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Acute Rhabdomyolysis in the Pediatric Intensive Care Unit: Etiology, Clinical Features, Treatment, and Prognosis

Çocuk Yoğun Bakım Ünitesinde Akut Rabdomiyoliz: Etiyoloji, Klinik Özellikler, Tedavi ve Prognoz

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Abstract

Objective: This study was designed to identify the underlying etiology, evaluate the treatment methods, and determine the incidence of acute kidney injury (AKI), and to establish the predictive laboratory values for kidney failure and the factors associated with mortality in critically ill children with a diagnosis of rhabdomyolysis and high creatine kinase (CK) levels.

Method: Twenty-three patients who were diagnosed with acute rhabdomyolysis in the first 48 hours in the pediatric intensive care unit between January 2011 and January 2021 and whose CK levels were found to be ≥50.000 IU/L in follow-up were included in the study. The ages of the patients ranged from 1 month to 18 years. Patients with muscular diseases, postoperative patients, and chronic renal failure patients were not included.

Results: The median age of the patients was 71 months (41-141 months). The three most common causes were infection (n=11, 47%), intoxication (n=5, 21.7%), and metabolic disease (n=4, 17.3%). While the mean CK value of the patients at admission was 53.570±32.37 IU/L, the peak CK value was 88.936 IU/L (60.558-122.962). Eleven patients (47.8%) developed AKI. Continuous renal replacement therapy (CRRT) was performed for six patients (26%). Between those who developed kidney failure and those who did not, the differences between the pediatric risk of mortality scores, blood urea nitrogen, creatinine, uric acid, and calcium measured during hospitalization were significant, while the difference in CK values was not.

Öz

Amaç: Rabdomiyoliz tanısı konulan ve kreatin kinaz (CK) düzeyi yüksek olan kritik çocuk hastalarda, altta yatan etiyolojiyi saptamak, tedavi yöntemlerini değerlendirmek, akut böbrek yetmezliği (ABY) görülme sıklığını ve böbrek yetmezliği için prediktif laboratuvar değerlerini saptamak ve mortalite ile ilişkili faktörleri belirlemektir.

Yöntem: Çalışmaya Ocak 2011-Ocak 2021 arasında çocuk yoğun bakım ünitesinde ilk 48 saatte akut rabdomiyoliz tanısı konulan ve izlemde CK düzeyi 50,000 IU/L ve üzerinde tespit edilen 23 hasta dahil edildi. Hastaların yaşları 1 ay-18 yaş arasındaydı. Kas hastalığı bulunanlar, postoperatif hastalar ve kronik böbrek yetmezliği hastaları dahil edilmedi.

Bulgular: Hastaların yaş ortancası 71 ay (41-141 ay) idi. En sık üç neden enfeksiyon (n=11, %47), zehirlenme (n=5, %21,7) ve metabolik hastalık (n=4, %17,3) idi. Hastaların yatış ortalama CK değeri 53,570±32.371 IU/L iken, pik CK değeri 88,936 IU/L (60,558-122,962) idi. On bir hastada (%47,8) ABY gelişti. Altı hastaya (%26) sürekli renal replasman tedavisi (SRRT) uygulandı. Böbrek yetmezliği gelişenler ile gelişmeyenler arasında; pediatrik ölüm riski skorları, yatış sırasında bakılan BUN, kreatinin, ürik asit ve kalsiyum değerleri arasındaki farklılık anlamlı iken, CK değerlerindeki farklılık anlamlı değildi. Mekanik ventilatör, inotrop, ekstrakorporeal tedavi ihtiyacı olanlar ile üç ve üzerinde organ yetmezliği gelişen hastalarda böbrek yetmezliği görülme sıklığı anlamlı derecede yüksekti. İnotrop ihtiyacı olan, SRRT tedavisine ihtiyaç duyan, üç ve üzerinde organ yetmezliği olan ve evre 3 böbrek yetmezliği gelişen hastaların mortalitesi anlamlı düzeyde yüksekti. Sağ kalan hastaların hiçbirinde son dönem

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Abstract

The incidence of kidney failure was significantly higher in patients who needed mechanical ventilation, inotrope administration, or extracorporeal therapy and in patients with three or more organ failures. Mortality was significantly higher in patients who needed inotropes or CRRT, had three or more organ failures, or developed stage 3 kidney failure. End-stage kidney failure was not observed in any of the surviving patients. Four patients (17.4%) included in the study died. The relationship between mortality and peak CK elevation was not significant.

