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Manifestations, Early Detection and Management of Rhabdomyolysis in Critically Ill Patients in ICU

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Abstract: Rhabdomyolysis is the rapid breakdown of striated muscles caused by wide variety of conditions including trauma, drugs, viruses, metabolic disorders; Rhabdomyolysis is a potential fatal condition with mortality of approximately 8%. In the ICU setting, the most common causes of rhabdomyolysis are muscular trauma and vascular obstruction. Rhabdomyolysis occurs in up to 85% of patients with traumatic injuries. Alcohol has been implicated in the development of rhabdomyolysis in up to 20% of cases. Patients with severe injuries that develop rhabdomyolysis induced renal failure have a mortality of approximately 20% but are higher if multiple organ dysfunction is present. Causes of rhabdomyolysis are divided into hereditary and acquired ones. The hereditary causes are mainly related to a lack or insufficiency of enzymes that participate in the catabolism of different energy macromolecules, the acquired causes are classified as traumatic and non-traumatic. The traumatic ones, such as crush syndrome, accidents, natural disasters, or intense exercise, cause direct muscle injury and rupture of the sarcolemma. The non-traumatic causes are the most common ones during peacetime and include alcohol abuse, medicines e.g., statins. The classic triad of symptoms of rhabdomyolysis includes muscle pain, weakness and dark urine. Diagnosis of rhabdomyolysis is based on elevated serum creatine kinase (CK) levels more than 1000u/L. Mild rhabdomyolysis can be treated by drinking lots of fluids. Severe cases require hospitalization and aggressive treatment with intravenous fluids to dilute the proteins to minimize their damage to the kidney and monitor the heart for dangerous rhythm changes from the surge of electrolytes. In severe cases, the kidneys may fail and immediate dialysis is needed to mechanically remove proteins and electrolytes from the blood. The complications of rhabdomyolysis include: hypovolemia, compartment syndrome, arrhythmia, disseminated intravascular coagulation, hepatic dysfunction and acute renal failure. Acute kidney injury associated with myoglobinuria is the most serious compilation of both traumatic and non-traumatic rhabdomyolysis, and it may be life-threatening. The reported incidence ranges from 13% to approximately 50%.

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1. Introduction

Rhabdomyolysis is a syndrome that is characterized by the disintegration of striated muscle and the leakage of intracellular muscular components into the blood and urine. It results in electrolyte disturbances and an elevation in the levels of sarcolemmal proteins, such as creatine kinase (CK) and myoglobin in body fluids **(Deyhle M, et al., 2013)**.

The presentation of this multifactorial and multicausal syndrome varies from an asymptomatic but detectable elevation of CK and myoglobin in blood to a life-threatening condition with fulminant acute renal failure **(Al-Ismaili Z, et al., 2011).**

The ability to predict rhabdomyolysis-induced acute kidney injury (AKI) is critical, because rhabdomyolysis is thought to be one of the leading causes of AKI. Indeed, 10–50% of patients with some degree of marked rhabdomyolysis develop AKI, and it has been suggested that rhabdomyolysis contributes to 5–25% of all cases of AKI **(Al-Ismaili Z, et al., 2011).**

Traumatic rhabdomyolysis resulting from crush injuries is an important cause of acute renal failure. 4% to 33% of cases with traumatic rhabdomyolysis develop acute renal failure (ARF), carrying a mortality rate of 3% to 50% **(Song J, et al., 2015).**

Causes of rhabdomolysis are divided into hereditary and acquired ones. The hereditary causes are mainly related to a lack or insufficiency of enzymes that participate in the catabolism of different energy macromolecules. The acquired causes are classified as traumatic and non-traumatic: The traumatic ones, such as crush direct muscle injury and rupture of the sarcolemma. The non-traumatic causes are the most common ones during peacetime and include alcohol abuse, medicines e.g., statins **(Chatzizitsis et al., 2008)**.

Although the causes of rhabdomyolysis are so diverse, the pathogenesis appears to follow a final common pathway, ultimately leading to myocyte destruction and release of muscle components into the circulation **(Khan, 2009)**.

The classic triad of symptoms of rhabdomolysis includes muscle pain, weakness and dark urine **(Huerta-Alardin et al., 2005)**. Diagnosis or rhabdomyolysis is based on elevated serum creatine kinease (CK) levels more than 1000u/L **(Luck and Verbin, 2008)**.

