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Original Article

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Epidemiological characteristics of intracranial pathologies and their association with fracture patterns in maxillofacial trauma: a retrospective cohort study

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ABSTRACT

Aims: This study aimed to investigate the epidemiological characteristics of intracranial pathologies associated with maxillofacial trauma, and to examine their relationship with fracture types.

Methods: This retrospective cohort study included a total of 1.048 patients who presented to the Emergency Department of Haydarpaşa Training and Research Hospital between 2012 and 2014. Demographic data, trauma mechanisms, seasonal distribution and fracture localisations were evaluated. The presence of intracranial pathology was determined based on computed tomography (CT) findings.

Results: The mean age of the patients was 34.7 years, with a predominance of males. No significant association was found between age, sex and cerebral injury. Fractures of the maxilla, zygoma, frontal sinus and orbit were significantly associated with intracranial pathology ($p<0.05$). Cerebral injury was observed in 16.17% of cases of nasal fracture, 41.48% of cases of frontal sinus fracture, and 50.00% of cases of orbital roof fracture. Seasonal analysis revealed that cerebral injuries were most frequently observed during spring and autumn. Falls were the most common cause of trauma, followed by traffic accidents.

Conclusion: Maxillofacial fractures, particularly those involving the midface and frontal regions, are important risk factors for cerebral injury. The predominance of simple falls as the leading cause and the higher frequency of injuries in autumn emphasise the importance of considering regional epidemiological patterns in trauma management.

Keywords: Maxillofacial trauma, intracranial pathology, fracture patterns, epidemiology, emergency medicine

INTRODUCTION

Nowadays, facial injuries constitute a significant proportion of emergency department visits. Global epidemiological data reveal that road traffic crashes are the leading etiological factor, particularly in low- and middle-income countries, followed by interpersonal violence and occupational accidents. In addition, assaults, falls, sports injuries, and other occupational accidents are also reported at significant rates. Geographical differences in trauma distribution are emphasised as being closely related to socio-cultural and environmental factors.[1]

The incidence of maxillofacial fractures worldwide increased by 19% between 1990 and 2019. This increase is reported to be more pronounced in males, with fractures due to falls increasing steadily in the elderly population.[2] In a review conducted by Adeleke et al.[3] in Sub-Saharan Africa, it was shown that maxillofacial injuries most commonly occur as a result of road traffic accidents (mostly motorcycle-related) and assaults; the incidence is significantly higher in males, and fractures are concentrated in the mandible and midface region. Similarly, studies conducted in different regions have reported that the distribution of maxillofacial trauma varies depending on geographical and socioeconomic conditions, with traffic accidents being the predominant cause in some regions and assault or falls being more prominent in others.[4,5]

Therefore, elucidating the etiology, distribution, and clinical outcomes of maxillofacial trauma; comparing the epidemiological characteristics of cases based on the presence of cerebral injury; and effectively managing diagnostic and treatment processes are of great importance.

METHODS

Ethics

Ethics committee approval is not required for retrospective patient file reviews that do not involve direct patient intervention or identification. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Study Design and Patient Selection

This study was designed as a retrospective cohort study. The medical records of patients who presented to the Emergency Department of Haydarpaşa Training and Research Hospital between 1 January 2012 and 31 December 2014 and were diagnosed with maxillofacial trauma were reviewed.

Inclusion criteria were defined as being over 16 years of age, having a diagnosis of facial fracture or soft tissue injury related to trauma, having a cranial computed tomography (CT) scan, and having complete medical records. Patients who presented for non-traumatic reasons, had incomplete records, or had a history of previous facial surgery were excluded from the study (**Figure 1**).

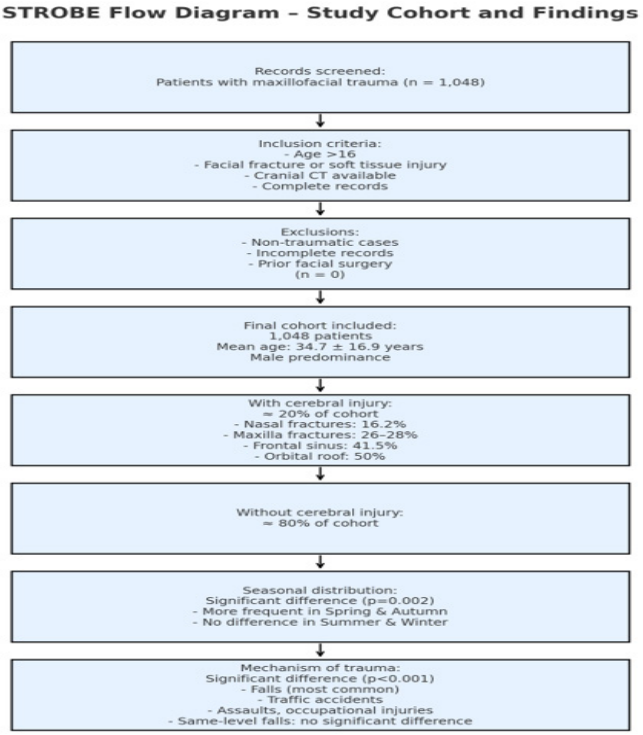

Figure 1. Strobe flow diagram

Variables

Demographic characteristics (age, gender), trauma mechanism, time of trauma (season: spring, summer, autumn, winter), and injury sites were recorded for all cases.

Facial fractures were classified as nasal, maxillary (right/left), mandibular (body, condyle, symphysis), zygomatic arch, zygomatic fracture, frontal sinus, and orbital fractures (lateral, roof, floor).

Patients were divided into two groups based on the presence of cerebral injury. Cerebral injury was defined as the presence of intracranial haemorrhage (epidural, subdural, subarachnoid, intraparenchymal), contusion, or diffuse axonal injury on CT.

Outcomes

The primary outcome was defined as determining the relationship between the presence of cerebral injury and demographic characteristics, trauma time, trauma mechanisms, and fracture locations.

Statistical Analysis

Data were analysed using SPSS v.28 (IBM Corp., Armonk, NY, USA). Continuous variables were presented as mean±standard deviation; Independent samples t-test was used for intergroup comparisons. Categorical variables were expressed as numbers (%) and Pearson Chi-square test was applied for comparisons. Post hoc subgroup analyses were conducted to evaluate the source of differences in variables found to be statistically significant. The significance level was set at $p<0.05$.

RESULTS

The mean age of the total 1.048 patients included in the study was 34.73±16.95 years (**Table 1**). No significant relationship was found between age and cerebral injury (p=0.169). When gender distribution was examined, cerebral injury was found in 21.0% of females and 19.4% of males; this difference was not statistically significant (p=0.636).

When evaluated according to fracture locations (**Table 1** and **Figure 2**);

- Nasal fractures were associated with cerebral injury in 16.18% of cases (p=0.035).
- Cerebral injury was detected in 26.38% of patients with left maxillary fractures (p=0.042) and in 27.70% of patients with right maxillary fractures (p=0.01).
- Mandibular body fractures had a 8.66% rate, mandibular condylar fractures had a 5.49% rate, and mandibular symphyseal fractures had no cerebral injuries (p<0.001 for all comparisons).
- Zygomatic arch fractures had a cerebral injury rate of 13.58%, while zygomatic fractures had a rate of 27.61% (p=0.032 and p=0.02, respectively).
- The rate of cerebral injury in cases of frontal sinus fractures was 41.48% (p<0.001),
- While it was 50.0% in orbital roof fractures (p<0.001).
- No significant relationship was found between age and gender variables and lateral orbital (26.58%) and orbital floor (18.66%) fractures (p>0.05).

Statistically significant differences were found in the frequency of cerebral injury according to seasonal distribution (p=0.002). Post hoc subgroup analyses revealed that this difference was particularly evident in the spring and autumn months (p<0.05). No significant difference was found between the groups in the summer and winter seasons (**Table 2**).

An evaluation based on trauma mechanisms also revealed a significant association with cerebral injury (p<0.001). Post hoc analyses revealed that the significant difference originated from the groups of falls from a height, traffic accidents, assault, syncope, collision with an object, and work-related accidents (**Table 3** and **Figure 3**). However, no statistically significant difference was found in the fall from the same level group (p>0.05).

Table 1. Demographic characteristics and distribution of cerebral injury according to facial fracture sites

Variable	Total (n, %)/mean (SD)	Serebral injury		p-value/difference (95% CI)
		No	With	
Age (years)	34.73 (16.95)	34.34 (16.38)	36.32 (19.04)	0.169/-4.81- 0.84*
Sex				
Female	224 (21.37%)	177 (79.01%)	47 (20.98%)	0.636**
Male	824 (78.62%)	664 (80.58%)	160 (19.41%)	
Fracture site				
Nasal	371 (35.40%)	311 (83.82%)	60 (16.17%)	0.035**
Left maxilla	144 (13.74%)	106 (73.61%)	38 (26.38%)	0.042**
Right maxilla	148 (14.12%)	107 (72.29%)	41 (27.70%)	0.01**
Mandibular corpus	127 (12.11%)	116 (91.33%)	11 (8.661%)	<0.001**
Mandibular condyle	91 (8.683%)	86 (94.50%)	5 (5.494%)	<0.001**
Mandibular symphysis	62 (5.916%)	62 (100%)	0 (0%)	<0.001**
Zygomatic arch	162 (15.45%)	140 (86.41%)	22 (13.58%)	0.032**
Zygomatic	134 (12.78%)	97 (72.38%)	37 (27.61%)	0.02**
Frontal sinus	135 (12.88%)	79 (58.51%)	56 (41.48%)	<0.001**
Orbital lateral wall	79 (7.538%)	58 (73.41%)	21 (26.58%)	0.14**
Orbital roof	40 (3.816%)	20 (50%)	20 (50.00%)	<0.001**
Orbital floor	75 (7.156%)	61 (81.33%)	14 (18.66%)	0.881**

SD: Standard deviation, CI: Confidence interval, * Independent sample t test, mean (SD), **Pearson Chi-square, n (%)

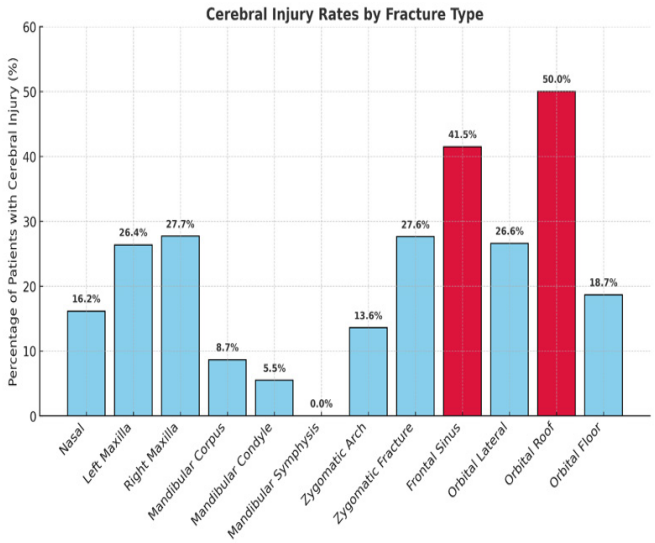

Figure 2. Cerebral injury types by fracture type

Table 2. Distribution of cerebral injury according to seasons

Season	Total n (%)	Serebral injury		p-value
		No	With	
Spring	289 (27.57%)	253 (87.54%)	36 (12.45%)	0.002
Summer	243 (23.18%)	188 (77.36%)	55 (22.63%)	
Autumn	283 (27.00%)	214 (75.61%)	69 (24.38%)	
Winter	233 (22.23%)	186 (79.82%)	47 (20.17%)	

Pearson Chi-square, n (%)

Table 3. Distribution of cerebral injury according to mechanisms of trauma

Mechanism of trauma	Total n (%)	Serebral injury		p-value
		No	With	
Same-level fall	286 (27.29%)	234 (81.81%)	52 (18.18%)	<0.001
Fall from height	65 (6.202%)	25 (38.46%)	40 (61.53%)	
Traffic accident	176 (16.79%)	110 (62.5%)	66 (37.5%)	
Assault	250 (23.85%)	221 (88.4%)	29 (11.6%)	
Syncope	83 (7.919%)	74 (89.15%)	9 (10.84%)	
Object-related injury	141 (13.45%)	133 (94.32%)	8 (5.673%)	
Occupational accident	47 (4.484%)	44 (93.61%)	3 (6.382%)	

Pearson Chi-square, n (%)

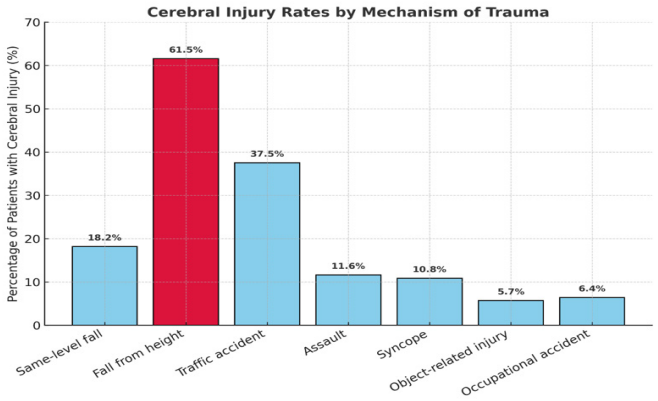

Figure 3. Cerebral injury rates by mechanism of trauma

DISCUSSION

Maxillofacial trauma is a clinical condition associated with serious morbidity and mortality, showing regional differences in aetiology and epidemiology. The literature emphasises that these injuries are closely related to intracranial pathologies. In our study, we demonstrated that fractures of the maxilla, zygoma, frontal sinus, and orbit are significantly associated with cerebral injuries.