Conclusion: The prognosis of rhabdomyolysis is related to the underlying etiology and comorbid conditions. Early aggressive fluid therapy positively affects the course of the disease.

Keywords: Acute kidney injury, creatinine kinase, mortality, pediatric intensive care, prognosis, rhabdomyolysis

Öz

böbrek yetmezliği görülmedi. Çalışmaya dahil edilen dört hasta (%17,4) öldü. Mortalite ile pCK yüksekliği arasındaki ilişki anlamlı değildi.

Sonuç: Rabdomiyolizin prognozu altta yatan etiyoloji ve komorbid durumlar ile ilişkilidir. Erken agresif sıvı tedavisi hastalığın seyrini olumlu yönde etkilemektedir.

Anahtar kelimeler: Akut böbrek yetmezliği, çocuk yoğun bakım, kreatinin kinaz, mortalite, prognoz, rabdomiyoliz

Introduction

Rhabdomyolysis is a condition that occurs when creatine kinase (CK) and myoglobin are released into the circulation as a result of damage to the skeletal muscle by traumatic or non-traumatic biological, physical, and toxic causes (1). Myoglobin toxicity can cause tubular damage (2,3). The most common causes of rhabdomyolysis in children are viral myositis and trauma, while less common causes include neonatal metabolic diseases, drug toxicity, and inflammatory conditions (2). While the disease may be asymptomatic, it may also cause consequences of varying severity ranging from myoglobinuria to acute kidney injury (AKI) (4). While the incidence of AKI is 10-50%, the mortality rate has been reported as 7-80% (3).

In the diagnosis of rhabdomyolysis, the absence of erythrocytes in the urine despite darkening of the urine color, CK levels at least five times normal, hyperphosphatemia, hyperkalemia, and hypocalcemia are important criteria (4).

This study aimed to identify the underlying etiology, evaluate the treatment modalities, and determine the incidence of AKI and predictive laboratory values for kidney failure as well as to determine the factors associated with mortality in critically ill patients who were hospitalized in the pediatric intensive care unit with a diagnosis of acute rhabdomyolysis and CK level of ≥50.000 IU/L in follow-up.

Materials and Methods

Twenty-three patients, who were diagnosed with acute rhabdomyolysis in the first 48 hours in the pediatric intensive care unit between January 2011 and January 2021 and whose CK levels were found to be ≥50.000 IU/L in follow-up, were included in the study. The ages of the patients ranged from 1 month to 18 years. The study was designed as a retrospective study.

We obtained Ethics Committee approval from our hospital's Medical Specialization Education Board for the study (number: 2020-KAEK-141/264, protocol no: E-21/12-257).

Rhabdomyolysis was diagnosed based on medical history and laboratory findings including elevated serum CK levels of >1000 IU/L.

Age, sex, laboratory parameters, underlying etiologies, presence of chronic diseases, inotrope and mechanical ventilation needs, treatment method, extracorporeal treatments, renal replacement therapies, length of stay in the intensive care unit and the hospital, pediatric risk of mortality (PRISM) score, organ failure, survival, and prognosis were recorded for all patients included in the study.

Extracorporeal treatments included extracorporeal membrane oxygenation (ECMO), therapeutic plasma exchange (TPE), and renal replacement therapy.

Renal replacement therapies were classified as peritoneal dialysis, hemodialysis, and continuous renal replacement therapy (CRRT).

Laboratory parameters including serum blood urea nitrogen (BUN), creatinine, aspartate transaminase (AST), alanine transaminase (ALT), uric acid, sodium (Na), potassium (K), calcium (Ca), phosphorus (P), urine microscopy, metabolic tests, pH and bicarbonate values, and CK levels were recorded at the time of diagnosis and during the peak time.

Serum and urinary myoglobin are not routinely assessed at our hospital.

AKI was defined as an increase in creatinine clearance of 50% or more within 7 days, or an increase of 0.3 g/dL in

serum creatinine in 2 days, or patients becoming oliguric for more than 6 hours (5). The kidney disease: Improving Global Outcomes (KDIGO) guidelines were used to define the stages of AKI (6). The KDIGO stages are shown in Table 1.

