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Original Article

Acute renal injury due to rhabdomyolysis: A tertiary hospital experience

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Abstract

Aim: Rhabdomyolysis (RML) is a clinical and biochemical syndrome caused by acute necrosis of striated muscle fibers and the subsequent transportation of potentially toxic cellular contents into the systemic circulation. In this study, we present data from rhabdomyolysis patients that developed acute renal failure who were hospitalized and treated in our clinic in 2019.

Materials and Methods: We reviewed all cases of RML treated in the tertiary hospital within a 12-month period, which was defined as serum creatinine kinase (CK) levels > five times the upper normal limit. The inclusion criteria were as follow: (a) being aged ≥ 18 years, (b) being treated for RML within the designated time period, (c) AKI development. The exclusion criteria are as follows: (a) being aged <18 years, (b) patients without AKI, (c) patients with End Stage Renal Disease(ESRD), (d) patients with neuromuscular diseases. Among a total of 583 patients with CK > 5 time upper normal limit (UNL), 14 conformed to the inclusion criteria and were selected as subjects

Results: A total of 14 patients were included in the study, 12 of which were male. The mean age of the patients was 48.1 (18–80). The etiologies were as follows: hypothyroidism, 3; prolonged exposure to sun, 2; electrolyte imbalance due to severe diarrhea, 1; viral upper respiratory tract infection (URTI), 3; intramuscular injection, 1; heavy exercise or falls.

Conclusion: Rhabdomyolysis is an interdisciplinary clinical condition that can lead to life-threatening outcomes including AKI. Rapid diagnosis and treatment can be life-saving. AKI is a significant potential complication of RML and renal function should be evaluated irrespective of CK levels or the presence of myoglobinuria.

Keywords: Acute kidney injury; creatininekinase; liver dysfunction; rhabdomyolysis

INTRODUCTION

Rhabdomyolysis (RML) is a clinical and biochemical syndrome caused by acute necrosis of striated muscle fibers and the subsequent transportation of potentially toxic cellular contents into the systemic circulation (1,2). There are various possible clinical manifestations, the most prevalent ones being myalgia, fatigue, and pigmenturia. It should be noted that this classic triad occurs in less than 10% of all RML patients (1). The causes of RML can be classified into three main categories: trauma- or compression-induced, nontraumatic exercise-induced, and nontraumatic and non-exercise-induced (1). Natural disasters, heavy exercise, and traffic and occupational accidents are among physical causes, while non-physical causes include electrolyte disorders (such as hypokalemia, hypocalcemia, hyponatremia, hypernatremia), infections, hereditary enzyme deficiencies, hypothyroidism, alcohol consumption, and certain drugs (lipid-lowering agents such as statins and fibrates, colchicine, corticosteroids, diuretics, and amphotericin B) (2–7). The most serious complication associated with RML is acute kidney injury (AKI) which leads to increased serum creatinine, myoglobinuria, and decreased output of urine. Rhabdomyolysis can also cause cardiac arrhythmia due to hyperkalemia (8) which is often accompanied by coagulopathy (9,10). RML is responsible for 5-10% of all AKI cases (11–13). Various factors take part in the development of AKI in RML patients. Most authors accept that the ischemic tubule damage and tubular obstruction caused by myoglobin – an actor in the complex mechanism of rhabdomyolysis – as the major pathophysiological explanation of RML-induced AKI (14). Anamnesis, clinical examination, and laboratory findings are all integral to diagnosis, where increased creatinine kinase (CK) levels (> 5 times UNL), absence of erythrocytes in urine despite darkened color, increased

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LDH, AST, ALT, phosphorus, and potassium, and decreased calcium levels indicate rhabdomyolysis. Despite being the most prominent laboratory finding associated with RML, increased myoglobin levels have little diagnostic value due to rapid clearance from the plasma within 6 hours. CK reaches its maximum level within 12-24 hours after the induction of RML (either by physical or non-physical causes) and has a half-life of 48 hours (1).

