



# Nephrological Follow-up of Children Victims of The Earthquake: A Single Center Experience

## Çocuk Deprem Mağdurlarının Nefrolojik İzlemi: Tek Merkez Deneyimi

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### ABSTRACT

**Objective:** We retrospectively examined the nephrological conditions of the victims who applied to the Pediatric Nephrology Clinic in our hospital in İzmir after the February 6, 2023 Kahramanmaraş earthquake.

**Method:** Age, gender, time spent under debris, number of crushed extremities, presence of acute kidney injury (AKI), creatine kinase (CK) levels and prognosis of all patients were evaluated. 5% dextrose-0.45% NaCl solution was given as 1500 cc/m<sup>2</sup>/day if the CK levels of the children were between 1000-3000U/L, and as 3000 cc/m<sup>2</sup>/day for those >3000U/L. If the bicarbonate value is <25, alkalization was achieved by applying NaHCO<sub>3</sub> treatment to 50 mEq/L. If CK values fell below 3000U/L, the amount of fluid was reduced by half, and if it was below 1000 U/L, it was discontinued. If blood gas pH is >7.50 and/or bicarbonate ≥30, alkalization treatment is discontinued; if 25-30 it is halved.

**Results:** Of the total 33 pediatric patients, 48.5% were girls and 51.5% were boys. The children had a mean age of 9.0±3.9 years. The mean stay under the rubble was 17.00 (4.25-48.00) hours. The CK values of 23 patients were >1000 U/L at the time of admission. Six patients had acute kidney injuries at admission. Four patients received hemodialysis and/or hemodiafiltration treatment. The CK values returned to normal in 5.0 (3.0-8.0) days in the patients who received fluid and alkalization treatments. The serum creatinine values of all patients normalized.

**Conclusion:** Even in the case of concomitant AKI in crush syndrome developing after an earthquake, full recovery can be achieved with aggressive fluid and alkalization treatment.

**Keywords:** Earthquake, child, crush syndrome

### ÖZ

**Amaç:** 6 Şubat 2023 Kahramanmaraş depremi sonrası İzmir'deki hastanemizin Çocuk Nefroloji Kliniği'ne başvuran mağdurların nefrolojik durumlarını retrospektif olarak inceledik.

**Yöntem:** Tüm hastaların yaşı, cinsiyeti, enkaz altında geçirilen süre, ezilen ekstremité sayısı, akut böbrek hasarı varlığı, kreatinin kinaz (CK) düzeyleri ve prognozları değerlendirildi. Çocukların CK düzeyleri 1000-3000 U/L arasında ise 1500 cc/m<sup>2</sup>/gün, >3000U/L ise 3000 cc/m<sup>2</sup>/gün olarak %5 dekstroz-%0,45 NaCl solüsyonu verildi. Bikarbonat değeri <25 ise 50 mEq/L olacak şekilde NaHCO<sub>3</sub> uygulanarak alkalinizasyon sağlandı. CK değerleri 3000 U/L'nin altına düşerse sıvı miktarı yarı yarıya azaltıldı, 1000 U/L'nin altına düşerse kesildi. Kan gazı pH'si >7,50 ve/veya bikarbonat ≥30 ise alkalinizasyon tedavisi kesildi; 25-30 ise yarıya düşürüldü.

**Bulgular:** Toplam 33 çocuk hastanın %48,5'i kız, %51,5'i erkekti. Çocukların yaş ortalaması 9,0±3,9 yıldı. Enkaz altında ortalama kalış süresi 17,00 (4,25-48,00) saatti. Başvuru sırasında 23 hastanın CK değeri 1000 U/L'nin üzerindeydi. Başvuru sırasında altı hastada akut böbrek hasarı mevcuttu. Dört hasta hemofiltrasyon ve/veya hemodiafiltrasyon tedavisi aldı. Sıvı ve alkalinizasyon tedavisi alan hastaların CK değerleri 5,0 (3,0-8,0) günde normale döndü. Tüm hastaların serum kreatinin değerleri normale döndü.

