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# Predictors of Acute Kidney Injury in Children Following the Kahramanmaraş Earthquakes: A Retrospective Analysis

Kahramanmaraş Depremleri ile Çocuklarda Oluşan Akut Böbrek Hasarı Risk Faktörlerinin Araştırılması: Retrospektif Bir Analiz

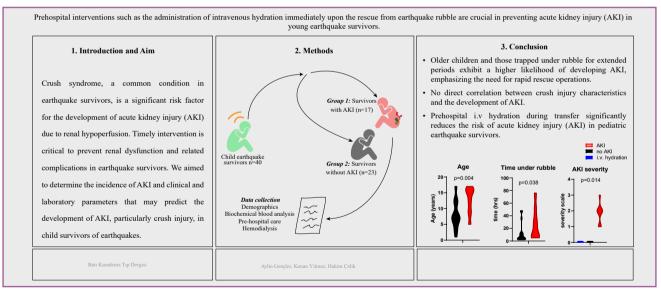
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## **GRAPHICAL ABSTRACT**



## ABSTRACT

**Aim:** The twin Kahramanmaraş earthquakes that occurred on February 6th, 2023, caused massive destruction in Turkey and Syria, affecting more than 16 million people in 11 provinces in Turkey alone. Crush syndrome, a common condition in earthquake survivors, is a significant risk element for the emergence of acute kidney injury (AKI) due to renal hypoperfusion. Therefore, timely intervention is critical to prevent renal dysfunction and related complications in earthquake survivors. In this particular situation, the current research was conducted to determine the occurrence of AKI and clinical and laboratory parameters that may predict the development of AKI, particularly crush injury, in child survivors of these earthquakes.

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Material and Methods: The sample of this retrospective multi-center study comprised child survivors of the Kahramanmaraş earthquakes admitted to two tertiary referral centers in the Şanlıurfa province of Turkey. Children's demographic, clinical, and laboratory characteristics were collected, and statistical tests were carried out to identify predictive factors for AKI development.

**Results:** The results shows that the median age of the 40 earthquake victims, 22 (55%) female and 18 (45%) male, was 9 years (1-17years). Of these children, 17 (42.5%) developed AKI (Group-1), while 23 (57.5%) did not (Group-2). Crush injuries were observed in 32 (80.0%) children. The median age of Group-1 was found significantly higher than Group-2 (p=0.004). The time to extrication from the rubble was also found significantly higher in Group 1 comparing to in Group 2 (p=0.028). Crush injury characteristics were not found to be associated with the development of AKI (p>0.05). However, receiving intravenous hydration during the transfer to the hospital was found significantly linked to a lower incidence of AKI (p=0.014). Hemodialysis was performed in 12 (70.6%) children with AKI. Of the 40 children in the sample, two (5%) in Group1 had died.

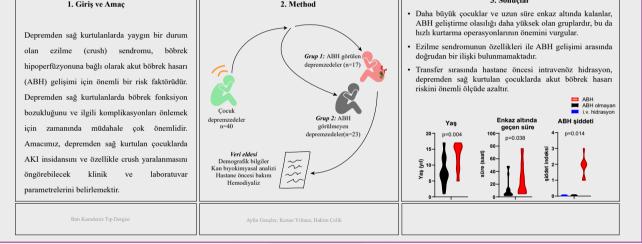
**Conclusion:** The findings of our study demonstrated the importance of timely implementation of necessary interventions, intravenous hydration in particular, in preventing AKI in child earthquake victims. This study did not find any significant correlation between crush injury characteristics and the development of AKI. On the other hand, we determined that children who were older and remained under earthquake rubble for longer were more likely to develop AKI.

Keywords: Earthquakes, crush injuries, acute kidney injury, trauma, extremities, fractures

#### **GRAFİKSEL ÖZET**

Deprem enkazından kurtarıldıktan hemen sonra intravenöz hidrasyon gibi hastane öncesi müdahaleler, genç depremzedelerde akut böbrek hasarını (AKI) önlemede hayati öneme taşımaktadır.