In this study, we present data from rhabdomyolysis patients that developed acute renal failure who were hospitalized and treated in our clinic in 2019.

MATERIALS and METHODS

We reviewed all cases of RML, which was defined as a serum creatinine kinase (CK) level > five times the upper normal limit, treated in a tertiary hospital within a 12-month period. The inclusion criteria were as follows: (a) being aged ≥ 18 years, (b) being treated for RML withing the designated time period, (c) developing AKI. The exclusion criteria are as follows: (a) being aged <18 years, (b) patients without AKI, (c) patients with End Stage Renal Disease(ESRD), (d) patients with neuromuscular diseases. Among the 583 patients with CK > 5 times the upper normal limit (UNL), 14 conformed to the inclusion criteria and were selected as subjects. Data regarding gender, age, serum creatinine values, length of hospital stay, etiology, and dialysis requirements were obtained from electronic medical records and discharge reports.

Ethical considerations: This study was approved by the Ethics Committee of the relevant University (decision number: 2019/384).

Statistical analysis: Statistical evaluation was performed using SPSS 22 for Windows (IBM SPSS Inc., Armonk, NY, USA). Chi-square test was used for the comparison of categorical data. $p<0.05$ was considered statistically significant.

RESULTS

A total of 14 patients were included in the study, 12 of whom were male. The mean age of the patients was 48.1 years (18–80). The etiologies of RML were as follows: hypothyroidism 3, prolonged sun exposure 2, electrolyte imbalance due to severe diarrhea 1, viral upper respiratory tract infection (URTI) 3, intramuscular injection 1, and heavy exercise or falls 4 (Figure 1).

The longest length of hospital stay was 14 days (where RML had developed after prolonged heavy exercise), and the shortest was 1 day. The average length of hospital stay was 7.7 days.

Only one subject required one round of dialysis due to anuria, the laboratory findings of all other subjects returned to normal after medical treatment. The patient with the highest CK value of 42,670 IU/L did not require dialysis. Admission hemogram and coagulation values were within normal limits. Admission biochemical parameters were summarized in Table 1.

Table 1. Biochemical parameters of patients

Patient	Age	Urea (mg/dL)	Creatinine (mg/dL)	Na (mmol/L)	K (mmol/L)	Ca (mg/dL)	LDH (IU/L)	CK (IU/L)	AST (IU/L)	ALT (IU/L)	Albumin (g/dL)	TSH (mIU/L)
1	80	51	1.6	129	3.5	7.7	290	1.217	61	18	3.2	3.5
2	45	27	1.4	139	3.9	9.4	553	4.267	93	29	4.6	>100
3	59	54	1.78	141	4.3	9.6	373	2.548	68	33	4.5	>100
4	53	106	2.04	140	3.7	9.2	387	2.480	38	17	3.7	4.2
5	70	140	6.76	136	4.7	8.36	885	11.406	427	158	3.78	1.06
6	33	41	1.63	139	4.2	8.14	510	2.014	46	27	4.57	>100
7	62	214	6.94	134	5.5	9.31	614	8.975	615	167	3.92	0.33
8	20	76	1.92	132	4.8	10.2	397	3.933	53	25	4.5	1.62
9	49	38	2.46	125	4.6	8.96	312	9.129	98	17	3.54	0.67
10	30	43	1.85	143	3.8	7.3	2.000	42.670	443	74	3.4	1.49
11	29	123	5.88	135	4.9	11.2	314	3.412	62	35	4.6	2.45
12	18	72	1.88	137	4.8	8.24	387	18.714	60	24	3.8	1.46
13	24	64	1.82	140	4.6	9.2	412	26.412	52	34	4.6	2.35
14	32	59	1.72	139	5.2	8.3	379	6.582	36	18	3.8	2.06