**Sonuç:** Deprem sonrası gelişen ezilme sendromunda akut böbrek hasarının eşlik etmesi durumunda bile agresif sıvı ve alkalinizasyon tedavisi ile tam iyileşme sağlanabilmektedir.

**Anahtar kelimeler:** Deprem, çocuk, ezilme sendromu

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## INTRODUCTION

On February 06, 2023, an earthquake with a magnitude of 7.7 Mw on the Richter scale occurred in the southeast of Turkey, centered in Kahramanmaraş. This massive earthquake affected approximately eleven provinces and fourteen million citizens<sup>(1)</sup>. Since the earthquake occurred early in the morning, it did not give people time to escape, which increased the impact of this catastrophe.

A wide variety of factors can affect the clinical condition of earthquake victims, including the timing and severity of the earthquake, geographical, demographic factors, the architectural structure, and the seismic safety of the buildings. Mortality rates increase mainly as a result of injuries to vital organs in major natural disasters such as earthquakes, landslides, in which large numbers of people are affected at the same time, or in human-made calamities such as wars and terrorist acts<sup>(2)</sup>. The second leading cause of death in such disasters is crush syndrome (CS) resulting from blunt muscle trauma<sup>(3)</sup>.

The main triggering event in the occurrence of CS is the release of components of striated muscle cells into the systemic circulation due to trauma or non-traumatic causes called rhabdomyolysis<sup>(4)</sup>. Most of the injured people pulled out of the rubble had acute kidney injury (AKI) due to rhabdomyolysis.

The most important cause of AKI is compartment syndrome, which induces hypovolemia. Since the rescued wounded do not have access to water under the wreckage, the fluid deficit is further increased by the ongoing losses. Development of AKI also depends on the severity of the muscle damage that occurs, the presence of underlying comorbid conditions, and the development of complications (e.g., sepsis). In addition, postrenal AKI due to supraventricular or infraventricular obstruction secondary to pelvic trauma, and AKI of renal origin due to the use of nephrotoxic agents, heart failure, arrhythmias or transfusion reaction can also be seen<sup>(2,5)</sup>.

Since the earthquake affected a very large geographical region, the injured who were removed from the rubble were first treated in the local health institutions. However, since the health institutions in the region and the health personnel working in these institutions were also affected by this disaster, some of the patients were referred to various hospitals throughout the country after their first emergency treatment. In this study, we retrospectively examined the nephrological conditions of the patients who applied to the Pediatric Nephrology

Clinic of our hospital after the earthquake, which can be described as the disaster of the century.

## MATERIALS and METHODS

The clinical and laboratory conditions of 33 children affected by the earthquake and followed in our clinic were retrospectively examined. Approval for the conduction of this review was obtained from the Ethics Committee of University of Health Sciences Turkey, İzmir Tepecik Training and Research Hospital (decision no: 2023/03-35, date: 05.04.2023).

Age, and gender of the patients, time remained under the rubble, cases of amputation, fasciotomy, AKI (if any), change in the amount and/or color of the voided/catheterized urine of all patients were evaluated. During the follow-up, the need for dialysis and the length of stay in the hospital were critically assessed. Systolic and diastolic blood pressures, urea, creatine (Cr), blood gas, sodium (Na), potassium (K), creatine kinase (CK), aspartate aminotransferase (AST), lactate dehydrogenase (LDH) values of the patients were evaluated, urine tests and imaging studies were performed immediately after admission.

Those who were removed from under the rubble after the earthquake and had a CK value of >1000 U/L were diagnosed with CS<sup>(6)</sup>. AKI was diagnosed when serum creatinine levels increased more than 3 times of its cut-off values, glomerular filtration rate <75%, or urine output <0.3 mL/kg for 24 or 12 hours of anuria<sup>(7)</sup>.

On the day of the earthquake, the Turkish Society of Pediatric Nephrology published practical guidelines for the management of victims to avoid development of kidney failure and disseminated this information to all hospitals that accepted or were required to admit the injured. These guidelines were related to the necessary examinations, treatment modalities and preventive measures to be implemented<sup>(8,9)</sup>.