1. Giriş ve Amaç
2. Method
3. Sonuçlar
- Daha büyük çocuklar ve uzun süre enkaz altında kalanlar, ABH geliştirme olasılığı daha yüksek olan gruplardır, bu da



## ÖΖ

**Amaç:** 6 Şubat 2023 tarihinde meydana gelen ve Türkiye ve Suriye'de büyük yıkıma neden olan ikiz Kahramanmaraş depremleri, yalnızca Türkiye'de 11 ilde 16 milyondan fazla insanı etkilemiştir. Depremzedelerde sık görülen bir durum olan ezilme (crush) sendromu, böbrek hipoperfüzyonuna bağlı akut böbrek hasarının (ABH) gelişimi için kayda değer bir risk etmenidir. Bu nedenle depremzedelerde böbrek fonksiyon bozukluğu ve buna bağlı komplikasyonların önlenmesi için zamanında müdahale çok önemlidir. Bu bağlamda bu çalışma, bu depremlerden sağ kurtulan çocuklarda ABH görülme sıklığını ve ezilme yaralanması başta olmak üzere ABH gelişimini öngörebilecek klinik ve laboratuvar parametrelerini belirlemek amacıyla yapılmıştır.

Gereç ve Yöntemler: Bu retrospektif çok merkezli çalışmanın evrenini, Kahramanmaraş depremlerinden sağ kurtularak Türkiye'nin Şanlıurfa ilindeki iki üçüncü basamak sevk merkezine kabul edilen çocuklar oluşturmuştur. Çocukların demografik, klinik ve laboratuvar özellikleri elde edilerek, ABH gelişimini öngören faktörleri belirlemek için istatistiksel analizlere tabi tutulmuştur.

**Bulgular:** Araştırmaya dahil edilen 40 depremzede çocuğun ortanca yaşı 9 yıl (1-17 yıl) idi. Bu çocukların 17(%42,5) 'sinde ABH gelişmiş (Grup-1), 23(%57,5) 'ünde gelişmemişti (Grup 2). Otuz iki (%80,0) çocukta ezilme yaralanması görülmüştü. Grup-1'in ortanca yaşı Grup-2'den istatistiksel olarak anlamlı derecede yüksek bulunmuştur (p=0,004). Enkazdan çıkarılma süresi de Grup-1'de Grup-2'ye göre istatistiksel olarak anlamlı derecede daha yüksek bulunmuştur (p=0,028). Ezilme yaralanması özelliklerinin ABH gelişimi ile ilişkili olmadığı belirlendi (p>0,05). Öte yandan, hastane öncesi intravenöz hidrasyonun daha düşük ABH insidansı ile anlamlı düzeyde ilişkili olduğu bulundu (p=0,014). ABH'lı çocukların 12 (%70,6)'sine hemodiyaliz uygulanmıştı. Çalışma grubundaki 40 çocuktan Grup-1'de yer alan iki (%5) çocuk ölmüştü.

**Sonuç:** Çalışmamızın bulguları, depremzede çocuklarda ABH'nin önlenmesinde başta intravenöz hidrasyon olmak üzere gerekli müdahalelerin zamanında uygulanmasının önemini ortaya koymuştur. Ezilme yaralanması özellikleri ile AKI gelişimi arasında anlamlı bir ilişki bulamadık. Öte yandan, yaşı daha büyük olan ve deprem enkazı altında daha uzun süre kalan çocuklarda ABH gelişme olasılığının daha yüksek olduğunu tespit ettik.

Anahtar Sözcükler: Depremler, ezilme yaralanması, akut böbrek hasarı, travma, ekstremiteler, kırıklar

## INTRODUCTION

The twin Kahramanmaraş earthquakes that occurred on February 6th, 2023, caused massive destruction in Turkey and Syria, affecting more than 16 million people in 11 provinces in Turkey alone (1-3). Crush syndrome, a consequence of traumatic rhabdomyolysis, is frequently encountered in the aftermath of earthquakes, mining disasters, industrial incidents, and traffic accidents (1,4,5-7). The prolonged entrapment of limbs or crushing of muscles beneath the rubble triggers the release of toxic intracellular components, including potassium, myoglobin, phosphorus, and nucleotides, leading to the primary pathophysiology of the crush syndrome (1,2,6,8). Crush syndrome leads to severe hypovolemia due to leakage of body water into injured muscles, resulting in renal hypoperfusion and acute kidney injury (AKI) if left untreated (1). The mortality rate associated with crush syndrome is guite high due to the circulatory shock, renal failure, and systemic inflammation it causes (2).

