provided with resuscitation care and followed up in the Intensive Care Unit. Patients under the age of 18, women over the age of 50, patients with trauma-related abdominal pain, and patients who could not provide informed consent were excluded from the study.

**Data analysis:** The sample size of the study was calculated with a test power of at least 80% and a type I error of 5% for each variable. The Kolmogorov-Smirnov test ( $n > 50$ ) was used to determine whether continuous variables were normally distributed; nonparametric tests were applied since they were not normally distributed. Descriptive statistics for continuous variables in our study were expressed as mean, standard deviation, median, minimum, and maximum values. For categorical variables, they were expressed as numbers and percentages. The Mann-Whitney U test was used to compare measurements according to admission and operation groups. Spearman

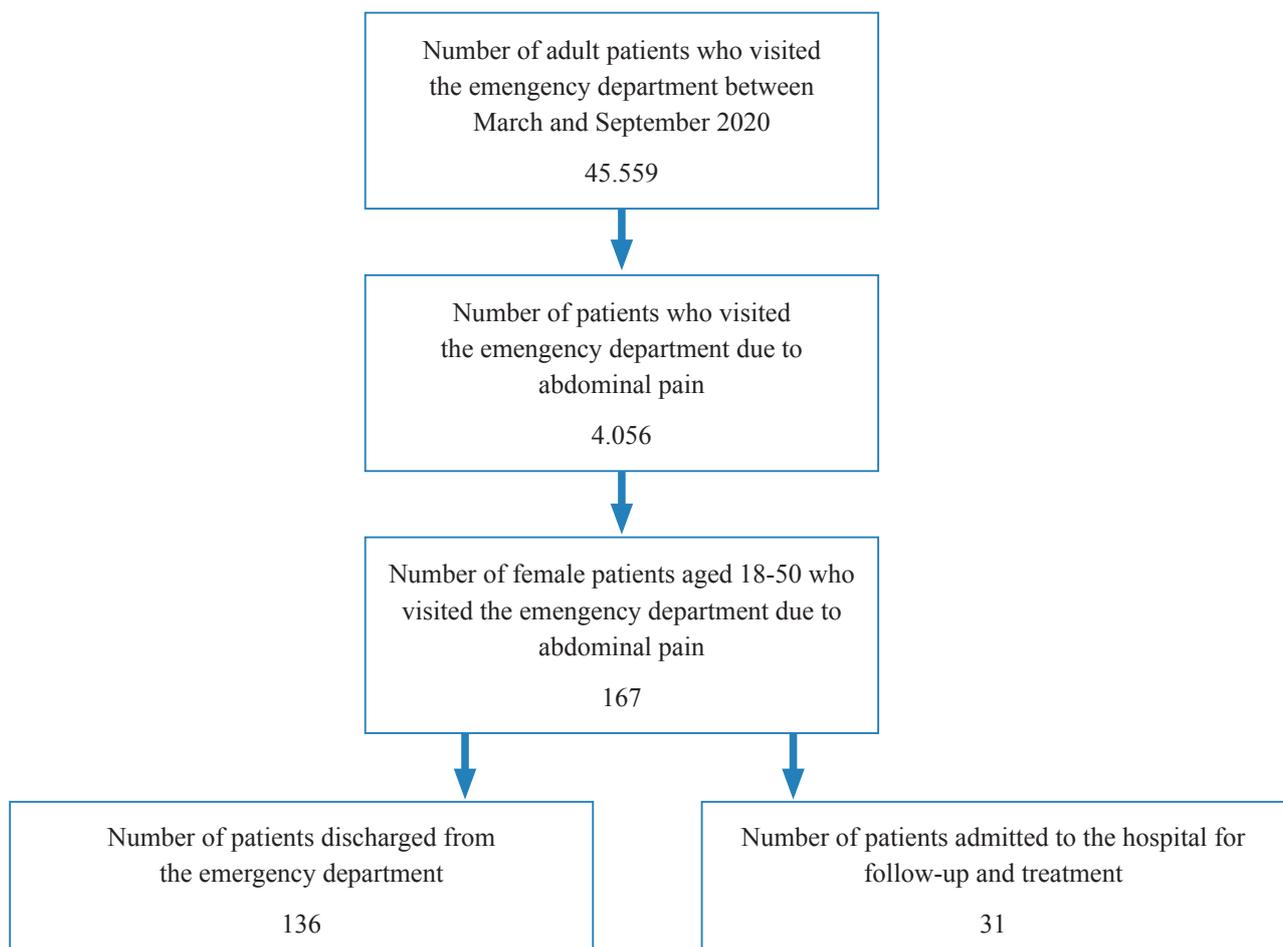


Figure 1. Flow chart diagram.

**Table 1.** Demographic characteristics, accompanying symptoms, and physical examination findings of reproductive-aged women presenting with abdominal pain, along with diagnostic tests requested.

Variable	% (n)
<b>Age (years), median (IQR)</b>	31 (24-37)
<b>Medical history</b>	%22.8 (38)
History of surgery	%8.4 (14)
Hypertension	%7.8 (13)
Diabetes mellitus	%3.6 (6)
Asthma	%3 (5)
Ureteral stone	%1.8 (3)
Colon polyp	%1.8 (3)
<b>Family history of diseases</b>	%6.6 (11)
Diabetes mellitus	%4.8 (8)
Hypertension	%4.2 (7)
Ureteral stone	%1.2 (2)
<b>The time between the onset of symptoms and presentation to the emergency department (hours), median (IQR)</b>	24 (6-48)
<b>Complaints accompanying abdominal pain</b>	
Nausea-vomiting	%41.3 (69)
Pelvic pain	%15.6 (26)
Heartburn	%11.4 (19)
Dysuria	%10.8 (18)
Diarrhea	%10.8 (18)
<b>Physical examination findings at the presentation</b>	%80.8 (135)
Tenderness	%74.9 (125)
Rebound	%18 (30)
Defense	%16.2 (27)
Costovertebral angle tenderness	%8.4 (14)
<b>Laboratory Tests</b>	
Complete blood count	%93.4 (156)
Biochemistry	%92.8 (155)
B HCG	%73.1 (122)
Complete urine analysis	%62.3 (104)
Coagulation	%22.2 (37)
Cardiac biomarkers	%10.8 (18)
Blood gas	%3.6 (6)
Stool analysis	%3.6 (6)
<b>Imaging Tests</b>	%61.7 (103)
Computed tomography	%35.3 (59)
Ultrasound	%32.9 (55)
Erect abdominal X-ray	%15.6 (26)
Magnetic resonance	%4.8 (8)

correlation coefficients were calculated to determine the relationships between measurements. The Chi-square test was used to determine the relationship between categorical variables. The Z-ratio test was used for proportional

comparisons between “Preliminary Diagnosis” and “Diagnosis.” The statistical significance level ( $\alpha$ ) was set at 0.05 for calculations, and SPSS (IBM SPSS for Windows, version 24) and Minitab (Statistical Software for Windows, version 17) statistical software packages were used for the calculations.

## Results

During the study period, 40,569 adult patients presented to the emergency department, of whom 4,056 (8.9%) presented with abdominal pain. Among this group, 167 women aged 18–50 years of reproductive age with abdominal pain were included in the study (Figure 1).

**Demographic characteristics, presenting complaints, physical examination findings, and requested tests:** The median age of the 167 female patients included in the study was 31 (IQR 18–48), and 38 (22.8%) had a history of any disease that could cause comorbidity. Of these, 14 (8.4%) had a history of previous surgical intervention, 13 (7.8%) had hypertension, and 6 (3.6%) had diabetes mellitus. In their family history, 8 (4.8%) had diabetes mellitus and 7 (4.2%) had hypertension (Table 1). The most commonly reported associated symptoms by the patients included nausea-vomiting in 69 (41.3%), pelvic pain in 19 (11.4%), and dysuria in 18 (10.8%). The median time between the onset of the presenting complaint and presentation to the emergency department was 24 hours (IQR, 6–48 hours). Vital signs were stable at the presentation. Physical examination revealed abdominal tenderness in 125 (74.9%), rebound tenderness in 30 (18%), and abdominal guarding in 27 (16.2%) patients. Laboratory tests were requested for 159 (95.2%) patients, and imaging studies were requested for 103 (61.7%) patients. Among laboratory tests, the most common were complete blood count (156, 93.4%), biochemical tests (155, 92.8%),  $\beta$  HCG 122 (73.1%) were performed, while imaging tests included computed tomography 59 (35.3%), ultrasound 55 (32.9%), and erect abdominal X-ray 26 (15.6%) (Table 1).

**Patients’ preliminary diagnosis, diagnosis, and follow-up areas:** Based on patients’ complaints and physical examinations, the preliminary diagnosis in the emergency department was urinary tract infection in 34 (20.4%), nonspecific abdominal pain in 33 (19.8%), and acute gastroenteritis in 17 (10.2%); the final diagnoses revealed urinary tract infection in 40 (24%) patients, nonspecific abdominal pain in 28 (16.8%) patients, and acute gastroenteritis in 19 (11.4%) patients. When evaluating the relationship between initial diagnosis and definitive diagnosis, greater agreement was observed in patients with suspected acute appendicitis and renal colic ( $p = 0.049$ )

**Table 2.** Preliminary diagnosis and diagnosis in the emergency department

	Preliminary Diagnosis % (n)	Final Diagnosis % (n)
Urinary Tract Infection	%20.4 (34)	%24 (40)
Nonspecific Abdominal Pain	%19.8 (33)	%16.8 (28)
Acute Gastroenteritis	%10.2 (17)	%11.4 (19)
Acute Appendicitis	%9.6 (16)	%4.2 (7)
Renal Colic	%9.6 (16)	%4.2 (7)
Peptic Ulcer	%8.4 (14)	%6.6 (11)
Ovarian Cyst	%4.8 (8)	%6 (10)
Acute Cholecystitis	%4.8 (8)	%1.8 (3)
Dysmenorrhea	%3.6 (6)	%3.6 (6)

(Table 2). Thirty-one patients (18.6%) were admitted for further management and treatment, with the most common departments being General Surgery (n = 14, 8.4%) and Obstetrics and Gynecology (n = 10, 6%). No deaths were reported among the patients following discharge from the emergency department or after treatment in the admitting department.

There was a statistically significant difference between the rates of hospitalization for treatment among patients presenting with abdominal pain accompanied by nausea-vomiting, dysuria, diarrhea, and constipation. The mean age of hospitalized patients was higher than that of patients treated on an outpatient basis ( $p = 0.012$ ). When laboratory tests were examined in this group, statistically significant differences were also found in glucose, CRP, leukocyte count, CK-MB, troponin, APTT, PT, INR, and the presence of ketones in the complete urine analysis (CUA) ( $p < 0.05$ ) (Table 3).

Surgical treatment was applied to 17 (10.2%) of the hospitalized patients. The mean age of the group that underwent surgical treatment was higher than that of the group that received medically treated. Laboratory test results showed that glucose, sodium, potassium, leukocyte, CK-MB, troponin, APTT, PT, and INR values were also higher in the group that underwent surgical treatment ( $p = 0.05$ ) (Table 3).

## Discussion

Non-traumatic abdominal pain is one of the most common complaints that cause patients to seek emergency care. During the six months of the study, non-traumatic abdominal pain accounted for 8.9% of all visits, and 4.11% of this patient group consisted of women of childbearing age. Data obtained from studies determining the overall burden of abdominal pain on emergency department visits were consistent with these findings (5, 6).

**Table 3:** Factors associated with age, diagnosis, laboratory findings, and treatment in hospitalized patients

Variable	Mean $\pm$ Std. Dev.	p
<b>Patients hospitalized for follow-up and treatment (n=31)</b>		
Age	34.61 $\pm$ 7.89	0.012
Glucose	108.32 $\pm$ 25.94	0.027
CRP	30.57 $\pm$ 72.45	0.010
Leukocyte	10.35 $\pm$ 3.58	0.002
CK-MB	24 $\pm$ 45	0.003
Troponin-I	88 $\pm$ 1.55	0.002
APTT	13.05 $\pm$ 14.00	<0.001
PT	6.73 $\pm$ 7.10	<0.001
INR	0.50 $\pm$ 53	<0.001
Presence of CUA-ketone	0.03 $\pm$ 0.18	0.036
<b>Patients who underwent surgical treatment (n=17)</b>		
Age	35.94 $\pm$ 8.25	0.018
Glucose	113 $\pm$ 17.89	0.048
Sodium	137.41 $\pm$ 1.54	0.033
Potassium	4.30 $\pm$ 0.37	0.047
Leukocyte	10.58 $\pm$ 3.49	0.012
CK-MB	0.28 $\pm$ 0.49	0.008
Troponin-I	0.94 $\pm$ 1.50	0.010
APTT	17.60 $\pm$ 13.89	<0.001
PT	9.06 $\pm$ 6.95	<0.001
INR	0.68 $\pm$ 6.20	<0.001

Demographic data such as age and gender, as well as medical history, symptoms, findings, and physical examination, are guiding factors in the differential diagnosis of the pathological condition causing abdominal pain (7). The history of comorbidities and other complaints in the medical history is significant in terms of preliminary diagnosis and planned tests. In this study, 8.4% of patients had a history of surgery, and the presence of additional symptoms such as nausea and vomiting in this patient group is important for the early diagnosis and treatment of diseases with high mortality and morbidity requiring surgical intervention (8). Additional symptoms accompanying abdominal pain may vary depending on the study population but are indicative (9).

Physical examination findings in patients play a role in the diagnosis. In this study, abdominal tenderness was the most common finding on physical examination, which was consistent with other studies in the literature (10,11). However, there were some differences in the proportions. This difference is due to the subjective nature of tenderness. Although the combined use of medical history, physical examination, and laboratory tests may seem insufficient for reaching a correct diagnosis, it is effective in selecting imaging tests and determining unstable

conditions with high mortality (12, 13). Here, laboratory tests were requested for 95.2% of patients based on their current condition, and imaging tests were requested for 61.7% of patients based on the findings obtained. Despite the widespread use of technological imaging techniques in recent years to prevent mortality and morbidity, plain abdominal radiographs are still the preferred method in patients with abdominal pain (14). In our study, they were used in patients presenting with constipation and in those with a suspected diagnosis of obstruction.

Computed tomography (CT) is recommended for the evaluation of patients with acute abdominal pain due to its high diagnostic accuracy and its ability to provide alternative diagnoses when the suspected diagnosis is not confirmed (15). Here, CT is the most frequently requested imaging method, although it differs from literature data (16, 17). This is primarily because, despite its ease of use at the bedside in the emergency department, ultrasound is user-dependent, prone to gas artifacts, and access to radiologists is often limited, resulting in lower usage rates compared to computed tomography (CT). Additionally, the high sensitivity and specificity of CT in acute abdominal syndromes reduce emergency department stay duration and prevent unnecessary surgical intervention, thereby increasing its preference (17).

Despite technological advances in laboratory and imaging methods used in the diagnostic phase, nonspecific abdominal pain remains one of the leading diagnoses (18, 19). In this study, it accounted for 19.8% of preliminary diagnoses and 16.8% of definitive diagnoses. In studies conducted on patients who presented to the emergency department with non-traumatic abdominal pain, the most common specific diagnosis reported was urinary tract infection (20). In our study, urinary tract infections were detected in 24% of cases, which is consistent with previous findings (21). However, differences in other diagnoses were observed, which we attribute to the study population. There was an agreement between the preliminary diagnoses based on the patient's histories and physical examinations and the definitive diagnoses determined after the tests in cases of acute appendicitis and renal colic. The relationship between the diagnoses varied by 33% and was similar to that reported in the literature (22).

Patients who presented to the emergency department with abdominal pain were discharged for outpatient follow-up after their symptoms subsided following symptomatic treatment, while some were admitted to different clinics (23). Here, 18.6% of patients were hospitalized for follow-up, and 10.2% were treated with surgical methods. The higher number of patients managed as outpatients compared to those admitted for inpatient care, or surgical treatment is primarily due to the increased diagnosis of nonspecific abdominal pain. The General Surgery and

Obstetrics and Gynecology Clinics frequently admitted patients who underwent surgical treatment. In this patient group, age, inflammatory markers, and coagulation parameters were found to be higher than in those who were followed up on an outpatient basis and received medical treatment. This suggests that the patients had high mortality and morbidity rates, which led to their presentation to the emergency department.

## Conclusion

During the diagnosis of pathological conditions causing abdominal pain, demographic characteristics, medical history, and physical examination are as important as laboratory and imaging tests in reaching the correct diagnosis. Comorbid conditions and history of previous surgeries must be thoroughly investigated. The use of technological imaging tests is viewed as a potential route in crowded emergency departments, particularly in terms of avoiding hospitalization and surgical treatment. However, the fact that our study was conducted in a single center with a small number of patients over a six-month period, during which the COVID-19 pandemic had a significant impact on the entire world, resulted in limited data.

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# Investigation of the Effect of Gender on Blood Parameters in Acute Renal Failure in Patients Presenting to the Emergency Department of a Hospital

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## Abstract

**Objective:** Acute renal failure (ARF) is a sudden change in renal function that prevents the excretion of nitrogenous wastes and disrupts the body's fluid and electrolyte balance. Identification of ARF risk factors and development of indicators that predict mortality are crucial to improve the success of medical care. We aim to evaluate the effect of age and gender factors in patients with ARF and to evaluate the course and frequency of the disease in female patients compared to male patients.

**Material and Methods:** The data of adult patients over 18 years of age who were hospitalized with a diagnosis of ARF between 01.02.2025-01.03.2025 in the emergency department of Malatya Training and Research Hospital were retrospectively analyzed. Blood laboratory parameters were recorded and analyzed to determine whether these data were positively or negatively associated with gender.

Results: A statistically significant difference was found between age and gender in patients with ARF ( $p=0.004$ ). Female patients with ARF were older than male patients. There was a statistically significant relationship between creatinine level and gender in patients with ARF ( $p=0,017$ ). Creatinine levels were higher in male ARF patients. There was no statistically significant difference between plt, hb, htc, ALT and HALP score and gender ( $p$  values 0.384; 0.078; 0.221; 0.221; 0.189; 0.174, respectively).