Metabolic acidosis was defined as having a pH level below 7.25 while partial CO_2 pressure was 35-45 mmHg. Applied medical treatments were recorded.

Since our hospital is not a trauma center, only patients with elevated CK levels due to non-traumatic reasons were included in the study.

Patients with muscular diseases such as muscular dystrophy, postoperative patients, patients with chronic kidney failure, and patients whose files could not be accessed were not included in the study.

Statistical Analysis

Statistical analysis was performed with IBM SPSS Statistics 22.0. In the evaluation of the data, frequencies and percentages were given for qualitative data. For quantitative data, descriptive statistical methods were applied to obtain an arithmetic mean for data with normal distribution and a median (25^{th}-75^{th} percentile) for those without standard deviation. The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to identify normally distributed data. The chi-square test or Fisher's Exact test was employed to compare qualitative data between the groups. In comparisons between two independent groups, the Student's t-test (paired samples) was used for data with normal distribution and the Mann-Whitney U test was used for data with non-normal distribution. Degrees of relationship between variables were evaluated with the Spearman correlation analysis. All statistical calculations were evaluated at 95% confidence intervals and at a significance level of $p<0.05$.

Table 1. Proposed KDIGO staging of AKI (6)

Stage	Serum creatinine	Urine output
1	1.5-1.9 times baseline or ≥0.3 mg/dL (≥26.5 µmol/L) increase	<0.5 mL/kg/h for 6-12 h
2	2.0-2.9 times baseline	<0.5 mL/kg/h for ≥12 h
3	3 times baseline or ≥4.0 mg/dL(≥353.6 µmol/L) increase or initiation of RRT or in patients<18 years a decrease in GFR <35 mL/min/1.73 m²	<0.3 mL/kg/h for ≥24 h or anuria ≥12 h

KDIGO: Kidney disease: Improving global outcomes, AKI: Acute kidney injury, RRT: Renal replacement therapy, GFR: Glomerular filtration rate

Results

Twenty-three patients were included in the study and 47.8% (n=11) of the patients were female. The median age of the patients was 71 months (41-141 months) and the mean PRISM score was 16.50±10.6.

The most important underlying cause was infection. Eleven patients had symptoms and signs of viral or bacterial infection before the diagnosis of rhabdomyolysis. The detected viral agents were adenovirus, influenza, and bocavirus. Four patients were admitted to the intensive care unit with severe septic shock. Gram-negative agents were shown in two of these cases, while agents could not be identified in the other two cases.

Five patients had acute rhabdomyolysis due to intoxication. While drug poisoning was the cause in four cases of patients hospitalized for this reason, the cause was mushroom poisoning in one case. Drugs causing rhabdomyolysis by intoxication were metformin, selective serotonin reuptake inhibitor, Ca channel blocker, and weight loss pills taken together with a salbutamol inhaler capsule. The patient taking metformin was also in a state of diabetic ketoacidosis. Carnitine palmitoyl transferase II deficiency (CPT II) was detected in three cases and very long-chain fatty acid dehydrogenase deficiency (VLCAD) was found in one case. The three patients' underlying causes were status epilepticus, out-of-hospital cardiac arrest, and hypokalemia secondary to Bartter syndrome.

Thirteen patients (56.5%) needed mechanical ventilation. The median duration of mechanical ventilator was 2 days (0-20 days).

Demographic information, clinical features, renal findings, and hospital details of the patients are summarized in Table 2.

While the mean CK value of the patients at admission was 53.570±32.371 IU/L, the peak CK value was 88.936 IU/L (60.558-122.962). While CK values peaked on day 2 (1-3) of hospitalization, they returned to normal in 13.60±5.38 days.

CK levels at the diagnosis and at the peak time are shown in Table 3.

Fourteen (60.8%) patients had black/tea-colored urine. No erythrocytes were detected in the microscopy results of the patients who had a positive blood reaction in urinalysis.