Crush injury-related AKI stands out as one of the important reasons of mortality in earthquake victims (6,9). Timely initiation of renal replacement therapy, intravenous hydration, and hemodialysis prevent renal dysfunction and its associated complications (2,4). Therefore, the prevention and early management of renal dysfunction in earthquake-affected children with crush injuries are critical in post-earthquake medical care to render effective interventions and improve outcomes.

In the aftermath of the Kahramanmaraş earthquakes, a pediatric cohort of earthquake victims, extricated from the rubble and transported to two of the tertiary referral centers on the periphery of the affected area, exhibited signs of crush syndrome. Thus, the current study was conducted to determine the incidence of AKI and clinical and laboratory parameters that may predict the development of AKI, particularly crush injury, in this specific patient population.

## MATERIAL and METHODS

## **Study Design**

The current research was a retrospective multi-center study and its protocol was approved by the Harran University Ethical Committee for Clinical Studies (Decision Number: HRU/23.09.19, Decision Date: May 22<sup>nd</sup>, 2023). The Declaration of Helsinki's ethical guidelines were followed when conducting the study. Because of the study's retrospective methodology and the uniformity of the data, legal guardians of the children included in the study were unable to provide written informed permission.

## **Population and Sampling**

The study population consisted of child survivors of children aged between 1 month and 18 years who survived the Kahramanmaraş earthquakes, were rescued from under the rubble in a nearby province, and transferred by ambulance to two tertiary referral centers in the province of Şanlıurfa, located on the edge of the affected region. One newborn baby and two children were excluded from the research due to incomplete data. Ultimately, the sample of the study was made up of 40 children hospitalized in these two referral centers. Of these children, 17 (42.5%) who developed AKI constituted Group-1, and 23 (57.5%) who did not develop AKI constituted Group-2.

## **Crush Injury and AKI Diagnoses**

Instead of traditional AKI diagnostic criteria (10), which could not be used because of the retrospective design of the research, the presence of at least one of the following laboratory findings was considered to indicate AKI: oliguria (urine production < 400 mL/day); blood urea nitrogen > 40 mg/dL; serum creatinine > 2 mg/dL; serum potassium > 6 mEq/L, phosphorus > 8 mg/dL, calcium < 8 mg/dL; and serum uric acid > 8 mg/dL (4,8).

## **Data Collection**

Children's baseline demographic (age, gender, city of residence), clinical (comorbidities, time to extrication from the rubble, type of injury, and details of coexisting extremity fractures and musculoskeletal crushing), and laboratory characteristics were obtained from the hospitals' information systems. Using children's laboratory findings, we calculated composite hematological and inflammatory parameters, including neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), C-reactive protein-to-lymphocyte ratio (CLR), C-reactive protein-to-albumin ratio (CAR), blood urea nitrogen-to-albumin ratio (BAR), and the systemic inflammatory index (SII) (11). Additionally, the medical treatments the children received, primarily intravenous hydration received before hospitalization, were obtained using ambulance transportation records. Early outcomes, such as amputation and fasciotomy, as well as details and outcomes of renal dysfunction, including polyuria, oliguria, or anuria, the requirement for hemodialysis and its metric data, and the development of AKI, were recorded. Other recorded parameters included the lengths of hospital and intensive care unit stays and associated consequences.

## **Statistical Analysis**

The main result of this research was the rate of patients with AKI, and the secondary result was the peril aspects for the development of AKI, crush injury in particular.

This study used descriptive statistics to review the data obtained from the study. The results for continuous (numerical) variables were given as mean  $\pm$  standard deviation median, minimum, or maximum. Numbers and percentages were used to summarize categorical variables. The normality of numerical variables was assessed using appropriate tests and visual tools, depending on the sample size and characteristics of the data. For comparisons involving small samples (n<50), the Shapiro-Wilk test was preferred. Additionally, visual tools such as histograms and Q-Q (quantile-quantile) plots were utilized to evaluate the assumption of normality.

In comparing the differences in categorical variables between the groups, For 2x2 tables with expected cells of 5 or more, the Pearson's chi-square test was employed; for 2x2 tables with expected cells of less than 5, the Fisher-Exact test was utilized; and for RxC tables, the Fisher-Freeman-Halton test was employed. Additionally, in comparing the differences in numerical variables between two independent groups, When it was found that a numerical variable did not fit the normal distribution, the Mann-Whitney U test was employed.