**Conclusions:** The finding in our study that ARF occurs at older ages compared to men may be explained by the interaction of biological, hormonal, clinical and sociocultural factors. The renal protective effects of estrogen are realized through protection of vascular structure, support of glomerular filtration rate (GFR) and reduction of oxidative stress. However, the decrease in estrogen levels in the postmenopausal period may be an important factor in the more rapid deterioration of renal function. The pro-inflammatory properties of testosterone and increased oxidative stress, as well as the earlier development of hypertension, atherosclerosis and chronic kidney disease in men, may be another reason why ARF occurs at a younger age in men compared to women. We found that creatinine levels were significantly higher in male patients with ARF compared to female patients. Men are known to have more muscle mass in general compared to women and this may lead to higher creatinine levels in men.

**Keywords:** Akut Renal Failure, Oxidative Stress, Testosterone, Estrogene

## Introduction

Acute renal failure (ARF) is generally defined as a sudden change in renal function that prevents the excretion of nitrogenous wastes (urea) from the body and disrupts the body's fluid and electrolyte balance. ARF is the sudden loss of renal function resulting in failure of urinary excretion and consequent increase in blood urea nitrogen (BUN: Blood urea nitrogen) and serum creatinine. (1) These definitions used for the diagnosis of ARF are quali-

tative and a quantitative definition has not yet been found and is still a matter of debate.(2-4) One of the difficulties in making the diagnosis of ARF is that increased serum creatinine or blood urea nitrogen levels do not provide information about whether renal failure is chronic or acute. (1,3). This situation is effective in determining patient treatment, follow-up and hospitalization. There are studies in the literature indicating that the detected laboratory values affect the clinical course. We think that gender

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**Received:** 05.06.2025 • **Accepted:** 20.06.2025

**DOI:** 10.55994/ejcc.1713230

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Available online at <https://dergipark.org.tr/pub/ejcc>

**Cite this article as:** Bilgehan Demir, Turgut Dolanbay, Suleyman Nogay, Fatih Tan, Omer Faruk Ongenli. Evaluation of Female Patients of Childbearing Age Who Applied to the Emergency Medicine Department with Abdominal Pain. Eurasian Journal of Critical Care. 2025;7(2): 7-11

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may also affect this clinic. No study has been found showing the relationship between ARF patients and gender. In our study, we aimed to examine the effects of both laboratory parameters and gender alone or together on clinical progression.

## Material Method

Our study was initiated after obtaining the ethics committee approval numbered 2025/74 dated 12.05.2025 from the non-interventional ethics committee of Malatya Turgut Ozal University Faculty of Medicine. The data of adult patients over 18 years of age who were admitted to the emergency department of Malatya Training and Research Hospital between 01.02.2025-01.03.2025 with a diagnosis of acute renal failure (ARF) were retrospectively analyzed. blood parameters [hemogram: leukocytes ( $10^3/uL$ ) (WBC), hemoglobin (g/dL) (hgb), hematocrit (%) (htc), platelets ( $10^3/uL$ ) (plt), mean erythrocyte volume (fL) (MCV), neutrophils ( $10^3/L$ ), lymphocytes ( $10^3/uL$ ), monocytes ( $10^3/uL$ ), neutrophil percentage (%neu); Biochemistry: C reactive protein (mg/dL) (CRP), urea (mg/dL), creatinine (mg/dL) (creat), aspartate aminotransferase (U/L) (AST), alanine aminotransferase (U/L) (ALT), albumin (g/dL) (alb), glucose (mg/dL) (glc), sodium (mmol/L) (Na), potassium (mmol/L) (K), chlorine (mmol/L) (Cl), calcium (mg/dL) (Ca), blood gas: pH, pO<sub>2</sub>(mmHg), pCO<sub>2</sub>(mmHg), lactate, FCOHB(%),

HALP score and its correlation with gender to determine whether it is an important parameter.

Biochemical markers were measured in the biochemistry laboratory of our hospital using About Device, CRP, urea, creatinine, AST, ALT, alb, glc, Na, K, Cl and Ca kits. Hemogram parameters were measured using Cell pack DST, DCL, WNR, WDF and SLS Lysercell kits on SYSMEX XN-1000 h device in the biochemistry laboratory of our hospital. In total, 55 pediatric patient data were accessed and our study was conducted with the data of 44 patients who met the inclusion and exclusion criteria.

## Inclusion Criteria

Patients over 18 years of age with a diagnosis of ARF and hospitalization.

Patients admitted to our hospital between 01.02.2025-01.03.2025 and hospitalized with a diagnosis of ARF, whose data were retrospectively accessed from the hospital information system.

## Exclusion Criteria

Patients under eighteen years of age.

Patients whose data cannot be fully accessed in the hospital data system.

All patients on anticoagulant and coagulant therapy.

Patients who were referred to different hospitals from the emergency department or who refused hospitalization

**Table 1.** Age, HALP score and laboratory parameters of patients

	<i>n</i>	Mean $\pm$ SD	Median (Min-Max)
Age (year)	44		77 (29-103)
Hgb (g/dL)	44	11,5 $\pm$ 2,5	
Htc (%)	44	35,5 $\pm$ 7,9	
Üre (mg/dL)	44	183 $\pm$ 71,8	
Alb (g/dL)	44	2,8 $\pm$ 0,6	
K (mmol/L)	44	5,5 $\pm$ 1,3	
WBC ( $10^3/uL$ )	44		12,1 (3,8-34,3)
Plt( $10^3/uL$ )	44		246 (98-801)
Lymp (mL)	44		1,3 (0-6)
Monocytes (mL)	44		0,7 (0-3,2)
Basophils ( $10^3/uL$ )	44		0,04 (0-0,2)
Eosinophils (mL)	44		0,06 (0-2,4)
Creatinine(mg/dL)	44		4,3 (1,4-19,5)
AST (U/L)	44		27,5 (7-4001)
ALT (U/L)	44		20 (4-2894)
LDH (U/L)	44		302,5 (127-4395)
Ca (mg/dL)	44		8,6 (5-11,9)
Na(mmol/L)	44		134 (122-166)
Crp (mg/ dL)	44		7,5 (0,1-35)
HALP	44		1,5 (0-10,5)

voluntarily and had a previous diagnosis of ARF were excluded from the study.

## Statistical Analysis

IBM SPSS statistics 27 program was used for statistical analyses while evaluating the findings obtained in the study. The conformity of the parameters to normal distribution was evaluated by shapiro wilk test. Descriptive statistical methods were given as mean, median, standard deviation, percentage (25-75% (Inter Quantile Range-IQR) and frequency. When comparing quantitative data, student t test was used for comparisons of normally distributed parameters between two groups and mann whitney u test was used for comparisons of non-normally distributed parameters between two groups. For quantitative data (blood parameters and inflammatory indices), correlation analysis was performed to determine the relationship between creatine and HALP score. Our study was planned retrospectively and all patients who met the inclusion and exclusion criteria were included.

## Results

Mean  $\pm$  SD values of the parameters with parametric distribution and median (min-max) values of the parameters with nonparametric distribution were 77 (29-103) years of age, respectively, hgb (g/dL) 11.5 $\pm$ 2.5 htc(%) 35.5 $\pm$ 7.9, urea (mg/dL) 183 $\pm$ 71.8, Alb (g/dL) 2.8 $\pm$ 0.6, K (mmol/L) 5.5 $\pm$ 1.3, WBC (103/uL) 12.1 (3.8-34.3), Plt (103/uL) 246 (98-801), Lymp (mcL) 1.3 (0-6), Monocyte (mcL) 0.7 (0-

3.2), Basophil (103/uL) 0.04 (0-0.2), Eosinophil (mcL) 0.06 (0-2.4), Creatinine (mg/dL) 4.3 (1.4-19.5), AST (U/L) 27.5 (7-4001), ALT (U/L) 20 (4-2894), LDH (U/L) 302.5 (127-4395), Ca (mg/dL) 8.6 (5-11.9), Na (mmol/L)134 (122-166), Crp (mg/dL) 7.5 (0.1-35), HALP 1.5 (0-10.5) and given in Table 1. P values of age and blood parameters in patients with ARF according to gender, respectively Age 0.004, WBC (103/uL) 0.170, Plt (103/uL) 0.384, Creatinine (mg/dL) 0.017, ALT (U/L)0.189, HALP 0.174, Hgb (g/dL) 0.078, Htc (%) 0.221 and p values of age and blood parameters according to gender are given in Table 2. A statistically significant difference was found between age and gender in patients with ARF (p= 0.004). In patients with ARF, women were older than men.

A statistically significant relationship was found between creatinine level and gender in patients with ARF (p=0.017). Creatinine level was higher in male ARF patients.

There was no statistically significant difference between plt, hb, htc, ALT and HALP score and gender (p values 0.384; 0.078; 0.221; 0.189; 0.174, respectively).

## Discussion

ARF is recognized as one of the most important causes of mortality and morbidity among patients followed up in hospitals in our country and worldwide. Patients diagnosed with ARF may present to hospitals in the presence of symptoms such as oliguria, edema and oral intake disorder, especially infection, and may rarely be asymptomatic (1-5). Identification of ARF risk factors and development of indicators predicting mortality are crucial to

**Table 2.** The Relations vereen Age, Blood Parameters and Gender in Patients with ARF

	Mortality	n	P value
Age	K	18	0,004**
	E	26	
WBC (103/uL)	K	18	0,170**
	E	26	
Plt(103/uL)	K	18	0,384**
	E	26	
Creatinine(mg/dL)	K	18	0,017**
	E	26	
ALT (U/L)	K	18	0,189**
	E	26	
HALP	K	18	0,174**
	E	26	
Hgb (g/dL)	K	18	0,078*
	E	26	
Htc (%)	K	18	0,221*
	E	26	

Notes. \*student t test, \*\*mann Whitney u

improve the success of medical diagnosis and care from both clinical and administrative perspectives.

As a result of our investigations, we evaluated the effect of age and gender factors in patients with ARF and found that ARF occurs at older ages in female patients compared to male patients. This finding may be explained by the interaction of biological, hormonal, clinical and sociocultural factors.

It would be a more rational approach to evaluate the effect of gender on renal function primarily through hormonal differences. The renal protective effects of estrogen are realized by protecting the vascular structure, supporting glomerular filtration rate (GFR) and reducing oxidative stress (6). In women, estrogen increases renal perfusion by regulating renal hemodynamics and protects renal cells from inflammation-related damage thanks to its anti-inflammatory properties (7). However, the decrease in estrogen levels in the postmenopausal period may be an important factor in more rapid deterioration of renal function (8). This may be considered as an important biological mechanism that may explain the occurrence of ARF at older ages in women in our study. In men, the effects of testosterone on renal functions are different. The proinflammatory properties of testosterone and its contribution to the increase in oxidative stress may lead to deterioration of renal function at an earlier age in patients with male ARF (9). In addition, hypertension, atherosclerosis and chronic kidney disease are known to develop at an earlier age in men, which may suggest another important reason why ARF in men occurs at a younger age than in women (10).

In addition to age and gender, the presence of chronic diseases parallel to that period may also be among the determining factors in the development of ARF. In men, factors that increase susceptibility to ARF such as diabetes mellitus and cardiovascular diseases usually occur at an earlier age (11). On the other hand, the development of these diseases in women occurs at older ages; the increase in hypertension and metabolic syndrome, especially in the postmenopausal period, leads to deterioration in renal function (12). In our study, the occurrence of ARF in women at older ages seems to be consistent with the effect of these clinical factors. In addition, it is known that the progression of ARF differs between genders. In a study in the literature, it was reported that ARF progressed faster in men and the risk of reaching terminal renal failure was higher in men than in women (8). This suggests that in addition to biological and clinical factors, sociocultural factors also play an important role in the development of ARF. The fact that women recognize health problems later or act later in seeking medical help may cause delays in the diagnosis of ARF. This may be one reason why ARF is often diagnosed at an older age in women. However, dietary habits and lifestyle factors can also affect kidney

health. factors such as higher salt consumption, smoking and obesity are common in men, which may predispose to the development of hypertension and diabetes and increase the risk of ARF (13-15). Although women generally have healthier eating habits, a rapid decline in renal function may be observed in the postmenopausal period due to metabolic changes (16).

Studies examining the effect of gender on ARF have reported that women can maintain renal function longer than men and that ARF occurs at older ages in women. In a recent study, it was reported that women are more resistant to the development of renal failure and this may be related to hormonal mechanisms (10). However, some studies suggest that gender has no significant effect on ARF (17). These differences may be due to methodologic approaches used in the studies and population differences. The findings of our study are generally consistent with previous studies supporting the effect of gender on the development of ARF.

Another important finding of our study was that creatinine levels were significantly higher in male patients with ARF compared to female patients. This difference may be due to physiologic, hormonal and muscle mass differences between the sexes. Serum creatinine is a by-product of muscle metabolism and is a widely used biomarker to assess renal function (18). It is known that men generally have more muscle mass compared to women, leading to higher creatinine levels in men (19,20). However, the difference in creatinine levels between the sexes is not only due to muscle mass. Previous studies have shown that men lose renal function earlier and have a more rapid decline in GFR compared to women (10). The reasons for this include hormonal factors, hemodynamic changes and cardiovascular risk factors (8,20).

Although serum creatinine levels are a commonly used parameter in the evaluation of renal function, they have some limitations. Creatinine levels reflect not only GFR but also many other factors such as muscle mass, diet, hydration status and metabolic rate (21). Therefore, it should be kept in mind that higher creatinine levels in men may not only indicate loss of renal function but may also be due to excess muscle mass (22). In recent years, biomarkers other than creatinine have been shown to be more reliable in assessing renal function. Especially cystatin C may provide a more accurate assessment of renal function because it is a marker independent of muscle mass. It has been reported that cystatin C shows less variability compared to creatinine and can detect renal dysfunction at an earlier stage (23).

The findings of our study show that male patients have a higher risk of ARF and their renal function deteriorates more rapidly. In this context, it is clinically important to monitor the renal health of male patients more closely and

to implement early screening programs especially in high-risk individuals. Although creatinine levels are a basic biomarker for assessing renal function, failure to consider gender-specific reference values may lead to misinterpretation. Higher creatinine levels in male patients may indicate a faster decline in renal reserve capacity, but may also be a physiologic variability due to muscle mass.

Therefore, the use of gender-specific GFR calculation methods and biomarkers other than creatinine is important for a more sensitive renal function assessment (23).

In conclusion, if we look at our study from a general perspective, it has limitations as well as strengths. Due to its retrospective design, it is not possible to determine the cause-and-effect relationship with certainty. In addition, factors that may affect creatinine levels such as muscle mass, dietary habits and hydration status of the participants were not analyzed in detail. Future prospective studies should more comprehensively examine the impact of gender on renal function and focus on the assessment of biomarkers other than creatinine. The finding that creatinine levels are higher in male patients compared to female patients may be explained by several mechanisms, including greater muscle mass in men, earlier deterioration of renal function and hormonal factors. In clinical practice, it is important to consider gender-specific reference values and to evaluate biomarkers other than creatinine for a more accurate disease management. Similarly, another important finding in our study, that ARF occurs at older ages in women compared to men, may be explained by the interaction of hormonal changes, comorbidities and sociocultural factors. We believe that these findings will enable and guide the identification of gender-specific risk factors and the development of new strategies for the prevention of ARF.

**Financing Support:** Financial support was provided by all authors. No external financial support was received.

**Conflict of Interest:** There is no conflict of interest between the authors.

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# A Toxic Threat: Determinants of Symptom Severity in Patients Under Intensive Care Due to Exposure to Aluminum Phosphide

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## Abstract

**Objective:** This study aims to identify the factors determining the severity of poisoning resulting from respiratory exposure to Aluminum Phosphide (AIP), commonly used as a rodenticide against pests in households in low socio-economic regions.

**Materials and Methods:** This is a single-center, retrospective observational study that reviewed the data of patients admitted to the emergency department due to AIP exposure and subsequently accepted into the toxicology intensive care unit between 2023 and 2024. The study utilized patients' demographic characteristics, mode and duration of exposure, clinical findings, and outcomes. Student's t-test was used for binary group comparisons, and one-way Analysis of Variance (ANOVA) was employed for comparisons among more than two groups. Continuous data not conforming to normal distribution were presented as median (interquartile range) and analyzed using the Mann-Whitney U test for two-group comparisons and the Kruskal-Wallis test for multiple-group comparisons. A p-value of <0.05 was considered statistically significant in all analyses.

**Results:** The median age of the 11 patients included in the study was 60 years (range 22–85). Of these, 64% were male (7 males, 4 females), and 36% were female. The relationship between Glasgow Coma Scale (GCS) and symptom severity was analyzed using the Kruskal-Wallis test and found to be significant ( $p = 0.027$ ). Similarly, the relationship between lactate levels and symptom severity was significant ( $p = 0.009$ ). Patients with lower GCS values exhibited higher lactate levels; for instance, all patients with  $GCS \leq 8$  had lactate levels  $>4$  mmol/L. A strong negative correlation was observed between GCS and lactate levels (Spearman's  $\rho \approx -0.82$ ,  $p < 0.01$ ). The relationship between gender and lactate levels was analyzed using the Mann-Whitney U test, revealing significantly higher lactate levels in females ( $p = 0.015$ ).

**Conclusion:** Advanced age, low GCS, high lactate levels, and female gender appear to necessitate more intensive monitoring and treatment in AIP poisonings. These findings may facilitate risk stratification.

