

# Evaluation of rhabdomyolysis patients who opted for emergency services

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## ABSTRACT

**OBJECTIVE:** Rhabdomyolysis is a clinical and biochemical syndrome caused by skeletal muscle injury. Our aim was to contribute to the existing data on rhabdomyolysis in our country by evaluating the etiologic, demographic, and clinical features of rhabdomyolysis patients who applied to a tertiary hospital emergency department.

**METHODS:** We retrospectively evaluated the data of patients who applied to the tertiary hospital emergency department from January 2015 to January 2016. The study population comprised patients admitted to the emergency department of our hospital with creatinine kinase levels above 5000 U/L at admission. The data of all cases that were included in the study were scanned by the researchers using the hospital's computer-based data recording system. Age, sex, creatine kinase levels, complaints, etiology, whether or not acute renal failure developed, hospitalization and discharge status, and clinic of hospitalization were screened for all patients.

**RESULTS:** The creatine kinase levels of the patients at admission ranged from 5052 to 59140 U/L [median 7882 U/L (IQR: 7840)]. The most frequent (23.5%) cause of admission was extremity pain. The most common reason (19.6%) in the etiology was exercise. Twenty-one patients (41.1%) were admitted to clinics, and 1 patient (1.9%) died. Acute renal failure was observed in 4 patients (8.8%).

**CONCLUSION:** Rhabdomyolysis is a clinical syndrome that can be life-threatening owing to muscle destruction. Although it is suspected after a traumatic injury, it should also be considered when other potential symptoms are observed. All clinicians should be aware of its common causes, diagnosis, and treatment options.

*Keywords: Acute renal failure; emergency department; rhabdomyolysis.*

Rhabdomyolysis is a clinical and biochemical syndrome characterized by entry of cell content into circulation owing to skeletal muscle injury. The important indicators of muscle injury are myoglobin, creatine kinase, and lactate dehydrogenase. The severity of the disease may change

from asymptomatic increase in muscle enzymes to life-threatening electrolyte disorders and renal failure [1].

Muscle injuries that cause rhabdomyolysis may occur secondary to muscle dystrophies, myositis, glycogen storage diseases, medications, and

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trauma. Muscle injury caused by various etiologic factors, myoglobin, and electrolytes released into circulation secondary to myocyte cell membrane injury are responsible for the development of complications. In particular, when hypovolemia and renal vasoconstriction accompany the accumulation of myoglobin in renal tubuli, acute renal failure may be observed [2].

Our aim was to investigate etiologic, demographic, and clinical characteristics of rhabdomyolysis patients who applied to the emergency department of a tertiary care hospital to contribute to the existing data pertaining to rhabdomyolysis in our country.

## MATERIALS AND METHODS

In our study, data of patients who applied to the emergency department of a tertiary care hospital between January 1, 2015 and January 1, 2016 were retrospectively evaluated. Necessary permission for conducting the study was obtained at the meeting of Committee of Scientific Studies of our hospital on January 25, 2016 (approval no. #121).

Study population comprised patients with creatine kinase values above 5000 U/L at admission who applied to our emergency department that admits 250.000 patients annually. The patients who were referred to our hospital for hospitalization or consultation or those diagnosed at an external center before applying to our hospital were excluded from the study.

Data of all patients included in the study were scanned by the investigators using the computerized database recording system of the hospital. Age, sex, creatine kinase levels, complaints at admission, etiologies, development of acute renal failure (if any), hospitalization, and discharge status of the patients along with their clinics of hospitalization were screened. Diagnosis of acute renal failure was made based on a 0.5 mg/dL increase in serum creatinine values, increase in serum creatinine values with unknown baseline values, or decrease in urine output. Complaints of patients at admission were grouped as extremity pain; abdominal pain and nausea; diarrhea; lassitude and malaise; trauma and agitation;

impaired general health status; dark-colored urine; symptoms of stroke; drowning; and seizures. Etiologies were grouped as exercise, pancreatitis, gastroenteritis, viral respiratory tract diseases, drug use, trauma, myopathy, sepsis, cannabinoid use, stroke, alcohol use, drowning, arterial occlusion, seizures, and pneumonia. The clinics where the patients were hospitalized were grouped as internal medicine and anesthesia; reanimation, general surgery, and neurology; and chest diseases. The discharge status of ambulatory patients (for patients treated and followed up at the emergency department) was grouped as no hospitalization, rejection of the treatment, and mortality.