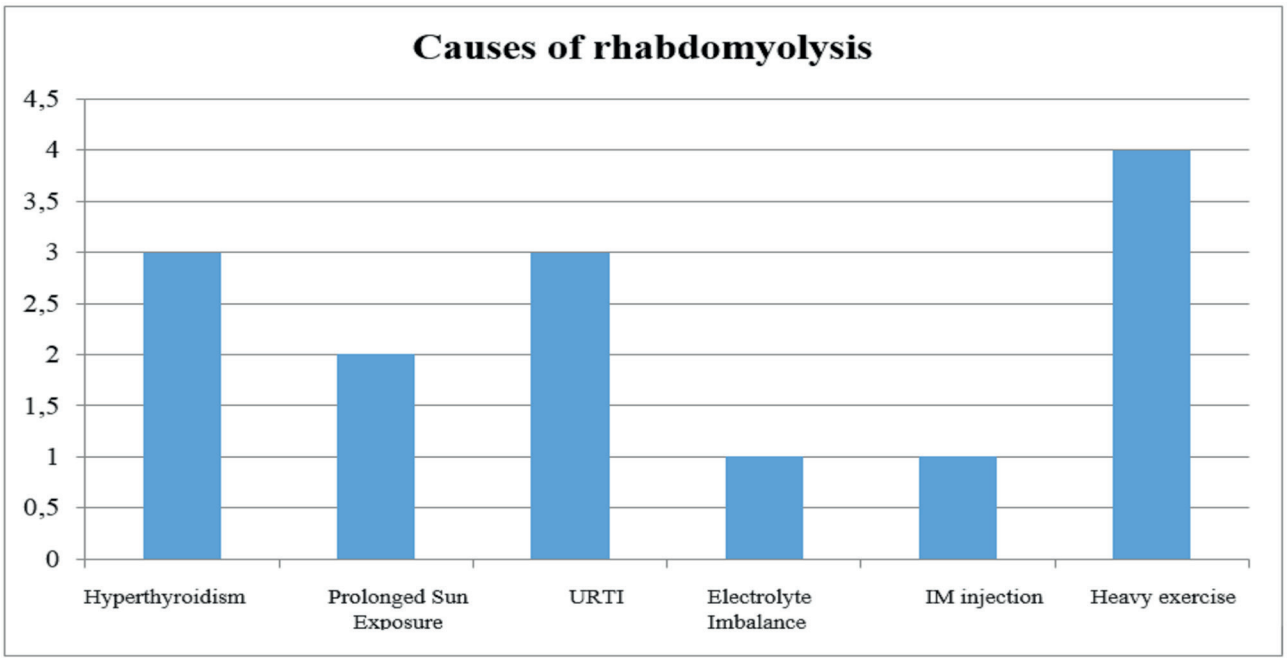

Figure 1. Distribution of causes of rhabdomyolysis

We found a statistically significant relationship between creatine and both AST and – more significantly – ALT levels (p = 0.009 for AST, p = 0.000 for ALT). The correlation analysis of age, creatine level, AST level, ALT level, and CK levels is presented in Table 2.

Intensive hydration, alkalinization of urine, and symptomatic treatment of electrolyte imbalances were sufficient to treat clinical and laboratory symptoms, after which the patients were discharged.

Table 2. Pearson correlation analysis

	Creatine		CK		AST		Age		ALT	
	r	p	r	p	r	p	r	p	r	p
Crea-tine	1.000		-0.076	0.795	**0.669**	**0.009**	0.669	0.325	**0.818**	**0.000**
CK	-0.076	0.795	1.000		0.416	0.139	-0.377	0.184	0.218	0.454
AST	**0.669**	**0.009**	0.416	0.139	1.000		0.336	0.240	**0.929**	**0.000**
Age	0.669	0.325	-0.377	0.184	0.325	0.240	1.000		0.400	0.157
ALT	0.669	0.325	0.218	0.454	**0.929**	**0.000**	0.400	0.157	1.000	