Univariate and multivariate logistic regression models were conducted to identify each independent variable, including age, time to extrication from the rubble, coexisting bodily trauma, and fracture, that may significantly predict the development of AKI. Independent variables found to significantly predict AKI's development in the univariate analysis were further analyzed using the multivariate analysis. To this end, odds ratios (OR), 95% confidence intervals (CI), and p-values were calculated separately for each independent variable analyzed.

The statistical analyses were conducted using software packages JASP 0.18.3 (Jeffreys' Amazing Statistics Program, version 0.17.3, 2024, retrieved from https://jasp-stats. org) and Jamovi project 2.3.28 (Jamovi, version 2.3.28.0, 2023, retrieved from https://www.jamovi.org). Statistical significance was considered to be shown by probability (p) statistics of < 0.05.

## RESULTS

The median age of the 40 earthquake victims included in the study, 22 (55%) female and 18 (45%) male, was 9 (min. 1, max. 17) years. Most (77.5%) of the children were from Adıyaman province, a neighboring city to Kahramanmaraş, where the earthquakes occurred. The median time to extrication from the rubble was 10.0 (min. 5.0, max. 76.0) hours. Trauma of any type and crush injuries were observed in 33 (82.5%) and 32 (80.0%) children, respectively. Crush injuries affected the lower extremities in the majority (68.8%) of children, while seven (21.9%) children experienced multiple crush injuries.

Of the 40 children included in the study, 17(42.5%) developed AKI (Group-1), while 23(57.5%) did not (Group-2).

The median age of Group-1 was significantly higher than Group-2 (median age: 14.0 vs. 7.0 years, p=0.004). The time to extrication from the rubble was also significantly higher in Group-1 than in Group-2(p=0.028). Other than this, there was no discernible difference between the groups' demographic and clinical traits. (p>0.05). Table 1 shows the distribution of children's demographic and clinical characteristics by the study groups.

Significant differences were also found in baseline laboratory characteristics between Group-1 and Group-2 (Table 2). The leukocyte count, blood urea nitrogen, potassium, serum creatinine, uric acid, C-reactive protein, aspartate aminotransferase, alanine aminotransferase, and creatine kinase levels were significantly higher in Group-1 comparing to Group-2 (p=0.043, p<0.001, p=0.001, p<0.001, p=0.004, p<0.001, p=0.003, and p=0.001, respectively). However, serum albumin and bicarbonate levels were significantly higher in Group-1 (p=0.018 and p<0.001, respectively). Of the composite hematological and inflammatory parameters investigated in this study, CLR, CAR, and BAR values were significantly higher in Group-1 comparing to in Group-2 (p<0.05), while SII was not significantly different between the groups (p=0.356).

The rate of children who received intravenous hydration during the transfer to the hospital was significantly higher in Group-2 comparing to in Group-1 (p=0.014). Notably, none of the cases that developed AKI had received intravenous hydration during the transfer to the hospital. Abnormal urine output (oliguria, anuria, or polyuria) within the first hours after admission was more frequent in Group-1 than in Group-2 (p<0.001) (Table 3). There were four (10.0%) and eight (20.0%) children with amputation and fasciotomy in the sample. No significant difference was found between the groups in other treatment characteristics (p>0.05) (Table 3).