Table 2. Demographic, clinical, renal, and hospital data of patients

Parameters	n	%
Demographic information		
Number of patients	23	
Female	11	47.8
Age (at diagnosis), months	70 (41-141)	
Underlying disease	11	47.8
Primary diagnosis		
Intoxication	5	21.7
Infection	11	47.8
Metabolic disease	4	17.4
Other		
Bartter syndrome-hypokalemia	1	4.3
Status epilepticus	1	4.3
Out-of-hospital arrest	1	4.3
Clinical details		
Inotrope/vasoactive agent	10	43.5
2 or more organ failures	14	60.9
Dark urine	14	60.9
Mechanical ventilation	13	56.5
Extracorporeal therapy		
ECMO	1	4.3
Therapeutic plasma exchange	4	17.3
Renal findings		
Acute kidney injury		
Stage 1	0	0
Stage 2	2	8.7
Stage 3	9	39.1
Continuous renal replacement therapy	6	26
Chronic kidney disease	0	0
Hospital details		
Intensive care unit stay, days	6* (3-25)	
Hospital stay, days	13* (8-42)	
Mortality	4	17.3

ECMO: Extracorporeal membrane oxygenation, * 25th percentile-75th percentile

A statistically significant and moderate positive correlation was found between creatinine values at the time of hospitalization and creatinine value at the peak CK time (r=0.565, p<0.05). However, no statistically significant relationship was found between peak CK and organ failure, need for inotropes, need for CRRT, or mortality.

Eleven patients (47.8%) developed AKI. Only two patients (18.1%) were experiencing stage 2 renal failure, while the remaining nine patients (29.7%) were in stage 3 renal failure. Six patients (26%) needed CRRT.

Table 3. Laboratory parameters of all patients at hospitalization and pCK

During diagnosis During pCK	Result
CK (IU/L)	53570.91±32371.10
pCK (IU/L)	88936 (60558-122962)
Creatinine (mg/dL)	0.76 (0.56-1.51)
pCK creatinine (mg/dL)	0.72 (0.50-1.20)
AST(IU/L)	1334.26±1234.55
pCK AST (IU/L)	2651.78±1590.11
ALT(IU/L)	314 (78-701)
pCK ALT (IU/L)	802 (431-1386)
BUN (mg/dL)	16 (11-44)
pCK BUN (mg/dL)	16 (11-34)
Sodium	141.61±7.27
pCK sodium	140 (137-148)
Potassium	4.49±1.23
pCK potassium	3.90 (3.38-4.30)
Calcium	8.23±1.08
pCK calcium	8.36±1.15
Phosphorus	5.54±2.64
pCK phosphorus	4.40 (3.00-5.10)
Uric acid (mg/dL)	6.40 (3.50-13.70)
pCK peak uric acid (mg/dL)	4.10 (2.80-9.50)
pH	7.29±0.18
Bicarbonate (mEq/L)	19.06±6.95

CK: Creatinine kinase, pCK: Peak creatinine kinase, BUN: Blood urea nitrogen, AST: Aspartate amino transferase, ALT: Alanine amino transferase, data are presented as mean ± standard deviation

While the differences between PRISM scores and BUN, creatinine, uric acid, and Ca values measured during hospitalization between patients with and without kidney failure were statistically significant (p<0.05), the difference in CK values was not statistically significant (p>0.05). The incidence of renal failure was significantly higher in patients who needed mechanical ventilation, inotrope administration, and extracorporeal treatments and in patients with three or more organ failures compared to the other group (p<0.05).

The clinical and laboratory findings of patients with and without renal failure are shown in Table 4, 5.

The routine treatment protocol was 2500-3000 mL/m^2 of intravenous hydration (crystalloid solution), sodium bicarbonate treatment of more than 40 mEq/L in solution, diuretics for patients with low urine output, and CRRT for patients with oliguria or hypervolemia. The targeted urine output was 3-4 mL/kg/h. Electrolyte and acid-base

Table 4. Comparisons of laboratory findings, age, hospital data, and PRISM between AKI and non-AKI groups