For hospitalized patients with prerenal AKI, IV fluid therapy was started at daily doses of 2000 cc/m<sup>2</sup>. If CK levels of these children were between 1000-3000 U/L, 5% dextrose and 0.45% NaCl solution were given at daily doses of 1500 cc/m<sup>2</sup>, if CK levels were >3000 U/L, then daily doses were increased to 3000 cc/m<sup>2</sup>. If serum bicarbonate level was <25 mEq/L, alkalization was achieved by applying NaHCO<sub>3</sub> treatment at a dose of 50 mEq/L. If CK values dropped below 3000 U/L in the follow-up, the amount of IV fluid replacement is halved and then stopped if CK levels fell below 1000 U/L. If blood gas pH was >7.50 and/or bicarbonate level was

$\geq 30$  mEq/L, alkalinization therapy was discontinued and halved when it is 25-30 mEq/L.

### Statistical Analysis

The SPSS 26.0 (SPSS Inc., Chicago, IL, USA) program was used for statistical analysis. Discrete variables were expressed as numbers (percentages), continuous variables with normal distribution as mean  $\pm$  standard deviation, and those with non-normal distribution as median (interquartile ranges; 25-75%). Spearman Bivariate Correlations and Mann-Whitney U tests were used for statistical analysis. P-values of less than 0.05 were accepted as statistically significant.

## RESULTS

Patients were firstly referred to our clinic or presented on their own on the 3<sup>rd</sup> day of the earthquake. The hospitalized children under the age of 18 (total n=33) consisted mostly of boys (51.5%) and then girls (48.5%). The children were between 2 and 16 years old, with a mean age of  $9.0 \pm 3.9$  years. Demographic and laboratory data of the patients are given in Table 1. The mean length

of stay under the rubble (was unknown in one patient) was 17.00 (4.25-48.00) hours. Average time to rescue was significantly longer in the group with CS, at 35.5 (7.50-48.00) hours ( $p < 0.005$ ).

The CK values of 23 patients were  $>1000$  U/L at the time of admission. CK values of  $>10,000$  U/L in 3 patients before admission, returned back to normal levels at our admission. There were a total of 12 children (36.4%) with a CK level of  $>10,000$  U/L at the time of admission. The mean CK levels were significantly higher in patients with CS at admission than in those without ( $p < 0.05$ ). CK values of the patients who received fluid and alkalinization therapies returned to normal within 5.0 (3.0-8.0) days.

Serum creatinine values of these patients at the time of admission ranged from 0.4 to 7.8 mg/dL, with a mean of 1.59 mg/dL. Serum creatinine values of all patients normalized in the follow-up. Five patients had AKI at admission and four patients received hemodialysis (HD) and/or hemodiafiltration (HDF) therapies. In renal ultrasonography, we did not detect any pathology