First line treatment for rhabdomyolysis is aggressive fluid repletion which reduces the accumulation of toxic intracellular content caused by rapid breakdown of muscle and subsequent renal damage, unfortunately few treatments are available for rhabdomyolysis beside those that address the underlying insult **(Cervellin et al., 2010)**.

The complications of rhabdomyolysis include: hypovolemia, compartment syndrome, hepatic dysfunction and acute renal failure **(Khan, 2009)**.

Aim of Work

The aim of this study was to investigate the incidence of rhabdomyolysis and AKI in severely injured trauma patients admitted to the intensive care unit (ICU). The patients were followed up for 3 days after admission to ICU, additional to that highlighting main lines of therapy in rhabdomyolysis and its complications.

2. Patients and Methods

Our study was a prospective cohort study conducted on 50 patients admitted to I.C.U at EL-HELAL trauma Centre and Ain Shams University hospital during the period from May 2018 to August 2019; all the studied populations were diagnosed to have multiple trauma.

In addition, all patients were followed-up for the first three days of admission.

Inclusion criteria:

Multiple trauma patients ISS > or = 16

- Duration of stay in ICU > or = 3 days
- **Injury severity socre (ISS):** Standardizes severity of traumatic injury based on worst injury of 6 body system which is:
- **Head and neck worst injury?** No injury 0 point, minor 1 point, moderate 4 point, serious 9 point, severe 16 point, critical 25 point, unsurvivable 75 point.
- **Face worst injury?** No injury 0 point, minor 1 point, moderate 4 point, serious 9 point, severe 16 point, critical 25 point unsurvivable 75 point.
- **Chest worst injury?** No injury 0 point, minor 1 point, moderate 4 point, serious 9 point, severe 16 point, critical 25 point, unsurvivalbe 75 point.
- **Abdomen worst injury?** No injury 0 point, minor 1 point, moderate 4 point, serious 9 point, severe 16 point, critical 25 point, unsurvivable 75 point.
- **Extremity (including pelvis) worst injury?** No injury 0 poiont, minor 1 point, moderate 4 point, serious 9 point, severe 16 point, critical 25 point, unsurvivalbe 75 point.
- **External worst injury?** No injury 0 point, minor 1 point moderate 4 point, serious 9 point, severe 16 point, critical 25 point, unsurvivalbe 75 point.

Exclusion criteria:

- Patients with chronic kidney diseases, e.g.; (Diabetic or hypertensive nephropathy).
- Injury severity score (ISS) = 75.

Data collection included:

I- Demographic data:

1- Age
2- Sex

II- Apache II:

APACHE II score was calculated. Clinical and laboratory data collected daily in the first three days of duration of stay in ICU from the studied population.

1- Blood pressure

Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) were measured manually by sphygmomanometer then Mean arterial blood pressure (MAP) was calculated.

MAP = Diastolic blood pressure+ 1/3 (systolic blood pressure - diastolic blood pressure). **(Magder SA, 2014)**

The lowest value of MAP in 24 hours period was used to calculate APACHE II score.

2- Heart Rate (HR):

Heart rate was recorded from monitor or by counting pulse rate in one minute. The highest value in 24 hours period was recorded.

3- Respiratory Rate (RR):

Respiratory rate was recorded from monitor or by counting respiratory cycle in one minute. The highest value in 24 hours period was recorded.

4- Temperature:

Body temperature was measured by applying the mercury - in glass thermometer to patient axillary temperature was measured due to difficulty of measuring oral temperature as in patients with disturbed conscious level and maxilla-facial injury. The highest value in 24 hour period was recorded.

Body temperature = axillary temperature + 0.5°C. **(Thompson at al., 2012)**

5- Laboratory data:

- Arterial PH, Pao2
- Serum sodium (Na), Serum potassium (k)
- Hematocrit, Tlc
- Serum creatinine

The worst value was recorded daily during the first 3 days of duration of stay in ICU and then an estimated approximate mortality percentage was measured (Figure:4-1).

III-Injury severity score (ISS)

The Injury Severity Score (ISS) is an anatomical scoring system that provides an overall score for patients with multiple injuries. Each injury is assigned an Abbreviated Injury Scale (AIS) score and is allocated to one of six body regions (Head, Face, Chest, Abdomen, Extremities (including Pelvis), External). Only the highest AIS score in each body region is used. The 3 most severely injured body regions have their score squared and added together to produce the ISS score.