DISCUSSION

The severity of AKI was the main determinant of hospitalization in RML patients. Only one of our subjects required dialysis, even though all subjects had developed AKI. The reported mortality rate of patients that develop AKI is 10%. In our study, all patients were discharged with recovery. We found the most common cause of RML to be heavy exercise and falls; however, it was surprising that viral URTI had caused RMI-induced AKI in 3 patients

Rhabdomyolysis is a potentially life-threatening condition treated by the emergency department and internal medicine clinics. Although it has been a well-known disease for more than a hundred years, there is not a universal agreement on the ideal treatment method. CK remains the most sensitive biomarker for assessing muscle damage, but there is no consensus regarding the diagnostic threshold, where different resources recommend from five up to ten times UNL (1,15). Stahl et al. reviewed 614 published articles and found that the most commonly used threshold was CK > 1000 IU/L (7). However, there is not a definite CK cut-off value for an increased risk of rhabdomyolysis-induced AKI (14). One meta-analysis found that the predictive value of CK could depend on the etiology of rhabdomyolysis. For instance, AKI risk was strongly correlated with the mean CK level in traumatic rhabdomyolysis (16).

Toxic accumulation of myoglobin is known to be a factor in the pathogenesis of AKI. A retrospective study of 484 patients with high serum myoglobin levels showed that myoglobin levels may be an early predictor of AKI in rhabdomyolysis patients (17). However, McKenna et al. detected urinary myoglobin in one-third of all rhabdomyolysis patients, yet only 24% of these patients ended up developing AKI (18). False negatives are attributed to the short half-life (2-3 hours) of myoglobin (15). The diagnostic value of myoglobin is minimal due to its rapid and unpredictable metabolism in the plasma (14).

If a patient presents with high CK levels, it is crucial to first rule out muscular and cardiovascular causes such as cerebrovascular disease and myocardial infarction. However, RML can also develop consequent to the aforementioned diseases, thus, it is important to include the chronological sequence of events (acute CK increase that peaks 1-3 days after muscle injury) in the evaluation of these patients.

Another significant finding was that 86% of our subjects were male. We did not find a correlation between CK levels and the development of AKI. The creatine levels of patients with CK levels of 42670 and 8975 IU/L were 1.85 and 6.94 mg/dL, respectively. We believe that AKI development in RML might be related to additional factors such as age, use of nephrotoxic drugs, and dehydration.

Liver dysfunction is another potential complication of rhabdomyolysis. Aspartate aminotransferase (AST) is elevated in approximately 93% of all RML patients, whereas alanine aminotransferase (ALT) is elevated only in 25% (1,19). Since AST is found in significant concentrations in the muscle, the AST elevation observed in rhabdomyolysis is usually attributed to its release from muscle tissues and therefore typically follows the CK trend. Therefore, ALT levels are a better indicator of hepatic damage in rhabdomyolysis (19). Our results were consistent with the literature, where 3 patients had increased ALT (21.4%) and 12 had increased AST (82.7%).We found a statistically significant relationship between creatine and both AST and – more significantly – ALT levels

The limitations of our study were as follows: (a) difficulties in assessing RML and RML-induced AKI due to incomplete or absent diagnostic codes, majority of patients with elevated CK levels were excluded due to our high cut-off value (> five times UNL), mild cases of rhabdomyolysis may have been excluded, and (b) some AKI patients did not have available CK measurements, some cases of rhabdomyolysis may have been overlooked.

CONCLUSION

Rhabdomyolysis is an interdisciplinary clinical condition that can lead to life-threatening outcomes, including AKI. Rapid diagnosis and treatment can be lifesaving. We recommend using the standard definition of rhabdomyolysis where CK > 1000 IU/L or CK > 5 times UNL is accompanied by acute muscle weakness and muscle pain. AKI is a significant potential complication of RML and renal function should be evaluated irrespective of CK levels or the presence of myoglobinuria.

Conflict of interest : The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports.

Ethical approval: This study was approved by the Ethics Committee of the relevant University (decision number: 2019/384).

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