It is consistently emphasised in the literature that maxillofacial trauma is most common in young adult males. The average age of approximately 35 and the predominance

of males in our study support this general trend. Asya et al.[6] reported that the incidence of trauma was highest in the 19–28 age group, with male patients being four times more affected than females. Similarly, Xiao-Dong et al.[7] reported an average age of 36.1 years, with the highest rate in the 20–29 age group and men being three times more affected than women. These findings indicate that the demographic results of our study are consistent with the data in the literature.

Seasonal distribution varies across different geographical regions. Gassner et al.[8] reported that maxillofacial injuries are most common during the summer months. Similarly, Işık et al.[9] reported that head injuries in the paediatric population occur most frequently during the summer season. In a study conducted in India, it was noted that trauma rates were higher during the monsoon season (July–October) compared to summer and winter.[10] In contrast, in our study, it is noteworthy that cerebral injuries were most common in autumn. This may be related to the decrease in population density in the region during the summer months and its increase in autumn.

When examining trauma mechanisms, Roccia et al.[11] reported that maxillofacial fractures most commonly resulted from falls from the same level ('slipping, tripping or stumbling').

A large-scale analysis conducted in 2019 also reported falls as the most common cause globally, but showed that assault and violence-related trauma were more prevalent in young adults.[12] The close relationship between maxillofacial trauma and traumatic brain injury (TBI) has also been demonstrated in many studies.

Suprabha et al.[13] noted that maxillofacial injuries are an important risk factor for TBI in paediatric patients. T V et al.[14] reported a significant association between maxillofacial trauma and brain injury in adults with multiple trauma. A multicentre study published in 2025 emphasised that this relationship is particularly pronounced in fractures of the midface and frontal region.[15] Additionally, it has been demonstrated that the presence of head and neck injuries increases the risk of TBI development.[16] Tung et al.[17] reported that life-saving interventions were required in 64 patients (6.2%) with facial fractures, with cerebral injuries being the most common cause of these interventions. Our findings also indicate that cerebral injuries are significantly associated and consistent with the literature.

Our study has revealed the relationship between maxillofacial trauma and cerebral injuries from a regional perspective. Our findings indicate that etiological causes and seasonal distributions may vary according to social conditions. The fact that simple falls are the most common trauma mechanism and that injuries are more frequent in autumn are important observations specific to the region where our study was conducted. When data from different geographical regions are also considered, it can be concluded that the separate evaluation of epidemiological parameters at the regional level is of great importance for the development of accurate diagnosis, treatment, and preventive approaches.

Limitations

This study has several limitations that should be considered when interpreting the findings.

First, the retrospective design inherently carries the risk of incomplete or missing data, which may have influenced the accuracy of recorded variables such as trauma mechanisms or associated comorbidities. In addition, CT scans were interpreted based on available medical records without standardized re-evaluation, which might have introduced variability in detecting cerebral injuries.

Second, the study was conducted in a single tertiary referral center, which may limit the generalizability of the results to other regions with different epidemiological, social, or cultural characteristics. Regional factors such as seasonal population density changes and trauma-related healthcare-seeking behavior may have contributed to the distribution observed in this cohort and may not reflect broader national or global patterns.

Third, although the sample size was relatively large, the subgroups for specific fracture localizations (e.g., orbital roof, mandibular symphysis) were small. This may have affected the statistical power to detect subtle associations, and thus, the reported rates should be interpreted with caution.

Finally, the study did not assess long-term outcomes, treatment modalities, or functional prognosis of patients with cerebral injuries. Therefore, the clinical implications of the identified associations remain limited to the acute diagnostic phase.

Future multicenter, prospective studies with standardized imaging review and long-term follow-up are warranted to validate and extend our findings.

CONCLUSION

This study revealed that maxillofacial trauma, especially fractures of the maxilla, zygoma, frontal sinus, and orbit, were significantly associated with cerebral injuries. Our findings also showed that simple falls were the most common etiological cause in the region where the study was conducted and that cerebral injuries were most frequently seen in autumn.

These results suggest that considering regional epidemiological data in the management of maxillofacial trauma could provide important contributions to diagnosis, treatment, and preventive strategies.

ETHICAL DECLARATIONS

Ethics Committee Approval

Ethics committee approval is not required for retrospective patient file reviews that do not involve direct patient intervention or identification.

Informed Consent

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

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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

Author Contributions

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

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Original Article

The importance of inflammatory indices in the early diagnosis and prognostic evaluation of patients with crush syndrome

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ABSTRACT

Aims: The increase in natural disasters has led to a higher incidence of crush injuries among individuals. Consequently, the development of disaster medicine in recent years has been accompanied by a rise in crush syndrome cases. In disaster medicine management, there is a need for rapid diagnostic and prognostic biomarkers in such cases. Creatine kinase (CK) and C-reactive protein (CRP) are among the most commonly used biomarkers for assessing the inflammatory process. In recent years, novel inflammatory indices such as the Systemic Inflammatory Response Index (SIRI), the Systemic Immune-inflammation Index (SII), and the Pan-immune-Inflammatory Value (PIV) have been shown to play a significant role in the rapid diagnostic and prognostic evaluation of various diseases. In this study, we aimed to determine the diagnostic value and clinical significance of the SII, SIRI, and PIV indices in the diagnosis of crush syndrome.

Methods: This retrospective observational study was conducted on patients diagnosed with crush syndrome who were affected by the earthquake that occurred in Hatay on February 6, 2023, and who were admitted to Ankara Etlik City Hospital between January 1 and December 31, 2023. The included patients were analyzed in terms of laboratory parameters and inflammatory indices and were compared with a control group.

Results: In the patient group included in the study, markers of inflammation, tissue damage, and metabolic disturbances were found to be significantly higher compared to the control group. Notably, levels of CRP, WBC, neutrophils, CK, AST, ALT, BUN, and potassium were markedly elevated, while calcium and pH levels were reduced. Systemic inflammatory indices such as SII, SIRI, PIV, and NLR were also found to be higher in the patient group. In logistic regression analysis, only the SIRI variable was identified as an independent predictor. ROC analyses demonstrated that parameters such as AST, ALT, and SIRI had high diagnostic power. The findings indicate that systemic inflammation and pathophysiological processes are more pronounced in the patient group.

Conclusion: The data obtained demonstrate that inflammatory indices play an important role in the diagnosis of crush syndrome. In particular, the SIRI may provide a stronger diagnostic value compared to other inflammatory indices. Therefore, the use of SIRI as a biomarker for early diagnosis and management of crush syndrome could be beneficial in clinical practice.

Keywords: Crush syndrome, early diagnosis, inflammation, creatine kinase, biomarker, earthquake

INTRODUCTION

The term "crush" refers to compression or crushing. Crush syndrome describes a condition in which the trunk or extremities of the body are exposed to an external compressive force.[1] Historically, in 1941, Bywaters and Beall[2] reported that many patients injured during the Blitz bombings died due to acute renal failure. They later identified a link between muscle damage caused by compression and the development of acute renal failure, coining the term "crush syndrome".[2] Causes of crush injuries include natural disasters such as earthquakes, as well as industrial, construction, or agricultural accidents.[3-5]

Following a compressive force, muscle injuries may occur in the affected regions, potentially accompanied by muscle necrosis, neurological dysfunction, and edema. As a result, crush syndrome can lead to acute kidney injury (AKI) and even multiple organ failure. Prolonged exposure to compression can cause cellular death, particularly

myonecrosis. Although individuals may appear stable after being rescued, the sudden release of potassium, phosphorus, and myoglobin into circulation from damaged tissues can trigger fatal ventricular fibrillation.[6]

The compression of skeletal muscles can result in AKI and, subsequently, rhabdomyolysis—a condition often associated with fatal outcomes. Nephrotoxic products released during rhabdomyolysis, together with tubular obstruction, contribute to AKI. Additionally, hypotension and hypoperfusion may exacerbate acute tubular necrosis. Other factors that increase mortality include advanced age and extensive muscle injury. Therefore, elevated levels of parameters such as serum potassium, aspartate aminotransferase (AST), and creatine kinase (CK), which indicate the severity of muscle injury, reflect both the extent of tissue damage and the severity of the clinical condition.[7]

Recent studies have shown that systemic inflammatory response syndrome (SIRS), triggered by muscle injury, may exacerbate tissue damage. It is suggested that this may create a vicious cycle. Following trauma, immune cells accumulate and become activated at the injury site. Activated lymphocytes, macrophages, and neutrophils contain enzymes in their intracellular granules that produce reactive oxygen species (ROS). Macrophages, which are rich in growth factors and cytokines, significantly contribute to ROS production. While ROS can intensify tissue damage, they also play a role in enhancing immune responses against tissue injury. Paradoxically, macrophages are involved in both muscle cell damage and regeneration.[8]

When the immune system detects danger signals released from injured tissues, inflammation is initiated.[9] This process leads to the release of inflammatory cytokines and ROS, activating lymphocytes, macrophages, and neutrophils, thereby exacerbating local tissue injury.[10] Numerous pro-inflammatory cytokines and chemokines are involved in the pathogenesis of skeletal muscle injury. Some of these inflammatory cytokines may enter systemic circulation and cause inflammation in distant tissues and organs.[11]

Among biomarkers derived from neutrophil, lymphocyte, and monocyte counts, the Systemic Inflammatory Response Index (SIRI) and the Systemic Immune-inflammation Index (SII) have previously been used in evaluating the prognosis of neoplastic diseases.[12,13] SII and SIRI incorporate multiple well-known inflammatory markers that reflect the balance between inflammation and immune response.[14]

Inflammation plays a key role in the pathogenesis of skeletal muscle injury in crush syndrome, and C-reactive protein (CRP) is the most widely used inflammatory marker. A newer parameter, the Pan-immune-Inflammatory Value (PIV), has emerged as a comprehensive and practical index for evaluating inflammation in clinical practice. Moreover, it has been shown to be associated with poor prognosis in various chronic diseases.[15-17]

METHODS

This study was designed as a retrospective analysis and was approved by the Ankara Etlik City Hospital Clinical Researches Ethics Committee (Date: 26.04.2023, Decision No: AEŞH-EK1-2023-099). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. The study included patients diagnosed with crush syndrome who were affected by the earthquake that occurred in Hatay on February 6, 2023, and who were admitted to Ankara Etlik City Hospital between January 1 and December 31, 2023.