The ISS score takes values from 0 to 75. If an injury is assigned an AIS of 6 (unsurvivable injury), the ISS score is automatically assigned to 75 and these patients were excluded from our study **(Baker SP, et al., 1974)**.

All patients were subjected to radiological investigations as part of trauma survey during the ER stay.

A-X-ray:

Plain x-ray was done to head, spine, chest, pelvis and limbs to detect fractures or any other pathological findings such as (pneumothorax or hemothorax).

B- Brain CT:

Brain CT was done for all patients ot confirm the presence or absence of intracranial pathology.

If CT brain did not show any significant findings and patient still had disturbed consciousness, Brain MRI was requested to exclude diffuse axonal injury.

C- Pelvic-abdominal Ultrasound:

Pelvic-abdominal ultrasound was performed to all patients with multiple trauma in the emergency room or at the bedside in the presence of hemodynamic instability to detect internal hemorrhage and severe abdominal trauma e.g. (Tear in abdominal organs as; liver or spleen) to calculate ISS.

Pelvic-abdominal Ultrasound was used to exclude the presence of chronic kidney disease.

IV- Laboratory data

Blood samples were withdrawn from all patients at least once daily in the first three days of duration of stay in ICU to do the following investigations.

A- Complete Blood Count (CBC)

Complete blood count was done for all patients to detect the lowest hematocrit and the highest TLC.

- Normal hematocrit: Males - 40-54%
- Females - 36-46%
- Normal TLC: 4.00-11.0 x 10 9/L

B- Serum potassium

Potassium level was measured daily. Above 5.5 mmol\L was considered as hyperkalemia.

C- Creatine phosphokinase (Ck)

Creatine phosphokinase and Ck-MB level were measured. We considered Ck >1160 diagnostic for rhabdomyolysis. The highest value was recorded.

D- Renal function tests:

Kidney function test was done to detect creatinine and blood urea nitrogen (BUN) Level and we considered AkI according to RIFLE criteria.

V- Icu management

During the duration of stay in ICU, data related to MV, Vasopressor medications, blood transfusion and the Flow rate of IV fluids were recorded to be correlated to the outcome.

VI- length of stay (LOS) in days

Date of admission and discharge from ICU were recorded to calculate the LOS in ICU for correlation with the outcome.

VII- Outcome

All patients were followed up during the ICU stay to determine the primary outcome:

I- Acute kidney injury

Patients who fulfilled RIFLE criteria were diagnosed as AkI and accordingly we devided patients into two groups

- ✓ Group I (GI): AkI
- ✓ Group II (GII): non AkI

Acute kidney injury is detected according to RIFLE criteria.

II-mortality

All ICU mortalities were documented whether related to AKI or not.

3. Results

O ur results were presented under the following headings:

I-Descriptive statistics of the whole study population

a) Demographic data
b) APACHE II score
c) Injury severity score (Iss)
d) Laboratory data
- Creatine kinase (CK)
- Renal function tests: (BUN & creatine)
- Serum potassium
- Heamoglobin
- Total leukocytic count

e) Icu management
- Mechanical ventilation

- Blood transfusion
- Vasopressor medications
- Intravenous fluids

f) Length of stay in ICU

g) Mortality

II- comparison between two patient groups according to the presence or absence of acute kidney injury (AKI):

- Group I: AkI (n=12)
- Group II: non AkI (n=38)

A-Descriptive statistics of the whole study population

I- Demographic data

1- Age

Our patient population had a mean age 35.18±14.22 years.

(Table 1).

Table (1): Age analysis of the whole study population

Variable	Mean±Sd	Minimum	Maximum
Age (year)	35.18±14.22	15	65

2- Gender

Male gender constituted 88% of our studied population compared to 12% female.

II- Acute physiology and chronic health evaluation (APACHE II)

When we calculated APACE II score for our patient population we found that:

- First day: median APACHE II score 7.
- Second day: median APACHE II score 7.
- Third day: median APACHE II score 5. (Table 2)

Table (2): Analysis APACHE II score of study population

APACHE II	Median	Minimum	Maximum
D1	7	2	27
D2	7	1	29
D3	5	1	33

III- Injury severity score (ISS)

ISS was calculated once on admission and our patient population had a mean ISS 28.94±12.13. (Table 3)

Table (3): Analysis of ISS among the study population

	Mean±sd	Minimum	Maximum
ISS	28.94±12.13	16	66

IV- laboratory data

1- Creatine kinase (Ck)

When we studied Ck levels for our patient population during the follow-up period our results revealed.