|  | One well (m. 40)  | Groups based on AKI |                  |                    |  |
|--|-------------------|---------------------|------------------|--------------------|--|
|  | Overall (n=40)    | Group 1 (n=17)      | Group 2(n=23)    | р                  |  |
| Age (year) <sup>§</sup>                    | 9.0 [6.0 - 14.2]  | 14.0 [5.0 – 17.0]   | 7.0 [1.0 – 17.0] | 0.004 °            |  |
| Sex <sup>‡</sup>                           |                   |                     |                  |                    |  |
| Female                                     | 22 (55.0)         | 8 (47.1)            | 14 (60.9)        | 0.505.2            |  |
| Male                                       | 18 (45.0)         | 9 (52.9)            | 9 (39.1)         | 0.585 ª            |  |
| City of earthquake <sup>‡</sup>            |                   |                     |                  |                    |  |
| Adıyaman                                   | 31 (77.5)         | 16 (94.1)           | 15 (65.2)        |                    |  |
| Şanlıurfa                                  | 7 (17.5)          | 1 (5.9)             | 6 (26.1)         | 0.085°             |  |
| Hatay                                      | 2 (5.0)           | 0 (0.0)             | 2 (8.7)          |                    |  |
| Time under rubble/extrication time (hr.) § | 10.0 [2.0 – 76.0] | 23.0 [5.0 – 76.0]   | 8.0 [2.0 - 48.0] | 0.038              |  |
| Coexisting bodily trauma <sup>‡</sup>      | 33 (82.5)         | 16 (94.1)           | 17 (73.9)        | 0.205 °            |  |
| Coexisting fracture <sup>‡</sup>           | 8 (20.0)          | 2 (11.8)            | 6 (26.1)         | 0.428 <sup>t</sup> |  |
| Fractured bone <sup>‡</sup>                | NIT FOR           |                     |                  |                    |  |
| Upper extremity                            | 2 (25.0)          | 0 (0.0)             | 2 (33.3)         |                    |  |
| Lower extremity                            | 3 (37.5)          | 1 (50.0)            | 2 (33.3)         | 0.400.0            |  |
| Pelvis                                     | 2 (25.0)          | 0 (0.0)             | 2 (33.3)         | 0.438°             |  |
| Upper and lower extremity                  | 1 (12.5)          | 1 (50.0)            | 0 (0.0)          |                    |  |
| Crush injury <sup>‡</sup>                  | 32 (80.0)         | 16 (94.1)           | 16 (69.6)        | 0.107 <sup>t</sup> |  |
| Anatomic parts of body crushed *           |                   | 0                   |                  |                    |  |
| Lower extremity                            | 22 (68.8)         | 10 (62.5)           | 12 (75.0)        |                    |  |
| Upper extremity                            | 2 (6.2)           | 0 (0.0)             | 2 (12.5)         | - 0.052            |  |
| Chest wall                                 | 1 (3.1)           | 0 (0.0)             | 1 (6.2)          | 0.052              |  |
| Multiple sites                             | 7 (21.9)          | 6 (37.5) 1 (6.2)    |                  |                    |  |
| Number of traumatized extremities §        | 1.0 [1.0 – 3.0]   | 1.0 [1.0 – 3.0]     | 1.0 [1.0 – 2.0]  | 0.206              |  |
| Type of crush injury <sup>‡</sup>          |                   |                     |                  |                    |  |
| Extremity trauma without fracture          | 31 (77.5)         | 15 (88.2)           | 16 (69.6)        |                    |  |
| Extremity trauma with fracture             | 7 (17.5)          | 2 (11.8)            | 5 (21.7)         | 0.0540             |  |
| Thoracic compression                       | 1 (2.5)           | 0 (0.0)             | 1 (4.3)          | 0.651°             |  |
| Pelvic fracture                            | 1 (2.5)           | 0 (0.0)             | 1 (4.3)          |                    |  |

Table 1. Demographic and baseline clinical characteristics of the groups.

\*: n (%), \*: Median [min-max]

AKI: acute kidney injury, Group-1: patients with AKI, Group-2: patients without AKI

a. Pearson Chi-Square test. b. Fisher's Exact test. c. Fisher Freeman Halton test. d. Mann-Whitney U test.

In the study, the timing and frequency of hemodialysis for children in Group 1 who developed AKI were as follows: Hemodialysis was initiated for most children (75%) within 5 to 24 hours after admission, highlighting the urgency and rapid response of the treatment following rescue. The median number of hemodialysis sessions was 20, with the typical duration lasting 5 days. These findings underscores the critical care provided to manage severe AKI in this pediatric population.

In the study, children who developed AKI exhibited a greater need for intensive care compared to those without AKI, with

76.5% requiring intensive care unit (ICU) admission versus 17.4% (p=0.001). The duration of ICU stay was also significantly longer for those with AKI, averaging 4 days, as opposed to no days for those without the condition (p=0.001). Despite the severity of their condition, the survival rate for children with AKI was high at 88.2%, although slightly lower than the 100% survival rate seen in children without AKI.

Both univariate and multivariate regression analyses revealed age as the factor predicting the development of AKI (OR=1.26, CI: 1.05-5.0, p=0.012, Table 4).