Demographic, clinical, and laboratory data of the patients were obtained from electronic medical records and hospital case report forms. The cases were divided into two groups: patients diagnosed with crush syndrome, and volunteers who had experienced crush injuries but did not develop the syndrome. Informed consent was obtained from both patient and control groups. Initial admission values were extracted from the hospital's "keydata" system. The results of both groups were compared. In all groups, the following parameters were analyzed: urea, creatinine, calcium, phosphorus, potassium, CK, AST, alanine aminotransferase (ALT), white blood cell (WBC) count, neutrophil count (NEU), lymphocyte count (LYMPH), monocyte count (MONO), platelet (PLT) count, neutrophil-to-lymphocyte ratio (NLR), SII, SIRI, PIV, CRP, pH, and lactate levels.

In the evaluation of cases diagnosed with crush syndrome, demographic data as well as clinical and laboratory findings were assessed. The control group included patients who had experienced crushing trauma but did not develop crush syndrome. The number of affected extremities, duration of entrapment under debris, and whether fasciotomy, dialysis, or intubation were performed were analyzed. Patients who did not survive (deceased cases) were also included in the analysis.

The following cases were excluded from the study: patients under the age of 18; pregnant patients who had experienced crushing injuries; patients admitted more than 24 hours after injury; patients who had experienced crushing trauma but had normal CK levels; patients with chronic renal failure undergoing routine hemodialysis; and patients who did not consent to participate in the study.

Diagnostic Criteria

The diagnosis of crush syndrome was established based on the clinical and laboratory findings of patients who had sustained crush injuries. Patients who had muscle damage due to crushing, presented clinical symptoms, and had CK levels >5000 U/L were included in the study. The study cohort consisted of 63 patients diagnosed with crush syndrome and 49 individuals who had experienced crushing injuries but did not develop the syndrome (control group).

Inflammatory indices were calculated using the following formulas:

- SII=Platelet count×neutrophil count)/lymphocyte count
- SIRI=Neutrophil count×monocyte count)/lymphocyte count
- PIV=Neutrophil count×monocyte count×platelet count)/lymphocyte count

Statistical Analysis

The data analysis of the study was conducted using The Statistical Package for Social Sciences (SPSS) for Windows, Version 23 (IBM Corp., Armonk, NY, USA). To evaluate the distribution characteristics of the variables, both analytical tests (Kolmogorov–Smirnov and Shapiro–Wilk tests) and visual methods (histogram inspection) were used. Descriptive

statistics were presented as mean±standard deviation for normally distributed variables and median (interquartile range [IQR]) for non-normally distributed variables.

For comparisons between groups, the Student's t-test was used for parametric variables, while the Mann–Whitney U test was employed for non-parametric variables. For categorical variables, the Chi-square test or, when appropriate, Fisher's exact test was used.

To assess relationships between variables, correlation analysis was performed. The Pearson correlation coefficient was used for parametric variables, while the Spearman correlation coefficient was applied for non-parametric variables. Variables showing strong correlations in the correlation analysis were evaluated for multicollinearity risk, and Variance Inflation Factor (VIF) values were examined for each independent variable. Variables with VIF>5 were excluded from the model. A multivariate logistic regression analysis was then conducted using variables deemed appropriate in terms of multicollinearity.

To evaluate the discriminatory power of laboratory and inflammatory indices used in the diagnosis of crush syndrome, a receiver operating characteristic (ROC) curve analysis was conducted, and optimal cutoff values were calculated for parameters such as NLR, SII, SIRI, and PIV. Additionally, differences between the areas under the curve (AUC) of the ROC curves were compared using the DeLong test.

A p-value <0.05 was considered statistically significant in all analyses.

RESULTS

A total of 112 cases were included in the study. Among the participants, 56.3% were in the patient group and 43.8% were in the control group. Regarding gender distribution, 34.8% of the cases were female and 65.2% were male. Fasciotomy was performed at the scene in 18.8% of the cases, while 81.3% did not undergo fasciotomy. The proportion of patients requiring dialysis was 17.9%, whereas 82.1% did not require dialysis. Intubation was required in 5.4% of the cases, and 94.6% were followed without intubation. The mortality (exitus) rate in the study group was 9.8%, while 90.2% of the patients were discharged alive (**Table 1**).

Table 1. Descriptive characteristics of the study group

Variable	Category	n	%
Group	Control	49	43.8
	Patient	63	56.3
Sex	Female	39	34.8
	Male	73	65.2
Fasciotomy on site	No	91	81.3
	Yes	21	18.8
Dialysis	No	92	82.1
	Yes	20	17.9
Intubated	No	106	94.6
	Yes	6	5.4
Deceased	No	101	90.2
	Yes	11	9.8

The mean age of the patient group was 40.9±17.1 years, while that of the control group was 44.3±18.2 years. Among inflammatory markers, CRP levels were significantly higher in the patient group (129.2±90.4 mg/L) compared to the control group (62.3±64.6 mg/L) (p<0.001). Similarly, WBC and neutrophil counts were significantly elevated in the patient group (WBC: 16.2±6.6 vs. 9.2±3.0×10^3/μL; NEU: 12.9±5.9 vs. 6.4±3.0×10^3/μL; p<0.001). Levels of CK and liver enzymes (AST, ALT) were also markedly higher in the patient group. Kidney function indicators, such as BUN and creatinine, were significantly elevated in patients (p<0.001).

Among electrolytes, potassium levels were increased and calcium levels were decreased in the patient group. Lactate levels were higher in patients (2.4±2.3 mmol/L) than in controls (1.7±1.1 mmol/L). The average duration of entrapment under debris was significantly longer in the patient group (17.6±20.5 hours) compared to the control group (3.9±11.4 hours) (p<0.001).

In comparisons between the two groups, most biochemical and hematological parameters showed statistically significant differences. Inflammatory and tissue damage markers were markedly elevated in the patient group. Levels of CRP, WBC, neutrophils, monocytes, CK, AST, ALT, BUN, and potassium were significantly higher (all p<0.001), while calcium and pH levels were lower (p=0.001 and p=0.016, respectively). Additionally, systemic inflammatory indices such as SII, SIRI, PIV, and NLR were significantly elevated in the patient group (p<0.001). The duration of entrapment under debris was significantly longer in the patient group (mean: 17.6 hours; p<0.001). No statistically significant differences were observed in PLT and LYMPH levels between the groups (p>0.05).

These findings indicate that systemic inflammation, tissue damage, and metabolic disruption were more pronounced in the patient group compared to the control group (**Table 2**).

The correlation analysis between the variable crush and various laboratory parameters revealed numerous significant positive associations. The strongest positive correlations were observed with WBC (r=0.548), NEU (r=0.560), CK (r=0.482), and MONO (r=0.474), indicating a notable increase in inflammatory and tissue damage markers in the patient group (all p<0.001). Additionally, CRP, AST, ALT, BUN, potassium (K), SII, SIRI, PIV, NLR, and the duration of entrapment also demonstrated significant positive correlations with the presence of crush syndrome (p<0.01).

Conversely, calcium (r=−0.351, p<0.001) and pH (r=−0.221, p=0.019) levels were negatively correlated with the crush variable, suggesting that lower levels of these homeostatic parameters are associated with patients diagnosed with crush syndrome.

In summary, a strong positive correlation exists between the crush variable and inflammatory markers (WBC, NEU, SII, CRP, SIRI, NLR), as well as metabolic parameters (BUN, K). In contrast, inverse correlations were found with calcium and pH, supporting the presence of more prominent systemic inflammation, metabolic disturbance, and tissue injury in the patient group compared to controls (**Table 3**).

Table 2. Distribution of basic laboratory and clinical data by group

Variable	Control mean±SD	Control median (IQR)	Control min–max	Patient mean±SD	Patient median (IQR)	Patient min–max	p (2-tailed)
Age (years)	44.33±18.20	45.0 (32)	18–85	40.89±17.12	40.0 (25)	18–90	0.320
CRP (mg/L)	62.35±64.60	39.0 (97)	1–266	129.21±90.41	120.0 (86)	18–400	<0.001
WBC (×10³/µL)	9.17±3.05	8.71 (3.08)	4.17–22.97	16.17±6.60	14.30 (8.80)	5.30–36.20	<0.001
NEU (×10³/µL)	6.38±2.99	5.88 (2.79)	2.26–19.88	12.91±5.88	11.50 (8.20)	3.40–29.60	<0.001
MONO (×10³/µL)	0.77±0.29	0.71 (0.37)	0.33–1.59	1.35±0.68	1.20 (0.70)	0.30–3.90	<0.001
LYMPH (×10³/µL)	1.80±0.82	1.70 (1.24)	0.64–4.30	1.80±0.86	1.60 (1.20)	0.39–4.49	0.830
PLT (×10³/µL)	254.82±93.48	255.0 (110.5)	94–592	229.83±85.88	217.0 (102.0)	81–455	0.116
CK (U/L)	392.63±266.08	359.0 (406)	41–952	42975.89±51661.56	24346.0 (50749)	1200–260334	<0.001
AST (U/L)	68.14±145.50	34.0 (27)	9–782	702.54±857.25	578.0 (751)	49–6419	<0.001
ALT (U/L)	39.61±60.04	20.0 (26)	8–358	271.29±392.95	158.0 (236)	19–2819	<0.001
BUN (mg/dl)	35.99±29.11	29.1 (27)	2–152	66.91±49.33	47.0 (74)	5–208	<0.001
Serum creatinine (mg/dl)	1.87±6.94	0.73 (0.42)	0.24–49.0	2.00±2.06	1.00 (1.97)	0.30–8.20	0.005
Potassium (K, mmol/L)	4.12±0.70	4.04 (0.6)	3.1–7.5	4.96±1.30	4.40 (1.6)	3.4–8.7	<0.001
Calcium (Ca, mg/dl)	8.64±0.80	8.61 (0.8)	5.8–9.9	7.90±1.12	8.00 (1.9)	5.6–10.0	0.001
pH	7.41±0.07	7.42 (0.08)	7.11–7.52	7.36±0.13	7.40 (0.10)	6.60–7.53	0.016
Lactate (mmol/L)	1.66±1.11	1.40 (0.68)	0.64–8.04	2.40±2.35	1.70 (1.40)	0.50–16.90	0.042
Time under debris (hr)	3.94±11.43	0.0 (2)	0–48	17.58±20.54	6.0 (27)	0–80	<0.001
SII	1117.96±933.29	879.0 (811)	192–4908	1999.26±1418.32	1554.0 (1889.08)	357.47–6685.0	<0.001
SIRI	3.51±3.48	3.00 (3.00)	0.00–22.00	13.34±13.52	8.60 (12.58)	1.81–70.20	<0.001
PIV	927.00±1181.90	598.0 (609.5)	132–7804	3149.05±3686.48	2131.8 (3528.86)	301.47–20568.60	<0.001
NLR	4.60±3.42	3.55 (3.72)	0.93–13.76	9.11±6.76	7.18 (5.93)	1.74–32.56	<0.001

SD: Standard deviation, IQR: Interquartile range, CRP: C-reactive protein, BUN: Blood urea nitrogen, WBC: White blood cell, AST: Aspartate aminotransferase, NEU: Neutrophil, ALT: Alanine aminotransferase, MONO: Monocyte, SII: Systemic Immune-inflammation Index, LYMPH: Lymphocyte, SIRI: Systemic Inflammatory Response Index, PLT: Platelet, PIV: Pan-immune Inflammatory Value, CK: Creatine kinase, NLR: Neutrophil-to-lymphocyte ratio, K: Potassium, Ca: Calcium

Table 3. Pearson correlations between crush syndrome and other variables

Variable	r	p-value
Age	-0.097	0.307
CRP	0.386	<0.001
WBC	0.548	<0.001
NEU	0.560	<0.001
MONO	0.474	<0.001
PLT	-0.139	0.145
LYMPH	-0.002	0.981
SII	0.338	<0.001
SIRI	0.427	<0.001
PIV	0.361	<0.001
BUN	0.348	<0.001
Serum creatinine (KREA)	0.013	0.894
Potassium (K)	0.360	<0.001
Calcium (Ca)	-0.351	<0.001
AST	0.439	<0.001
ALT	0.363	<0.001
pH	-0.221	0.019
Lactate	0.190	0.044
Duration under debris (hr)	0.343	0.001
NLR	0.377	<0.001

CRP: C-reactive protein, SII: Systemic Immune-inflammation Index, WBC: White blood cell, SIRI: Systemic Inflammatory Response Index, NEU: Neutrophil, PIV: Pan-immune-Inflammation Value, MONO: Monocyte., NLR: Neutrophil-to-lymphocyte ratio, LENF: Lymphocyte, PLT: Platelet

According to the results of the correlation analysis, a high level of positive correlation was identified among certain variables, indicating a potential risk of multicollinearity. Prior to model development, the VIF values for all independent variables were assessed. The final logistic regression model was constructed using variables that remained within acceptable limits for multicollinearity.