**Keywords:** Aluminum Phosphide, Respiratory Exposure, Gender, Lactate, Intensive Care

## Introduction

Aluminum Phosphide (AIP) is a fumigant commonly used for pest control in grain storage. In agricultural settings, grain warehouses, and occasionally in homes, it is utilized as a rodenticide. AIP tablets are available in the market as formulated products. When it reacts with moisture, water, or stomach acid, it releases phosphine ( $PH_3$ ) gas, which is primarily responsible for its toxicity (1). AIP is rapidly absorbed through the skin, gastrointestinal tract, and respiratory tract, depending on the mode of exposure. There are few case reports associated with AIP poisoning. The majority of cases involve poisonings resulting from oral ingestion with gastrointestinal absorption, while respira-

tory AIP poisonings are rare (2). In the literature, poisonings through oral ingestion are often reported as suicide attempts. When ingested orally, aluminum phosphide reacts with hydrochloric acid in the stomach, releasing  $PH_3$  gas, which is a potential source of poisoning (3,4). Respiratory exposure typically arises from the use of AIP for pest control within homes or agricultural areas. It is more readily available and widely used in underdeveloped countries. Although the exact mechanism of action is still not fully understood, various animal studies have indicated that its most significant effect is the inhibition of mitochondrial cytochrome c oxidase enzyme. This leads to impaired cellular oxygen utilization, accelerated formation of free oxygen radicals, lipid peroxidation in cell membranes,

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**Received:** 17.08.2025 • **Revision:** 21.08.2025 • **Accepted:** 23.08.2025

**DOI:** 10.55994/ejcc.1713230

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Available online at <https://dergipark.org.tr/tr/pub/ejcc>

**Cite this article as:** Emin Fatih Visneci, Osman Lutfi Demirci. A Toxic Threat: Determinants of Symptom Severity in Patients Under Intensive Care Due to Exposure to Aluminum Phosphide. Eurasian Journal of Critical Care. 2025;7(2): 13-17

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and protein denaturation. The net effect is multiple organ failure resulting from disrupted mitochondrial oxidative phosphorylation (5). The most commonly affected organs are the lungs, heart, kidneys, gastrointestinal system, and liver. Due to the absence of a known antidote, mortality rates remain high, especially in cases presenting late to the hospital, despite intensive care monitoring. In the literature, mortality rates following aluminum phosphide poisoning have been reported to range between 40% and 80%. In patients developing resistant myocardial dysfunction, this rate can rise up to 77% (37–100%) (6-8).

In contrast to the frequent suicide attempts through oral AIP ingestion reported in the literature, our study examined the management in the emergency department, intensive care monitoring, demographic characteristics, laboratory findings, and mortality rates of PH<sub>3</sub> gas poisonings resulting from respiratory exposure to AIP following fumigation intended to kill rodents and insects.

## Materials and Methods

### Study Design

This single-center, retrospective observational study analyzed data from patients who presented to the emergency department due to AIP exposure and were subsequently admitted to the toxicology intensive care unit between 2023 and 2024.

### Patient Population

A total of 11 patients who experienced respiratory AIP exposure during the specified period were included in the study. Cases involving intentional (deliberate) oral ingestion of aluminum phosphide and those with dermal contact exposure were excluded. Thus, only accidental poisoning cases resulting from inhalation exposure were evaluated.

### Data Collection

Demographic characteristics, mode and duration of exposure, clinical findings, and outcomes of all patients were

retrospectively obtained by reviewing hospital records. Data were compiled using a standard form and recorded digitally.

### Statistical Analysis

The conformity of continuous variables to normal distribution was evaluated using the Kolmogorov-Smirnov test. Normally distributed data were expressed as mean  $\pm$  standard deviation and analyzed using Student's t-test for two-group comparisons and one-way Analysis of Variance (ANOVA) for comparisons among more than two groups. Continuous data not conforming to normal distribution were presented as median (interquartile range) and analyzed using the Mann-Whitney U test for two-group comparisons and the Kruskal-Wallis test for multiple-group comparisons. A p-value of <0.05 was considered statistically significant in all analyses.

## Results

The median age of the 11 patients included in the study was 60 years (range 22–85). Of these, 64% were male (7 males, 4 females), and 36% were female. Regarding symptom severity, 3 patients (27%) were classified as mild, 5 patients (45%) as moderate, and 3 patients (27%) as severe. The median Glasgow Coma Scale (GCS) score at presentation was 11 (range 6–15). The initial mean lactate level was  $3.1 \pm 1.2$  mmol/L, with a median value of 3.0 mmol/L (range 1.2–5.0). The demographic data of the patients are presented in Table 1. The relationship between age and symptom severity was evaluated using the ANOVA test, with values presented as mean  $\pm$  standard deviation (SD). A significant relationship was found between age and symptom severity ( $p = 0.041$ ) (Table 2). The relationship between GCS and symptom severity was analyzed using the Kruskal-Wallis test, with values presented as mean  $\pm$  SD. A significant relationship was found between GCS and symptom severity ( $p = 0.027$ ) (Table 3). The relationship between lactate level and

**Table 1.** Symptoms and Severity by Duration of Exposure

	Symptoms					Duration of Exposure
	Skin Lesions (itch)	Mild neurological symptoms (dizziness, headache)	Gastrointestinal Symptoms (Nausea vomiting)	Shortness of breath, chest pain	Severe neurologic alteration (Change of consciousness)	
Cases with mild symptoms (n:3)	+	-	-	-	-	4 hours
Cases with moderate symptoms (n:5)	-	+	+	+	+	15 hours
Cases with severe symptoms (n:5)	-	-	+	+	+	48 hours

**Table 2.** Demographic and Clinical Characteristics of Patients

Characteristic	Value
Age (years)	60 (median), Range (22-85)
Gender (Female/Male)	4/7 (4 females,7 males)
Symptom Severity	3 Mild (%27), 5 Moderate (%45), 3 Severe (%27)
Glasgow Coma Scale (GCS)	11 (median) Range (6-15)
Lactate (mmol/L)	3.0 (median), Range (1.2-5.0)

Note: The data is presented as median values and ranges; gender and symptom severity are indicated categorically by the number of patients (percentage, %).

**Table 3.** Symptom Severity Scores by Age Group

Age Group (years)	n	Symptom Severity Score (mean ± SD)
≤30	3	5.7 ±1.3
31-60	4	6.0 ±1.4
≥60	4	6.5 ±1.5

Note: Relationship between Age and Symptom Severity (ANOVA Test Results). Distribution of symptom severity scores by age groups (age: categorical; symptom severity score: continuous). Values are presented as mean ± standard deviation (SD). ANOVA test result  $p = 0.041$ .

**Table 4.** Lactate Levels by Symptom Severity Level

Symptom Severity Level	n	Lactate (median [IQR],(mmol/L))
Mild	3	1.2 ± [0.8-1.8]
Moderate	5	2.5 ± [1.9-3.5]
Severe	3	4.0 ± [3.2-5.6]

Note: Relationship between Lactate Level and Symptom Severity (Kruskal-Wallis Test Results). Distribution of lactate levels by symptom severity categories (symptom severity: categorical; lactate level: continuous). Values are presented as median [interquartile range [IQR]]. Kruskal-Wallis test result  $p = 0.009$ .

symptom severity was analyzed using the Kruskal-Wallis test, with values presented as median [interquartile range (IQR)]. A significant relationship was found between lactate level and symptom severity ( $p = 0.009$ ) (Table 4). Patients with severe symptoms had notably higher lactate levels compared to those with mild symptoms (mean  $\approx 4.6$  mmol/L vs  $\approx 1.7$  mmol/L). Similarly, patients with lower GCS scores exhibited higher lactate levels; for instance, all patients with  $GCS \leq 8$  had lactate levels  $>4$

**Table 5.** Glasgow Coma Scale Scores by Symptom Severity Level

Symptom Severity Level	n	Glasgow Coma Scale (GCS) (mean ± SD)
Mild	3	14.0 ±1.2
Moderate	5	12.8 ± 2.1
Severe	3	11.0 ± 3.0

Note: Relationship between GCS and Symptom Severity (Kruskal-Wallis Test Results). The distribution of Glasgow Coma Score (GCS) values according to symptom severity levels (symptom severity level: categorical; GCS: continuous). Values are presented as mean ± standard deviation. Kruskal-Wallis test result  $p = 0.027$ .

mmol/L. A strong negative correlation was observed between GCS and lactate levels (Spearman's  $\rho \approx -0.82$ ,  $p < 0.01$ ), indicating that increased lactate levels are associated with decreased levels of consciousness. (Table 5). The relationship between gender and age was evaluated using the t-test, with values presented as mean ± SD. The independent samples t-test result ( $p = 0.055$ ) indicated no significant relationship between gender and age (Table 6). The relationship between gender and lactate levels was analyzed using the Mann-Whitney U test, with values presented as median [IQR]. Lactate levels were found to be significantly higher in females ( $p = 0.015$ ) (Table 7).

## Discussion

The data obtained in this study highlight the prognostic importance of parameters such as age, level of consciousness, and lactate in clinical toxicology. Firstly, it was observed that older patients had significantly increased symptom severity. This finding is consistent with previous studies in the literature; for example, large patient series have reported that advanced age is associated with more severe clinical presentations and a higher risk of mortality in poisoning cases (9,10). The effect of age may be explained by reduced physiological reserves and comorbidities in elderly patients, which can exacerbate the outcomes of toxic effects. However, it should also be noted that in certain specific types of poisoning, age has not always been found to be a significant prognostic indicator; variations in population characteristics and the speed of intervention may lead to these differing results. Inhalation poisonings resulting from rodent use in small, enclosed spaces like homes have generally been reported in limited numbers and in limited cases. The symptoms of inhalation exposure in our

**Table 6.** Age Distribution by Gender

Gender	n	Age (mean ±SD,years)
Male	7	54.3 ± 17.5
Female	4	47.8 ± 18.9

Note: Relationship Between Gender and Age (T-Test Results). Comparison of mean age of male and female patients (gender: categorical; age: continuous). Values are presented as mean ± standard deviation. Independent sample T-test result  $p = 0.055$ .

**Table 7.** Lactate Levels by Gender

Gender	n	Lactate (median [IQR], (mmol/L)
Male	7	1.7 [1.0-2.6]
Female	4	2.5 [1.8-3.6]

Note: Relationship Between Gender and Lactate Level (Mann-Whitney U Test Results). Comparison of lactate levels of male and female patients (gender: categorical; lactate level: continuous). Values are presented as median [IQR]. Mann-Whitney U test result  $p = 0.015$ .

study are consistent with the symptoms presented in the cases, ranging from simple gastrointestinal symptoms to shock. (11). In our study, the inverse relationship between GCS and symptom severity is also an important finding. As GCS values decreased, symptom severity worsened, indicating a deterioration in the patient's neurological status. This supports the use of GCS as a prognostic indicator in acute poisonings, aligning with the literature. Indeed, a study on organophosphate poisoning reported that the mean GCS at admission was as low as 4 in patients who did not survive, while it was approximately 12 in survivors (12). The same study found a strong correlation between low GCS and mortality, emphasizing the prognostic value of GCS. Similarly, Eddleston et al. recommended that patients presenting with critical GCS levels ( $\leq 13$ ) in pesticide poisonings should receive intensive care monitoring and aggressive treatment, as a significant portion of these patients experienced deterioration and death (13). Therefore, a low GCS score can be considered an early indicator of severity not only in trauma but also in toxicology patients. On the other hand, some studies have noted that GCS alone may not be a reliable prognostic indicator in all types of poisoning. In a study involving cases of mixed drug ingestion, no statistical relationship was found between initial Glasgow Coma Scale (GCS) scores and hospital course (e.g., length of stay), suggesting that GCS may have limited predictive power in heterogeneous overdose groups (14). These conflicting results indicate that the prognostic value of GCS may depend on the type of poisoning and accompanying factors. However, our findings generally confirm that patients with particularly low GCS scores may be in critical condition and require close monitoring.

Another significant result of our study is the close association between lactate levels and the clinical picture. As patients' blood lactate levels increased, symptom severity and clinical deterioration were observed to escalate. Lactate is considered a biomarker of tissue hypoxia and perfusion disorders; therefore, high lactate values in acute poisoning cases may indicate severe systemic involvement. Indeed, the literature has repeatedly demonstrated the prognostic value of lactate levels in various toxicology scenarios. For instance, a study on patients with carbon monoxide poisoning found a positive correlation between initial lactate

levels and clinical severity, with higher lactate associated with worse outcomes. Abd El Razik et al. emphasized that lactate could be a prognostic indicator in acute CO poisoning, reporting significantly elevated initial lactate levels in severe cases (15). Similarly, recent studies have identified serum lactate as a strong predictor of mortality in pesticide intoxications such as paraquat. For example, Huang et al.'s (2014) study on paraquat poisoning showed that patients with high initial lactate levels had a significantly increased risk of death (OR  $\sim 7$ ) (16). Additionally, a carbon monoxide poisoning study conducted in our country revealed that lactate concentration at emergency admission predicted whether patients would develop neurological and cardiac complications. When these data are considered alongside our findings, it suggests that lactate measurement could serve as a simple yet effective risk indicator in acute poisonings (17). In patients with elevated lactate, early initiation of more aggressive oxygenation, fluid therapy, and, if necessary, advanced supportive treatments may help improve prognosis. Conversely, normal lactate levels may indicate relatively better tissue perfusion, guiding the identification of mild poisoning cases.

Another noteworthy finding in our study is the biochemical difference between genders: female patients had significantly higher average lactate levels compared to male patients. Interestingly, although some toxicology series in the literature report that male gender is associated with more severe outcomes (18), our data suggest that female patients may be under greater metabolic stress. Several mechanisms could explain this phenomenon. Firstly, physiological differences: female patients may generally have lower average body mass and baseline hemoglobin levels. At the same exposure level, receiving a higher toxin dose per kilogram or having relatively lower oxygen-carrying capacity could lead to tissue hypoxia and, consequently, more rapid lactate accumulation in women. Secondly, hormonal and metabolic differences may also play a role. Estrogen and other sex hormones affect cardiovascular and metabolic responses; during stress responses, catecholamine release, microcirculation distribution, and lactate clearance may differ between women and men. Indeed, gender differences have been observed in critical illnesses: some large-scale studies have reported higher mortality in female patients with severe sepsis and shock, suggesting that women may be at a disadvantage under severe physiological stress (19). On the other hand, animal models and some human studies have proposed that women have immunological advantages against infectious stress; the impact of gender differences on outcomes can be inconsistent in the literature (20-22). Therefore, our finding of higher lactate levels in women may be specific to our patient group's characteristics or reflect an underlying pathophysiological difference. Other factors,

such as delayed hospital admission, gender-related differences in the amount of toxin ingested, or variations in distribution/metabolism within the body, may also contribute to this disparity. The lack of a significant relationship between gender and age ( $p=0.055$ ) suggests that age is not a confounding factor and that the higher lactate levels in women may be directly related to gender. Future studies examining whether similar findings are replicated could provide a better understanding of physiological response differences between male and female patients.

## Limitations

The limited number of cases in our study stems from the rarity of aluminum phosphide rodenticide use in small, enclosed areas. Although some variables reached statistical significance, the small sample size limits the generalizability and strength of the results. The aluminum phosphide level was not measured.

## Conclusion

Advanced age, low GCS scores, elevated lactate levels, and female gender are associated with greater severity in AIP poisoning. These factors may guide risk stratification and management, though larger studies are needed to confirm these findings and clarify gender-related differences.

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# Analysis of Factors Affecting Mortality in Patients with Acute Aortic Dissection Admitted to the Emergency Department

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## Abstract

**Objective:** Acute aortic dissection is a life-threatening cardiovascular emergency. The dissection may be admitted to the emergency department with different clinical pictures, depending on the place of involvement in the aorta. It is extremely important to know the factors affecting mortality, as delays in diagnosis and treatment can increase mortality rates. Our aim of this study is to evaluate the factors that may affect mortality rates.

**Materials and Methods:** One thousand two hundred and eighty-three patients were analyzed from the database. A definitive diagnosis of acute aortic dissection was identified in 48 patients. Two patients voluntarily refused treatment and left the emergency department. SPSS 27.0 program was used for data analysis. The p value was analyzed for the statistical significance of the data.

**Results:** The effects of patients' demographic data, age, gender, complaints on admission to the emergency department, onset time of complaints, duration of diagnosis, imaging and laboratory values on mortality were evaluated. We concluded that renal failure is associated with mortality at the time of first admission, especially in syncope and comorbid conditions.

**Conclusion:** It was evaluated that syncope, one complaint at admission, and renal failure, one of the accompanying diseases, increased mortality. Although our other data are not statistically significant, they contain significant differences. Bigger data analyzes will help identify risk factors.

**Keywords:** Aort dissection, emergency department, mortality

## Introduction

Acute aortic dissection (AAD) is a life-threatening cardiovascular emergency due to rupture of the intima layer of the aorta from the outer layers (1,2). Aortic dissection is part of acute aortic syndromes and was described about 200 years ago (3). While it is seen 4-6 per 100 thousand in the general population, it peaks at 50-60 years (4). Especially in the 6th and 7th decades of life, this rate can reach up to 30 people per 100 thousand (2,4). AAD is an extremely fatal clinical situation (2). Quick and convenient diagnosis is crucial for successful management (5). For each hour of delay in treatment, the mortality rate increases by approximately 1-2% (6). It may cause delays in diagnosis because patients apply to the emergency depart-

ment (ED) with different clinical presentations (5). The clinical condition is caused by the compression of the true lumen by the false lumen, resulting in various degrees of malperfusion depending on the involved aortic segment and the affected aortic branches (2).

In this study, we think that determining the factors affecting mortality will facilitate patient management. Therefore, we aimed to determine the factors affecting mortality before and after hospitalization of AAD patients.

## Material and Methods

The study was initiated after obtaining approval from Van Yüzüncü Yıl University Hospital on 12/02/2021 with the local ethics committee number 2021/02-20. We reviewed

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**Received:** 31.07.2025 • **Revision:** 11.08.2025 • **Accepted:** 18.08.2025

**DOI:** 10.55994/ejcc.1600996

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Available online at <https://dergipark.org.tr/tr/pub/ejcc>

**Cite this article as:** Ramazan Sami Aktas, Idris Tuzun, Ayşe Ertekin, Sahin Sahinalp, Analysis of Factors Affecting Mortality in Patients with Acute Aortic Dissection Admitted to the Emergency Department. Eurasian Journal of Critical Care. 2025;7(2): 19-24

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the consultation notes, epicrisis and radiology reports of 1283 patients with suspicion of dissection, who applied to the ED between January 2010 and January 2021. We reached 48 patients diagnosed with AAD. Since two patients left the hospital voluntarily without treatment, we conducted a study with 46 patients who met the criteria. Although aortic dissection was suspected in the ED, patients with different or misdiagnosed patients were not included in the study.

Demographic data of the patients, such as age, gender, and comorbidities, were defined. Complaints records, blood parameters and treatment processes at the time of admission were examined from the hospital database. The imaging data used for diagnosis was re-evaluated by one specialist doctor, confirming dissection and measuring the aortic diameters. The ascending aorta was measured just above the valve, the arcus aorta was measured between the truncus brachiocephalic and the left carotid artery, and the descending aorta was measured at the level of the thoracic 4 vertebrae. From the database, the patients who died in the hospital were determined. The effects on mortality were evaluated by comparing these data. Patients who did not accept treatment or died after discharge were not included in the mortality.