Data obtained in the study were evaluated for statistical analyses using SPSS for Windows 16.0 and Microsoft Office Excel 2007 programs. For the statistical evaluation of data and fitness of parameters to the normal distribution pattern, descriptive analyses (mean, percentage, and median) and Shapiro–Wilk test, respectively, were employed.

## RESULTS

A total of 51 (male,  $n=37$ , 72.55% and female,  $n=14$ , 27.45%) patients who applied to the emergency department of our hospital between January 2014 and January 2015 with creatine kinase levels above 5000 U/L at admission were included in the study. Patient ages ranged between 17 and 96 years. Creatine kinase levels of the patients at admission changed between 5052 and 59140 U/L (median, 7882 U/L; IQR: 7840 U/L). Complaints at admission of the patients who applied to the emergency department were as follows: extremity pain ( $n=12$ ; 23.5%), abdominal pain and nausea ( $n=5$ ; 9.8%), diarrhea ( $n=3$ ; 5.8%), malaise and lassitude ( $n=6$ ; 11.7%), agitation ( $n=7$ ; 13.7%), impaired general health status ( $n=6$ ; 11.7%), dark-colored urine ( $n=3$ ; 5.8%), symptoms of stroke ( $n=1$ ; 1.9%), drowning ( $n=1$ ; 1.9%), and seizures ( $n=1$ ; 1.9%) (Figure 1). Most frequent (23.5%) complaint was extremity pain.

When etiologic factors involved in rhabdomyolysis were evaluated, exercise ( $n=10$ ; 19.6%), pancreatitis ( $n=2$ ; 3.9%), gastroenteritis ( $n=4$ ; 7.8%), viral respiratory tract infection ( $n=8$ ; 15.6%), drug use ( $n=3$ ;

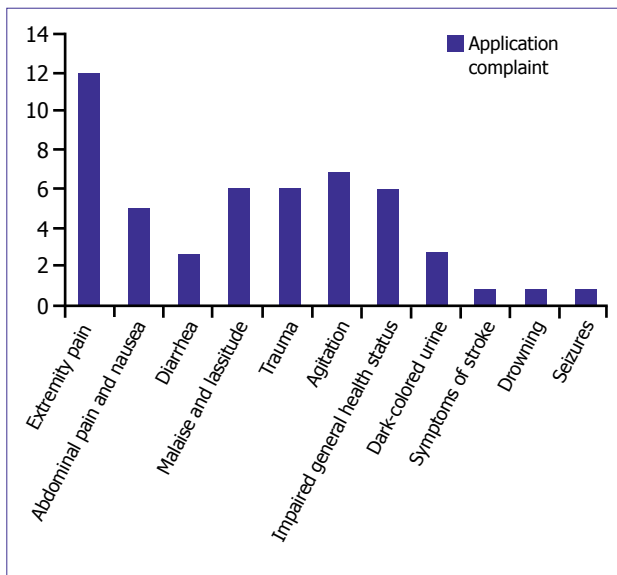


FIGURE 1. Complaints at admission of the patients.