- First day: median Ck level was 1489 U/L.
- Second day: median Ck level was 1986 U/L.
- Third day: median Ck level was 1330 U/L. (Table 4).

Table (1): Analysis of Ck among the study population

Ck (U/L)	Median	Minimum	Maximum
D1	1489	53	31459
D2	1986	64	25340
D3	1330	51	19230

Among our patient population 32 patient (64%) were diagnosed with rhabdomyolysis. (Table 5)

Table (5): Prevalence of rhabdomyolysis among the studied population

		Number	Percent%
Rhabdomyolysis	Positive	32	64%
	Negative	18	36%

2- Renal function tests:

A- Blood urea nitrogen (BUN):

During the follow-up period, analysis of BUN levels of our patient population showed that:

- First day: median BUN level 17.95 mg/dL.
- Second day: median BUN level 18 mg/dL.
- Third day: median BUN level 17 mg/dL. (Table6)

Table (6): Analysis of BUN among the study population.

BUN (mg/dL)	Median	Minimum	Maximum
D1	17.95	7	57
D2	18	8	85
D3	17	7	113

B- Serum Creatine (creat.) level

Ceat. Level showed a median 0.9 mg/dL in D1 compared to 0.85 mg/dL in D2 and 0.9 mg/dL in D3 of the follow-up period. (Table 7)

Table (7): Analysis of creat. levels among the study population

Creat. (mg/dL)	Median	Minimum	Maximum
D1	0.9	0.4	1.7
D2	0.85	0.3	6.2
D3	0.9	0.9	8.8

3- Serum Potassium (K^+)

As for k+ level of our study population during the follow-up period, we found that:

- D1: Mean value 4±0.44 mEq/L.
- D2: mean value 4.15±0.78 mEq/L.
- D3: mean value 3.8±0.5 mEq/L. (Table 8).

Table (8): Analysis of k^+ among the study population

k+ (mEq/L)	Mean±SD	Minimum	Maximum
D1	4±0.44	2.8	4.9
D2	4.15±0.78	3	6.2
D3	3.8±0.5	3.2	5.3

Out of 50 patients only 6 patients (12%) developed hyperkalemia. (Table 9).

Table (9): Prevalence of hyperkalemia among the studied population

		Number	Percent%
Hyperkalemia	Positive	6	12%
	Negative	44	88%

4- Hemoglobin (Hb)

Analysis of Hb levels of our study population during the follow-up period revealed mean Hb level 11.03±2.40 g/dL in day 1 compared to 9.90±2.27 g/dL in day 2 and 9.89±1.64 g/dL in day 3. (Table10)

5- Total leucocytic count (Tlc)

Analysing TLC levels of our patient population, our results showed:

- Day 1: mean Tlc 16.69±5.93 /mcL.

- Day 2: mean Tlc level 11.84±3.53 /mcL.
- Day 3: mean Tlc level 11.11±3.11 /mcL. (Table 11).

Table (10): Analysis of hemoglobin level among the study population

Hb (g/dL)	Mean±SD	Minimum	Maximum
D1	11.03±2.40	4.2	16.3
D2	9.90±2.27	4	14.8
D3	9.89±1.64	6.1	13.7

Table (11): Analysis of Tlc among the study population

Tlc (/mcL)	Mean±SD	Minimum	Maximum
D1	16.69±5.9	6.1	31
D2	11.84±3.5	8.3	21
D3	11.11±3.1	3.6	19.8

V- ICU management

Out of 50 patients admitted to the ICU when 20 patients (40%) were mechanically ventilated, 15 patients (30%) received blood transfusion, 7 patients (14%) received Vasopressor medications and all patients received IV fluids. (Table 12)

Table (12): Descriptive analysis of ICU management among the studied population

		Number	Percent%
Mechanical ventilation	Positive	20	40%
	Negative	30	60%
Blood transfusion	Positive	15	30%
	Negative	35	70%
Vasopressor medications	Positive	7	14%
	Negative	43	86%
IV fluids	Positive	50	100%
	Negative	0	0%

VI- Length of stay in ICU

Analyzing the period of stay in ICU, our patients had median 7 days of stay. (Table 13)

Table (13): Analysis of length of stay in ICU among the studied population

	Median	Minimum	Maximum
ICU LOS (days)	7	3	25

VII-Outcome

Our patient population was followed-up during the ICU stay to determine patients who had.