**Statistical Analysis:** In the descriptive statistics of the data, the mean, standard deviation, median (minimum-maximum), frequency, and ratio values were used.

The distribution of the variables was measured by the Kolmogorov-Smirnov test. Mann-Whitney u test was used in the analysis of quantitative independent data. The chi square test in the analysis of qualitative independent data, and the chi-square test conditions were not met, and the Fischer test was used. Statistical Package for the Social Sciences (SPSS) 27.0 program was used for analysis.

## Results

Of the 46 patients included in the study, 30 (65.2%) were male. The mean age was  $58.7 \pm 14.6$  years. The median age was 58.5 (26-91) years. Age was found to have no effect on mortality ( $p=0.358$ ). The most common comorbid condition is hypertension, and the other descriptive data are given in Table-1. The meantime between the first onset of the complaint and the admission to the ED was  $8.5 \pm 25.5$  hours. The most common symptom was chest pain, with 84.8%. Type A aortic dissection was seen 3 times more than Type B. The most used imaging method is direct chest X-ray. The in-hospital mortality rate was found to be 21.7% (Table 2). Statistically, syncope at first admission and renal failure in comorbid conditions were associated with mortality. The mean time from the onset of symptoms to diagnosis was  $8.5 \pm 25.5$  hours, and the mean waiting time from ED presentation to diagnosis was  $92.5 \pm 56.5$  minutes. No statistically significant difference was

**Table 1.** Effects of demographic data and comorbid conditions on mortality

		In-Hospital			p
		Deaths n (%)	Survivors n (%)	Total n (%)	
<b>Gender</b>	Male	6 (60%)	24(66.7%)	30 (65.2%)	0.695
	Female	4 (40%)	12(33.3%)	16 (34.8%)	
<b>Smoking</b>	yes	6 (60%)	20(55.6%)	26 (56.5%)	0.802
	non-smoker	4 (40%)	16(44.4%)	20 (43.5%)	
<b>Co-morbidity</b>					
	Hypertension	6 (60%)	23 (63.9%)	29 (63.0%)	0.822
	CAD	4 (40%)	17 (47.2%)	21 (45.7%)	0.685
	DM	0 (0%)	1 (2.8%)	1 (2.2%)	1.000
	COPD	0 (0%)	3 (8.3%)	3 (6.5%)	1.000
	Stroke	0 (0%)	1 (2.8%)	1 (2.2%)	1.000
	<b>RF</b>	<b>6 (60%)</b>	<b>1 (2.8%)</b>	<b>7 (15.2%)</b>	<b>&lt;0.001</b>
	BPH	1 (10%)	0 (0%)	1 (2.2%)	0.217
	Asthma	0 (0%)	1 (2.8%)	1 (2.2%)	1.000
	Cancer	0 (0%)	1 (2.8%)	1 (2.2%)	1.000
	No	0 (0%)	3 (8.3%)	3 (6.5%)	1.000
	CD/ID	0 (0%)	0 (0%)	0 (0%)	1.000
	Unknown	1 (10%)	2 (5.6%)	3 (6.5%)	0.230

CAD: Coronary artery disease, DM: Diabetes mellitus, COPD: Chronic obstructive pulmonary disease  
RF: Renal failure, BPH: Benign prostatic hypertrophy, CD/ID: Congenital disease/ Inflammatory diseases

**Table 2.** Effect of Clinical Features on Mortality

	In-Hospital			p
	Deaths n (%)	Survivors n (%)	Total n (%)	
<b>Admitted Complaint</b>				
Chest pain	7 (70%)	32 (88.9%)	39 (84.8%)	0.163
Back pain	3 (30%)	15 (41.7%)	18 (39.1%)	0.504
<b>Syncope</b>	<b>4 (40%)</b>	<b>2 (5.6%)</b>	<b>6 (13%)</b>	<b>0.015</b>
Stomachache	4 (40%)	9 (25%)	13 (28.3%)	0.351
Dyspnea	1 (10%)	3 (8.3%)	4 (8.7%)	1.000
Hemoptysis	0 (0%)	1 (2.8%)	1 (2.2%)	1.000
Hematemesis	0 (0%)	0 (0%)	0 (0%)	1.000
Trauma	0 (0%)	4 (11.1%)	4 (8.7%)	0.562
<b>Location of Pain</b>				
Chest	7 (70%)	32 (88.9%)	39 (84.8%)	0.163
Back (interscapular)	5 (50%)	20 (55.6%)	25 (54.3%)	0.755
Abdomen	5 (50%)	13 (36.1%)	18 (39.1%)	0.426
Other	0 (0%)	2 (5.6%)	2 (4.3%)	1.000
<b>Imaging</b>				
Chest X-Ray	10 (100%)	32 (88.9%)	42 (91.3%)	0.562
Transthoracic Echocardiography	6 (60%)	23 (63.9%)	29 (63%)	0.822
Contrast-Enhanced CT	7 (70%)	24 (66.7%)	31 (67.4%)	0.842
Unknown	0 (0%)	1 (2.8%)	1 (2.2%)	1.000
<b>Dissection type</b>				
A	6 (60%)	29 (80.6%)	35 (76.1%)	0.178
B	4 (40%)	7 (19.4%)	11 (23.9%)	
<b>Treatment</b>				
Surgical	7 (70%)	26 (72.2%)	33 (71.7%)	0.795
Non-surgical	3 (30%)	9 (25%)	12 (26.1%)	0.929
Transfer to Outer Center	0 (0%)	1 (2.8%)	1 (2.2%)	1.000

AD: Aorta Diameter, CT: Computed Tomography

found between aortic diameter dimensions measured by echocardiography and the incidence of death and survival ( $p>0.05$ ). Furthermore, no statistically significant difference was found between the patients' blood values and the incidence of death and survival ( $p>0.05$ ) (Table 3).

## Discussion

Acute aortic dissection is a rare but serious cardiovascular syndrome that can cause different clinical presentations (1,5). Although AAD can occur in any part of the aorta, it most commonly occurs in the right lateral wall of the ascending aorta. The most common clinical causes of AAD are malperfusion syndromes, aortic insufficiency, heart failure and stroke (2,7).

Although it is reported in the literature that AAD is seen at an early age in collagen tissue diseases, it is stated that the most common age range is 59-65 years (1,4,5,7). Some authors acknowledge age as a risk factor (2,7). Christoph et al. reported that mortality rates in-

crease with increasing age (7). In our study, most of the patients were in the 6th decade and their mean age was 58 years. Although age did not affect mortality, the average age of those who died was higher. We believe this is due to the ease and frequency of access to emergency services in the region where the study was conducted. The frequency of visits gradually decreases with age. We have also observed AAD in younger patients. For this reason, AAD should be considered when there are clinically unexplained symptoms regardless of age group.

In studies, the male-female ratio is seen between 7/3 and 6/4 (1,5,7). Male gender is reported as a risk factor for AAD according to a study conducted in Switzerland (2). In the present study, the male-female ratio of AAD was 7.5/4. We evaluated gender did not affect mortality, since the female-male ratio was similar between the groups. Although the risk is higher in men, we believe that rapid diagnosis and treatment in the emergency department does not cause a difference in mortality rates between genders.

Although dissection because of trauma is extremely

**Table 3.** The Effects of Time, Aortic Diameter and Blood Values on Mortality

	In-Hospital		Total	p	
	Deaths	Survivors			
	Mean ± sd	Mean ± sd			
CST (hour)	23.9 ± 52.6	4.2 ± 6.3	8.5 ± 25.5	2.0 (0.5-168)	0.351
WTED (minutes)	94.5 ± 77.1	91.9 ± 50.8	92.5 ± 56.5	60 (45-240)	0.558
Ascending AD (mm)	44.2 ± 12.3	42.3 ± 11	42.7 ± 11.1	40.4 (25-87)	0.567
Arcus AD (mm)	31.7 ± 6.1	33.4 ± 4.7	33.1 ± 5	33.2 (25-45.7)	0.215
Descending AD (mm)	36.8 ± 8.2	34.9 ± 8.1	35.3 ± 8.1	34 (24-62)	0.651
D-dimer (mg/L)	14.5 ± 12.7	9.6 ± 7.2	11.4 ± 9.4	9.6 (0.8-30)	0.386
Troponin (ng/ml)	0.3 ± 0.6	0.6 ± 2	0.5 ± 1.7	0 (0-9)	0.351
Hemoglobin (g/dl)	12.3 ± 3	13.3 ± 2.2	13.1 ± 2.4	13.7 (7.2-16.6)	0.077
Sodium (mmol/L)	140.2 ± 4.5	137.5 ± 3.5	138.1 ± 3.8	138.9 (129-147)	0.947
Potassium (mmol/L)	4.2 ± 0.8	4.1 ± 0.5	4.1 ± 0.6	4.1 (2.4-5.5)	0.593
Calcium (mg/dL)	8.8 ± 1	8.7 ± 0.7	8.8 ± 0.8	8.9 (7-10.4)	0.142
Magnesium (mg/dL)	2.5 ± 0.2	2.1 ± 0.5	2.2 ± 0.5	2 (1.7-3)	0.640
INR	1.7 ± 0.8	1.2 ± 0.2	1.3 ± 0.5	1.2 (0.9-3.2)	0.219

CST: Complaint Start Time, WTED: Waiting Time in the Emergency Department, INR: International normalized ratio

rare, according to the study of Eduardo et al., the mortality rate in traumatic aortic dissection is reported to be >80% (7,8). However, there were no deaths in 4 (8.7%) patients who developed AAD due to trauma. We think that this is because of the rapid diagnosis of trauma with advanced imaging.

In the present study, the most common complaints were chest, back and abdominal pain. Although only 6 (13%) of patients with AAD have syncope, it is the only symptom associated with mortality. We think that the reason for this situation is the sudden brain damage that occurs because of syncope.

The most common symptom is a sudden onset of tearing, typically in the chest and back (6). These symptoms can be confused with other diseases that can cause mortal chest pain, especially acute coronary syndrome (6,9). We found no correlation between the location of pain and mortality in this study.

Late diagnosis of AAD increases mortality(2,5). According to the study of Booher et al., if the onset of symptoms is in the first 24 hours, hyperacute, 2-7 days acute, 8-30 days subacute, and over 30 days are chronic aortic dissection (10). The time interval with the highest mortality is the first 48 hours after the onset of symptoms (7). In Zaszke's study, it was reported that early suspicion of AAD reduced the time from pain onset to surgery from 8.6 hours to 5.5 hours (6). Harris et al. reported that the diagnosis time would be shortened if the symptoms of admission to the ED were typical (chest, back and leg pain) (5). In a study conducted on 750 patients, the time from admission to the ED to the diagnosis of AAD was approximately 4.3 hours (5). In the presented study, the average time from the onset of the complaints to the diagnosis was

8.5 hours, and the time from admission to the ED to the diagnosis was approximately 92 minutes (~1.5 hours). We would like to state that only hyperacute and acute included patients in the study. Even though it is seen that this period does not have a statistically significant effect on in-hospital mortality, we saw that most of the deceased applied to the hospital almost 24 hours after the onset of their complaints. We think that by increasing the awareness of AAD, early diagnosis will decrease mortality.

Cigarette smoking is recognized as an independent risk factor in most studies (2,4,7). In this study, there were more smokers. However, we think that since we do not include the duration of smoking in the records as pack-years, its relationship with mortality cannot be determined.

The most common comorbid condition in AAD is hypertension (11). Congenital diseases such as Marfan syndrome, Loeys-Dietz syndrome, vascular Ehlers-Danlos syndrome, Turner's syndrome, aortic coarctation and bicuspid aortic valve are considered being risk factors for AAD (2,4,7). It is stated that hypertensive people increase the risk of AAD approximately 4 times compared to normotensives, and it is seen in 75% of patients (7,11). The most common comorbid conditions in the present study were hypertension and coronary artery disease. Its incidence was consistent with the literature, but the only comorbid condition affecting mortality among comorbid conditions was renal failure. According to the study of Chen et al., it is reported that there is a short and long-term mortality relationship between type-B dissection and renal failure (12). We found no connective tissue disease among the cases. We think that contrasting nephropathy developing after intravenous computed tomography for

the diagnosis of AAD aggravates the underlying renal failure and increases mortality.

Since chest and back pain are common, the first imaging method is direct chest X-ray (2,5). However, it should be known that the radiograph is normal in approximately 20% of Type A aortic dissections (5). Transthoracic echocardiography (TTE) or transesophageal echocardiography (TEE) may be performed where AAD is suspected and cannot be diagnosed (2,7). Echocardiography has the advantages of being rapid, reproducible and radiation-free in an unstable patient, but the possibility of false positives or negativity is known depending on the operator (7). The most widely used method is computed tomography with intravenous contrast, because of its rapid image acquisition and processing capability (2). Magnetic resonance imaging (MRI) is the most accurate diagnostic method for dissection, but it is not used very often due to the disadvantages of the imaging technique (5). The frequency of use of the triple CT protocol, which is used to show acute coronary syndrome, pulmonary embolism and AAD in a single session, is increasing (7). One disadvantage of CT is that it can cause renal failure due to ionizing radiation and contrast material (2). In our patients diagnosed with AAD, X-ray (91%), CT (67%) and echocardiography (63%) imaging methods were used, respectively. X-ray, echocardiography and CT were performed together in some patients, but MRI was not performed on any of the patients urgently. Images of a patient diagnosed in an external center could not be accessed from the database, only the reports of the images were accessed. Each method has its advantages and disadvantages. We think that with the widespread use of affordable MRI devices that can shoot quickly, they can be used instead of direct radiography, echocardiography and CT.

One of the most used classification methods in clinical practice is Stanford (12). If the first dissected segment is in the ascending aorta, it is called type A, and the other segment that is affected is called type B (2). According to Zschke's study in 2020, the incidence of type AAD is 2.9-11.9/100000 persons annually (6). According to the Stanford classification, it is stated that Type A dissections can be seen at earlier ages than B (2). In the current study, it was seen that 76.1% of the patients were type A, 60% of those who died were type A and 40% were type B. We observed that Stanford classification did not affect mortality in AAD patients in the hyperacute and acute phases. We would like to point out that in-hospital and post-hospital mortality rates were not evaluated after hospitalization. We think that mortality rates may vary according to the type of dissection in long-term follow-ups.

The greater the aortic diameter, the greater the risk of dissection (2). According to Christoph, those with aortic diameter greater than 55 mm increase the mortality rate

by 4 times compared to those with an aortic diameter less than 55 mm (7). In the study of Koechlin et al., the mean aortic diameter of the ascending aorta, aortic arch and thoracic aorta was reported as less than 45 mm in AAD (1). In the present study, the mean aortic diameter was measured as ascending/ arcus/ descending 42/ 33/ 35 mm, respectively. The aortic diameter was similar between both groups, but no statistically significant difference was detected. When evaluated according to the literature, we can say that the risk is less because the average of the measured aortic diameters is less than 55 mm.

It is stated that blood parameters contribute little to the diagnosis in AAD patients (2). There may be variability in blood values, depending on the affected organ (13). However, even if D-dimer is used more in the diagnosis of pulmonary embolism if it is <500 ng in the first 24 hours from the onset of symptoms, it is one parameter that can exclude dissection (2,7). It is stated that troponin is elevated in half of AAD patients (13). We think that the reason why troponin elevation had no effect on mortality in this study was that patients applied to the emergency room within an average of 2 hours after the symptoms began, thus preventing the development of heart failure and consequently, preventing hypoperfusion. Although the d-dimer value was high in the presented study, we did not evaluate it as a risk factor for mortality. Even though the use of blood parameters is helpful in rapid diagnosis and differential diagnosis, the diagnostic value is low in AAD. AAD should be considered if there is an unexplained blood parameter.

Medical treatment aims to reduce pain and complications by reducing blood pressure and heart rate and stopping its progression in the affected aortic segment (2,7). Initially, it is aimed to have a heart rate of 60-80/min and a blood pressure of 100-120 mmHg (7). Patients with malperfusion syndrome (clinically and radiologically) should have immediate surgical intervention (1). Surgical treatment aims to close the false lumen entrance and re-design the internal structure of the aorta to provide reperfusion (7). It has been reported that up to 90% of patients with type A dissection are treated surgically, even if they have comorbid conditions (1,2,4). If malperfusion syndromes are not revealed in patients with type B, conservative intervention can be performed (1,2). According to Bossone et al., surgical treatment has increased from 79% to 90%, and the mortality rate has been reported to have decreased from 31% to 22% (9). Trimarchi et al. report that the rate of surgical intervention decreases, and the rate of medical treatment increases in the treatment of patients with AAD as age progresses (11). In this study, 71.7% of the patients underwent surgery immediately after diagnosis. We decided on medical treatment depending on the clinical situation, advanced age, comorbid conditions, or the patient

and their relatives' refusal to have surgery. The effect of the patients' decision to undergo surgery immediately on mortality was not determined. We think it does not affect the mortality rates since the patients are followed closely in the intensive care unit and surgical treatment is available 24 hours if necessary.

There are many parameters affecting mortality in aortic dissection. Some external factors, such as hospital admission time, rapid diagnosis and treatment availability, change mortality rates (8). Some factors found to be associated with mortality may be recurrent chest and back pain and expanding refractory hypertension (2,4,7). The increase in troponin values after hospitalization was found to be associated with mortality (2). Therefore, close follow-up is very important. Mortality rates have decreased to 12% depending on the developing surgical methods (2). According to a study conducted at the University of Michigan, the hospital mortality rate was reported as 23.8% (11). In our study, 21.7% of patients with AAD died in the hospital shortly after admission. We think these rates will decrease with the patient's admission to the hospital before the development of malperfusion syndromes, rapid diagnosis and treatment.

**Study Limitations:** The limitations of this study are that the post-hospital and long-term results were not evaluated in the study, and that it was a retrospective and single-center study with a relatively low number of participants.

## Conclusion

Despite the improvement in the rate of diagnosis and surgical techniques, the mortality rate of AAD is still very high. There are too many unknowns in parameters that affect mortality. In this study, which we conducted to reveal these unknowns, we found that renal failure is associated with increased mortality, especially in syncope and comorbid conditions, at the first admission. We believe that mortality-related factors will be determined in studies with more patients and more centers. In the light of these findings, we think that more effective health services will be provided.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study received no financial support.