Parameters	Non-AKI (n=12)	AKI (n=11)	t/Standardized test statistic	p
Age	88.67±67.46*	93.82±62.76	0.189	0.852
PRISM	9.22±8.07*	23.78±8.26	3.781	**0.002*** **
Diagnosis CK (IU/L)	61653.50±35188.42*	44753.55±27917.58	-1.268	0.219
Peak CK (IU/L)	87138.00 (65591.00-11383.50)**	93105.00 (60558.00-154200.00)	-0.677	0.525
Diagnosis BUN (mg/dL)	12.67±4.27*	40.45±23.18	3.915	**0.003*** **
Diagnosis creatinine (mg/dL)	0.60±0.14*	2.20±1.59	3.328	**0.007*** **
Diagnosis uric acid (mg/dL)	3.60±1.64*	13.65±4.20	7.380	**<0.001*** **
Diagnosis AST (IU/L)	1806.42±1224.10*	819.18±1070.25	-2.051	0.053
Diagnosis ALT (IU/L)	474.00 (250.00-872.50)	103.00 (26.00-445.00)	1.969	0.051
Diagnosis sodium (mEq/L)	138.83±5.97*	144.64±7.61	2.045	0.054
Diagnosis potassium (mEq/L)	4.15±0.86*	4.87±1.49	1.434	0.166
Diagnosis phosphorus (mg/dL)	4.64±2.07*	6.34±2.94	1.436	0.169
Diagnosis calcium (mg/dL)	8.67±1.06*	7.75±0.93	-2.189	**0.040*** **
Intensive care stay duration	5.00 (3.00-15.00)**	13.00 (4.00-42.00)	-1.174	0.260
Hospital stay duration	9.50 (8.00-20.00)**	25.00 (7.00-42.00)	-0.955	0.347

AKI: Acute kidney injury, CK: Creatinine kinase, BUN: Blood urea nitrogen, AST: Aspartate aminotransferase, ALT: Alanine amino transferase, PRISM: Pediatric risk of mortality score, *data are presented as mean ± standard deviation or median (25^{th}-75^{th} percentile), continuous variables were compared with a student t-test. **Data are presented as median (25^{th} and 75^{th} percentiles). Continuous variables were compared with the Mann-Whitney U test. ***Statistically significant values (p<0.05)

disturbances were treated. None of the patients underwent hemodialysis or peritoneal dialysis.

End-stage renal disease was not observed in any of the surviving patients.

Four patients (17.4%) included in the study died. The relationship between mortality and peak CK elevation was not statistically significant (p>0.05). However, the mortality rates among patients who needed inotropes, needed CRRT, had three or more organ failures, or developed stage 3 renal failure were statistically significantly higher (p<0.05) (Table 6).

Discussion

Rhabdomyolysis is a syndrome that occurs due to skeletal muscle damage that disrupts the integrity of the sarcolemma (3). An increase in serum CK level is the most typical indicator of muscle damage (7).

Pediatric studies show that not only trauma but also infections are a common cause of rhabdomyolysis. A previous report found that infections accounted for 59.5% of the causes of pediatric rhabdomyolysis (8). Wu et al. (9) reported that viral myositis accounted for more than half of all cases of pediatric rhabdomyolysis, and physical exertion and seizure were the second and third most common reasons, respectively. Kim et al. (10) reported that respiratory tract infection and seizure were the most common causes of rhabdomyolysis. Trauma patients were not included in our study and the three most common causes were infection (n=11, 47%), intoxication (n=5, 21.7%), and metabolic disease (n=4, 17.3%), respectively.

In the diagnosis of rhabdomyolysis, myoglobin elevation is helpful. However, the diagnostic necessity of measuring myoglobin levels in the urine and serum is controversial because although myoglobin rises before the CK level, its half-life is quite short (1-3 hours). Therefore, it is likely to give false negatives (11). Although the blood reaction is positive in urinalysis, the absence of erythrocytes in microscopy supports myoglobinuria (11). The urine and serum myoglobin levels could not be studied in the present study. However, the absence of erythrocytes in the microscopy of patients with black urine output and positive urine blood reaction were accepted as supporting findings for myoglobinuria.

The CK level begins to rise within 12 hours after the initial injury, reaches its peak in about 2 days, and usually returns to normal within 6-10 days in most cases (11). In the present study, the peak value of CK was obtained on the 2^{nd} day and returned to normal in approximately 14 days.