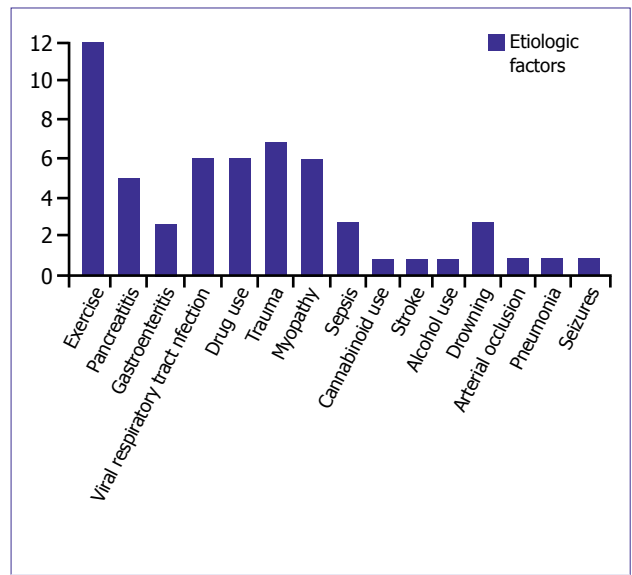


FIGURE 2. Etiologic factors involved in rhabdomyolysis.

5.8%), trauma (n=6; 11.7%), myopathy (n=1; 1.9%), sepsis (n=4; 7.8%), cannabinoid use (n=7; 13.7%), stroke (n=1; 1.9%), alcohol use (n=1; 1.9%), drowning (n=1; 1.9%), arterial occlusion (n=1; 1.9%), pneumonia (n=1; 1.9%), and seizures (n=1; 1.9%) were observed (Figure 2). Most frequent etiologic factor was exercise (19.6%).

When emergency service outcomes were evaluated, it was determined that 23 (45.1%) patients were followed up and treated in the emergency department before they were discharged. Six (11.7%) patients rejected the treatment and left the emergency room. However, 21 (41.1%) patients were hospitalized in relevant clinics, and one (1.9%) patient died.

The patients were hospitalized in the clinics of internal medicine (n=12; 57.1%), anesthesia and reanimation (n=5; 23.8%), general surgery (n=1; 4.7%), neurology (n=2; 9.5%), and chest diseases (n=1; 4.7%).

The patients were evaluated with respect to the development of renal failure, and the data of patients who rejected the treatment could not be obtained. In 8.8% (n=4) of the patients with available data, acute renal failure developed. Data of these patients are summarized in Table 1.

## DISCUSSION

Rhabdomyolysis was first defined by Fleisher in the year 1881 when hemoglobinuria was observed in soldiers after a long and tedious march [3]. Explanation of its pathogenesis and its association with myoglobin entering into circulation following muscle injury and acute tubular necrosis were revealed by Bywaters and Beall in the year 1941 [1].

Ion channels and pumps in muscle cells maintain  $Ca^{2+}$  and  $Na^{+}$  ions at lower and  $K^{+}$  ions at higher concentrations. Direct injury of the muscle cell or inability to produce intracellular energy induces rhabdomyolysis. When energy production cannot be realized, ATP-dependent ion pumps, namely, Na/K ATPase and  $Ca^{2+}$  ATPase, cannot exert their functions [4]. Increased intracellular calcium levels enhance activation of calcium-dependent proteases and phospholipases and subsequently induce apoptosis. With onset of apoptosis, myofibrils, cytoskeletal proteins, and membrane proteins degrade. Intracellular proteins, namely, aldolase, myoglobin, creatine kinase, lactate dehydrogenase, aspartate transaminase, and intracellular metabolites such as potassium, phosphate, and urate enter into systemic circulation and induce rhabdomyolysis [5].