**Table 2.** Admission laboratory parameters of the groups.

|                                    | Groups based on AKI        |                          |         |
|------------------------------------|----------------------------|--------------------------|---------|
|                                    | Group 1 (n=17)             | Group 2(n=23)            | pª      |
| Leukocyte count§                   | 20.1 [6.6 – 39.0]          | 15.0 [5.4 – 33.4]        | 0.043   |
| Platelet count §                   | 272.0 [59.0 – 670.0]       | 323.0 [152.0 – 571.0]    | 0.163   |
| Lymphocyte count §                 | 1.8 [0.5 – 15.0]           | 2.3 [0.9 - 6.6]          | 0.267   |
| Blood urea nitrogen (mg/dL) §      | 76.0 [38.0 – 165.0]        | 19.0 [8.5 – 169.0]       | < 0.001 |
| Potassium (mEq/L)§                 | 6.2 [2.0 – 7.7]            | 4.6 [3.3 – 7.3]          | 0.001   |
| Creatinine (mg/dL) §               | 2.5 [0.7 - 6.1]            | 0.4 [0.2 – 1.1]          | < 0.00  |
| Uric acid (mg/dL) §                | 10.8 [2.5 – 209.0]         | 4.0 [1.9 – 15.0]         | 0.004   |
| C-reactive protein (mg/dL) §       | 110.0 [23.0 – 242.0]       | 7.0 [1.7 – 151.0]        | < 0.00  |
| Creatine kinase (U/L) §            | 50000.0 [826.0 - 190618.0] | 3750.0 [27.0 – 97020.0]  | 0.001   |
| Albumin (mg/dL) §                  | 3.2 [2.0 – 4.4]            | 3.7 [2.8 – 4.7]          | 0.018   |
| Bicarbonate (mEq/L) §              | 15.9 [10.8 – 25.8]         | 21.7 [13.0 – 29.0]       | < 0.00  |
| Aspartate aminotransferase (U/L) § | 1054.0 [346.0 – 2493.0]    | 157.0 [16.0 – 3327.0]    | 0.003   |
| Alanine aminotransferase (U/L) §   | 332.0 [47.0 – 2298.0]      | 73.0 [11.0 – 728.0]      | 0.004   |
| NLR§                               | 5.2 [1.2 – 24.2]           | 3.4 [0.8 – 33.3]         | 0.165   |
| MLR§                               | 0.8 [0.1 – 2.1]            | 0.4 [0.1 – 5.4]          | 0.085   |
| PLR§                               | 135.7 [40.0 – 264.8]       | 115.8 [38.3 – 474.4]     | 0.914   |
| CLR§                               | 50.0 [5.1 – 258.0]         | 3.7 [0.3 – 79.5]         | < 0.00  |
| NPR§                               | 0.0 [0.0 – 0.2]            | 0.0 [0.0 – 0.1]          | 0.051   |
| CAR§                               | 33.3 [8.2 - 103.5]         | 2.1 [0.4 – 45.8]         | < 0.00  |
| BAR§                               | 21.7 [9.5 – 54.0]          | 5.0 [2.2 – 49.7]         | < 0.00  |
| SII§                               | 1302.0 [439.5 – 5780.7]    | 1025.5 [244.0 - 14233.3] | 0.356   |

<sup>§</sup>: Median [min-max]. AKI: acute kidney injury, Group-1: patients with AKI, Group-2: patients without AKI NLR: neutrophil-to-lymphocyte ratio, PLR: platelet-to-lymphocyte ratio, MLR: monocyte-to-lymphocyte ratio, CLR: C-reactive protein-to-lymphocyte ratio, CAR: C-reactive protein-to-albumin ratio, BAR: blood urea nitrogen-to-albumin ratio (BAR), SII: the systemic inflammatory index. a. Mann-Whitney U test.

Table 3. Pre-hospital interventions and treatment details in the study groups.