A-) acute kidney injury (AkI):

Our results showed that 12 patients out of 50 (24%) developed AkI, (41.7%) of them were in risk stage, (8.3%) were in the injury stage and (50%) were in the failure stage. (Table 14)

B-) Mortality:

Our results showed that 10 patients (20%) died. (Table 15)

Table (14): Analysis of AkI among the studied population

		Number	Percent%
AkI	Positive	12	24%
	Negative	38	76%

Table (15): Analysis of mortality among the studied population

		Number	Percent%
Mortality	Positive	10	20%
	Negative	40	80%

B-comparison between two patient groups

I- According to development of acute kidney injury (AkI):

We have classified our patients into two groups

- Group I: AkI (n=12)
- Group II: non AkI (n=38)

I- Demographic data

1- Age (years)

Upon analyzing age, there was no significant difference between both groups (group I had mean age 36.08±15.58 years vs. 34.89±13.98 in group II, P value 0.804. (Table 16)

Table (16): Analytical comparison data of age between AkI and Non-AkI groups

	AkI (n=12)	Non-AkI (n=38)
Mean	36.08±15.58	34.89±13.98
Minimum	19	15
Maximum	63	65
P Value	0.804	

2- Gender

Upon analysis gender, there was no significant difference between males and females in relation to AkI, P-value 0.142. (Table: 17)

Table (17): Analytical comparison data of gender between AkI and Non-AkI groups

Gender	Number, %	AKI (n=12)	Non-AKI (n=38)
Male	Number	12	32
	%within outcome	100%	84.2%
Female	Number	0	6
	%within outcome	0%	15.8%
P -value	0.142		

II-Acute physiology and chronic health evaluation (APACHE II)

When we compared the results of APACHE II scoring system in relation to AKI throughout the follow-up period we found highly significant difference between both groups as follows

- First day: median APACHE II was 14 in group I, Vs 6 in group II; P value 0.002.
- Second day: median APACHE II was 13 in group I, Vs 4 in group II; P value 0.000.
- Third day: median APACHE II was 15 in group I, Vs 4 in group II; P value 0.002. (Table 18)

Table (18): Analytical comparison data of APACHE II between AKI and Non-AKI groups during the follow-up period

APACHE II		AKI (n=12)	Non-AKI (n=38)	P-value
D1	Median	14	6	0.002
	Range	7-27	2-22	
D2	Median	13	4	0.000
	Range	6-29	1-26	
D3	Median	15	4	0.002
	Range	3-33	1-26	

III- Injury severity score (ISS)

ISS showed highly significant difference between both groups (Mean 40.33±16.73 in group I Vs. 25.34±7.50 in group II), P-value 0.000. (Table 19).

Table (19): Analytical comparison data of ISS between AKI and Non-AKI groups

ISS	AKI (n=12)	Non-AKI (n=38)
Mean	40.33±16.73	25.34±7.50
Minimum	17	16
Maximum	66	43
P Value	0.000	

IV- Laboratory data

1- Creatine kinase (CK)

When we compared the results of CK levels in relation to AKI throughout the follow-up period we found that:

- Day 1: there was a significant difference between both groups; median CK was 2468.5 U/L in group I, Vs. 783 U/L in group II; P value 0.013.
- Day 2: there was a highly significant difference between both groups; median CK was 4344 U/L in group I, Vs. 1489 U/L in group II; P value 0.000.
- Day 3: there was a highly significant difference between both groups; median CK was 3661.5 U/L in group I, Vs. 733.5U/L in group II; P value 0.000. (Table 20).

Table (20): Analytical comparison data of CK between AKI and Non-AKI groups

CK (U/L)		AKI (n=12)	Non-AKI (n=38)	P-value
D1	Median	2468.5	783	0.013
	Range	342-31459	53-5534	
D2	Median	4344	1489	0.000
	Range	3179-25340	64-5359	
D3	Median	3661.5	733.5	0.000
	Range	2145-19230	51-4667	

Further analysis showed highly significant difference between both groups regarding rhabdomyolysis, as all patients in group I Vs. only 20 patients (52.6%) in group II had rhabdomyolysis. P-value0.003. (Table; 21)

Table (21): Incidence of rhabdomyolysis among the studied population

	Number, %	**AKI (n=12)**	**Non-AKI (n=38)**
Rhabdomyolysis	Number	12	20
	%within outcome	100%	52.6%
P -value	0.003		

Day 1: cutoff point >1385U/L to be related to AKI (AUC 0.73, sensitivity 91.7%, and specificity 60.5%).