**Ethical Statement:** Ethical approval for this study was obtained from Van Yüzüncü Yıl University Hospital Ethics Committee (decision no: 2021/02-20, date:12.02.2021).

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# A Retrospective Study, Analysis of Syrian Patients Under Temporary Protection Presenting to the Emergency Department

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## Abstract

**Objective:** The immigration problem, driven by war and economic hardships, is a global social and economic issue. Following the Syrian civil war, millions migrated, mainly to neighboring countries. As of 2024, Turkey hosts the largest Syrian population. Syrians frequently use emergency departments (ED) due to limited primary healthcare access. This study analyzes the demographic data, ED usage patterns, and outcomes of Syrian patients, comparing findings with existing literature.

**Materials and Methods:** Demographic data, ED usage characteristics, and outcomes of Syrian patients who applied to the ED between October 1, 2023, and April 1, 2024, were analyzed retrospectively.

**Results:** A total of 1780 patients were included in the study. Most patients presented to the ED during off-duty hours (57.1%), on weekdays (70%), and as self-presentation (97.7%). The most common reason for presentation was symptoms of upper respiratory tract disease (27%). Many patients stayed in the ED for less than an hour (71%). The length of stay in the ED was significantly higher in patients who arrived by ambulance and for whom consultation was requested ( $p < 0.001$ ). Consultation was not requested for most patients (87.8%). The rate of consultation requests was significantly higher in patients who arrived by ambulance than in self-presentation ( $p < 0.001$ ).

**Conclusion:** Syrian patients' visits to the ED for non-urgent reasons are a significant health problem. Educating patients about the functioning of the health system and effectively planning and implementing primary health services will significantly reduce the burden on ED and the cost of health services.

**Keywords:** Emergency department, ED, Syrian, refugee, health services accessibility

## Introduction

The immigration problem, because of war and economic difficulties, stands out as a multidimensional social and economic issue worldwide. Following the Syrian civil war, millions of people were forced to leave their country and migrate to different regions, especially neighboring countries. As of 2024, Turkey is hosting the most significant number of Syrians worldwide. People from Syria who live in Turkey are under the "Temporary Protection" status, and these individuals can benefit from free healthcare services. In this context, the number of Syrians under temporary protection has been recorded as 2,901,478, and 114,599 reside in the province of Izmir<sup>1</sup>.

These people have problems with basic shelter, nutrition, hygiene, and access to health services. In terms of health services, it is known that ED are the units that these people use most intensively<sup>2-3</sup>. This is due mainly to the lack of access to primary health services<sup>4-6</sup>. This situation has led to a significant increase in ED application rates. In addition, it creates additional costs for the health system and causes difficulties in operation. This study aims to fill the gap in knowledge in this area by examining the diagnoses, demographic data, and outcomes of Syrian patients who applied to the ED of local hospital.

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**Received:** 23.05.2025 • **Accepted:** 29.07.2025

**DOI:** 10.55994/ejcc.1703884

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Available online at <https://dergipark.org.tr/tr/pub/ejcc>

**Cite this article as:** Ali Unal, Yagiz Kagan Ergun, Servan Kucuk, Abdulaziz Dogan. A retrospective study, analysis of Syrian patients under temporary protection presenting to the emergency department. Eurasian Journal of Critical Care. 2025;7(2): 25-29

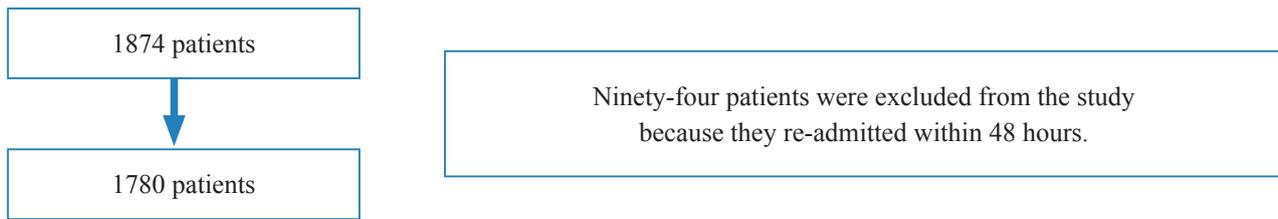
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**Figure 1.** Study flow chart.

## Materials And Methods

This study was conducted single-center and retrospective-ly in a tertiary ED. The hospital where the study was performed has an average of 15000-18000 patients admitted to the ED monthly. Ethical approval was received from a local ethics committee (Decision number: 2024/07-09 Date: 19/08/2024). The tenets of the Declaration of Helsinki performed the study.

**Population Study:** Patient information was obtained through the Hospital Information Management System (HIMS). The study enrolled all patients who visited the ED between October 01, 2023, and April 01, 2024.

**Inclusion Criteria:** In our hospital, Syrian patients with temporary protection status' social security are selected as "Syrian Patients." Therefore, patients whose social security coverage was selected as "Syrian Patients" in their ED applications and registered were included in the study.

**Exclusion Criteria:** Patients who re-applied with similar complaints within 48 hours were excluded from the study.

**Data Collection and Standards:** Data on patients admitted to the hospital were collected retrospectively through the HIMS. The collected information was grouped as follows:

- Patients' age, gender, application day and time information, application methods, and reasons.
- Diagnoses received in the ED [grouped according to ICD-10 (International Classification of Diseases) diagnosis codes].
- Length of stay in the ED
- Consultation requirements
- ED outcome information (discharge, hospitalization, referral, or death)
- If hospitalization occurred, in-hospital outcome information (discharge, referral, or death)

**Statistical Analysis:** Statistical analyses were performed using the JAMOVI v. 2.3.28 software package (The Jamovi Project, Sydney, Australia). The Kolmogorov-Smirnov test was used to check the normality of data distribution. Categorical data were presented as frequency and percentages; numerical data were presented as mean and standard deviation if normally distributed, and median

and interquartile range (IQR) values otherwise. Pearson's chi-square test will be used to test whether the differences between pairwise dependent groups are significant. Fisher's exact test will be used when a table has a cell with an expected frequency of less than 5. Mann-Whitney U test was used to compare two groups regarding non-normally distributed data. All analyses will be performed at a 95% confidence level, and p-value <0.05 will be considered statistically significant.

## Results

A total of 1874 patients were enrolled in the study that matched the inclusion criteria. Subsequently, 94 patients who met the exclusion criteria were excluded from the study (**Figure 1**). 1780 patients were included in the study. 53.1% (n=946) of the patients were male and the median age was 31 (IQR:24-42) years. 57.1% (n=1017) of the patients applied to the ED between 16:00 and 08:00, 70% (n=1246) on weekdays, and 97.7% (n=1739) as self-presentation (**Table 1**). The most common presenting complaint was symptoms of upper respiratory tract disease. (n=480, 27%) (**Table 2**). There were 1263 (71%) patients who were followed in the ED for less than 1 hour (**Table 3**). We observed that patients arriving by ambulance and patients for whom consultation was requested stayed in the ED for a statistically significant longer time (p<0.001). No consultation was requested in 1562 patients (87.8%) applying to the ED. The rate of consultation requests from

**Table 1.** Analysis of emergency department application times and types

	Number(n)	Percentage (%)
<b>Application time</b>		
08:00-16:00	763	42.9%
16:00-08:00	1017	57.1%
<b>Application day</b>		
Mid-week	1246	70%
Weekend	534	30%
<b>How to apply</b>		
Self-presentation	1739	97.7%
Ambulance-arrival	41	2.3%

**Table 2.** Reasons for application of patients

Reason for Application	Number(n)	Percentage (%)
Symptoms of upper respiratory tract disease	480	27.0%
Trauma	299	16.8%
Gastroenterological symptoms	250	14.0%
Musculoskeletal symptoms	250	14.0%
Symptoms associated with the urinary system	111	6.2%
Eye-related symptoms	90	5.1%
Neurological symptoms	86	4.8%
Cardiological symptoms	86	4.8%
Dermatological symptoms	82	4.6%
Other symptoms	46	2.7%
<b>Total</b>	<b>1780</b>	<b>100%</b>

patients arriving by ambulance was statistically significantly higher than from self-presentation ( $p < 0.001$ ).

The most frequently requested consultation was ophthalmology ( $n=67$ , 30.7%). Of all patients for whom consultation was requested, 52 (23.9%) were hospitalized. This rate was 32.5% ( $n=49$ ) for consultations requested from branches other than ophthalmology. 1700 patients (95.5%) were discharged from the ED, while 52 patients (2.9%) were admitted to hospital. (Table 4). Patient diagnoses were recorded in accordance with the ICD-10 diagnosis coding system. The most common diagnosis group was diseases of the musculoskeletal system and connective tissue (28.7%), entered with the code "M" (Table 5).

## Discussion

In our study, the most common presenting complaints of Syrian patients were upper respiratory tract disease,

**Table 4.** Outcomes of patients in the emergency department and during hospitalization

Patient outcomes	Number (n)	Percentage (%)
Discharged from the emergency department	1700	95.6%
Hospitalization	52	2.9%
Discharged from hospital	46	
Transfer to another hospital	3	
Death in hospital		
Leaving the emergency department with a treatment refusal signature	24	1.3%
Transfer from the emergency department to another hospital	4	0.2%
<b>Total</b>	<b>1780</b>	<b>100%</b>

**Table 3.** Length of stay of patients in the emergency department

Length of stay	Number (n)	Percentage (%)
Less than an hour	1263	71%
One to four hours	486	27.3%
More than four hours	31	1.7%
<b>Total</b>	<b>1780</b>	<b>100%</b>

trauma, and gastroenterological symptoms. We observed similar findings in many studies<sup>3,7,8</sup>. In a study, the most common reason for admission was found to be gunshot wounds<sup>9</sup>. This difference may be because the province where the study was conducted is on the Syrian border, the camps are not used effectively, and the war has decreased in intensity over the years. However, compared to the findings of Gulacti et al. (2017)<sup>3</sup>, the rate of trauma cases was higher in our study. This difference may be because the war was intense at the time Gulacti et al. conducted the study, and people were mostly living in isolated camps. Also, the fact that Syrian people today live in settlements rather than in isolated camps may have increased their exposure to minor/major traumas. Some studies emphasize the economic burden of refugees on health systems<sup>3,7,10</sup>. In 2022, total health expenditures in

**Table 5.** Patients' diagnosis code groups

Patients' diagnosis code groups	Number(n)	Percentage (%)
M: Diseases of the musculoskeletal system and connective tissue	510	28,7%
J: Diseases of the respiratory system	454	25.5%
R: Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	399	22.4%
N: Diseases of the genitourinary system	115	6.5%
S and T: Injury, poisoning and certain other consequences of external causes	92	5.2%
L: Diseases of the skin and subcutaneous tissue	59	3.3%
K: Diseases of the digestive system	57	3.2%
H: Diseases of the eye and adnexa	28	1.6%
I: Diseases of the circulatory system	17	0.9%
Y: External causes of morbidity and mortality	17	0.9%
Other diagnosis	32	1.8%
<b>Total</b>	<b>1780</b>	<b>100%</b>

Turkey were recorded at 606 billion 835 million TL<sup>11</sup>. The impact of health services for Syrian patients on these total expenditures is significant. This situation reveals the need for more international cooperation regarding the financing and accessibility of health services. In addition, the use of primary health services by Syrian patients can effectively reduce costs. In a study conducted in a tertiary hospital like ours (earlier than the arrival of Syrian people in our country), the average length of stay of patients in the ED was observed to be two hours. Again, it was found that 12.5% of patients were hospitalized<sup>12</sup>. We found that the average length of stay of Syrian patients in the ED was shorter, and they were hospitalized at a much lower rate. As in our study, studies show that the rate of consultation requests is significantly higher in patients who apply by ambulance and that the length of stay in the ED increases when consultation is requested<sup>13</sup>. This finding may indicate that Syrian patients use ambulances for more serious reasons. In the study by Donmez et al., the hospitalization rate of patients who requested consultation was 27.9%<sup>14</sup>. Our study is also consistent with the literature in this respect. The consultation threshold was used appropriately, resulting in a high hospitalization rate in that population. In our study, the rate of discharge of Syrian patients after applying to the ED was 95.6%. Gulacti et al. (2017)<sup>3</sup> also found high early discharge rates in their study. This indicates that Syrian patients prefer ED to primary health-care services institutions. In another study done between 2012 and 2016 years, the hospitalization rate of Syrian patients was determined as 46.8%<sup>9</sup>. This difference may be because, today, Syrian patients use ED with non-urgent complaints rather than serious complaints. This is another indicator that patients do not use primary healthcare services effectively.

**Limitations:** Some centers did not allow patient data to be collected. For this reason, our study is single-center, and the number of patients is limited. The province where our study was conducted has a larger population of former immigrants and settled people than new immigrants because it is far from the Syrian border. This may be the reason why patients apply more for non-traumatic and non-urgent reasons. Studies to be conducted in patient groups, including provinces close to and far from the border, will provide better information on this subject. Although rare, some patients may have a different ICD diagnosis entry than the original diagnosis. Since our study is retrospective, this cannot be ignored.

## Conclusion

Syrian patients often visit the ED with non-urgent complaints and have high discharge rates. This situation further increases the existing pressure on the functioning of

ED. Redirecting Syrian patients to primary health services, increasing the accessibility of these services, and educating patients on this issue is important in reducing the burden on ED and ensuring more effective use of health services. After these are done, solutions such as not covering the service fee, billing the service recipient, etc., may be applicable in case of applications with non-urgent complaints. In addition, policies that will facilitate the integration of Syrian patients into health services, as well as international cooperation and support, will make significant contributions to the sustainability of the health system. This study is consistent with similar findings in the literature. The study is intended to guide the future of emergency health services provided to Syrian patients and all patients. As a result, primary health care services should be improved when planning health services, and patients under temporary protection status should be encouraged in primary health care units.

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## Aminoglycoside Resistance in Common Pathogens

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### Abstract

**Objective:** This study investigated the resistance patterns to aminoglycosides among 137 bacterial isolates derived from various clinical specimens submitted to the Microbiology Laboratory at XXX Training and Research Hospital in the year 2005.

**Materials and Methods:** The bacterial isolates were *Escherichia coli* (n=34), *Klebsiella pneumoniae* (n=30), *Pseudomonas aeruginosa* (n=30), *Acinetobacter baumannii* (n=23), and *Staphylococcus aureus* (n=20). *Staphylococcus aureus* was further classified into methicillin-susceptible strains (MSSA, n=13) and methicillin-resistant strains (MRSA, n=7). We examined the susceptibility against eight distinct aminoglycosides.

**Results:** Isepamicin exhibited the lowest overall resistance rates within Gram-negative bacilli, particularly among isolates of *P. aeruginosa* and *A. baumannii* derived from intensive care units (ICUs). Streptomycin presented the highest levels of resistance. Statistically significant differences in resistance rates were observed between ICU and non-ICU isolates for gentamicin ( $\chi^2 = 11.19$ ,  $p = 0.0037$ ), amikacin ( $\chi^2 = 8.82$ ,  $p = 0.0121$ ), and isepamicin ( $\chi^2 = 9.67$ ,  $p = 0.0079$ ). This suggests an increased resistance rate in intensive care units.

**Conclusion:** MRSA strains were more resistant to various aminoglycosides, including gentamicin, tobramycin, and isepamicin, in comparison to MSSA strains. These observed differences were not statistically significant. These resistance patterns highlight the limitations of older drugs like streptomycin and kanamycin. The sustained efficacy of isepamicin and netilmicin positions them as viable treatment alternatives, particularly for infections caused by multidrug-resistant organisms. The results point to the necessity for routine susceptibility testing, careful antimicrobial stewardship, and judicious antibiotic selection to enhance patient outcomes and address resistance in high-risk environments such as the ICU.

**Keywords:** Amikacin, Aminoglycoside resistance, Intensive Care Unit, Isepamicin

### Introduction

Aminoglycosides have played a significant role in antibacterial treatment since their discovery, following the introduction of streptomycin in 1944. The concentration-dependent bactericidal activity is crucial for the treatment of severe infections, including tuberculosis, and remains influential in modern medicine. Subsequent introductions of other aminoglycosides, which include neomycin, kanamycin, gentamicin, tobramycin, amikacin, and netilmicin, expanded the therapeutic options for bacterial infections, specifically those caused by Gram-negative organisms (1, 2).

Aminoglycosides have a chemical structure characterised by a 6-membered aminocyclitol ring connected to

different sugar molecules. This configuration contributes to their high solubility and limited lipophilicity, which are necessary for their ability to kill bacteria (3). Their mechanism of action entails an initial electrostatic interaction with the bacterial outer membrane, leading to a disruption of its permeability through the displacement of ions consisting of magnesium and calcium. Upon entering the cell, they irreversibly bind to the 30S ribosomal subunit, obstructing protein synthesis by inducing misreading of mRNA, ultimately leading to bacterial demise (3, 4). Aminoglycosides exhibit enhanced action in alkaline settings and diminished efficacy in acidic situations. This property is particularly significant in clinical settings, as infection sites may exhibit variable pH levels (1, 5).

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**Received:** 01.07.2025 **Accepted:** 05.08.2025

**DOI:** 10.55994/ejcc.1729315

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Available online at <https://dergipark.org.tr/pub/ejcc>

**Cite this article as:** Yasemin Durdu, Kadriye Kart Yasar. Aminoglycoside Resistance in Common Pathogens. Eurasian Journal of Critical Care. 2025;7(2): 31-37

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Aminoglycosides exhibit optimal efficacy against aerobic Gram-negative bacilli, such as *Pseudomonas* species, while demonstrating limited effectiveness against Gram-positive bacteria and negligible activity against most anaerobes. Synergy can arise when combined with cell wall-active agents such as beta-lactams; aminoglycosides may exhibit enhanced efficacy. But bacteria often become resistant to them, which makes them less effective. The post-antibiotic effect (PAE) of aminoglycosides keeps bacteria from growing even after the drug level drops below the Minimum Inhibitory Concentration (MIC). This effect depends on the dose (2, 3). Because aminoglycosides don't absorb well in the gut, they need to be given parenterally. They show good tissue distribution, but they have trouble getting through certain biological barriers, like the blood-brain barrier. The main way that aminoglycosides leave the body is through the kidneys. When they build up in kidney and auditory cells, they can cause nephrotoxicity and ototoxicity, which are serious side effects (1, 2, 3). In the clinic, it is used to treat serious infections like blood infections that are hospital-acquired, urinary tract infections, endocarditis, and infections that are linked to cystic fibrosis (1).