**TABLE 1.** Data of these patients

Age	Sex	Complaints at admission	Etiology	Creatine kinase (U/L)	Emergency service outcome	Clinic of hospitalization
26	Male	Abdominal pain and vomiting	Drug use	12564	Hospitalization	Department of internal diseases
86	Female	Trauma	Trauma	26850	Hospitalization	Department of internal diseases
96	Female	Impaired general health status	Sepsis	5374	Death	-
48	Male	Impaired general health status	Sepsis	6230	Hospitalization	Department of internal diseases

Rhabdomyolysis manifests itself with myalgia, weakness of the injured muscle, and is generally associated with myoglobinuria. In addition, atypically, nausea, vomiting, and fever are observed. Clinically, muscle pain as its characteristic feature, is associated with increased serum creatine kinase levels [6]. Its classical triad includes muscle pain, weakness, and tea-colored urine. This classical triad can be seen in only 10% of the patients. In more than 50% of the patients, muscle pain and weakness are not observed. The patients more often apply with causes related to primary pathology [2]. In our study, the most frequent symptom was muscle pain, and the classical triad was observed in 5.8% of the patients.

Many clinical conditions may cause rhabdomyolysis. These etiologic factors may be classified as hereditary, acquired or traumatic, and non-traumatic causes. Acquired causes are more frequently observed and constitute 75% of all cases [7]. Melli et al. indicated most frequently observed causes as substance use (34%), medications (11%), trauma (9%), and epileptic seizures (7%) [8]. Other rarely observed causes include metabolic disorders, infections, local, and muscle ischemia, widespread muscle ischemia, prolonged immobilization, exercise, and exposure to extreme heat [5]. However, in 60% of the patients, more than one etiologic factor was observed [5, 8, 9]. Also, in our study, acquired causes were more frequently observed (98.1%). Assessment

of acquired causes revealed incidence rates comparable to those observed in the literature.

Creatine kinase is a muscle protein, and its levels increase 2–12 h after muscle injury and reach their peak 24–72 h later. Within 3–5 days, they return to normal. Brown et al. conducted a study with 2083 patients and demonstrated the correlation between acute renal failure and creatine kinase levels above 5000 U/L. [10] Veenstra et al. detected the risk of developing acute renal as 35% in patients with creatine kinase levels between 5000 and 15000 U/L and as 75% in those with creatine kinase levels above 15000 U/L [11]. In our study, the risk of developing acute renal failure in patients with creatine kinase levels between 5000 and above 15000 U/L was 7.3% and 10%, respectively. We believe that the difference between our estimates and the values reported in the literature stems from the fact that 45.1% of our patients were treated in the emergency department on an outpatient basis contrary to previous studies, which had been performed on inpatients.

In serum, myoglobin is bound to serum globulins while transporting. As a result of excessive degradation, greater amounts of myoglobin exceed the myoglobin binding capacity of globulin and circulate freely in the blood. Mechanical occlusion of renal tubuli caused by free myoglobin is an important factor in the development of acute renal failure. Renal toxic effects of accompanying vasospasm, hypovolemia,

and myoglobin contribute to the development of acute renal failure [12].

The most important complication induced by free myoglobin, i.e., development of acute tubular necrosis and acute renal failure secondary to increased free myoglobin concentrations have been detected in various studies at a rate of 14–46% [13, 14]. In a study by Günel et al. on inpatient trauma patients in our country, the authors found incidence of the development of acute renal failure to be 25% [15]. In our study, the incidence was 8.8%.

In the management of rhabdomyolysis, first, the underlying cause should be treated. Aggressive fluid resuscitation at an early phase to improve renal perfusion and increasing the urine output have been considered to be the main interventions for prevention and treatment of acute renal failure [16]. The decision to start renal replacement treatment should not be based on myoglobin or creatine kinase concentrations but on the development or prediction of the development of life-threatening hyperkalemia, hypercalcemia, hyperazotemia, anuria, or renal failure [17]. Scarce evidence is available concerning routine sodium carbonate, loop diuretic, or mannitol administration [18].

In conclusion, rhabdomyolysis is a potentially life-threatening clinical syndrome caused by muscle injury. Although it is suspected after a traumatic injury, other potential causes should also be contemplated. All clinicians should be aware of common causes and diagnostic and therapeutic alternatives.

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