Day 2: cutoff point >3114U/L to be related to AKI (AUC 0.955, sensitivity 100%, and specificity 89.47%).

Day 3: cutoff point >1723U/L to be related to AKI (AUC 0.9, sensitivity 100%, and specificity 84.21%). (Fig.5-6)

2- Renal function tests

A- Blood urea nitrogen (BUN)

When we compared the results of BUN levels in relation to AKI throughout the follow-up period we found a significant difference in the first day and a highly significant difference between both groups in the second and third day as follows:

- First day: median BUN was 22 mg/dL in group I, Vs 16.5 and mg/dL in group II; P value 0.017.
- Second day: median BUN was 31 mg/dL in group I, Vs 15 mg/dL in group II; P value 0.000.
- Third day: median BUN was 39.5 mg/dL in group I, Vs 15 mg/dL in group II; P-value 0.000. (Table 22)

Table (22): Analytical comparison data of BUN between AKI and Non-AKI groups

BUN (mg/dL)		AKI (n=12)	Non-AKI (n=38)	P-value
D1	Median	22	16.5	0.017
	Range	12-57	7-38	
D2	Median	31	15	0.000
	Range	25-85	8-36	
D3	Median	39.5	15	0.000
	Range	21-113	7-44	

B-Serum creatine

Comparing creatinine level in both groups revealed the following:

- First day: there was non significant difference between both groups, median 1

mg/dL in group I Vs. 0.9 mg/dL in group II, P-value 0.279.

- Second day: there was highly significant difference between both groups, median 2.05 mg/dL in group I Vs. median 0.8 mg/dL in group II, P- value 0.000.
- Third day: there was highly significant difference between both groups, median 3.15 mg/dL in group I Vs. median 0.8 mg/dL and in group II, P-value 0.000. (Table 23)

Table (23): Analytical comparison data of Creat. between AKI and Non-AKI groups

Creat. (mg/dL)		AKI (n=12)	Non-AKI (n=38)	P-value
D1	Median	1	0.9	0.297
	Range	0.8-1.7	0.4-1.3	
D2	Median	2.05	0.8	0.000
	Range	1.6-6.2	0.3-1.3	
D3	Median	3.15	0.8	0.000
	Range	1.2-8.8	0.5-1.1	

3- Serum potassium (K^+)

Potassium level showed significant difference between both groups in day 1 (mean 4.26±0.41 mEq/dL in group I Vs 3.92±0.42 mEq/dL in group II, P-value 0.017). However it showed highly significant difference in day 2 (mean 5.11±0.77 in group I Vs 3.85±0.48 mEq/dL in group II, P-value 0.000.3) and day 3 (mean 4.31±0.67mEq/dL In group I Vs 3.64±0.29mEq/dL in group II, p-value 0.000). (Table 24)

Table (24): Analytical comparison data of K^+ between AKI and Non-AKI groups

K^+ (mEq/dL)	Mean±SD, Range	AKI (n=12)	Non-AKI (n=38)	P-value
D1	Mean	4.26±0.41	3.92±0.42	0.017
	Range	3.5-4.9	2.8-4.6	
D2	Mean	5.11±0.77	3.85±0.48	0.000
	Range	3.9-6.2	3-5	
D3	Mean	4.31±0.67	3.64±0.29	0.000
	Range	3.5-5.3	3.2-4.4	

Hyperklemia (>5.5 mEq/dL) was highly correlated with AKI (6 patients (50%) in group I vs no patients 0% in group II developed hyperkalemia, P-value 0.000 (Table 25)

Table (25): Analytical comparison data of hyperkalemia between AKI and non-AKI groupFigur

		AKI (n=12)	Non-AKI (n=38)
Hyperkalemia	Number	6	0
	%within outcome	50%	0%
P-value	0.000		

4- Hemoglobin

When we compared the results of Hb levels in relation to AKI throughout the follow-up period we found a highly significant difference between both groups in the three days of the follow-up period as follows:

First day: mean Hb was 9.11±2.76 gm/dL in group I, Vs 11.64±1.95 gm/dL in group II; P value 0.001.