Mechanisms of resistance are complicated and multifactorial and include changing the ribosomal target, making the drugs less permeable, and modifying the drugs with aminoglycoside-modifying enzymes (AMEs) (1, 7). This study shows how important it is to keep doing surveillance on resistance rates so that clinicians can make precise decisions about when to use aminoglycosides. Researchers often believe that certain bacterial strains, like *Escherichia coli* and *Pseudomonas aeruginosa*, are resistant because they have certain resistance genes (2). Aminoglycosides are still an important part of antibiotherapy, even though they are hard to use because of resistance. This is why researchers are still looking into how they work and what new derivatives might be able to get around existing resistance pathways (1, 2, 3).

## Materials and Methods

This study included a total of 137 bacterial strains isolated from biological specimens submitted to the Microbiology Laboratory of the University of Health Sciences, XXX Training and Research Hospital, throughout the year 2005. The isolates were 20 strains of *Staphylococcus aureus*, 34 strains of *Escherichia coli*, 30 strains of *Klebsiella pneumoniae*, 30 strains of *Pseudomonas aeruginosa*, and 23 strains of *Acinetobacter baumannii*. This study was conducted following the Principles of the Declaration of Helsinki. The isolates were used with institutional permission. The susceptibility of these isolates to the following aminoglycoside antibiotics was assessed: streptomycin,

neomycin, kanamycin, gentamicin, amikacin, netilmicin, tobramycin, and isepamicin. We applied Gram staining to all bacterial isolates. We used the catalase test on Gram-positive cocci. The tube coagulase test was done to examine isolates that tested positive for catalase. Those with positive results were identified as *Staphylococcus aureus*. We divided gram-negative bacilli into two groups: fermentative and non-fermentative. Then, we applied standard biochemical methods to identify the species. On MacConkey agar, *E. coli* isolates were lactose-positive, citrate-negative, acid-producing on Triple Sugar Iron Agar (TSI), fermentative in oxidation-fermentation (OF) medium, motile, indole-positive, and methyl red (MR)-positive. *K. pneumoniae* isolates were lactose-positive on MacConkey agar, citrate-positive, acid or acid/alkaline on TSI, non-motile, indole-negative, fermentative, MR-negative, Voges-Proskauer (VP)-positive, and urease-positive. *P. aeruginosa* was found to be oxidase-positive, citrate-positive, alkaline on TSI, motile, and capable of producing pyocyanin pigment in the chloroform test. It could also grow at +42°C. *A. baumannii* was oxidase-negative, citrate-positive, non-motile, alkaline on TSI, and able to grow at +44°C. We followed the Clinical and Laboratory Standards Institute (CLSI) guidelines for antimicrobial susceptibility testing. The Kirby-Bauer disk diffusion method was used to determine the susceptibility of isolates to aminoglycoside antibiotics such as streptomycin, neomycin, kanamycin, gentamicin, amikacin, netilmicin, tobramycin, and isepamicin.

**Statistical Analysis:** Descriptive statistics were used to characterise the distribution of bacterial isolates across clinical departments, specimen types, and patient demographics. Categorical variables, including species identification, isolation sources, and aminoglycoside resistance profiles, were summarised using frequencies and proportions. Antimicrobial resistance rates were calculated and reported as percentages for each pathogen-antibiotic pairing. Inferential statistical analysis employed the chi-square ( $\chi^2$ ) test of independence to assess differences in antimicrobial susceptibility profiles (resistant, intermediate, and susceptible categories) between isolates from intensive care units (ICU) versus the broader clinical population. Two-by-three contingency tables were constructed for each aminoglycoside agent tested. Statistical significance was defined as  $p < 0.05$ . All statistical computations were performed using IBM SPSS Statistics version 28. Comparative analyses were conducted to elucidate resistance patterns across bacterial taxa and hospital departments, with a focused examination of ICU-derived isolates. Resistance data were stratified by Gram staining characteristics (Gram-positive versus Gram-negative organisms). Data visualisation techniques were employed to illustrate temporal trends in isolate recovery and resis-

**Table 1.** Distribution of isolates among the clinics where they have originated

Clinics	<i>E. coli</i>	<i>K. pneumoniae</i>	<i>P. aeruginosa</i>	<i>A. baumannii</i>	<i>S. aureus</i>	Total
Intensive Care Unit	3	7	23	19	6	58
Internal Medicine	8	3	4	2	2	19
Pediatrics	5	9	-	-	1	15
Surgery	6	3	-	-	3	12
Infectious Diseases	3	2	1	1	2	9
Orthopedics	-	1	2	-	5	8
Others	9	5	-	1	1	16
<b>Total</b>	<b>34</b>	<b>30</b>	<b>30</b>	<b>23</b>	<b>20</b>	<b>137</b>

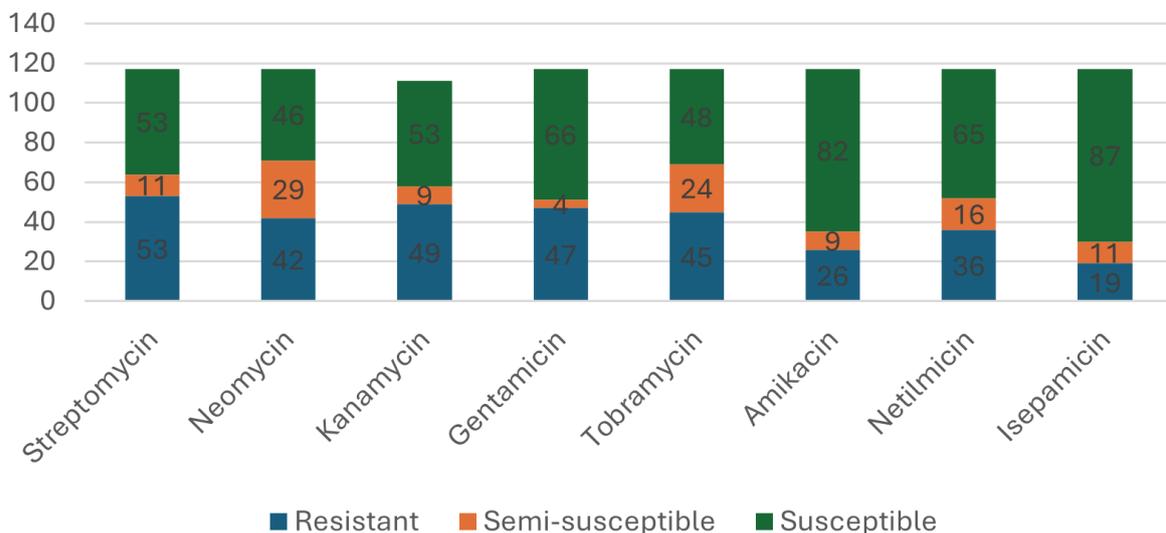
tance prevalence. Raw data management and preliminary statistical tabulations were performed using Microsoft Excel, with subsequent figureical representations generated to facilitate interpretation of resistance patterns and epidemiological trends.

## Results

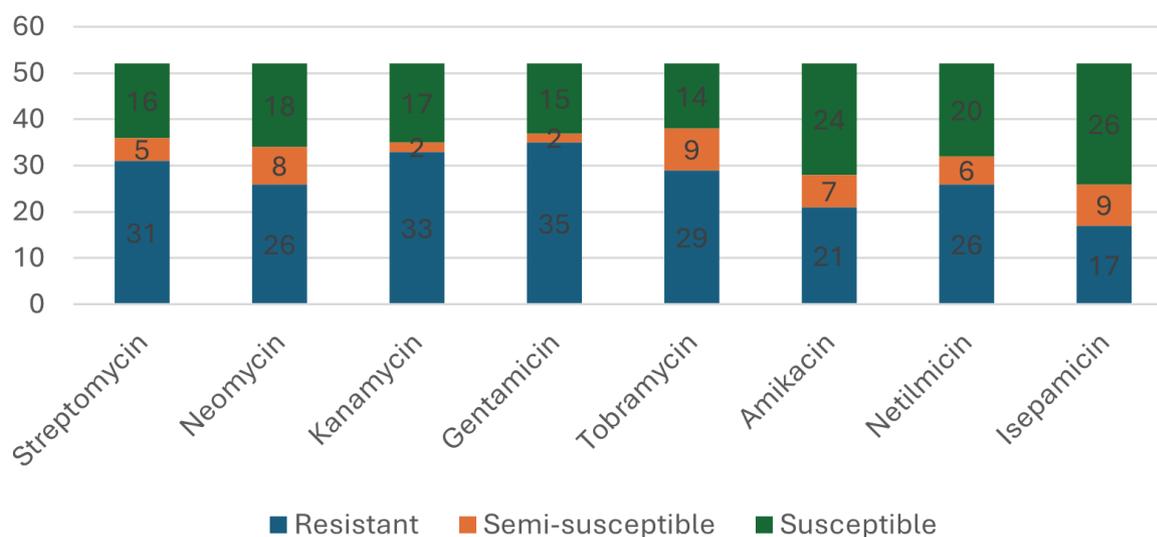
A total of 137 bacterial isolates were included in the study, consisting of 34 *E. coli*, 30 *Klebsiella pneumoniae*, 30 *Pseudomonas aeruginosa*, 23 *Acinetobacter baumannii*, and 20 *Staphylococcus aureus* strains. These were isolated from various clinical specimens submitted in 2005 to the Microbiology Laboratory of XXX Training and Research Hospital. Sample Origins: Most isolates were obtained from urine (33%), followed by sputum (24%), blood (23%), swab (12%), and abscess (9%) samples. Clinical Distribution: The Intensive Care Unit (ICU) accounted for the highest proportion of isolates (42%), with

*P. aeruginosa* and *A. baumannii* being the most prevalent organisms in that setting. (Table 1). Age Distribution: 86% of isolates were from adult patients, while 14% were from paediatric cases. Antimicrobial Resistance: Among Gram-negative isolates, isepamicin demonstrated the highest overall efficacy, showing the lowest resistance rate (16%), followed by amikacin (28%) and netilmicin (32%) (Figure 1). Streptomycin exhibited the highest resistance rate (45%) among Gram-negative isolates. In the ICU subgroup, isepamicin remained the most effective agent, especially against *P. aeruginosa* and *A. baumannii*. (Figure 2) (Table 2). Among the eight aminoglycosides evaluated, statistically significant differences were observed for gentamicin ( $\chi^2 = 11.19$ ,  $p = 0.0037$ ), amikacin ( $\chi^2 = 8.82$ ,  $p = 0.0121$ ), and isepamicin ( $\chi^2 = 9.67$ ,  $p = 0.0079$ ), indicating a higher resistance rate among ICU isolates. Other antibiotics, including streptomycin, neomycin, kanamycin, tobramycin, and netilmicin, did not show statistically significant differences, although kana-

## Aminoglycoside Susceptibilities of all Gram Negative Isolates

**Figure 1.** Aminoglycoside Efficacies of all Gram-Negative Isolates.

## Aminoglycoside Susceptibilities of Gram Negative Isolates in the ICU



**Figure 2.** Aminoglycoside Efficacies of Gram-Negative Isolates in the Intensive Care Unit (ICU).

mycin and netilmicin approached significance ( $p = 0.065$  and  $p = 0.054$ , respectively). (Table 3)

Among *E. coli* isolates, resistance to isepamicin was as low as 3%, while streptomycin resistance reached 47%. *K. pneumoniae* isolates showed 0% resistance to isepamicin, making it the most effective option against this pathogen. *A. baumannii* isolates demonstrated high levels of resistance across all aminoglycosides, although isepamicin remained more effective. The total resistance rates for all the isolates from all the clinics are summarised in Table 4. There were 20 *S. aureus* isolates. 35% of *S. aureus* isolates were identified as methicillin-resistant *S. aureus* (MRSA). The total resistance rates of *S. aureus*, MSSA, and MRSA are summarised in Table 5. The resistance rates are also displayed in Figure 3. While some antibiotics showed trends toward higher resistance in MRSA isolates, particularly gentamicin, tobramycin, and isepamicin ( $p \approx 0.062$ ) (Fisher Exact test), the overall resistance distribution did not differ significantly between MRSA and MSSA groups. ( $p > 0.05$ )

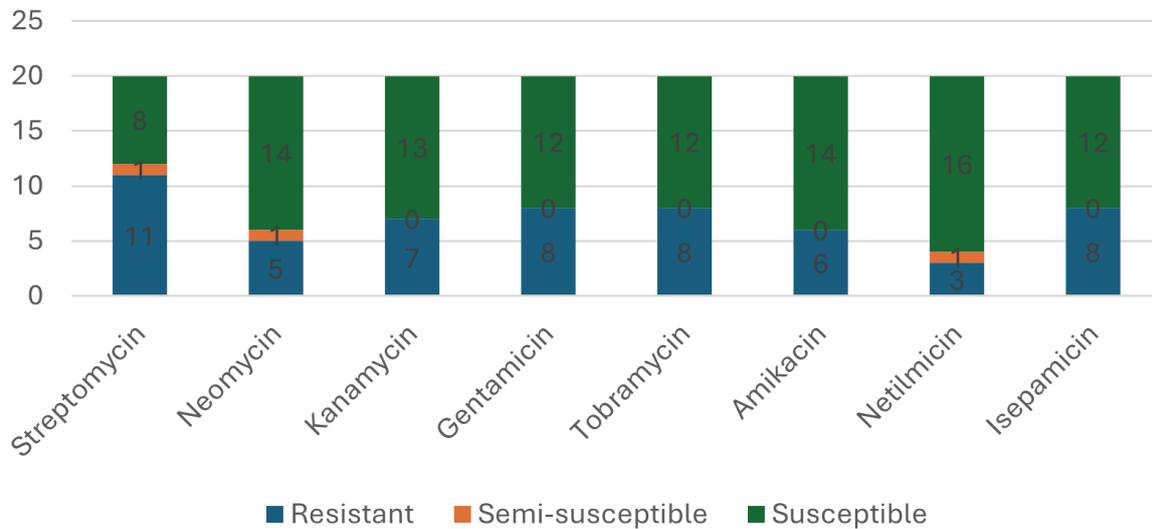
## Discussion

In our study of 137 bacterial isolates collected in 2005, isepamicin demonstrated exceptional efficacy against Gram-negative organisms, corroborating findings from both Turkey and Greece that highlight its stability against prevalent aminoglycoside-modifying enzymes, such as AAC (6')-I, and its improved efficacy over older agents like gentamicin and tobramycin (8, 9, 10). This is especially important because rates of resistance are rising in clinical settings. Notably, isepamicin's ability to work against multidrug-resistant strains makes it an even better candidate for being the mainstay of antimicrobial therapy, especially in severe infections where traditional aminoglycosides have stopped working (11, 12). On the other hand, streptomycin had very high resistance rates—almost 60% among isolates of *Pseudomonas aeruginosa* and *Acinetobacter baumannii*—showing that it is less useful in the clinic (13). This trend shows how streptomycin has been used too much in the past, which has led

**Table 2.** Resistance Rates of the different Aminoglycosides of the ICU Gram-negative isolates

Aminoglycosides	<i>E. coli</i> (n=3) %	<i>K. pneumoniae</i> (n=7) %	<i>P. aeruginosa</i> (n=23) %	<i>A. baumannii</i> (n=19)%
Isepamicin	0	0	30	53
Neomycin	0	43	57	53
Gentamicin	33	57	74	68
Tobramycin	33	43	52	68
Amikacin	33	14	26	68
Netilmicin	33	14	52	63
Streptomycin	67	29	70	58
Kanamycin	100	57	61	63

## Aminoglycoside Susceptibilities of all *S. aureus* Isolates



**Figure 3.** The total resistance rates of all *S. aureus* isolates

**Table 3.** The statistical difference between all isolates and ICU isolates

Aminoglycosides	Chi <sup>2</sup>	p-value	Significant (p < 0.05)
Streptomycin	3.35	0.188	No
Neomycin	3.44	0.179	No
Kanamycin	5.45	0.066	No
Gentamicin	11.19	0.0037	Yes
Tobramycin	4.60	0.100	No
Amikacin	8.82	0.0121	Yes
Netilmicin	5.85	0.054	No (but close)
Isepamicin	9.67	0.0079	Yes

to bacteria developing ways to resist it. The production of aminoglycoside-modifying enzymes, like acetyltransferases and phosphotransferases, which are becoming more common in clinical isolates (14), is what mostly causes resistance to older aminoglycosides. For instance, Strateva et al. found that a large number of *P. aeruginosa* strains

were resistant because of these modifying enzymes. This shows how difficult it is to control bacterial infections around the world (15). Aminoglycosides kill bacteria by stopping protein synthesis by binding to the 30S ribosomal subunit in a way that can't be undone. This causes translation errors and eventually kills the bacterial cell (12). This characteristic enables aminoglycosides to demonstrate notable efficacy in managing multidrug-resistant infections, particularly in the ICU (16). When we looked at isolates obtained from the ICU, we found that gentamicin ( $p = 0.0037$ ), amikacin ( $p = 0.0121$ ), and isepamicin ( $p = 0.0079$ ) had resistance rates that were statistically significantly higher than those of all Gram-negative isolates. These results are in accordance with what we know about how intensive care settings often put selective pressure on microorganisms because they use too many broad-spectrum antibiotics. This makes it easier for strains that are resistant to more than one drug to grow and spread (17, 18). The high level of resistance seen in ICU isolates

**Table 4.** Resistance Rates of the different Aminoglycosides of all Gram-negative isolates

Aminoglycosides	<i>E. coli</i> (n=34) %	<i>K. pneumoniae</i> (n= 30) %	<i>P. aeruginosa</i> (n=30) %	<i>A. baumannii</i> (n=23) %
Isepamicin	3	0	23	48
Neomycin	18	23	57	52
Gentamicin	15	33	60	61
Tobramycin	24	23	50	65
Amikacin	9	7	23	61
Netilmicin	12	20	40	61
Streptomycin	47	23	60	52
Kanamycin	29	33	53	57

**Table 5.** The total resistance rates of *S. aureus*, MSSA, and MRSA

Aminoglycosides	<i>S. Aureus</i> (n=20) %	MSSA (n=13) %	MRSA (n=7) %
Isepamicin	40	23	71
Neomycin	25	31	14
Gentamicin	40	23	71
Tobramycin	40	23	71
Amikacin	30	15	57
Netilmicin	15	8	14
Streptomycin	55	46	71
Kanamycin	35	23	57

shows how important it is to carefully prescribe antibiotics in these situations to avoid more problems caused by antibiotic resistance (19). Of the *Staphylococcus aureus* isolates that were investigated at, 35% were found to be methicillin-resistant *S. aureus* (MRSA). MRSA strains were less sensitive to gentamicin, tobramycin, and isepamicin than methicillin-sensitive *S. aureus* (MSSA), but these differences were not statistically significant ( $p > 0.05$ ). For some antibiotics, though, they were almost significant (for example, gentamicin,  $p = 0.0623$ ). The *aac(6')/aph(2'')* bifunctional gene makes MRSA isolates more resistant to a number of aminoglycosides. This gene is often found in MRSA isolates that were acquired in hospitals (20, 21). There is a lot of proof that this gene makes bacteria very resistant, especially to gentamicin. This makes us think of other ways to get rid of MRSA infections that work. Even though resistance makes things complicated, agents like netilmicin and amikacin are still suitable alternative therapies because they are less likely to be broken down by enzymes (9, 14). Our results show how important it is to include local resistance data when choosing aminoglycoside treatments. Netilmicin may be a good choice for treating infections that don't respond to other drugs because it has consistently low resistance rates in both Gram-positive and Gram-negative organisms. On the other hand, streptomycin's high resistance rates make it of little use in the medical setting. Amikacin is especially important when it comes to multidrug-resistant infections because it works against a wide range of resistant Gram-negative pathogens and is an important part of combination therapies. Studies have shown that when amikacin is used with cell wall active drugs, it can have synergistic effects that make it easier to eradicate bacteria, especially *Pseudomonas aeruginosa* and *Acinetobacter baumannii* (22, 23). This possibility of synergism is especially important when dealing with pathogens that are very resistant and common in ICUs. Researchers are also working on reformulating amikacin and making it more bioavailable, such as through the development of

nanoparticle delivery systems, which could lead to better therapeutic outcomes and help overcome current resistance problems (6, 23).