**Table 1. Some remarkable demographic and laboratory data of the patients**

	Crush syndrome		p-values
	Without	With	
	10 (30.3%)	23 (69.7%)	
Age (years)	9.5 (6.00-14.00)	8.00 (6.00-11.00)	0.576
Gender			
Male, n (%)	6 (60)	11 (47.8)	0.603
Female, n (%)	4 (40)	12 (52.2)	
Time spent under earthquake rubble (h)	4.50 (1.75-21.25)	35.5 (7.50-48.00)	0.035
CK level at admission (U/L)	145.00 (67.75-539.00)	11,838.00 (2,049.00-38,700.00)	0.00
Mean CK level (U/L)	87.02 (49.55-274.00)	3,145.50 (900.40-12,083.70)	0.00
Maximum CK level (U/L)	167.50 (67.7-539.00)	11,838.00 (2,353.00-48,860.00)	0.00
Cr level at admission (mg/dL)	0.50 (0.48-0.62)	0.50 (0.50-0.60)	0.954
Mean Cr level (mg/dL)	0.49 (0.42-0.57)	0.50 (0.40-0.57)	0.743
Maximum Cr level (mg/dL)	0.55 (0.48-0.62)	0.50 (0.50-0.70)	0.985
AST level at admission (U/L)	34.50 (24.75-65.75)	175.00 (78.00-891.00)	0.00
Mean AST level (U/L)	30.40 (24.00-41.85)	93.00 (42.20-346.60)	0.00
Maximum AST level (U/L)	53.50 (32.25-71.00)	175.00 (85.00-1,046.00)	0.00
LDH level at admission (U/L)	300.50 (223.50-453.50)	860.00 (457.00-1,991.00)	0.002
Mean LDH level (U/L)	258.60 (232.27-287.12)	449.30 (312.20-979.10)	0.002
Maximum LDH level (U/L)	375.00 (264.75-525.25)	860.00 (496.00-2,003.00)	0.001
Presence of AKI, n (%)	-	5 (21.7)	
HD/HDF, n (%)	-	4 (17.4)	
Length of hospital stay (days)	36 (16.50 - 44.75)	29.00 (17.00 - 47.00)	0.985

CK: Creatine kinase, AST: Aspartate aminotransferase, LDH: Lactate dehydrogenase AKI: Acute kidney injury, HD/HDF: Hemodialysis/hemodiafiltration

except for one patient with a right ectopic kidney, which was not known previously. Length of hospital stay was not significantly different in patients with or without CS ( $p=0.985$ ).

The correlations between the maximum serum creatinine values of the patients and the duration of their stay under the rubble, and the maximum CK, AST, LDH and K levels are shown in Table 2. We have found positively significant correlations between maximum creatinine levels and serum CK, AST and LDH levels of our patients (Table 2). The corresponding Spearman's rank correlation coefficients ( $r_s$ ) were 0.734, 0.598 and 0.790 and  $p<0.001$ , respectively. Serum K levels were positively but not significantly correlated with maximum creatinine values ( $r_s$  value 0.340,  $p=0.053$ ).

Six patients developed AKI and underwent HD/HDF during follow-up (Table 3). Patients #16 and #31 applied with a picture of prerenal AKI, and patient #16 received IV alkalinized fluid therapy due to CS presented at admission. Patient #22 was applied with AKI and a very high CK level without any damage to the extremities, and received HDF therapy for a short period of 24 hours, together with alkaline fluid. Despite the fact that our male patient #23 who was admitted to our hospital on the 3<sup>rd</sup> day of the earthquake remained under the rubble

for only 5 hours, he had not any obvious fracture, or underwent fasciotomy, etc. in his extremities, HD was performed because he had hyperkalemia that did not respond to medical treatment. In the follow-up, HDF was required for another 12 days. Our patient #24 was also admitted on the post-earthquake 3<sup>rd</sup> day. This patient who had multiple extremity injuries and, as expected, very high CK levels and AKI, received HD for 21 days. Our patient #25 was a 4-year-old patient who had a history of cardiopulmonary resuscitation after she was rescued from the wreckage and underwent HD in an external center. CS was present at admission, and creatinine values were normal when she arrived. She received HDF for 2 days. Figure 1 shows the change in kidney function test parameters during the hospitalization period of 4 patients who underwent HD/HDF.

## DISCUSSION

This study aims to evaluate the nephrological status of pediatric patients followed in our clinic after the Kahramanmaraş-centered earthquake that occurred on February 6, 2023. Besides, our study conveys importance because it emphasizes that in such possible future disasters, even in the presence of AKI accompanying CS, fluid replacement therapy can reverse the situation when applied effectively.