Second day: mean Hb was 7.83±1.93 gm/dL in group I, Vs 10.56±1.98 gm/dL in group II; P value 0.000.

Third day: mean Hb was 8.81±1.48 gm/dL in group I, Vs 10.23±1.55 gm/dL in group II; P value 0.007. (Table 26)

5- Total leukocytic count

When we analyzed Tlc levels among our study population we found that there was no significant difference between both groups through out the follow-up period as follows;

- First day: mean 4.26±0.41/mcL in group I Vs median 3.92±0.42/mcL in group II, P-value 0.403.
- Second day: mean 5.11±0.77/mcL in group I Vs median 3.85±0.48 /mcL in group II, P-value 0.688.

Third day: mean 4.31±0.67/mcL in group I Vs 3.64±0.29/mcL in group II, P-value 0.523. (Table 27)

Table (26): Analytical comparison data of Hb between AKI and Non-AKI groups

Hb (gm/dL)		AKI (no=12)	Non-AKI (no=38)	P-value
D1	Mean	9.11±2.76	11.64±1.95	0.001
	Range	4.2-11.8	7.6-16.3	
D2	Mean	7.83±1.93	10.56±1.98	0.000
	Range	4-10	6.9-14.8	
D3	Mean	8.81±1.48	10.23±1.55	0.007
	Range	6.1-10.7	8.1-13.7	

Table (27): Analytical comparison data of Tlc between AKI and Non-AKI groups

Tlc (/mcL)		AKI (no=12)	Non-AKI (no=38)	P-value
D1	Mean	17.95±6.25	16.29±5.85	0.403
	Range	(9-24.6)	(6.1-31)	
D2	Mean	11.48±2.84	11.95±3.82	0.688
	Range	(9.1-17)	(8.3-21)	
D3	Mean	10.61±2.02	11.27±3.38	0.523
	Range	(9-16)	(3.6-19.8)	

V- ICU management

1- mechanical ventilation

Our results showed that mechanical ventilation had a highly significant effect on AKI (10 out of 12 patients (83.3%) in group I Vs only 10 out of 38 patients (26.3%) in group II were mechanically ventilated.

P-value 0.000. (Table 28)

Table (28): Effect of MV on AKI

AKI	Number, %	AKI (no=12)	Non-AKI (no=38)
Positive	Number	10	10
	%within outcome	83.3%	26.3%
Negative	Number	2	28
	%within outcome	16.7%	73.7%
P -value	0.000		

2- Blood transfusion

On the contrary blood transfusion showed no significant effect on developing AKI (5 patients (41.7%) in group I Vs 10 patients (26.3%) in group II received blood transfusion. P-value 0.312. (Table29)

Table (29): Effect of blood transfusion on AKI

Blood transfusion	Number, %	AKI (no=12)	Non-AKI (no=38)
Positive	Number	5	10
	%within outcome	41.7%	26.3%
Negative	Number	7	28
	%within outcome	58.3%	73.7%
P -value	0.312		

3- Vasopressor medications

Patients who received Vasopressor medications were at high risk for developing AKI (6 patients (50%) in group I Vs only 1 patient (2.6%) in group II received vasopressor medications. P-value 0.000. (Table 30)

4- IV fluids

The infusion rate of IV fluids had a highly significant effect on AKI (mean in group I 141.82±49.76ml/h and range 60-200ml/h Vs 99.74±25.31ml/h and range 60-200ml/h).

Further analysis of IV fluids among patients who developed AKI revealed a negative relation between

creat. level and infusion rate of IV flluids, (P-value 0.020 and r -0.684). (Table 31)

Table (30): Effect of vasopressor medications on AKI

Vasopressor medications	Number, %	AKI (no=12)	Non-AKI (no=38)
Positive	Number	6	1
	%within outcome	50%	2.6%
Negative	Number	6	37
	%within outcome	50%	97.4%
P -value	0.000		

Table (31): relation between IV fluids and creat. among patients with AKI

Creat	IV fluids (mL/h)	r	P-value
(mg/dL)	141.82 ± 49.76	-0.684	0.020

VI- Length of stay in ICU

Our results showed that AKI has no significant impact on length of stay in ICU (5 days in AKI group vs days in non-AKI group, p-value 0.655). (Table 32)