In conclusion, aminoglycosides like isepamicin and netilmicin are still very important treatment options, especially in ICUs and against Gram-negative pathogens that are resistant to multiple drugs. However, our findings show that antimicrobial stewardship, regular susceptibility monitoring, and careful antibiotic prescribing are very important, especially in critical care settings where resistance develops quickly. To keep these important antimicrobial agents working and patients safe, clinicians must constantly adapt to the changing microbial landscape.

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# Demographic and Clinical Analysis of Shoulder Dislocations in the Emergency Department

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## Abstract

**Objective:** The shoulder joint is the most frequently dislocated joint in the human body due to its wide range of motion, accounting for approximately 50% of all joint dislocations. This study was designed to retrospectively evaluate the demographic characteristics, etiological factors, treatment methods, surgical outcomes, and recurrence rates in patients with shoulder dislocation.

**Materials and Methods:** Between January 2008 and June 2014, 740 patients (1,063 presentations) who presented to the emergency department with shoulder dislocation were retrospectively reviewed. In addition to data obtained from the automation system, supplementary information—including dominant hand, cause of dislocation, post-reduction recurrence, and surgical intervention—was collected via telephone from 248 reachable patients. The data were analyzed in terms of demographic characteristics, dislocation type, reduction method, and complications.

**Results:** The mean patient age was  $37.7 \pm 19.2$  years, with 74.3% being male. Dislocations occurred most frequently in the third decade of life (30.6%), in the dominant arm (64.5%), and in the right shoulder (58.1%). Falls were identified as the primary etiology in 69.8% of cases. Anterior dislocation was detected in 93.1% of cases, and 91.5% were successfully reduced in the emergency department without requiring general anesthesia. While the overall post-reduction recurrence rate was 53.2%, this rate decreased to 15.2% in surgically treated patients. Males were observed to have a significantly higher risk of recurrence.

**Conclusion:** Shoulder dislocations occur more frequently in young males, predominantly in the dominant arm and as anterior-type dislocations. Although surgical treatment significantly reduces recurrence rates, only a small proportion of patients opt for surgical intervention. These findings highlight the need for more active consideration of surgical options in high-risk patients with recurrent dislocations.

**Keywords:** Emergency room, Shoulder dislocation, Shoulder reduction

## Introduction

Shoulder instability is a prevalent and complex orthopedic condition characterized by abnormal mobility of the humeral head within the glenohumeral joint. This condition manifests with pain, muscle weakness, and recurrent dislocations, occurring particularly frequently among young active individuals, athletes, and those who engage in repetitive overhead activities (1). Traumatic causes account for approximately 95% of shoulder dislocations, typically resulting from falls, impacts, or sudden movements (2). In young patients, especially those under 20 years of age, recurrence rates following initial dislocation

may exceed 90%, underscoring the critical importance of early and effective treatment (2, 3). Chronic instability can lead to serious long-term complications including osteoarthritis, joint stiffness, and functional limitations (4). From an economic perspective, the management of shoulder instability creates a multibillion-dollar burden due to medical interventions, rehabilitation, and lost productivity (5). Therefore, accurate diagnosis and treatment of shoulder instability are of paramount importance at both individual and societal levels (6). The history of shoulder instability traces back to the earliest medical records. The Edwin Smith Papyrus (circa 3000 BCE) contains information about the treatment of shoulder dis-

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**Received:** 10.05.2025 • **Revision:** 05.08.2025 • **Accepted:** 22.08.2025

**DOI:** 10.55994/ejcc.1696676

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**Cite this article as:** Mustafa Yalimol, Nusin Yalimol, Ali Saridas, Nedim Uzun, Fatih Buyukcam. Demographic And Clinical Analysis Of Shoulder Dislocations In The Emergency Department. Eurasian Journal of Critical Care. 2025;7(2): 39-44

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locations (7). Hippocrates (460 BCE) developed various reduction techniques using hands, heels, and wooden implements, and recommended cauterization to prevent recurrent dislocations (8). These methods remained in widespread use until the 19th century. During the 20th century, open surgical techniques such as the Putti-Platt procedure were developed, though these methods often restricted joint range of motion and increased osteoarthritis risk (4). The advent of arthroscopic techniques in the late 20th century enabled less invasive and more successful treatments, with arthroscopic Bankart repair now considered the gold standard for recurrent anterior instability (9). The shoulder complex consists of the glenohumeral, acromioclavicular, sternoclavicular, and scapulothoracic joints. The glenohumeral joint is the most mobile joint in the human body and also the most frequently dislocated (10). The stability of this joint is maintained by static and dynamic stabilizers. Static stabilizers include the glenoid labrum, joint capsule, and ligaments; the labrum increases the depth of the glenoid cavity by up to 50% (11). Dynamic stabilizers comprise the rotator cuff muscles (supraspinatus, infraspinatus, teres minor, subscapularis), biceps tendon, and periscapular muscles (12). The deltoid muscle provides power for joint movement and controls scapular position (13). The relatively small size of the glenoid cavity compared to the humeral head predisposes the joint to instability (10). Two main clinical types are recognized: TUBS (Traumatic, Unidirectional, Bankart lesion, requiring Surgery) and AMBRII (Atraumatic, Multidirectional, Bilateral, Rehabilitation/Inferior capsular shift) (14). Diagnosis is established through detailed patient history, physical examination, and imaging studies. Physical examination includes specialized tests such as the Sulcus Sign, Load and Shift Test, Apprehension Test, and Jobe Relocation Test (15). Imaging modalities include plain radiographs, CT, MRI, and MR arthrography; these techniques are critical for identifying associated injuries such as Bankart or Hill-Sachs lesions (11). The management of shoulder instability depends on the type and severity of instability, as well as the patient's age and activity level. For initial dislocations, particularly in elderly patients, conservative treatment is preferred (16). This typically involves 3 weeks of immobilization followed by rehabilitation exercises (16). However, surgical intervention is often necessary in young patients due to their high risk of recurrence (2, 3). The most common surgical procedure is arthroscopic Bankart repair, in which the torn labrum is reattached to the glenoid rim, with success rates exceeding 90% (17). The Latarjet procedure may be performed in patients with significant bone loss (3). Thermal capsulorrhaphy was previously used for multidirectional instability but

has fallen out of favor due to high failure rates (18). Post-operative rehabilitation is crucial for restoring joint range of motion, strength, and stability, and generally includes periods of immobilization followed by passive and active exercises along with strengthening protocols (19). This study aims to examine the demographic and clinical characteristics of patients with shoulder instability, their rates of emergency department visits, and post-treatment recurrence rates. By analyzing data from patients treated at our institution over the past five years, we will identify risk factors for recurrence and evaluate the effectiveness of current treatment protocols (20). Additionally, we will investigate the role of advanced imaging techniques in identifying associated lesions and guiding surgical decision-making (58, 64). The findings of this study will contribute to the existing body of knowledge on shoulder instability management and aid in the development of future clinical guidelines (21). Due to its high prevalence and recurrence rates, shoulder instability remains an important research topic in orthopedics. This thesis seeks to improve understanding and management of this condition through examination of patient demographics, clinical characteristics, and treatment outcomes (5). Early diagnosis, appropriate treatment, and effective rehabilitation are critically important for optimizing patient outcomes (22).

## Materials and Methods

This study was conducted at Bağcılar Training and Research Hospital Emergency Department after obtaining ethics committee approval. The study was designed retrospectively. Patients diagnosed with shoulder dislocation in the emergency department between February 2009 and June 2014 were included in the study. Patient records were retrieved from the hospital information system using ICD codes for shoulder dislocation, and through contact information obtained, patients were reached by phone to collect data on age, sex, side of dislocation, location where reduction was performed, dominant arm, presence of recurrent dislocations, post-reduction surgical intervention, causative event, associated pathologies, and post-reduction complications. Among the causative events, assault and sports injuries were classified as direct trauma. Additionally, classifications included traffic accidents, falls, and non-traumatic forced joint movements. All patients were contacted by phone using the contact information available in hospital records. Telephone contact was established with 248 patients, who were questioned about whether they underwent surgery at our hospital or another center following the procedure, whether recurrent dislocation occurred, and whether any complications developed.

**Table 1.** Age distribution by decades of shoulder dislocations in reachable patients

	Number of patients	Percentage (%)	Number of recurrences	Recurrence rate (%)
0-9 Age	1	0.4	1	0.8
10-19 Age	38	15.3	24	18.2
20-29 Age	69	27.8	50	37.9
30-39 Age	45	18.1	25	18.9
40-49 Age	29	11.7	16	12.1
50-59 Age	22	8.9	6	4.5
60-69 Age	21	8.5	6	4.5
70-79 Age	17	6.9	3	2.3
80-89 Age	6	2.4	1	0.8

Data were analyzed using SPSS 20.0 for Windows software package. Continuous data were expressed as mean and standard deviation, while categorical data were presented as percentages and numbers. Normal distribution of continuous variables was assessed using histograms and the Kolmogorov-Smirnov test. For normally distributed data, the Student's t-test was used to compare means, while the Mann-Whitney U test was used for non-normally distributed data. Differences between categorical variables were evaluated using the Chi-square test. A p-value <0.05 was considered statistically significant.

**Table 2.** Characteristics of Shoulder Dislocations in Reachable Patients

	Number of Cases	Percentage (%)
<b>Cause of Dislocation</b>		
Falls	173	69.8
Motor vehicle accidents	18	7.3
Direct trauma	25	10.1
Non-traumatic forced joint motion	32	12.9
<b>Side of Lesion</b>		
Right	144	58.1
Left	95	38.3
Bilateral	9	3.6
<b>Dislocation Type</b>		
Anterior	231	93.1
Posterior	12	4.8
Inferior	5	2.0
<b>Dominant Side Involvement?</b>		
Dominant	156	62.9
Non-Dominant	92	37.1
<b>Number of dislocation episodes</b>		
1	121	48.8
2	25	10.1
>2	102	41.1

## Results

The patients' mean age was  $37.7 \pm 19.2$  years, with 545 males (74.3%) and 189 females (25.7%). The mean age of female patients was  $55.3 \pm 19.9$  years, while the mean age of male patients was  $31.6 \pm 14.6$  years. The mean age of female patients was significantly higher than that of male patients ( $p < 0.001$ ).

Shoulder dislocations were most frequently observed in the third decade of life. Similarly, the highest recurrence rates also occurred in this decade. A marked decline in both incidence and recurrence rates was observed beyond the sixth decade.

Table 2 presents the characteristics of shoulder dislocations in reachable patients. Among these patients, falls were the most common cause of dislocation, occurring in 173 cases (69.8%). Dislocations were most frequently observed in the right arm (58.1%), and in 62.9% of patients, the dislocation occurred in their dominant arm. The anterior direction was the most common dislocation type (93.1%).

**Table 3.** Reduction-Related Data in Reachable Patients with Shoulder Dislocations

	Number of Cases	Percentage (%)
<b>Location of reduction</b>		
Emergency Department	227	91.5
Operating Room	21	8.5
<b>Recurrence status</b>		
Recurrence present	132	53.2
No recurrence	116	46.8
<b>Post-Reduction Surgery</b>		
Surgical intervention perform	33	13.3
No surgical intervention	215	86.7
<b>Postoperative Recurrence Rate</b>		
Recurrence occurred	5	15.2
No recurrence	28	84.8

**Table 4.** Distribution of Shoulder Dislocation Types by Reduction Location in Accessible Patients

	Emergency Department	Operating Room
Anterior	211	20
Posterior	11	1
Inferior	5	0

Among the accessible patient cohort, 227 shoulder dislocations (91.5%) were successfully reduced in the emergency department, while 21 cases (8.5%) required reduction in the operating room. As detailed in Table 4, the distribution by dislocation type revealed that all inferior dislocations were managed in the emergency setting, whereas only one posterior dislocation necessitated operating room intervention. Statistical analysis demonstrated no significant association between reduction location and dislocation type ( $p=0.573$ ).

Reachable patients were asked whether their shoulder dislocation recurred after reduction; 132 patients (53.2%) reported recurrence, while 116 (46.8%) reported no recurrence. It was observed that the likelihood of redislocation is high after experiencing a shoulder dislocation once. Among reachable patients, 13.3% underwent surgery after reduction. Recurrent shoulder dislocation occurred in 5 (15.2%) of the surgically treated patients. The recurrence rate was lower in those who had surgery. Additionally, postoperative recurrence was identified in 4 patients under 40 years of age compared to only 1 patient over 40. Fourteen patients (5.6%) had a proximal fracture accompanying their shoulder dislocation. In 7 of these patients (50%), the fractured bone was the humerus.

Recurrent shoulder dislocation was present in 31.0% of female patients compared to 62.1% of males, demonstrating significantly higher recurrence rates in male patients ( $p<0.001$ ).

## Discussion

Shoulder dislocation is a medical problem as ancient as our historical records of medicine. It was described during Ancient Egyptian and Hippocratic eras, with treatment approaches emerging concurrently with medical history (8). The shoulder joint is the most mobile joint in the human body and is at higher risk of injury compared to other joints (23). The humeral head's articular surface is four times larger than the glenoid fossa's articular surface, and its "ball-and-socket" configuration - combined with the joint capsule's accommodating elasticity - provides extensive range of motion. Consequently, the shoulder joint is the most frequently dislocated joint in the body due to its high susceptibility to trauma. In patients with shoulder

**Table 5.** Distribution of Recurrent Shoulder Dislocation by Gender

Recurrence status	Sex		
	Female	Male	Total
No	49	67	116
Yes	22	110	132
Total	71	177	248

dislocation, fear of recurrence may lead to limitations in daily activities and occupational performance (22). The reported prevalence of shoulder dislocation in adults aged 18-70 is 1.7% (24). Shoulder dislocation occurs more frequently in males (21). Simonet et al. demonstrated higher incidence rates in males compared to females, particularly among young male patients (25). Michael et al. reported that 71.8% of dislocations occurred in males, with peak incidence between 20-29 years (47.8%) and 15-29 years (46.8%), identifying young age and male sex as risk factors (5). Taş et al. found 96.5% male predominance in 21-30 year-olds versus 66.7% females in 61-70 year-olds (20). Owens et al.'s US military study identified significant demographic risk factors: male sex, Caucasian race, military service, junior rank, and age <30 years (26). Hazmy et al. reported 77% male cases (27), while Yeap et al. documented 71.4% males and 28.6% females, with peak incidence in males aged 21-30 (28). Owens et al.'s 9-month study of 4,141 military academy students identified 117 new dislocations (86.3% male, 13.7% female) (29). Our study similarly showed 74.3% male and 25.7% female cases, with peak incidence at 20-29 years (27.8%), confirming young male sex as a risk factor. Michael et al. reported falls (58.8%) as the most common mechanism, with 47.7% occurring at home and 34.5% during sports/recreation; 48.3% of injuries occurred during sports/leisure activities (5). Taş et al. attributed 74.5% of dislocations to falls (20). Hazmy et al. reported etiologies as: falls (37%), traffic accidents (23%), sports injuries (17%), and pathological causes (13%) (27). Yeap et al. found falls (particularly in patients  $\geq 40$  years) and motor vehicle accidents (predominantly younger patients) as main causes (28). Te Slaa et al. reported 37% sports-related and 28% home-related injuries (30). Owens et al. documented 43.6% contact and 41% non-contact mechanisms (29). Our study similarly showed falls (69.8%) as the leading cause, followed by forced joint motion (12.9%), direct trauma (10.1%), and traffic accidents (7.3%). Hazmy et al. reported 68% right-sided dislocations (27), while our study found 58.1% right, 38.3% left, and 3.6% bilateral cases. Antero-inferior dislocations comprise 95% of cases, with 3% posterior and 2% other types (26). Taş et al. reported 93.4% anterior dislocations (20), Hazmy et al. 96.2%, Yeap et al. 98% anterior vs 2% posterior, and

Owens et al. 80.3% anterior, 10.3% posterior, and 9.4% multidirectional. Our findings were consistent: 93.1% anterior, 4.8% posterior, and 2% inferior dislocations.