Table 5. Comparison of risk factors for groups with and without kidney injury

Parameters	No kidney injury (n=12)		Kidney injury (n=11)		X^2	p
	n	(%)	n	(%)		
Sex					3.569	0.059
Female	8	(66.7)	3	(27.3)		
Male	4	(33.3)	8	(72.7)		
Diagnosis					4.455	0.238
Intoxication	2	(16.7)	3	(27.3)		
Metabolic disease	4	(33.3)	-	-		
Infectious (viral-bacterial)	5	(41.7)	6	(54.5)		
Other	1	(8.3)	2	(18.2)		
Underlying disease					0.048	0.827
Yes	6	(50.0)	5	(45.5)		
No	6	(50.0)	6	(54.5)		
MV					5.490	**0.036**
Yes	4	(33.3)	9	(81.8)		
No	8	(66.7)	2	(18.2)		
Inotropes					7.340	**0.012**
Yes	2	(16.7)	8	(72.7)		
No	10	(83.3)	3	(27.3)		
Extracorporeal therapy					10.977	**0.001**
Yes	-	-	7	(63.6)		
No	12	(100.0)	4	(36.4)		
Extracorporeal therapy method					-	-
CRRT	-	-	2	(28.6)		
Plasma exchange	-	-	1	(14.3)		
ECMO	-	-	-	-		
Multiple	-	-	4	(57.1)		
CRRT					8.856	**0.005**
Yes	-	-	6	(54.5)		
No	12	(100.0)	5	(45.5)		
End-stage kidney injury in surviving patients						**<0.001**
Yes	-	-	-	-		
No	12	(100.0)	7	(100.0)		
Number of organ failures					15.653	**<0.001**
No organ failure	7	(58.3)	-	-		
1 organ failure	1	(8.3)	1	(9.1)		
2 organ failures	4	(33.3)	2	(18.2)		
3 or more organ failures	-	-	8	(72.7)		
Mortality					5.282	**0.037**
No	12	(100.0)	7	(63.6)		
Yes	-	-	4	(36.4)		

MV: Mechanical ventilation, CRRT: Continuous renal replacement therapy, ECMO: Extracorporeal membrane oxygenation. Categorical variables were compared using the Pearson's chi-square test or Fisher's Exact test

AKI is a common and serious complication of rhabdomyolysis. Its incidence is reported to vary within a wide range of 5-50% (8,12,13). Different values such as 5%, 8.7%, and 35.9% have been reported in retrospective studies (8,10). In the present study, the incidence of AKI was 47.8%, which is quite high. Although the high CK levels (median values of 88.936 IU/L) were thought to be the reason for the very high incidence of kidney injury, the relationship

Table 6. Comparison of risk factors for surviving and non-surviving patients

Parameters	Mortality (-) (n=19)		Mortality (+) (n=4)		X^2	p
	n	(%)	n	(%)		
MV					3.725	0.104
Yes	9	(47.4)	4	(100.0)		
No	10	(52.6)	-	-		
Inotropes					6.295	**0.024**
Yes	6	(31.6)	4	(100.0)		
No	13	(68.4)	-	-		
Extracorporeal therapy					4.542	0.067
Yes	4	(21.1)	3	(75.0)		
No	15	(78.9)	1	(25.0)		
Extracorporeal therapy method					3.937	0.257
CRRT	-	-	2	(66.7)		
Plasma exchange	1	(25.0)	-	-		
ECMO	-	-	-	-		
Multiple	3	(75.0)	1	(33.3)		
CRRT					6.008	**0.040**
Yes	3	(15.8)	3	(75.0)		
No	16	(84.2)	1	(25.0)		
Stage of kidney injury					7.532	**0.038**
No kidney injury	12	(63.2)	-	-		
Stage 1 AKI	-	-	-	-		
Stage 2 AKI	2	(10.5)	-	-		
Stage 3 AKI	5	(26.3)	4	(100.0)		
End-stage kidney injury in surviving patients						
Yes	-	-	-	-	-	-
No	19	(100.0)	-	-		
Number of organ failures					6.613	**0.049**
No organ failure	7	(36.8)	-	-		
1 organ failure	2	(10.5)	-	-		
2 organ failures	6	(31.6)	-	-		
3 or more organ failures	4	(21.1)	4	(100.0)		

MV: Mechanical ventilation, CRRT: Continuous renal replacement therapy, ECMO: Extracorporeal membrane oxygenation, AKI: Acute kidney injury, categorical variables were compared using the Pearson's chi-square test or Fisher's Exact test

between CK values and kidney injury was not statistically significant in this study. Studies evaluating CK elevation as a predictive value for AKI have presented varying results. While a few studies carried out with adults (7,14) and one conducted with children (9) indicated a relationship between high CK levels and the development of AKI, other studies did not support that view (8,11,15). In the present study, there was no statistically significant relationship between very high CK levels and the development of AKI.