|   | Overall (n=40) | Groups based on AKI |               | р                     |
|---|----------------|---------------------|---------------|-----------------------|
|   |                | Group 1 (n=17)      | Group 2(n=23) |                       |
| Pre-hospital intravenous hydration <sup>‡</sup> | 7 (17.5)       | 0 (0.0)             | 7 (30.4)      | 0.014ª                |
| Urine output in the first hours <sup>‡</sup>    |                |                     |               |                       |
| Normal  | 29 (72.5)      | 7 (41.2)            | 22 (95.7)     |                       |
| Oliguria  | 6 (15.0)       | 6 (35.3)            | 0 (0.0)       |                       |
| Anuria  | 3 (7.5)        | 3 (17.6)            | 0 (0.0)       | - <0.001 <sup>b</sup> |
| Polyuria  | 2 (5.0)        | 1 (5.9)             | 1 (4.3)       |                       |
| Amputation <sup>‡</sup>                         | 4 (10.0)       | 0 (0.0)             | 4 (17.4)      | 0.123ª                |
| Anatomical location <sup>+</sup>                |                |                     |               |                       |
| Upper extremity                                 | 1 (25.0)       | -                   | 1 (25.0)      |                       |
| Lower extremity                                 | 3 (75.0)       | -                   | 3 (75.0)      |                       |
| Fasciotomy <sup>‡</sup>                         | 8 (20.0)       | 2 (11.8)            | 6 (26.1)      | 0.428ª                |
| Anatomical location for fasciotomy <sup>‡</sup> |                |                     |               |                       |
| Lower extremity                                 | 2 (25.0)       | 0 (0.0)             | 2 (33.3)      | 0.000 c               |
| Upper extremity                                 | 6 (75.0)       | 2 (100.0)           | 4 (66.7)      | – 0.999ª              |
| Hyperbaric oxygen treatment <sup>‡</sup>        | 1 (2.5)        | 1 (5.9)             | 0 (0.0)       | 0.425ª                |

\*: n (%). **AKI:** acute kidney injury, **Group-1:** patients with AKI, **Group-2:** patients without AKI. **a.** Fisher's Exact test. **b.** Fisher Freeman Halton test.

|  | Univariate analysis |       | Multivariate analysis |       |
|--|---------------------|-------|-----------------------|-------|
|  | Odds ratio [95% CI] | р     | Odds ratio [95% CI]   | р     |
| Age  | 1.27 [1.07 – 1.51]  | 0.005 | 1.26 [1.05 – 1.5]     | 0.012 |
| Extrication time                             | 1.03 [0.99 – 1.06]  | 0.083 | 1.03 [0.99 – 1.06]    | 0.202 |
| Coexisting bodily trauma: Present vs. absent | 5.65 [0.61 – 52.22] | 0.127 | 6.07 [0.47 – 78.11]   | 0.166 |
| Coexisting fracture: Present vs. absent      | 0.38 [0.07 – 2.16]  | 0.274 |                       |       |

Table 4. Univariate and multivariate regression analysis in predicting the development of AKI.

AKI: acute kidney injury.

## DISCUSSION

Our findings reveal that older children who remained trapped under rubble for extended periods faced a greater risk of developing AKI. This risk was particularly elevated in those who did not receive intravenous hydration during their transfer to the hospital. Contrary to expectations, the specific characteristics of the trauma and crush injuries did not significantly correlate with the development of AKI.

A limited number of studies have investigated the factors that can significantly predict AKI in earthquake victims (1,2,4,12). In one of these studies focusing on the Marmara Earthquake, Sever et al. emphasized the importance of administering renal replacement therapy to earthquake victims with crush syndrome, noting higher rates of morbidity and mortality in dialyzed patients (4). In another study, it was concluded that age, the time lapse between disaster and admission to referral centers, type of trauma, comorbidities, and complications during treatment were the risk factors for developing AKI in victims of catastrophic earthquakes (13). Hu et al. found that male gender, time to extrication from the rubble, surgical interventions, infections, multiple crush injuries, and creatine kinase level were significantly correlated with the development of AKI (14). On the other hand, the findings on the effect of fasciotomy on morbidity and mortality of patients with crush injury-induced AKI are contradictory (8,12). Karakaya et al. investigated the significance of a renal score, which is calculated using estimated glomerular filtration rate (eGFR), creatine phosphokinase level, time to extrication from the rubble, amputation or fasciotomy, and amount of urine, in predicting child survivors of earthquakes needing kidney replacement treatment (2). In another study conducted with child survivors of earthquakes who had crush injuries, Atmis et al. found that creatine kinase level, percentage of body area subject to crushing to total body area, and phosphorus level significantly predicted the patients needing dialysis treatment. They did not find a significant relationship between time to extrication from the rubble and the development of AKI (1). In comparison, we found that among the baseline demographic and clinical variables we investigated, only age significantly predicted the development of AKI in child survivors of earthquakes.