Without proper medical/surgical treatment, shoulder dislocations carry high recurrence risk (31). Taş et al. reported 82.7% first-time vs 17.3% recurrent cases, noting younger age in recurrent cases (20). Hazmy et al. documented 73.6% first-time dislocations (27), Yeap et al. 69.2% vs 30.8% recurrent (28). Te Slaa et al. reported 26% 4-year recurrence probability, with 64% recurrences in patients <20 vs 6% in >40 year-olds, and no significant sport participation difference (31). Our study showed 53.2% overall recurrence (20% in <20 year-olds, 57.9% in <30 year-olds), with higher rates in males (62.1%) vs females (31.0%), confirming increased recurrence in younger patients.

Taş et al. performed 79.3% reductions in ED vs 20.7% under general anesthesia (20). Hazmy et al. achieved 92.4% successful closed reductions, with 7.6% requiring surgical reconstruction (27). Yeap et al. successfully reduced 97% without general anesthesia (28). Our study similarly showed 91.5% ED closed reductions vs 8.5% OR procedures under general anesthesia. Yeap et al. identified greater tuberosity fractures in 16.9% of patients (half aged 41-50) (28). Te Slaa et al. reported fracture-associated dislocations in 19% and nerve injuries in 21% (31). Our study found associated fractures in 5.6% of dislocations, 50% involving the humerus.

## Conclusion

The study determined that shoulder dislocation occurs more frequently, particularly in young males, with falls being the most common cause, and predominantly manifests as anterior dislocation. Dislocations were observed more commonly in the dominant limb and right shoulder region. However, the vast majority of cases were successfully reduced in the emergency department without requiring general anesthesia and without complications. Male sex was identified as a risk factor for recurrent dislocation. The recurrence rate was found to be significantly lower in patients who underwent surgical treatment compared to those who did not. Nevertheless, despite this positive effect of surgery in reducing recurrence, it is noteworthy that the rates of surgical intervention after dislocation remain considerably low

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### Chronic Methemoglobinemia: A Rare Case with Dramatic Response to Methylene Blue Following Informed Refusal and Recurrent ICU Indication

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#### Abstract

A 46-year-old female patient with a lifelong history of cyanosis affecting the lips and fingertips since childhood presented to the emergency department. On admission, she exhibited mild dyspnea and low oxygen saturation (84%). Arterial blood gas analysis revealed a pH of 7.4, pCO<sub>2</sub> of 40 mmHg, HCO<sub>3</sub><sup>-</sup> of 24 mmol/L, hemoglobin level of 17 g/dL, and a methemoglobin (MetHb) level of 38%. The patient initially refused referral and left the hospital, but returned two days later with recurrent symptoms. Intravenous methylene blue was administered at a dose of 1–2 mg/kg. Following treatment, the MetHb level decreased to 3%, and the patient's symptoms resolved. This case highlights that acute episodes in patients with chronic methemoglobinemia can be effectively managed with early diagnosis and timely intervention.

#### Introduction

Methemoglobinemia is a rare hematologic disorder characterized by the oxidation of hemoglobin's iron from the ferrous (Fe<sup>2+</sup>) to the ferric (Fe<sup>3+</sup>) state due to oxidative agents, impairing its oxygen-carrying capacity. Under normal physiological conditions, methemoglobin levels in the blood remain between 1–2% (1). Clinically, methemoglobinemia presents with decreased oxygen saturation and central cyanosis that does not respond to oxygen therapy. The diagnosis is confirmed by arterial blood gas analysis, and treatment involves the use of reducing agents such as methylene blue (2).

#### Case Report

A 46-year-old female patient presented to the emergency department with complaints of cyanosis of the lips and fingertips. The patient reported a history of intermittent cyanosis of the lips and fingers since childhood. Physical examination revealed no pathological findings in either lung, with equal bilateral respiratory movements. Respi-

ratory rate was 15 breaths/min, blood pressure 135/65 mmHg, heart rate 90 bpm, and peripheral oxygen saturation (SpO<sub>2</sub>) was 84%. The patient was neither tachypneic nor dyspneic. She denied any recent medication use, but reported frequent consumption of beetroot in Konya, raising the possibility of a dietary etiology. Referral to a tertiary care center for further evaluation and treatment was requested via the national referral system. However, the patient declined the referral, stating that her symptoms were not new and had occurred intermittently since childhood. After signing an informed refusal form, she left the hospital voluntarily.

Two days later, the patient presented to a tertiary emergency department as an outpatient with similar complaints. Blood gas analysis revealed results nearly identical to the previous visit. Due to the indication for intensive care, intravenous methylene blue therapy was initiated in the emergency department. Venous blood gas analysis revealed the following values: pH 7.394, pCO<sub>2</sub> 40.7 mmHg, pO<sub>2</sub> 37.6 mmHg, HCO<sub>3</sub><sup>-</sup> 23.9 mmol/L, lactate 1.8 mmol/L, and methemoglobin (MetHb) level of 38%, confirming the diagnosis of methemoglobinemia. Follow-up

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**Received:** 21.06.2025 • **Accepted:** 25.07.2025

**DOI:** 10.55994/ejcc.1724553

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Available online at <https://dergipark.org.tr/tr/pub/ejcc>

**Cite this article as:** Abdullah Yaser Guney, Bilal Arac, Deniz Zeynep Tekir, Sena Nur Sigirci. Chronic Methemoglobinemia: A Rare Case with Dramatic Response to Methylene Blue Following Informed Refusal and Recurrent ICU Indication. Eurasian Journal of Critical Care. 2025;7(2): 45-46.

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blood gas analysis performed two hours after treatment showed stable values: pH 7.394, pCO<sub>2</sub> 40.7 mmHg, pO<sub>2</sub> 37.6 mmHg, HCO<sub>3</sub><sup>-</sup> 23.9 mmol/L, lactate 1.8 mmol/L, and a significantly decreased MetHb level of 3%.

## Discussion

In this case, the patient was found to have chronic methemoglobinemia resulting from a clinical condition to which she had grown accustomed. Chronic methemoglobinemia is typically congenital in origin and may be triggered by specific stressors or environmental factors. The condition often resolves spontaneously. We believe that the patient's refusal to be transferred from the initial facility was primarily due to her previous experiences with similar episodes that had resolved without treatment. In this case, no clear trigger for the methemoglobinemia episode was identified; however, it was noted that the patient consumed large quantities of beetroot in her hometown, which may have played a contributing role. No medication-related cause was found. In a review published by Hord et al. in 2009, the biological transformations of dietary nitrates and their potential health effects were comprehensively discussed. It was emphasized that excessive consumption of high-nitrate foods (e.g., beets) could increase the risk of methemoglobinemia under certain conditions [3]. The treatment of methemoglobinemia varies depending on the patient's clinical status and the level of methemoglobin. In mild cases, withdrawal of oxidative agents and supportive care may be sufficient. However, in cases where methemoglobin levels exceed 20% or severe symptoms are present, specific treatment becomes necessary [4].

Conclusion: This case illustrates that the diagnosis of chronic methemoglobinemia may be delayed due to stable vital signs and the presence of long standing symptoms. Prompt recognition and administration of methylene blue led to rapid symptom resolution in this patient, emphasizing the importance of a multidisciplinary approach in such rare presentations.

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### Hemorrhagic Shock Due to Tubal Ectopic Pregnancy Following Curettage: A Case Report

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#### Abstract

Ectopic pregnancy occurs when a blastocyst implants outside the uterine cavity, most commonly in the fallopian tube. Heterotopic pregnancy refers to the simultaneous presence of intrauterine and extrauterine gestations. The presence of an intrauterine pregnancy often masks the ectopic component, making diagnosis challenging. A ruptured ectopic pregnancy can cause intra-abdominal bleeding and shock. Here, we present a case of heterotopic pregnancy in a patient who underwent curettage for an unintended pregnancy and subsequently developed hemorrhagic shock, along with a review of the relevant literature.

**Keywords:** Heterotopic Pregnancy, Ectopic Pregnancy, Hemorrhagic Shock, Curettage, Salpingectomy

#### Introduction

Ectopic pregnancy is defined as implantation of the blastocyst outside the endometrial cavity (1). The fallopian tube is the most common site, accounting for about 96% of cases (2). Ectopic pregnancy constitutes approximately 1–2% of all pregnancies (3), but the incidence rises to 6–16% among reproductive-age women presenting to emergency departments with abdominal pain or vaginal bleeding. Thus, ectopic pregnancy must always be considered in the differential diagnosis of such cases. It accounts for roughly 4% of all pregnancy-related deaths (4). Without early diagnosis, complications such as rupture, internal bleeding, and hemodynamic instability frequently occur. Heterotopic pregnancy describes the coexistence of intrauterine and extrauterine pregnancies. Although rare in natural conceptions (0.003–0.005%), the incidence increases to 0.1–1% with assisted reproductive technologies (ART), particularly in vitro fertilization (IVF) (5). Because the intrauterine pregnancy often conceals the ectopic component, heterotopic pregnancy is difficult to diagnose (6). In this report, we describe a patient who de-

veloped hemorrhagic shock due to a heterotopic pregnancy after curettage for an unintended pregnancy.

#### Case Report

A 26-year-old woman presented to our emergency department with abdominal and lower back pain. The patient gave written consent for publication of this case.

She had no history of chronic disease. A few days earlier, she had undergone uterine curettage for an unintended pregnancy at a private clinic and had been prescribed oral antibiotics. She reported minimal vaginal bleeding. On examination, tenderness was noted in the lower abdominal quadrants. Laboratory findings revealed Hb: 11.6 g/dL, WBC: 23.67 K/uL, and CRP: 0.4 mg/dL. Because of persistent abdominal pain and the need to exclude potential complications of recent curettage, we performed a contrast-enhanced abdominal CT (Figure 1). The radiology report described mild uterine edema and heterogeneity, enlargement of the left ovary, and a 2×2 cm cystic lesion adjacent to the left fallopian tube.

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• **Received:** 18.08.2025 • **Revision:** 28.08.2025 • **Accepted:** 30.08.2025

**DOI:** 10.55994/ejcc.1613104

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Available online at <https://dergipark.org.tr/tr/pub/ejcc>

**Cite this article as:** Onuralp Caliskan, Aysegul Akcebe, Tufan Akin Giray, Ali Saglik, Tarik Ocak. Hemorrhagic Shock Due to Tubal Ectopic Pregnancy Following Curettage: A Case Report. Eurasian Journal of Critical Care. 2025;7(2): 47-49.

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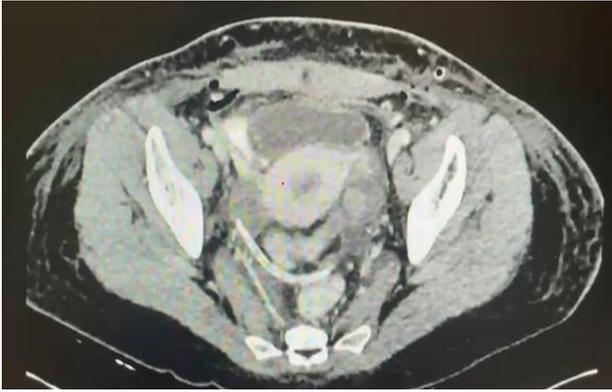
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**Figure 1.** Axial view of the contrast-enhanced abdominal CT showing cystic-like lesion near the left fallopian tube.



**Figure 2.** Intraoperative image revealing massive hemoperitoneum and a ruptured left tubal ectopic pregnancy.

We admitted the patient for observation to our emergency medicine department and requested a gynecology consultation. Within two hours, her abdominal pain worsened, accompanied by dizziness and near-syncope. Initially, her blood pressure was 130/70 mmHg with a heart rate of 105 bpm. During near-syncope, her blood pressure dropped to 75/45 mmHg and heart rate increased to 137 bpm. Abdominal examination revealed acute abdomen findings. Repeat laboratory results showed  $\beta$ -hCG: 12,015 mIU/mL and Hb: 6.0 g/dL. We performed blood typing and crossmatching. In the emergency department, she received 2 units of packed red blood cells and 2 units of fresh frozen plasma after seeing decrease in her hemoglobin levels.

Bedside ultrasonography revealed a 90 hemorrhagic fluid collection in the pouch of Douglas, which had not been present on the CT two hours earlier. The presence of free fluid on ultrasonography in the setting of hemodynamic instability, a sudden hemoglobin drop, and acute abdomen findings strongly indicates intra-abdominal bleeding. We urgently recalled the gynecology team. They initially planned hematoma evacuation via vNOTES (vaginal natural orifice transluminal endoscopic surgery). However, laparoscopy revealed massive intra-abdominal bleeding, prompting conversion to laparotomy. We evacuated the hemoperitoneum. The uterus, bilateral ovaries, and right fallopian tube were intact, but the left fallopian tube was ruptured. Active bleeding originated from a ruptured left tubal ectopic pregnancy (Figure 2). We performed a left salpingectomy and achieved hemostasis. The procedure was completed successfully, and the patient was discharged on postoperative day 4 in stable condition.

## Discussion

This case illustrates a tubal ectopic pregnancy presenting with hemorrhagic shock after spontaneous conception and curettage. An intrauterine pregnancy had been confirmed earlier, and curettage was performed. However,

the subsequent onset of shock revealed an overlooked tubal ectopic pregnancy. This highlights how heterotopic pregnancies—although rare—are easily missed in clinical practice (7).

Heterotopic pregnancy refers to the simultaneous occurrence of intrauterine and extrauterine gestations. Its incidence is approximately 1 in 30,000 in natural cycles but rises to 1 in 100 with ART (12). In our patient, removal of intrauterine tissue likely led the physician to exclude ectopic pregnancy, a common diagnostic pitfall in heterotopic cases. This raises an important question: could careful evaluation of adnexal structures at the initial presentation have revealed the ectopic component earlier?

Modern ultrasonography and transvaginal assessment (8) can detect signs of ectopic pregnancy, such as adnexal masses, the “ring of fire” sign (9), or free pelvic fluid. Because ectopic pregnancy is uncommon, clinicians often evaluate extrauterine structures less thoroughly once intrauterine pregnancy is confirmed. In our patient, this practice likely delayed the diagnosis. Heterotopic pregnancy often presents with nonspecific symptoms. Post-curettage abdominal pain, minimal vaginal bleeding, and low  $\beta$ -hCG levels can mislead clinicians toward alternative diagnoses such as cervical trauma, uterine perforation, or incomplete abortion (10). However, rapid hemodynamic deterioration and worsening abdominal tenderness mandate reconsideration of the diagnosis. For this reason, clinicians must always examine adnexal regions in patients presenting with abdominal pain or shock after abortion, curettage, or intrauterine pregnancy (11).

Kajdy et al. described a case of heterotopic pregnancy diagnosed at 26 weeks of gestation, showing that intrauterine pregnancy can delay detection of the ectopic component for an extended period (12). Like in our case heterotopic pregnancy diagnosed only after intra-abdominal bleeding occurred. These cases emphasize the need to view heterotopic pregnancy as a real clinical entity rather than a theoretical possibility.

This case demonstrates that persistent or new-onset abdominal symptoms after curettage may indicate rare but life-threatening conditions such as heterotopic pregnancy. Although infrequently reported, delayed diagnosis carries a high mortality risk.

## Conclusion

Clinicians should always consider heterotopic pregnancy in patients presenting with persistent abdominal pain after curettage, even if an intrauterine pregnancy has been documented. Inadequate evaluation of adnexal regions may delay diagnosis and lead to life-threatening complications such as hemorrhagic shock. Early recognition and prompt surgical intervention are essential to achieve favorable outcomes.

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### Is the Widespread Use of Electronic Cigarettes a Fatal Threat?

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#### To the Editor,

In recent years, with the increasing use of electronic cigarettes (e-cigarettes), there has been a noticeable rise in poisoning incidents caused by these devices. The potential health hazards of these devices, commonly known as electronic puffs (e-puffs), are becoming more widely discussed. As research examining the health effects of e-cigarette use grows, it also highlights the importance of how poisonings caused by these devices should be managed in Emergency Departments and the necessary interventions for effective treatment.

E-cigarettes are devices that operate by vaporizing nicotine and other chemicals. However, poisonings associated with e-cigarette use are usually based on nicotine toxicity. Nicotine, when taken in high doses, can quickly lead to poisoning and cause fatal consequences. Electronic puffs, especially with improper use of nicotine-containing liquids, pose a significant poisoning risk for children and adolescents [1].

The symptoms of e-puff poisoning in patients presenting to the Emergency Department may include nausea, vomiting, dizziness, excessive sweating, rapid heart rate (tachycardia), and neurological symptoms (seizures, muscle tremors). These symptoms are generally caused by the rapid absorption of nicotine into the body [2]. Furthermore, other chemicals in e-cigarette liquids may damage the respiratory tract, potentially leading to respiratory failure [3].

Regarding treatment in the Emergency Department, the first intervention in e-puff poisoning should be quick and effective to treat nicotine toxicity. In nicotine poisoning, symptomatic treatment is prioritized, including rapid fluid therapy, antiemetics, and sedative treatment. In se-

vere cases, especially if respiratory failure has developed, advanced treatments like intubation and ventilation may be required [4]. The composition of the e-puff liquid and the type of device used can affect the poisoning presentation, so a thorough evaluation of the patients is essential for an accurate diagnosis and treatment process.

With the rise in e-cigarette use, the public health risks in this area are also increasing. Electronic puffs used among children and adolescents are contributing to an increase in nicotine poisoning cases and leading to serious health complications. It is crucial for healthcare professionals, especially those in Emergency Departments, to be knowledgeable about managing these types of poisonings. Additionally, public health initiatives should focus on providing more education and awareness about the use of these devices [5].

In conclusion, awareness about the health impacts of electronic puffs and the emergency treatment of nicotine poisoning should be raised. Healthcare professionals and the public need to become more conscious of the potential dangers of these devices, and necessary measures should be taken, especially for the safety of children and adolescents.

Sincerely,  
Ali Saridas

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**Received:** 07.02.2025 • **Accepted:** 02.04.2025

**DOI:** 10.55994/ejcc.1635454

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**Cite this article as:** Ali Saridas. Is the Widespread Use of Electronic Cigarettes a Fatal Threat?. *Eurasian Journal of Critical Care*. 2025;7(2): 51-52

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