**Table 2. Correlation of maximum creatinine levels with other clinical and laboratory parameters**

	Maximum creatinine level (mg/dL)	
	r	p-value
Time spent underearth quake rubble (h)	-0.154	0.399
Maximum CK level (U/L)	0.734	<0.001
Maximum AST level (U/L)	0.598	<0.001
Maximum LDH level (U/L)	0.790	<0.001
Maximum K level (mmol/L)	0.340	0.053

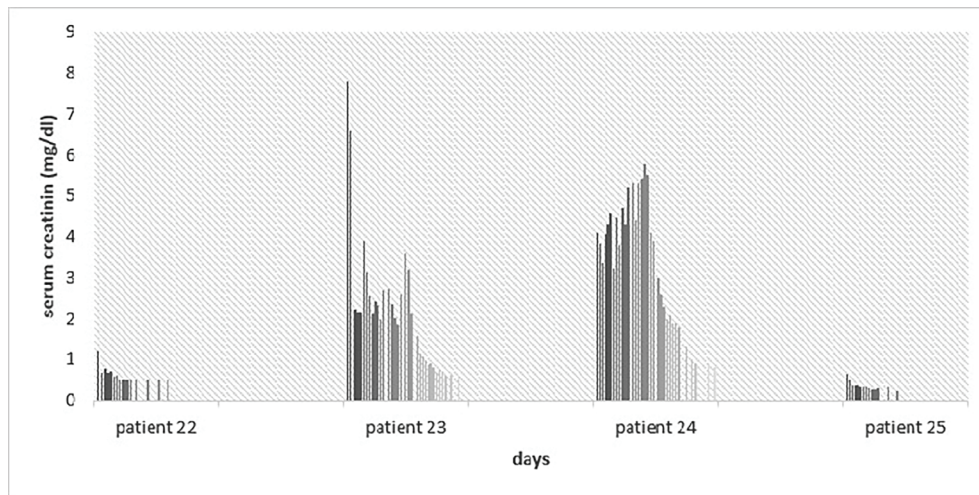
CK: Creatine kinase, AST: Aspartate aminotransferase, LDH: Lactate dehydrogenase, K: Potassium

**Table 3. Some remarkable demographic and laboratory data of 6 patients with acute kidney injury and/or HD/HDF**

Patient no	Time spent under earthquake rubble (hours)	Extremities affected (n)	Fasciotomy procedures performed (n)	Maximum CK level (U/L)	CK recovery time (days)	Maximum Cr level (mg/dL)	Cr recovery time (day)	HD /HDF	Duration of dialysis therapies (day)
16	12	2	3	62.140	8	1.5	6	-	-
22	35	0	0	98.400	12	1.37	2	HDF	1
23	5	0	0	158.980	9	7.80	32	HDF	12
24	8	4	4	284.560	10	4.40	34	HD	21
25	48	3	3	11.838	10	0.42	-	HDF	2
31	48	3	3	69	-	3.42	10	-	-

CK: Creatine kinase, Cr: Creatinine, HD/HDF: Hemodialysis/hemodiafiltration





**Figure 1.** Serum creatinine tests during hospitalization of patient

Although there is no definitely established diagnostic criteria of CS, we accepted CK values  $>1000$  U/L as CS in victims who were rescued from the earthquake rubble<sup>(6,10)</sup>. CS was present in 23 of a total of 33 patients. After the 1999 Marmara earthquake, Dönmez et al.<sup>(11)</sup> specified crushing injury of a large skeletal muscle mass, sensory and motor disturbances in the extremities, myoglobinuria and/or hematuria, and serum CK levels  $>1000$  U/L as diagnostic criteria for CS in the children followed. Iskit et al.<sup>(12)</sup> reported that they accepted children with myoglobinuria or AKI (the cases with serum creatinine levels above 1.2 mg/dL or oliguria accepted as AKI) with crush injury as CS.

After crush injury, large amounts of fluid can be retained in the injured muscles, leading to compartment syndrome, hypovolemia, and ultimately AKI due to poor perfusion of the kidneys<sup>(4)</sup>. Therefore, appropriate and intensive fluid therapy should be initiated in a timely manner. Insufficient or delayed fluid administration increases the likelihood of AKI<sup>(13,14)</sup>. The prognostic factor in CS is the development of AKI, and although it is potentially preventable, it is still considered the most serious complication<sup>(15)</sup>. We also make the diagnosis of AKI when serum creatinine levels increased more than 3 times the upper limit of normal, glomerular filtration rate  $<75\%$ , or urine output  $<0.3$  mL/kg for 24 hours or 12 hours of anuria<sup>(7)</sup>.