In this multivariable model, only the SIRI (Systemic Inflammation Response Index) variable was found to be statistically significant (β=0.269, p=0.026, OR=1.308, 95% CI: 1.032–1.660). This finding indicates that even when controlling for the effects of other variables, SIRI independently increases the likelihood of being in the patient group and stands out as the strongest predictor in the model (**Table 4**).

According to the ROC analysis, many biochemical and hematological parameters were found to have high diagnostic power in distinguishing the patient group from the control group. AST (AUC=0.968) and ALT (AUC=0.940) were identified as the parameters with the highest discriminative ability. These were followed by duration under debris (AUC=0.876), neutrophil count (AUC=0.852), WBC (AUC=0.849), SIRI (AUC=0.811), and monocyte count (AUC=0.792). These results indicate that inflammatory and tissue damage markers were significantly elevated in the patient group and possess strong diagnostic discriminative value.

Parameters with moderate diagnostic power included BUN (AUC=0.731), NLR-2 (AUC=0.746), and potassium (AUC=0.712), while creatinine (AUC=0.676) and lactate (AUC=0.603) demonstrated lower discriminative ability. The fact that calcium (AUC=0.289) and pH (AUC=0.358) values were below 0.5 indicates an inverse relationship, suggesting

Table 4. Logistic regression analysis results (dependent variable: group=patient)

Predictor variable	β (estimate)	SE	z	p-value	Odds ratio	95% CI (lower–upper)
Intercept	0.5663	4.0891	0.138	0.890	1.762	0.0006–5327.79
SII	-0.000206	0.000507	-0.407	0.684	1.000	0.999–1.000
SIRI	0.2687	0.1210	2.221	0.026	1.308	1.032–1.660
NLR	-0.0930	0.1560	-0.597	0.551	0.911	0.671–1.240
Potassium (K)	0.3992	0.4324	0.923	0.356	1.491	0.639–3.480
Calcium (Ca)	-0.3497	0.3651	-0.958	0.338	0.705	0.345–1.440
Duration under debris (hours)	0.0456	0.0245	1.862	0.063	1.047	0.998–1.100

SE: Standard error, CI: Confidence interval, SII: Systemic Immune-inflammation Index, SIRI: Systemic Inflammatory Response Index NLR: Neutrophil-to-lymphocyte ratio

that lower levels of these parameters were associated with the patient group (**Figure, Table 5**).

In conclusion, the ROC analysis revealed that indicators of inflammatory response (WBC, NEU, MONO, SII, SIRI, NLR), tissue damage (AST, ALT), and metabolic deterioration (BUN, K, Ca, pH) possessed strong discriminative power in the patient group. These findings support that, in clinical evaluation, parameters such as CK, AST, ALT, and duration under debris stand out prognostically.

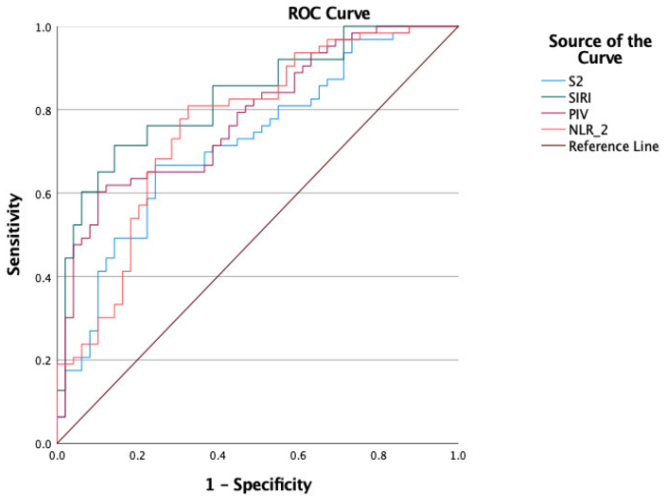

Figure. ROC curve
ROC: Receiver operating characteristic

Table 5. ROC analysis results

Variable	AUC	SE	p-value	95% CI (lower–upper)
CRP	0.777	0.055	<0.001	0.669–0.884
WBC	0.849	0.044	<0.001	0.764–0.935
NEU	0.852	0.044	<0.001	0.765–0.938
MONO	0.792	0.050	<0.001	0.694–0.889
SII	0.710	0.057	0.001	0.598–0.821
SIRI	0.811	0.047	<0.001	0.720–0.903
PIV	0.764	0.052	<0.001	0.662–0.866
BUN	0.731	0.054	<0.001	0.624–0.837
Serum creatinine (KREA)	0.676	0.058	0.006	0.563–0.789
Potassium (K)	0.712	0.055	0.001	0.604–0.819
Calcium (Ca)	0.289	0.054	0.001	0.182–0.395
AST	0.968	0.021	<0.001	0.926–1.000
ALT	0.940	0.027	<0.001	0.887–0.993
pH	0.358	0.060	0.028	0.241–0.476
Lactate	0.603	0.062	0.111	0.482–0.723
Time under debris (hrs)	0.876	0.045	<0.001	0.788–0.965
NLR	0.746	0.056	<0.001	0.636–0.856

SE: Standard error, CI: Confidence interval, ROC: Receiver operating characteristic, AUC: Areas under the curve, CRP: C-reactive protein, BUN: Blood urea nitrogen, WBC: White blood cell, ALT: Alanine aminotransferase, NEU: Neutrophil, NLR: Neutrophil-to-lymphocyte ratio, MONO: Monocyte, SII: Systemic Immune-inflammation Index, SIRI: Systemic Inflammatory Response Index, PIV: Pan-immune Inflammation Value, AST: Aspartate aminotransferase

In the pairwise comparisons of ROC curves, the SII parameter was found to have significantly lower discriminative power compared to SIRI and PIV (p<0.001 and p=0.010, respectively). In contrast, no statistically significant difference was observed between SII and NLR (p=0.155).

SIRI was found to have a significantly higher AUC value than NLR (p=0.014), while no significant difference was noted between PIV and NLR (p=0.611).

These results indicate that the SIRI index is one of the strongest discriminative parameters in terms of inflammation and prognosis, whereas SII has a more limited diagnostic capability (**Table 6**).

Table 6. Comparison of AUC differences between ROC curves

Comparison (test pair)	z	p (2-tailed)	AUC difference	SE	95% CI (lower–upper)
SII–SIRI	-3.510	<0.001	-0.112	0.289	-0.174–-0.049
SII–PIV	-2.575	0.010	-0.062	0.296	-0.108–-0.015
SII–NLR	-1.422	0.155	-0.042	0.302	-0.099–0.016
SIRI–PIV	2.221	0.026	0.050	0.280	0.006–0.095
SIRI–NLR	2.446	0.014	0.070	0.286	0.014–0.126
PIV–NLR	0.509	0.611	0.020	0.295	-0.056–0.096

SE: Standard error, CI: Confidence interval, ROC: Receiver operating characteristic, AUC: Areas under the curve, SII: Systemic Immune-inflammation Index, SIRI: Systemic Inflammation Response Index, PIV: Pan-immune Inflammation Value, NLR: Neutrophil-to-lymphocyte ratio

DISCUSSION

Crush syndrome is a serious clinical condition characterized by systemic damage caused by compressive force applied externally to the trunk, extremities, or other parts of the body. This trauma results in extensive musculoskeletal tissue damage, which can lead to limb loss and organ dysfunction. Post-traumatic muscle damage causes significant changes in blood parameters, notably a marked elevation in CK levels, which correlates with the severity of the disease. In recent years, inflammatory indices developed to assist in the diagnostic process of various diseases have also been evaluated for their potential utility in diagnosing crush syndrome.

This study aimed to investigate the diagnostic value and prognostic role of inflammatory indices in crush syndrome.

Accordingly, we sought to determine the role of the SII, the Systemic Inflammation Response Index (SIRI), and the PIV in diagnosing crush syndrome and to evaluate their correlation with CK, CRP, WBC, and neutrophil-lymphocyte ratio (NLR).

Previous studies have investigated the use of various scoring systems and indices in diagnosing crush syndrome. However, studies examining the role of SII, SIRI, and PIV specifically in crush syndrome remain limited.

In cases of crush syndrome, an increased number of affected extremities and more extensive muscle injury are associated with a higher risk of AKI, increased need for hemodialysis, and significantly elevated CK levels. In our study, 17.9% of all patients exposed to crush injury required hemodialysis, which is consistent with previous research. CK levels in our cohort increased proportionally to the severity of muscle damage. Consequently, AKI may develop in these patients. Elevated CK may serve as an early indicator of AKI. A significant correlation was observed between CK and inflammatory indices, suggesting that these indices may be used as prognostic markers for disease severity.

Ischemia-reperfusion injury plays a critical role in the pathogenesis of crush syndrome. Restoration of blood flow to ischemic muscle tissue triggers an inflammatory response, with neutrophils being the first immune cells to infiltrate the affected area, becoming activated within minutes. In our study, similarly, patients with severe muscle damage showed significant elevations in inflammatory indices.

The pathophysiology of crush syndrome includes renal failure due to rhabdomyolysis, electrolyte imbalances, fatal arrhythmias, and SIRS. In our findings, patients with elevated renal function test results (BUN, creatinine) and abnormal electrolyte levels (potassium) also exhibited significant increases in inflammatory indices.

Neutrophils, lymphocytes, monocytes, and platelets—key components of the immune system—respond to systemic inflammation, trauma, and physiological stress. The neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), SII, SIRI, and PIV are considered prognostic markers in inflammatory processes. Moreover, early changes in neutrophil and lymphocyte counts (<6 hours) may reflect systemic inflammation more rapidly than traditional markers like WBC and CRP. Therefore, due to their practicality and low cost, inflammatory indices can be used to support clinical decision-making.

In a study by Wang and colleagues,[27] inflammatory indices were found to be clinically significant in predicting the occurrence and severity of pneumonia in patients with intracerebral hemorrhage. Similarly, our study demonstrated a meaningful correlation between inflammatory indices and the patient group. Thus, inflammatory indices may be practically used to predict the severity of crush syndrome in affected individuals.

According to the ROC curve analysis conducted in our study, neutrophil (AUC=0.852), WBC (AUC=0.849), SIRI (AUC=0.811), and monocyte (AUC=0.792) levels showed high diagnostic power in differentiating patients with crush syndrome. Pairwise comparisons of AUC values revealed that SIRI had higher AUC values compared to other indices, indicating its superior diagnostic utility in identifying crush syndrome among patients exposed to crush injuries.

In recent years, the use of inflammatory indices in predicting disease prognosis has garnered increasing attention. For instance, in a cross-sectional study by Li et al.,[28] SIRI was found to possess the highest discriminatory capacity and accuracy in predicting chronic kidney disease and low glomerular filtration rate (GFR). Consistently, our study also found that SIRI had significant diagnostic utility and a high AUC value in crush syndrome.

In a retrospective cohort study by Zhang et al.,[29] SIRI was found to positively correlate with stroke severity. In our logistic regression analysis, SIRI was identified as an independent predictor of the likelihood of having crush syndrome. This suggests that patients with elevated CK levels also had high SIRI values. Therefore, SIRI may be a valuable marker for both diagnosis and severity assessment in patients exposed to crush injury.

In a retrospective observational study by Yaman et al.,[18] the McMahon score was used to predict mortality in earthquake-related rhabdomyolysis. The study demonstrated that in disasters such as earthquakes, the McMahon score plays an important role in rapid decision-making regarding mortality prediction. Similarly, our study showed that in patients affected by natural disasters, SIRI and other inflammatory indices may serve as useful markers in rapid diagnosis and severity assessment of crush syndrome.