The relationships between crush syndrome, extremity injuries, and renal failure have complex, interrelated pathophysiological aspects. Although crush syndrome is expected in earthquake victims with severe or multiple extremity trauma with and without fractures, no statistically significant correlation between crush injury and AKI was found, unlike several studies that found a positive correlation between the number of extremity injuries and the incidence of AKI. On the other hand, some studies found the development of AKI in patients with crush syndrome a poor prognostic factor (5,15). The studies that focus on the Marmara earthguake reported that 58% of the children who did not receive intravenous hydration before their admission to the hospital developed AKI, even if they received aggressive fluid treatment after hospitalization. In parallel, in our study, none of the children who developed AKI had received intravenous hydration before their admission to the hospital. Tahmasebi et al. reported that the incidence of AKI was directly related to the time until medical aid was first provided (16). Hence, providing adequate volume replacement to earthquake victims after rescue is a vital preventive measure in maintaining normal kidney function (3,16,17).

Various laboratory parameters, including creatine kinase level, have been investigated to predict the severity of crush syndrome in earthquake victims. Mertsoy et al. reported that high creatine kinase levels may indicate the severity of muscle damage in traumatized pediatric patients with crush syndrome (18). Similarly, Donmez et al. reported that serum creatine kinase level, as well as other laboratory parameters such as potassium, uric acid, urea, creatinine, aspartate aminotransferase, lactic dehydrogenase, alanine aminotransferase, and calcium levels, may help predict the severity of crush injury (5). Composite systemic inflammatory indices, including NLR, PLR, MLR, and SII, have also been investigated for their prognostic power in predicting the need for hospitalization and dialysis and found helpful in improving patient management in disaster scenarios (11). In comparison, we categorized the child survivors of the earthquakes based on whether they developed AKI. However, as in other studies (1,14), we observed that creatine kinase levels were significantly higher in children with AKI. In addition, various laboratory parameters, including leukocyte

count, blood urea nitrogen, potassium, serum creatinine, uric acid, C-reactive protein, alanine aminotransferase, and aspartate aminotransferase levels, as well as composite indices, such as CLR, CAR, and BAR were significantly higher in earthquake-affected children with AKI than in those without AKI. Due to the lack of data that would otherwise enable us to conduct the relevant correlation analyses, we could not conclude that elevated creatine kinase levels or other laboratory parameters indicate severe crush injuries. Then again, the finding of higher inflammatory parameters should be considered for early assessment of anatomic sites and providing aggressive fluid resuscitation in order to prevent future morbidities.

The relationship between AKI and time to extrication from the rubble is another speculated subject (9,14,19,20). The percentage of body area subject to crushing to total body is reportedly another critcal factor for the development of AKI (14). Although we found that the time to extrication from the rubble was statistically significantly higher in children with AKI than in those without AKI, we did not find any significant correlation between the characteristics of crush injury and the development of AKI, contrary to our expectations.

The primary limitation of the current study was its retrospective design, which may introduce biases. Additionally, including only pediatric cases without excluding those without crush injuries may have affected the generalizability of our findings, as it led to the heterogeneity of the sample.

This study provides valuable insights into the incidence of AKI and the risk factors that can predict the development of AKI in child survivors of earthquakes. Although we could not find a significant correlation between crush injury characteristics and AKI, we found that older age and longer time spent under rubble were significant risk factors for renal complications, particularly in children who did not receive intravenous hydration before they were admitted to the hospital. These findings underscore the importance of timely resuscitation and systemic inflammation management in preventing AKI in this vulnerable population. Further prospective studies are needed to corroborate our findings and elucidate additional factors influencing renal outcomes in child survivors of earthquakes, guiding targeted interventions aimed at reducing the burden of AKI and improving the overall prognosis in this sensitive patient population.

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#### Author Contributions

Aylin Gençler: Concept, Design, Data collection or processing, analysis or interpretation, literature search, writing, approval. Kenan Yılmaz: Design, Data collection or processing, literature search, writing. Hakim Çelik: Design, analysis or interpretation, writing, approval

#### **Conflicts of Interest**

The authors confirm there are no conflicts of interest to declare

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The authors confirm that the study did not receive any funds.

#### Ethical Approval

The study protocol was approved by the Harran University Ethical Committee for Clinical Studies on May 22, 2023 (Approval no: HRU/23.09.19). The study was carried out in accordance with the ethical principles outlined in the Declaration of Helsinki. Written informed consent could not be obtained from the legal guardians of children included in the study due to the study's retrospective design and the data's unanimity.

#### **Review Process**

Externally and extremely peer-reviewed.

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