AKI was detected in 5 of our patients, and it should not be overlooked that the patients applied to us on the 3<sup>rd</sup> day at the earliest, and that some patients may have been protected from the adverse effects of AKI with fluid replacement therapy in the early period. AKI

of our two patients regressed with fluid replacement therapy, while HD/HDF was applied to the other three patients. In addition, patients #16, #23 and #24 were admitted on the 3<sup>rd</sup> day after the incident of earthquake and had myoglobinuria when they were admitted, which disappeared in the first two days with fluid replacement and alkalization therapies.

Dönmez et al.<sup>(11)</sup> reported the highest CK levels in pediatric patients with CS followed up after the Marmara earthquake as 27,558 U/L in those with multiple extremity injuries. In the study of Iskit et al.<sup>(12)</sup>, the development of AKI was not correlated with serum CK levels, and serum CK levels were above 10,000 U/L in only three out of 33 patients. Four of our five patients with AKI had CS and their mean CK level was 151,085 U/L. The highest CK level was found to be 284,500 U/L in our patient #24.

Oda et al.<sup>(16)</sup> reported the incidence of AKI in children with one, two, and three extremity injuries as 50.5%, 74.5%, and 100%, respectively. In the same study, they stated that they had observed AKI in only 14.3% of children with one and 85.7% of those with multiple extremity injuries and that the number of affected extremities is an important factor in determining the severity of CS. Iskit et al.<sup>(12)</sup> reported that they could not find any relationship between the time spent under the rubble, the number of damaged extremities and the development of AKI. In our study, the mean time to stay trapped under the rubble was significantly longer in the group with CS. This is important in that it shows that the delayed rescues will expose the victims to a greater risk for CS and therefore the development of AKI.

One of the most common causes of death in injured survivors after an earthquake is cardiac arrhythmias caused by hyperkalemia. Hyperkalemia has been reported as a prominent feature of CS<sup>(17)</sup>. In their study involving 20 children, Dönmez et al.<sup>(11)</sup> stated that the increase in K levels was positively correlated with serum CK, AST, urea and creatinine levels and that CS was more severe in these children. Iskit et al.<sup>(12)</sup> detected hyperkalemia (5.6-8.2 mEq/L) in only four of the patients who developed AKI. Among the patients who applied to us, patients #23 and #24 also had hyperkalemia upon admission to the hospital. K values in other patients were within the normal range. We observed that maximum creatinine and serum CK, AST and LDH levels of our patients were positively and significantly correlated.

Isotonic sodium chloride is the preferred, and easily available electrolyte solution because it is difficult to obtain bicarbonate solutions in times of disaster<sup>(2)</sup>. The rationale for administering bicarbonate solution is that raising the urine pH above 6.5 can prevent heme-protein precipitation, intratubular plug formation, and uric acid precipitation with Tamm-Horsfall protein which will reduce the rates of metabolic acidosis and hyperkalemia. Alkalinization can also reduce the release of free iron from myoglobin and the formation of F2-isoprostane, which can increase the severity of renal vasoconstriction<sup>(18)</sup>. For this reason, we provided alkalinization with bicarbonate solutions in patients presenting with CS.

Iskit et al.<sup>(12)</sup> followed up 33 trauma patients hospitalised in the 1999 Marmara earthquake, and indicated development of AKI in 10 out of 15 cases with crush injuries. They reported that 4 of these patients received IV infusion of 0.33% or 0.45% NaCl solution at daily doses of 6000 mL/m<sup>2</sup> or at least 3000 mL/m<sup>2</sup> and despite these aggressive fluid resuscitations, two of them needed HD<sup>(12)</sup>. They stated that since AKI is seen only in children with crush injuries, this type of injury is the main cause of AKI in pediatric patients who are trapped under earthquake rubble. Dönmez et al.<sup>(11)</sup> reported that they did not detect AKI in any of the eight pediatric patients in whom fluid resuscitation was initiated in the rescue area after the Marmara earthquake, and that AKI occurred in seven (58%) of 12 children who had not started to receive fluid therapy in the early period. They reported that even though they administered fluid replacement therapy at an average daily dose of 2500-3000 mL/m<sup>2</sup>, four children needed treatment with HD<sup>(11)</sup>. Sanadgol et al.<sup>(19)</sup> stated that in the Iran-Bam earthquake, none of the