Limitations

- The sample size was relatively small; thus, validation of the study findings could be enhanced with a larger cohort.
- The study was conducted retrospectively.
- The number of fatal cases (exitus) was limited, preventing a reliable statistical assessment of mortality prediction.

CONCLUSION

Natural disasters occurring around the world—especially earthquakes—frequently expose individuals to compressive forces. In disaster and emergency medicine, the importance of rapid and effective decision-making mechanisms is increasingly emphasized over time. In this context, our study suggests that inflammatory indices may serve as useful tools in the diagnostic process and prognostic evaluation of patients exposed to crush injuries in natural disasters such as earthquakes.

Among these indices, the SIRI stands out as the most effective and significant marker. Since it can be calculated using early and routinely obtained blood test results, it may accelerate the diagnostic process. Furthermore, it is easy to compute and does not incur additional cost.

With these characteristics, SIRI may be used as a practical and cost-effective biomarker for both diagnosis and prognosis in patients with crush syndrome during natural disasters.

ETHICAL DECLARATIONS

Ethics Committee Approval

Was approved by the Ankara Etlik City Hospital Clinical Researches Ethics Committee (Date: 26.04.2023, Decision No: AEŞH-EK1-2023-099).

Informed Consent

As this was a retrospective study, formal written informed consent was not required and was therefore not obtained.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

Financial Disclosure

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Author Contributions

All authors contributed significantly to the study's conception, design, data acquisition, analysis, and interpretation. All authors reviewed and approved the final version of the manuscript.

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Acute gastroenteritis in children in Turkiye: epidemiological trends, etiological agents, changing patterns, and management approaches

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ABSTRACT

Aims: This comprehensive bibliographic review aims to systematically evaluate the published literature on acute gastroenteritis (AGE) in Turkiye, focusing on epidemiological trends, distribution of etiological agents, temporal changes in disease patterns, and current management approaches over the past three decades.

Methods: A systematic literature search was conducted across PubMed/MEDLINE, Web of Science, Turkish Medical Index, and Google Scholar databases for studies published between 1987 and 2024. Search terms included combinations of "Turkiye," "gastroenteritis," "rotavirus," "norovirus," "diarrhea," and "epidemiology." Studies providing epidemiological data, clinical findings, or treatment approaches for AGE in Turkish populations were included. Data extraction encompassed study characteristics, pathogen detection rates, clinical outcomes, and temporal trends.

Results: Analysis of 98 studies revealed rotavirus as the leading cause of childhood AGE in Turkiye, with a median detection rate of 31.8% (95% CI: 31.3-32.4) among 117,741 children with diarrhea. Despite rotavirus vaccines not being included in the national immunization program, self-financed vaccination (12-17% coverage) resulted in significant reductions: rotavirus-positive AGE incidence decreased from 4.4/1,000 in 2012 to 2.48/1,000 in 2018 (44% reduction), while rotavirus-related hospitalizations declined from 1.9/1,000 to 0.45/1,000 (76% reduction). Norovirus genotype II emerged as the most frequently detected viral agent in national surveillance studies, with increasing relative importance following rotavirus vaccination. The influx of 3.5 million Syrian refugees significantly impacted infectious disease epidemiology, with 158,058 diarrheal episodes reported between 2012-2016. Seasonal patterns showed peak rotavirus activity during winter months (January-March), while bacterial pathogens predominated in summer.

Conclusion: AGE remains a significant public health burden in Turkiye. The evidence strongly supports incorporation of rotavirus vaccine into the national immunization program, enhanced norovirus surveillance, expansion of molecular diagnostic capabilities, and establishment of a systematic AGE surveillance network.

Keywords: Acute gastroenteritis, Turkiye, rotavirus, norovirus,diarrheal disease

INTRODUCTION

Acute gastroenteritis (AGE) constitutes one of the most prevalent infectious diseases globally, resulting in significant morbidity and mortality, particularly among children under five years of age. According to the World Health Organization, diarrheal diseases account for approximately 1.8 million deaths annually, making them the second leading cause of death in children under five worldwide.[1] The incidence of the disease is disproportionately higher in low- and middle-income countries, where access to clean water, sanitation, and healthcare services may be limited.[2]

Viral pathogens are responsible for roughly 70% of infectious diarrhea cases in the pediatric population. Among these, rotavirus has traditionally been the primary causative agent of severe gastroenteritis necessitating hospitalization in children under five years of age.[3] The introduction of rotavirus vaccines in 2006 marked a significant milestone in the prevention of AGE, with numerous countries subsequently integrating these vaccines into their national immunization schedules and observing substantial reductions in disease burden.[4]

Turkiye occupies a distinctive geographical and socioeconomic position, bridging Europe and Asia, with characteristics of both developed and developing nations. This transitional status significantly influences the epidemiology of infectious

diseases in the country. Furthermore, since 2011, Turkiye has hosted the world's largest refugee population, comprising over 3.5 million Syrian refugees seeking safety within its borders.[5] This demographic shift has introduced additional complexities to its public health landscape, particularly concerning communicable diseases.

Notably, rotavirus vaccines have not yet been incorporated into Turkiye's national immunization program and remain available solely through self-financing within the private healthcare sector. This policy choice has resulted in vaccination coverage rates of only 12-17%, creating a distinctive epidemiological context that diverges from many European and North American nations where universal rotavirus vaccination is commonplace.[6]

The objective of this comprehensive bibliographic review is to systematically examine the existing literature on AGE in Turkiye, synthesizing evidence regarding epidemiological trends, the distribution and temporal variations of etiological agents, and current management approaches. This review seeks to establish a foundation for evidence-based policy recommendations and to identify gaps in current knowledge that warrant further investigation.

METHODS

Ethics

This study did not involve human participants, patient data, or any biological material. Therefore, ethics committee approval was not required.

Search Strategy and Data Sources

A comprehensive systematic literature search was conducted across multiple electronic databases including PubMed/MEDLINE, Web of Science Core Collection, Scopus, Turkish Medical Index, Turkiye Citation Index, and Google Scholar. The search encompassed publications from January 1987 through December 2024, representing nearly four decades of research on AGE in Turkiye.

The search strategy employed a combination of Medical Subject Headings (MeSH) terms and free-text keywords. The primary search string included: ("Turkey" OR "Türkiye" OR "Turkish") AND ("gastroenteritis" OR "gastroenterit" OR "diarrhea" OR "diarrhoea" OR "ishal") AND ("rotavirus" OR "norovirus" OR "adenovirus" OR "astrovirus" OR "viral" OR "bacterial" OR "*Salmonella*" OR "*Campylobacter*") AND ("epidemiology" OR "prevalence" OR "incidence" OR "outbreak" OR "surveillance"). Secondary searches were conducted using specific pathogen names combined with geographic identifiers.

Additionally, reference lists of identified articles and relevant review papers were manually searched to identify studies potentially missed by electronic database searches. Conference abstracts from major Turkish medical congresses and international infectious disease meetings were also reviewed for relevant unpublished data.

Inclusion and Exclusion Criteria

Studies were eligible for inclusion if they met the following criteria: (1) conducted within Turkiye or involving Turkish populations; (2) reported original epidemiological data, clinical findings, or treatment outcomes related to AGE; (3) published in English or Turkish languages; (4) encompassed a study period of at least one year to account for seasonal variations; and (5) utilized standardized diagnostic methods for pathogen identification.

Exclusion criteria comprised: (1) case reports involving fewer than 10 patients; (2) editorials, letters to the editor, or commentaries without original data; (3) studies focusing exclusively on travelers' diarrhea in non-Turkish populations; (4) animal studies without human relevance; (5) studies with incomplete methodology descriptions preventing quality assessment; and (6) duplicate publications of the same dataset.

Data Extraction and Quality Assessment

Data extraction was performed using a standardized form capturing: publication year, study design, study period, geographic region within Turkiye, healthcare setting (hospital-based vs. community-based), patient demographics (age distribution, sample size), diagnostic methods employed, pathogens identified and their detection rates, clinical severity assessments, treatment modalities, and outcomes including hospitalization rates and mortality.

Study quality was assessed using the Newcastle-Ottawa Scale for observational studies and the Cochrane Risk of Bias tool for clinical trials where applicable. Studies were categorized as high, moderate, or low quality based on selection criteria, comparability of groups, and outcome assessment methodology. Only studies rated as moderate or high quality were included in quantitative analyses.

Data Synthesis and Analysis

Data synthesis employed a narrative approach given the heterogeneity of study designs, populations, and outcome measures across included studies. Where possible, pooled prevalence estimates were calculated using random-effects meta-analysis models to account for between-study variability. Temporal trends were analyzed by stratifying studies according to publication periods (pre-2006, 2006-2015, post-2015) corresponding to key milestones in rotavirus vaccine availability. Geographic variations were examined by categorizing studies according to Turkiye's statistical regions (NUTS-1 classification). Subgroup analyses were performed based on age groups, healthcare settings, and diagnostic methodologies.

RESULTS

Overview of Included Studies

The systematic search identified 1,247 potentially relevant records. Following removal of duplicates and screening of titles and abstracts, 312 full-text articles were assessed for eligibility. Ultimately, 98 studies meeting all inclusion criteria were included in this review, collectively encompassing 117,741 children with diarrhea and spanning 37 years of research (1987-2024) (**Table 1**). The majority of studies (72%) were hospital-based prospective or retrospective cohort studies, with the remainder comprising community-based surveillance studies (18%) and outbreak investigations (10%) (**Figure 1**).

Rotavirus Epidemiology and Burden of Disease

Rotavirus emerged as the predominant etiological agent across all included studies, with a median detection rate of 31.8% (95% CI: 31.3-32.4) among children under five years presenting with AGE (**Figure 2**). This translates to approximately 26,566 rotavirus-positive cases identified from the cumulative study population. The detection rate

Table 1. Characteristics of included studies on acute gastroenteritis in Turkiye (1987-2024)

Study period	No. of studies	Study design	Sample size	Age group	Region	Diagnostics
1987-1999	18	Hospital (89%)	12.458	<5 years	Marmara, C.Anatolia	EM, LA
2000-2005	22	Hospital (82%)	24.892	<5 years	Aegean, Medit.	ELISA, LA
2006-2010	24	Hospital (75%)	31.547	<5 years	Nationwide	ELISA, RT-PCR
2011-2015	19	Hospital (68%)	28.156	<5 years	Nationwide + Refugee	RT-PCR, Multiplex
2016-2024	15	Hospital (60%)	20.688	All ages	Nationwide	Multiplex PCR
Total	98	-	117.741	-	-	-

EM: Electron microscopy, LA: Latex agglutination, ELISA: Enzyme-linked Immunosorbent Assay; RT-PCR: Reverse transcription polymerase chain reaction

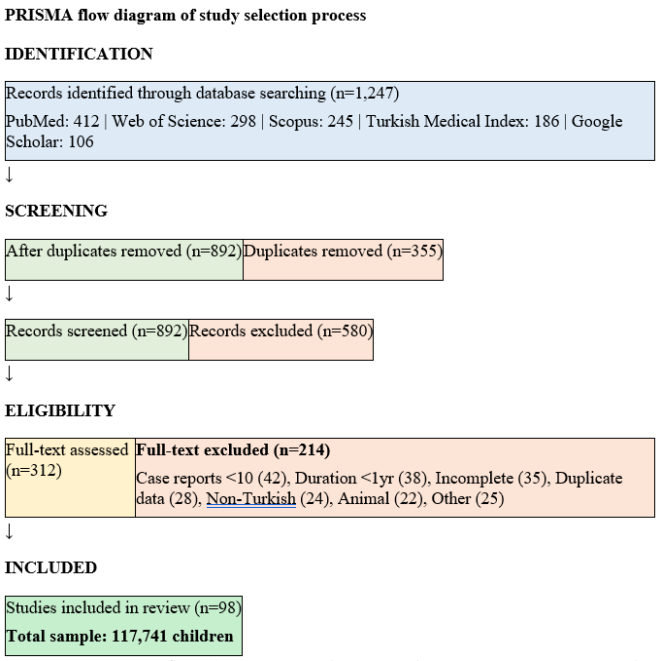

Figure 1. PRISMA flow diagram. Database searches: January 1987-December 2024

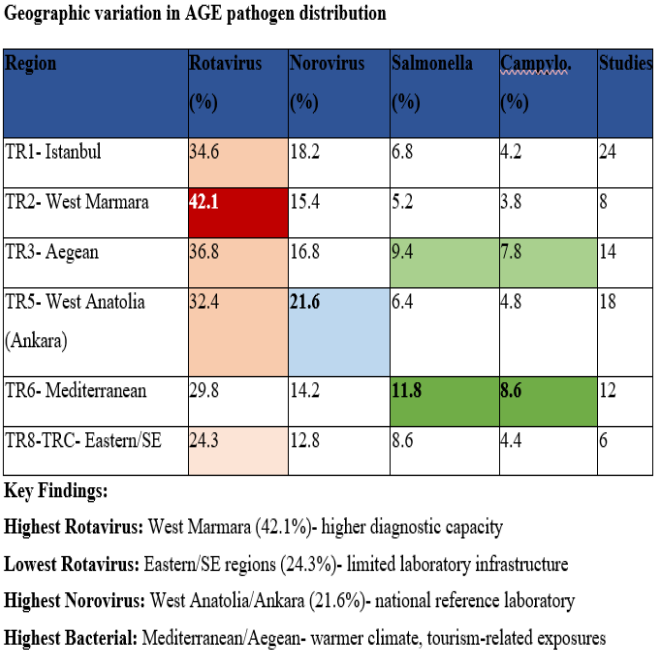

Figure 3. Geographic distribution across NUTS-1 regions. Pooled estimates reflect regional diagnostic capacity, climate, and population characteristics

demonstrated considerable regional variation, ranging from 24.3% in southeastern Turkiye to 42.1% in the Marmara region, potentially reflecting differences in healthcare-seeking behaviors, diagnostic capabilities, and population demographics (Figure 3).