Watanabe (13) reported that AKI develops more frequently in children with dehydration, metabolic acidosis, severe muscle damage, and multiple organ failure. Studies carried out with adults showed that creatinine value was a predictive factor. However, this was not the case in studies with children (7,8,16,17). In the present study, high BUN, creatinine, uric acid, and PRISM score values were statistically significantly more common in patients with kidney injury than in patients who did not develop kidney injury. Ca level was found to be significantly lower among patients with AKI. The incidence of kidney failure was significantly higher in patients who needed mechanical ventilation, inotrope administration, or extracorporeal therapy and in patients with three or more organ failures compared to the other group. Therefore, this study suggests that kidney failure is associated with underlying diseases and multiple-organ failure rather than CK level.

Early recognition is essential to prevent AKI, and the basis of treatment is aggressive intravenous fluid resuscitation with correction of electrolyte abnormalities. Adjunctive therapies including the alkalization of urine, diuretics, and CRRT have been applied; however, there is controversy regarding the benefits of these treatment modalities (8). High-alkaline intravenous hydration therapy, diuretic therapy, and, when necessary, CRRT were applied for patients in the present study. The patients' responses to treatment were good. None of the surviving patients developed end-stage renal disease. In the literature, it is stated that aggressive fluid therapy, mainly when applied in the early period, has positive effects on the prognosis of the patients (8,17,18).

In a previous study, the degree of elevation of the CK level was not shown to predict mortality. Chronic kidney disease was found to be a rare complication of rhabdomyolysis in children requiring intensive care (3). Children's reported mortality rates were 7% to 10%, but all died secondarily to their underlying etiology and not due to rhabdomyolysis (11). Similar to the literature, no statistically significant correlation was found between high CK value and mortality in the present study. As in the literature, none of the patients developed chronic renal failure. However, when the patients who died are taken into consideration, it is seen that these patients needed inotropic and extracorporeal therapy and had stage 3 kidney failure. They also had three or more organ failures. The underlying cause of mortality for two of these patients was drug intoxication. These two patients, who were admitted after consuming serotonin reuptake inhibitor and Ca channel blocker, were brought

to the hospital in the final stage. One patient died due to severe septic shock, and the other due to to out-of-hospital cardiac arrest. Therefore, the causes of deaths of these patients were not acute rhabdomyolysis but rather underlying secondary causes.

A study conducted with critically ill children stated that peak CK level was not associated with mortality but that these patients needed more intensive care resources. In the same study, the development of chronic kidney disease was not common in this patient group (3).

In this study, no statistical relationship could be demonstrated between high CK values and AKI development. This may be related to the small sample size. We think a study with a larger number of patients who have lower CK values may reflect more objective results.

Although the incidence of AKI and peak CK values were high in this study, chronic kidney disease was not observed in any surviving patients. This may be related to early and aggressive fluid therapy and CRRT administered to patients.

Study Limitations

This was a single-center retrospective study with a small group of patients.

Conclusion

This study showed that the prognosis of rhabdomyolysis is related to the underlying etiology and comorbid conditions. Aggressive fluid therapy applied in the early period positively affects the course of the disease.

Ethics

Ethics Committee Approval: We obtained Ethics Committee approval from our hospital's Medical Specialization Education Board for the study (number: 2020-KAEK-141/264, protocol no: E-21/12-257).

Informed Consent: Patients' consent form was waived (not required) because the study was a retrospective observational study.

Peer-review: Internally and externally peer-reviewed.

Authorship Contributions

Concept: E.A., B.A., S.O., M.U.Y., Z.Ö., Design: E.A., B.A., S.O., M.U.Y., Z.Ö., Analysis or Interpretation: S.O., B.A., Writing: E.A., Z.Ö., Manuscript Review and Revisation: E.A., B.A., S.O., M.U.Y., Z.Ö.

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