pediatric patients could be started on fluid therapy in the rescue area because the earthquake was severe and all the medical facilities in the region were damaged. They stated that they had given alkaline solution (15 mEq/L bicarbonate/isotonic sodium chloride) in cases where serum CK levels were 3-5 times the upper limit of normal, serum K values were above 5.5 mEq/L, and in the concomitant presence of myoglobinuria. They reported that AKI had not developed in any patient without crush injury, but it had occurred in 8 (53%) of 15 patients with crush injury, but none of these patients had required dialysis. Here, too, since AKI had been observed only in their patients with crush injuries, they also emphasized that crush injury was the main cause of AKI in these patients. They concluded that the amount of fluid that should be administered to prevent the development of AKI in children with crush injuries should be greater than 4.8 times the amount of the maintenance fluid<sup>(19)</sup>. There is no clear data on the amount, content and alkalinization amount of the fluid to be given to children presenting with CS. First of all, we used 5% dextrose and 0.45% NaCl solution because of its easy accessibility. We adjusted the bicarbonate dose to be administered according to the blood bicarbonate level. With the aggressive fluid therapy and alkalinization we applied, all patients who developed CS recovered within a short time.

The extent of the damages caused by the earthquakes is associated with many factors such as earthquake resistance of the buildings, the condition of the water supplies, and weather conditions in the region. For example, the Marmara earthquake occurred during the summer months when the air temperature was higher. It should not be overlooked that fluid loss in victims also contributes to AKI. The study conducted by Bakkaloğlu et al.<sup>(20)</sup> presented the most comprehensive nationwide post-earthquake kidney disaster data in pediatric victims.

The strength of our study is the detailed description of fluid therapy in the presence of limited literature on children victims of the earthquake.

### Study Limitations

Scarce number of patients included in our study, our inability to measure height of the patients, and calculate their eGFRs accordingly due to the fact that almost all of the children had lower extremity damage were limitations of our study. In addition, since the first medical interventions of the patients were performed in an external center. we could not reach the previous impressions of some patients due to communication problems in the first days of the earthquake.

## CONCLUSION

CS-induced AKI resolves in the long term without any damage to the kidneys. It should be noted that even when dialysis is not possible in cases with post-earthquake CS, these patients should never be left untreated, because the effects of CS can be prevented by aggressive fluid and alkalization therapies.

## Ethics

**Ethics Committee Approval:** Approval for the conduction of this review was obtained from the Ethics Committee of University of Health Sciences Turkey, İzmir Tepecik Training and Research Hospital (decision no: 2023/03-35, date: 05.04.2023).

**Informed Consent:** Retrospective study.

## Author Contributions

Surgical and Medical Practices: C.B., Ö.Ö.Ş., D.A., S.A.Ç., F.M., A.B.A., B.K.D., Concept: C.B., Ö.Ö.Ş., D.A., S.A.Ç., F.M., A.B.A., B.K.D., Design: C.B., Ö.Ö.Ş., D.A., S.A.Ç., F.M., A.B.A., B.K.D., Data Collection and Processing: C.B., Ö.Ö.Ş., D.A., S.A.Ç., F.M., A.B.A., B.K.D., Analysis and Interpretation: C.B., D.A., S.A.Ç., F.M., A.B.A., B.K.D., Literature Search: C.B., B.K.D., Writing: C.B., B.K.D.

**Conflict of Interest:** The authors have no conflict of interest to declare.

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