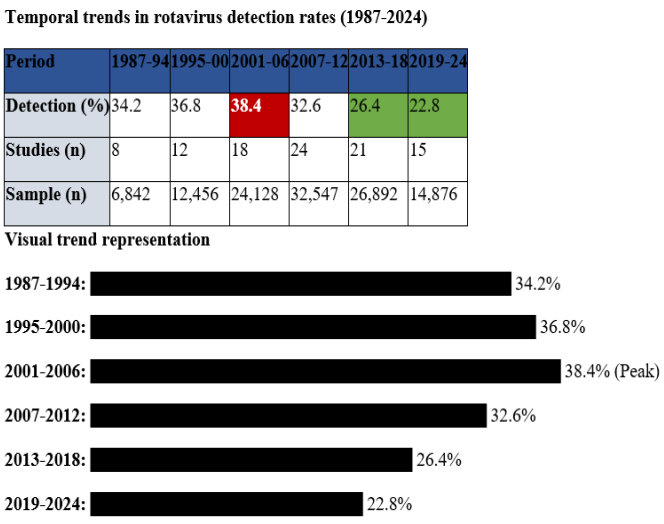

Figure 2. Temporal trends. Detection peaked in 2001-2006 (pre-vaccine) and declined after vaccine introduction in 2006.

Age-specific analysis revealed that 80.7% of rotavirus-positive cases occurred in children under 24 months of age, with peak incidence observed between 6-12 months. This age distribution aligns with global patterns and underscores the importance of early vaccination. Marked seasonality was observed, with 67% of rotavirus cases occurring during the winter months (December through March), peaking in January-February. This seasonal pattern remained consistent across different geographic regions of Turkiye (Figure 4).

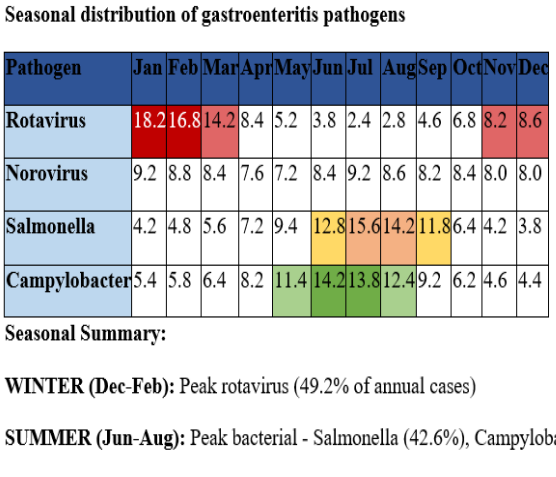

Figure 4. Monthly distribution (% of annual cases). Highlighted cells indicate peak months. Rotavirus peaks in winter; bacterial pathogens in summer

Genotype distribution analysis from 34 studies employing molecular characterization revealed G1P[8] as the predominant strain, accounting for 38-45% of typed isolates, followed by G2P[4] (15-22%), G9P[8] (12-18%), G3P[8] (8-12%), and G4P[8] (5-8%). Notably, the emergence of G9P[8] as a significant circulating strain was documented beginning in 2008, with increasing prevalence in subsequent years. G12 strains, while uncommon, were identified in surveillance studies from 2015 onwards (**Table 2**).

Clinical severity assessment using the Vesikari Clinical Severity Scoring System demonstrated that rotavirus gastroenteritis was significantly more severe than non-rotavirus gastroenteritis. Across studies employing this scoring system, 69% of rotavirus-positive children had severe gastroenteritis (Vesikari score ≥11), compared to 34% of rotavirus-negative cases (p<0.001). Hospitalization rates for rotavirus-positive AGE ranged from 31% to 58% across studies, substantially higher than the 12-24% hospitalization rates observed for non-rotavirus AGE.

Impact of Rotavirus Vaccination

Despite rotavirus vaccines not being included in Turkiye's national immunization program, self-financed vaccination through the private healthcare sector achieved coverage rates estimated between 12-17% during the 2012-2018 study period. Analysis of vaccination impact from two large tertiary care hospitals in Istanbul (representing approximately 20% of Turkey's population) demonstrated significant reductions in disease burden even at these modest coverage levels.

Rotavirus-positive AGE incidence decreased from 4.4 per 1,000 children in 2012 to 2.48 per 1,000 in 2018, representing a 43.6% reduction over the seven-year observation period (p<0.001 for trend). More dramatically, rotavirus-related hospitalizations declined from 1.9 per 1,000 children to 0.45 per 1,000, a 76.3% reduction. The prevalence of rotavirus among children presenting to emergency departments with AGE decreased by nearly 40%, from 28.3% in 2012 to 17.1% in 2018 (**Table 3**).

These findings suggest that even partial vaccination coverage generates measurable herd immunity effects, reducing disease transmission and protecting unvaccinated individuals. Extrapolation of these results to national-level implementation suggests that incorporation of rotavirus vaccine into Turkiye's universal immunization program could prevent an estimated 50,000-70,000 hospitalizations and 150,000-200,000 outpatient visits annually.

Table 3. Impact of rotavirus vaccination on AGE incidence and hospitalization (2012-2018)

Parameter	2012	2015	2018	% change	p-value
Vaccination coverage (%)	12.0	15.2	17.0	+41.7	-
RV+ AGE incidence (/1,000)	4.40	3.21	2.48	-43.6	<0.001
RV hospitalization (/1,000)	1.90	0.98	0.45	-76.3	<0.001
RV prevalence in AGE (%)	28.3	22.6	17.1	-39.6	<0.001
Mean hospital stay (days)	4.2±1.8	3.8±1.6	3.4±1.4	-19.0	0.024
Severe dehydration (%)	18.4	14.2	11.8	-35.9	0.008
IV fluid requirement (%)	62.4	54.8	48.2	-22.8	0.012

RV: Rotavirus, AGE: Acute gastroenteritis, IV: Intravenous. Data from tertiary care hospitals in Istanbul (~20% of Turkiye's population). p-values by Chi-square test for trend.

Norovirus and Other Viral Pathogens

Norovirus has emerged as an increasingly important pathogen in Turkish AGE epidemiology, particularly following rotavirus vaccine introduction. National reference laboratory surveillance from 2009 demonstrated norovirus genotype II as the most frequently detected viral agent, identified in 28.6% of tested samples, followed by rotavirus (22.4%), astrovirus (4.1%), and adenovirus (2.7%). Co-infections involving multiple viral pathogens were detected in 6.8% of samples (**Table 4**).

Table 4. Distribution of viral pathogens in pediatric acute gastroenteritis across Turkish studies

Viral pathogen	No. of studies	Detection rate (%)	95% CI	Peak season
Rotavirus	98	31.8	31.3-32.4	January-March
Norovirus GII	24	18.4	14.2-22.6	Year-round
Norovirus GI	18	4.2	2.8-5.6	Year-round
Adenovirus 40/41	42	5.4	3.8-7.0	Summer months
Astrovirus	28	3.8	2.4-5.2	Winter-Spring
Sapovirus	12	2.1	1.2-3.0	Winter months
Co-infections (≥2 viruses)	18	6.8	4.5-9.1	Winter months

CI: Confidence interval, GI: Genogroup I, GII: Genogroup II

A comprehensive 8-year retrospective study from Ankara examining children aged 0-5 years with AGE documented significant norovirus GI/GII prevalence. The study noted that rotavirus vaccination is predicted to result in relative increases in norovirus-attributable gastroenteritis, a phenomenon

Table 2. Rotavirus genotype distribution in Turkiye: temporal trends (2000-2024)

Genotype	2000-2005 (%)	2006-2010 (%)	2011-2015 (%)	2016-2024 (%)	Overall (%)
G1P[8]	48.2	42.5	38.4	35.8	41.2
G2P[4]	22.4	18.6	16.2	19.4	19.2
G9P[8]	4.8	14.2	18.6	16.8	13.6
G3P[8]	12.4	10.8	9.4	8.2	10.2
G4P[8]	8.6	7.2	6.8	5.4	7.0
G12P[8]	0	0.8	2.4	4.6	2.0
Mixed/untypeable	3.6	5.9	8.2	9.8	6.8
Total typed (n)	2.845	4.128	3.654	2.186	12.813

Note: G9P[8] emerged as a significant circulating strain beginning in 2008. G12 strains were first identified in 2015.

already observed in countries with high rotavirus vaccination coverage. Norovirus-associated AGE demonstrated year-round occurrence without the pronounced winter seasonality characteristic of rotavirus.

Adenovirus (serotypes 40/41) was identified in 3-8% of pediatric AGE cases across studies employing appropriate diagnostic methods. Astrovirus detection rates ranged from 2-6%, with higher prevalence noted in institutional settings. Sapovirus, while less commonly tested for, was identified in 1-3% of cases in studies employing comprehensive viral panels.

Bacterial Pathogens and Seasonal Patterns

Bacterial pathogens demonstrated distinct seasonal patterns compared to viral agents, with peak incidence during summer months (June-September). *Salmonella* species were the most commonly identified bacterial pathogen, detected in 4-12% of AGE cases depending on the study population and geographic region. Campylobacter jejuni was identified in 3-8% of cases, with higher rates observed in the Aegean and Mediterranean regions where poultry consumption is particularly high.

Shigella species, while less common than *Salmonella*, were associated with more severe clinical presentations including bloody diarrhea and higher fever. Enterotoxigenic *E. coli* (ETEC) and enteropathogenic *E. coli* (EPEC) were identified in 5-15% of cases in studies employing advanced molecular diagnostics, though detection rates varied substantially based on methodological approaches.

Impact of Syrian Refugee Influx

The influx of over 3.5 million Syrian refugees since 2011 significantly impacted Turkiye's infectious disease landscape. Between 2012 and 2016, surveillance data from temporary protection centers documented 158,058 diarrheal episodes, including 59 cases of bloody diarrhea. Additionally, 1,354 hepatitis A cases were reported, reflecting the interaction between gastrointestinal infections and sanitation conditions.

Children arriving from conflict zones demonstrated lower baseline vaccination coverage due to disrupted healthcare services. However, intensive immunization campaigns within temporary protection centers achieved vaccination coverage exceeding 95%, substantially mitigating outbreak risks. The receptiveness of the refugee population to vaccination programs facilitated rapid achievement of protective coverage levels.

Diagnostic Approaches and Laboratory Capacity

Diagnostic methodologies employed across studies evolved substantially over the review period. Early studies (1987-2000) relied primarily on electron microscopy and latex agglutination assays. The period 2000-2010 saw widespread adoption of enzyme immunoassays (EIA/ELISA) for rotavirus and adenovirus detection. More recent studies have increasingly employed molecular methods including RT-PCR and multiplex PCR panels enabling simultaneous detection of multiple pathogens.

However, access to advanced molecular diagnostics remains limited outside major academic centers. A survey of diagnostic capabilities indicated that only 23% of hospitals in Turkiye routinely test for viral gastroenteritis pathogens beyond rotavirus. This diagnostic gap likely results in underestimation of norovirus, astrovirus, and sapovirus contribution to AGE burden. Third-generation ELISA kits for stool antigen detection remain the most practical and economical routine diagnostic approach in most clinical settings.

DISCUSSION

This comprehensive bibliographic review synthesizes nearly four decades of research on AGE in Turkiye, revealing several key findings with significant implications for public health policy and clinical practice. The evidence consistently demonstrates that AGE, particularly rotavirus-associated disease, remains a substantial public health burden requiring targeted intervention interventions.[2]

Rotavirus Disease Burden and Vaccination Policy

The median rotavirus detection rate of 31.8% among Turkish children with AGE is comparable to pre-vaccination era estimates from European countries (25-40%) and higher than current rates in countries with universal rotavirus vaccination programs (8-15%).[2,7] This persistent high detection rate directly reflects Turkiye's policy decision not to include rotavirus vaccines in the national immunization program.[8]

The economic implications of this policy deserve careful consideration. Rotavirus gastroenteritis imposes substantial direct costs (hospitalizations, emergency department visits, outpatient consultations, diagnostic tests) and indirect costs (parental work loss, productivity reduction).[9] Cost-effectiveness analyses from comparable middle-income countries consistently demonstrate favorable cost-effectiveness ratios for rotavirus vaccination, often achieving cost savings when both direct and indirect costs are considered.[10]

Particularly compelling is the evidence that even partial vaccination coverage (12-17%) achieved through self-financing generated substantial reductions in disease burden. The 76% reduction in rotavirus-related hospitalizations observed over seven years represents thousands of prevented hospitalizations, reduced healthcare system strain, and diminished family burden. These herd immunity effects suggest that universal vaccination could achieve even greater impact, potentially approaching the 85-95% reductions in rotavirus hospitalizations observed in countries with high vaccination coverage. Recent global evidence continues to support the critical importance of rotavirus vaccination in reducing childhood gastroenteritis burden, with meta-regression analyses demonstrating substantial variation in vaccine efficacy and effectiveness across settings, generally higher in high-income and low child-mortality countries and lower in high-mortality, low-resource contexts; and clinical severity studies using modified Vesikari and Clark scoring systems confirm the continued vulnerability of pediatric populations to viral gastroenteritis, with children comprising the majority of cases and significant disease severity documented by validated scoring tools.[11,12] Similarly, a 2024 comprehensive study evaluating viral gastroenteritis severity using modified Vesikari and Clark scoring systems emphasized the continued vulnerability of pediatric populations to viral pathogens, with children accounting for over 72% of viral gastroenteritis cases. These contemporary findings reinforce the urgency of expanding rotavirus vaccination coverage in Turkiye and highlight the need for

context-specific implementation strategies that account for local epidemiological patterns and healthcare system characteristics.[13]

Emerging Importance of Norovirus

The emergence of norovirus as the leading viral pathogen in Turkish surveillance studies signals an important epidemiological transition. In countries with established rotavirus vaccination programs, norovirus has become the predominant cause of childhood AGE requiring medical attention. This pattern appears to be emerging in Turkiye despite incomplete rotavirus vaccination coverage.[8]

Unlike rotavirus, no licensed norovirus vaccine is currently available, though several candidates are in advanced clinical development. Until vaccine availability, norovirus prevention relies on non-pharmaceutical interventions including hand hygiene, environmental disinfection, and food safety measures. The high transmissibility of norovirus and its resistance to many common disinfectants present ongoing challenges for outbreak control, particularly in institutional settings such as hospitals, nursing homes, and schools.[14]

Strengthening norovirus surveillance capacity is essential for understanding the true burden of disease and preparing for future vaccine implementation. Current diagnostic limitations likely result in substantial underestimation of norovirus contribution to AGE. Investment in molecular diagnostic infrastructure would improve pathogen attribution and inform targeted prevention strategies.

Refugee Health and Vulnerable Populations

The Syrian refugee crisis introduced unprecedented challenges to Turkiye's public health infrastructure. The documentation of over 158,000 diarrheal episodes among the refugee population between 2012-2016 highlights the vulnerability of displaced populations to gastrointestinal infections. Contributing factors include crowded living conditions, compromised water and sanitation infrastructure, disrupted vaccination histories, and psychological stress affecting immune function.[15]

However, the Turkish health system's response demonstrated remarkable capacity for rapid adaptation. Achievement of greater than 95% vaccination coverage within temporary protection centers represents a public health success story with lessons for future humanitarian responses. The integration of refugee healthcare into the existing health system, coupled with targeted immunization campaigns, effectively mitigated potential epidemic risks.[16]

Diagnostic Challenges and Surveillance Gaps

The heterogeneity of diagnostic approaches across studies represents both a limitation of this review and a broader challenge for AGE surveillance in Turkiye. The absence of a standardized national surveillance system results in fragmented data collection, inconsistent case definitions, and variable diagnostic methodologies that complicate temporal and geographic comparisons.[14] The relative underrepresentation of bacterial pathogens in the reviewed studies warrants careful interpretation. Several methodological factors may contribute to this observation: inconsistent stool culture collection practices across healthcare settings, suboptimal specimen transport conditions affecting bacterial viability, limited availability of selective and differential culture media for fastidious organisms such as Campylobacter species, and the restricted deployment of molecular diagnostic panels capable of detecting bacterial pathogens in many Turkish healthcare facilities. Furthermore, empirical antibiotic administration prior to specimen collection, a common practice in clinical settings, may significantly reduce bacterial isolation rates. These diagnostic limitations suggest that the true burden of bacterial gastroenteritis in Turkish children is likely underestimated in the current literature.[17,18]

Establishment of a systematic AGE surveillance network, modeled on successful programs in European countries, would substantially improve understanding of disease epidemiology. Such a system should incorporate standardized case definitions, representative sentinel sites spanning different geographic regions and healthcare settings, consistent diagnostic protocols including molecular methods for comprehensive pathogen detection, and electronic data capture enabling real-time analysis and outbreak detection.[19,20]

Limitations

Several limitations should be acknowledged when interpreting these findings. First, the predominance of hospital-based studies may overestimate disease severity and pathogen detection rates compared to community-based estimates. Mild cases managed at home or in primary care are underrepresented in the literature. Second, publication bias may have resulted in overrepresentation of positive findings and studies from major academic centers. Third, the evolving diagnostic methodologies across the review period complicate direct comparisons of pathogen detection rates between earlier and more recent studies.

Additionally, data on AGE in adult populations is notably sparse compared to pediatric data, representing an important knowledge gap. Adults, particularly elderly individuals and those with comorbidities, also experience significant AGE-related morbidity that warrants greater research attention.

Future Directions and Recommendations

Based on the evidence synthesized in this review, several recommendations emerge for policy and practice. First and foremost, incorporation of rotavirus vaccine into Turkiye's national immunization program should be prioritized. The evidence of benefit even at low coverage levels, combined with extensive global experience demonstrating vaccine safety and effectiveness, provides a compelling case for this policy change.

Second, investment in laboratory infrastructure for comprehensive viral gastroenteritis diagnostics would improve pathogen attribution and inform targeted interventions. Multiplex molecular panels capable of detecting rotavirus, norovirus, adenovirus, astrovirus, and sapovirus should become standard diagnostic tools in reference laboratories and major healthcare centers.

Third, establishment of a national AGE surveillance network with standardized protocols would generate the systematic data necessary for evidence-based policy development and outbreak response. Such a system should include both hospital-based and community-based sentinel sites to capture the full spectrum of disease severity.

Beyond rotavirus vaccination, comprehensive prevention strategies are essential for reducing the burden of pediatric

gastroenteritis in Turkiye. Public health measures should prioritize ensuring access to safe drinking water through improved water treatment and distribution infrastructure, particularly in underserved regions.[21] Promotion of proper sanitation facilities and waste management systems can significantly reduce fecal-oral transmission of enteric pathogens. Hand hygiene education campaigns targeting families, schools, and healthcare settings represent cost-effective interventions, with systematic reviews demonstrating that handwashing with soap can reduce diarrheal disease incidence by 30-47%.[22] Food safety practices, including proper food handling, storage, and preparation techniques, should be emphasized through community health education programs. For vulnerable populations, including refugee communities and children in institutional settings, targeted interventions addressing overcrowding, ensuring adequate water supply, and implementing systematic hygiene protocols are particularly important.[23] These complementary measures, combined with vaccination programs, constitute a comprehensive approach to reducing gastroenteritis morbidity and mortality in Turkish children. Finally, continued attention to vulnerable populations, including refugees and internally displaced persons, is essential. Health equity considerations should inform resource allocation and program design to ensure that all residents of Turkiye benefit from advances in AGE prevention and treatment.

CONCLUSION

AGE remains a significant public health challenge in Turkiye, with rotavirus continuing as the leading cause of severe childhood diarrhea despite the availability of effective vaccines. This comprehensive review demonstrates that even partial rotavirus vaccination coverage generates meaningful reductions in disease burden, strongly supporting universal vaccine implementation. The emergence of norovirus as an increasingly important pathogen necessitates enhanced surveillance and diagnostic capabilities. Addressing the identified gaps in surveillance infrastructure, diagnostic capacity, and vaccination policy would substantially reduce the burden of AGE in Turkiye and position the country among leaders in gastrointestinal infection prevention.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study did not involve human participants, patient data, or any biological material. Therefore, ethics committee approval was not required.

Informed Consent

Since no human participants or patient information were included in this research, informed consent was not required.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

Financial Disclosure

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Author Contributions

All authors contributed significantly to the study's conception, design, data acquisition, analysis, and interpretation. All authors reviewed and approved the final version of the manuscript.

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The Intercontinental Journal of Emergency Medicine

Case Report

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Coexistence of iliac artery thrombosis and acute myocardial infarction: a rare clinical entity

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ABSTRACT

Acute myocardial infarction (AMI) concomitant with iliac artery thrombosis in the absence of underlying hematological disorders or cardiac arrhythmias is an exceedingly rare clinical entity. We report a case of a 55-year-old male with a history of hypertension and chronic smoking who presented with epigastric pain and nausea. On initial evaluation, electrocardiography showed no ST-segment elevation. While under observation, the patient developed abrupt-onset, severe pain in the left lower limb. A subsequent electrocardiogram demonstrated ST-segment elevation in leads II, III, and aVF, consistent with an inferior ST-segment elevation myocardial infarction (STEMI). Given the concomitant onset of lower limb pain, thoracoabdominal computed tomographic angiography was promptly performed, revealing complete occlusion of the left common iliac artery with extension into the internal and external iliac arteries. The patient underwent emergent primary percutaneous coronary intervention with successful stent deployment in the right coronary artery, followed by referral to a tertiary vascular surgery center for definitive management of the iliac artery thrombosis. This case underscores the importance of maintaining a high index of suspicion for multiple simultaneous vascular events in the setting of acute coronary syndromes, particularly when novel or atypical symptoms develop.

Keywords: Acute myocardial infarction, iliac artery thrombosis, smoking, hypertension, case report

INTRODUCTION

Inferior myocardial infarction is a critical cardiac emergency that occurs due to the occlusion of the coronary arteries, resulting in decreased perfusion of the affected myocardial territory, potentially leading to serious complications and mortality. This condition is most frequently caused by occlusion of the right coronary artery (RCA). Compared to anterior wall infarctions, inferior MIs generally have a more favorable prognosis. Although the mortality rate is less than 10%, patients may still develop complications such as hypotension, malignant arrhythmias, conduction disturbances, and cardiogenic shock.[1-4]

Iliac artery occlusion is a subtype of peripheral arterial disease, often referred to as aortoiliac occlusive disease. Similar to other arterial conditions, this pathology can present with a wide range of symptoms, from being asymptomatic to progressing to limb-threatening ischemia. Risk factors including diabetes, hyperhomocysteinemia, hypertension, hyperlipidemia, and tobacco use play a significant role in its development. Chronic smoking contributes to inflammation and endothelial dysfunction, potentially promoting thrombosis formation.[5,6]

According to the U.S. Food and Drug Administration (FDA), approximately 800,000 people die annually due to cardiovascular diseases. Smoking doubles the risk of cardiovascular disease, and both smoking and hypertension are considered key modifiable risk factors for such events.[7]

In this case report, we present a rare occurrence of simultaneous inferior myocardial infarction and iliac artery occlusion.

CASE

A 55-year-old male patient with a known history of hypertension and a 35 pack-year smoking background presented to a regional hospital with complaints of sharp epigastric pain and nausea during the morning hours. It was learned that he had taken a non-steroidal anti-inflammatory drug (NSAID) and a proton pump inhibitor (PPI) before admission.

At initial presentation, his vital signs and physical examination were unremarkable, and electrocardiography (ECG) showed normal sinus rhythm. However, approximately one hour after admission, he developed sudden severe pain in

his left leg and was referred to our hospital with a preliminary diagnosis of aortic dissection for further evaluation and treatment.

Upon arrival, the patient reported continued epigastric pain, with new-onset left leg pain. Vital signs were stable, and there was no significant bilateral blood pressure difference. On physical examination, his left leg was cold and pale.

A repeat ECG revealed ST-segment elevation in leads DII, DIII, and aVF, and ST-segment depression in leads DI, aVL, V4–V6 (**Figure 1**). The Troponin T level was elevated at 41.15 ng/L. Due to the "knife-like" nature and distribution of the pain, contrast-enhanced CT angiography was performed to rule out aortic dissection, and no aortic dissection was detected. Aneurysmal dilatation was observed proximal to the abdominal aortic bifurcation. No contrast opacification was observed in the middle-distal segment of the left common iliac artery or in either the internal or external iliac arteries, and these findings were interpreted as consistent with total occlusion (**Figure 2**).

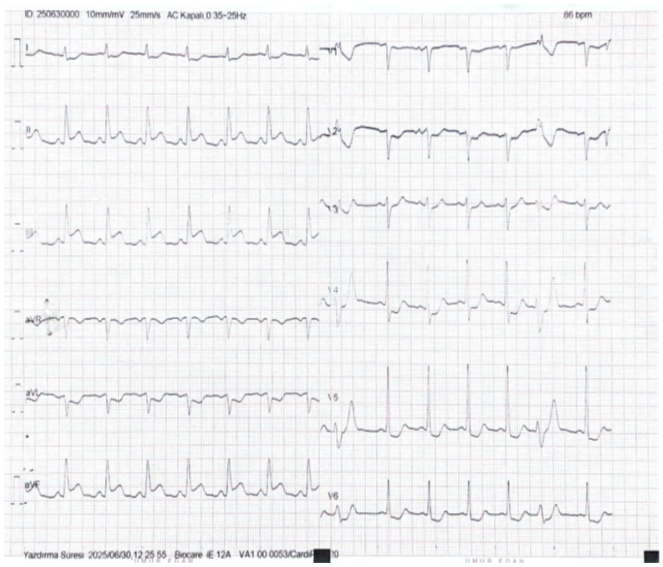

Figure 1. The patient's electrocardiogram (ECG) demonstrates ST-segment elevations and depressions

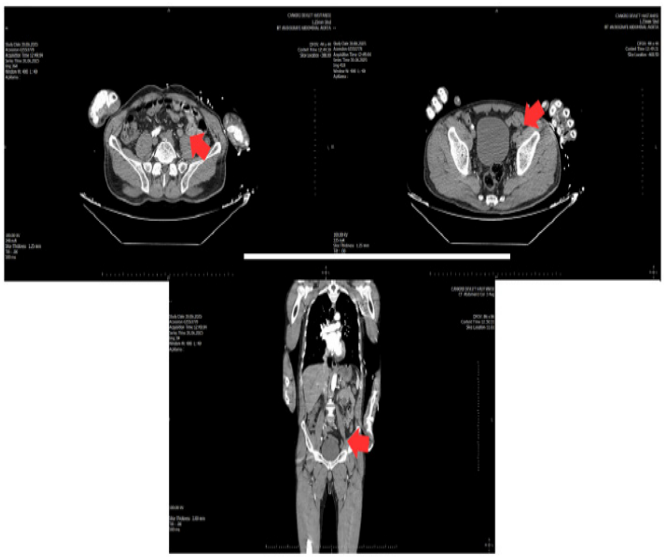

Figure 2. Transverse and coronal images from thoracoabdominal computed tomographic angiography demonstrating iliac occlusion from different angles

Since our hospital lacks a cardiovascular surgery unit, the patient was managed by the cardiology department. He was admitted to the coronary intensive care unit with a preliminary diagnosis of acute inferior myocardial infarction. Primary percutaneous coronary intervention (PCI) was performed (**Figure 3**), and a balloon and stent were placed in the RCA. The patient was subsequently referred to a tertiary center for further intervention regarding the iliac artery occlusion.

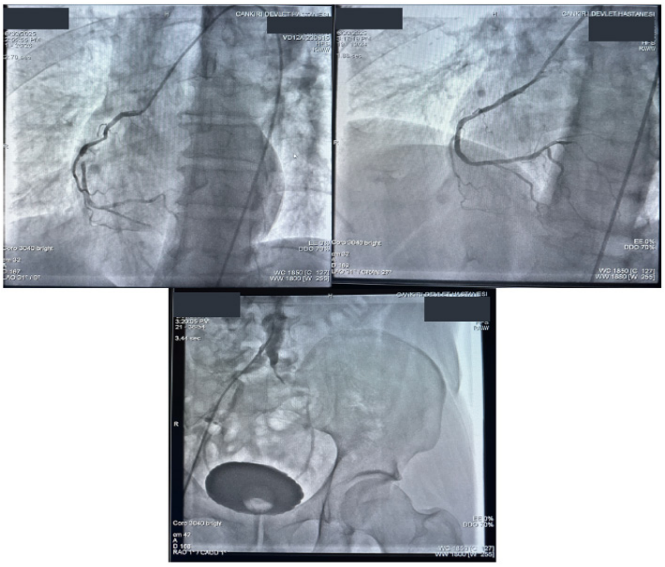

Figure 3. Interventional imaging demonstrating right coronary artery (RCA) occlusion and iliac artery occlusion prior to stent placement

DISCUSSION

Simultaneous arterial thrombosis involving different vascular territories is an exceptionally rare clinical occurrence, particularly in patients without underlying hematological disorders or arrhythmias such as atrial fibrillation that predispose to thrombus formation.[8] In the present case, the patient had no known prothrombotic condition or arrhythmia, and his only identified risk factors were hypertension and chronic smoking, both of which are well-established but modifiable contributors to cardiovascular disease.

The coexistence of an acute inferior myocardial infarction and an iliac artery occlusion in the same patient highlights the complexity of vascular events and the importance of comprehensive diagnostic evaluation. Inferior myocardial infarction generally has a better prognosis compared to anterior infarctions; however, if not recognized and treated promptly, it poses significant risks of morbidity and mortality Similarly, iliac artery thrombosis, often associated with advanced peripheral arterial disease, can progress rapidly from asymptomatic disease to acute limb-threatening ischemia.

Diabetes is perhaps the most important underlying factor in silent myocardial infarction, but it has been reported that the prevalence of silent MI decreases when hypertensive individuals maintain lower blood pressure levels.[9,10] Although our patient did not experience a silent myocardial infarction, the chest pain was atypical rather

than characteristic. This atypical finding may be attributed to uncontrolled hypertension, highlighting the importance of adequate blood pressure control, although this association cannot be definitively proven.

One of the critical clinical challenges underscored by this case is that, in the presence of a life-threatening diagnosis such as myocardial infarction, other coexisting vascular pathologies may be overlooked, particularly when presenting symptoms overlap or evolve rapidly. This underscores the need for a high index of suspicion and a more comprehensive evaluation, particularly when patients develop new or atypical symptoms during acute coronary syndromes.

CONCLUSION

This case underscores the rarity and clinical significance of simultaneous occlusions in two distinct arterial territories in a patient with no hematologic abnormality or arrhythmic predisposition. It further highlights that clinicians, while focusing on critical diagnoses such as myocardial infarction, must remain vigilant for other potentially life-threatening vascular conditions that may present concurrently and require urgent attention.

ETHICAL DECLARATIONS

Informed Consent

Written informed consent was obtained from the patient included in this report. Signed consent forms are retained by the authors and are available upon request.

Peer Review Process

This report underwent external peer review.

Conflict of Interest

The authors declare no conflicts of interest.

Financial Disclosure

This case report did not receive any financial support.

Author Contributions

All authors made substantial contributions to the clinical documentation, interpretation, and manuscript preparation. All authors approved the final version of the manuscript.

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Letter to the Editor

Hypertensive crisis following mepolizumab in a patient with severe eosinophilic asthma: a letter to the editor

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Keywords: Hypertension, interleukin-5, mepolizumab, asthma, immunology

Dear Editor,

Mepolizumab, an IL-5 targeting humanized monoclonal antibody, has become a key treatment option for patients with severe eosinophilic asthma by effectively reducing eosinophilic inflammation and asthma exacerbations.[1-3] Although generally considered safe, its full adverse effect profile remains to be fully characterized. Herein, we report a rare but potentially serious adverse event not previously documented in the literature.

We describe a 52-year-old female with a longstanding history of asthma and idiopathic thrombocytopenic purpura (ITP), who developed a hypertensive crisis shortly after receiving her first dose of mepolizumab. Her maintenance therapy included inhaled corticosteroids and long-acting beta-agonists. Initial lab results showed a white blood cell count of

Table 1. Laboratory findings on admission

White blood count (x10^9/L)	7.22
Neutrophil (x10^9/L)	4.63
Lymphocyte (x10^9/L)	1.9
Eosinophil (x10^9/L)	0.22
Hemoglobin (g/dl)	12.6
Platelets (x10^9/L)	184

Within 15 minutes of administration, the patient experienced dyspnea, chest pain, and elevated blood pressure (140/90 mmHg). She was treated with 10 mg of amlodipine, and her ECG was unremarkable. However, within an hour, her blood pressure escalated to 180/100 mmHg, accompanied by unilateral blurred vision and headache. Neuroimaging with cranial CT and diffusion MRI showed no abnormalities. Notably, her eosinophil count had decreased to 10/mm^3.

Treatment with 4 mg doxazosin at 30 and 60 minutes post-injection resulted in gradual normalization of blood pressure and clinical recovery. The patient was monitored for 24 hours before discharge (Table 2).

Table 2. Post-treatment blood pressure monitoring

Time	Blood pressure (mmHg)	Treatment
15. minutes	140/90	Amlodipin 10 mg
30. minutes	155/90	Doxazosin 4 mg
45. minutes	170/95	
60. minutes	180/100	Doxazosin 4 mg
120. minutes	155/90	
240. minutes	130/80	

Common side effects of mepolizumab reported in previous studies include headache, injection site reactions, back pain, and fatigue.[4,5] There are also rare reports of non-cardiac chest pain.[6] To our knowledge, this is the first report describing hypertensive crisis accompanied by transient visual symptoms immediately following mepolizumab administration.

This case underscores the importance of vigilant cardiovascular monitoring, particularly within the first hour after injection. Although the exact mechanism remains uncertain, potential interactions between eosinophil depletion and vascular regulation merit further research.

We recommend clinicians to closely monitor blood pressure after mepolizumab administration, especially in patients with risk factors for hypertension or cardiovascular disease.

ETHICAL DECLARATIONS

Informed Consent

Written informed consent was obtained from the patient for the publication of this correspondence and any related clinical details.

Peer Review Process

This letter was externally peer-reviewed.

Conflict of Interest

The authors declare no conflicts of interest.

Financial Disclosure

No financial support was received for the preparation or publication of this letter.

Author Contributions

All authors contributed to the conceptualization and drafting of this correspondence and approved the final version for publication.

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