Table (32): Relation between AKI and LOS in ICU

		AKI (n=12)	Non-AKI (n=38)
Length of stay (days)	Median	5	7
	Range	4-21	3-25
P-value	0.655		

VII-) Outcome

Our results showed that AKI had a significant impact on mortality as (58.3% of patients died in AKI group Vs.7.9% of patients in non-AKI group, P-value=0.000). (Table 33)

Table (33): Effect of AKI on mortality

		AKI (n=12)	Non-AKI (n=38)
Yes	Number	7	3
	% within outcome	58.3%	7.9%
No	Number	5	35
	% within outcome	41.7%	92.1%
P-value	0.000		

4. Discussion

Rhabdomyolysis is a clinical entity characterized by the destruction of skeletal muscle with resultant release of intracellular enzymatic content into the bloodstream that leads to systemic complications, marked elevation of serum creatine kinase (CK) five to ten times above the upper limit of normal serum levels is characteristic of rhabdomyolysis.

The term “crush syndrome” is usually used to describe muscle destruction after direct trauma, injury, or compression.

Acute kidney injury (AKI) is the most common systemic complication of rhabdomyolysis. It occurs at an incidence ranging between 10 and 55 % and is associated with a poor outcome, particularly in the presence of multiple organ failure.

Therefore, preservation of renal function with intravenous (IV) fluid therapy remains the cornerstone of rhabdomyolysis treatment.

Our study was a Prospective chort study conducted on 50 patients admitted to I.C.U at EL-HELAL trauma Centre and Ain Shams University hospital during the period from May 2018 to August 2019; all the studied populations were diagnosed to had multiple trauma.

In addition, all patients were followed-up for the first three days of admission.

The aim of our study is to detect the incidence of rhabdomyolysis among the polytrauma patients, to detect the effect of rhabdomyolysis on developing acute kidney injury (AKI), to detect the effect of rhabdomyolysis on mortality and it's effect on the duration of stay in intensive care unit (ICU), additional

to that heighlighting main lines of therapy in rhabdomyolysis and its complications.

We compared between variables in two groups according to the presence or absence of acute kidney injury (AkI)

Ø Group I: AkI (n=12)

Ø Group II: non AkI (n=38)

I-Demographic data

1-Age

Our study revealed that age of our patient population had no significant effect on developing AKI (35.88 in AKI group vs 32.4 in Non-AKI group).

Our data were in concordance with data collected by **Sara Ramtinfar et al. 2014** and revealed that there was no significant impact of age on developing AKI (mean age was 36 years in AKI group vs 32 years in Non-AKI group).

On the contrary data collected by **Mikael Eriksson et al. 2015** revealed highly significant effect of age on developing AKI (median age was 36 years in non-AKI group vs 54 years in AKI group.

2-Gender

Our study showed that there was no significant impact of gender on developing AKI as males represented 100% of patients who developed AKI were males vs 84.2% of patients who didn't develop AKI.

Our data were in agreement with data collected by **Sara Ramtinfar et al. 2014** who revealed that there was no significant impact of gender on developing AKI as males represented 95.2% of patients in AKI group vs 93.5% in non-AKI group, p-value 0.617.

On the contrary data collected by **Mikael Eriksson et al. 2015** showed significant effect of gender on developing AKI as males represented 75.2 % of patients in AKI group vs 86.4% in non-AKI group, p-value 0.17).

II-Acute physiology and chronic health evaluation II (APACHE II)

Our patient population had a highly significant difference between both groups regarding APACHE II (median APACHE II score 14 in day 1, 13 in day 2 and 15 in day 3in group I Vs 6 in day 1, 4 in day 2 and 3 in day 3 in group II, P-value < 0.002 in day 1, 0.000 in day 2 and 0.002 in day 3).

Our data were in concordance with data collected by **Luis Alberto et al. 2014** found that APACHE II had a significant impact on AKI in ICU as The APACHE-II of the patients who developed AKI was higher than those of the non-AKI (20 for AKI vs. 15.4 for non-AKI) with a statistically significant difference (P-value = 0.000).

Also, **William L. Macias et al. 2011** who evaluated 547 patients, 127 (23.2%) of whom developed AKI. Patients who developed AKI, had higher APACHE II score (24.8 in AKI group versus 22.0 in No-AKI group; P = 0.0002),

On the contrary, a study performed by **Sara Ramtinfar et al. 2016** showed that APACHE II score has no significant effect on AKI (14.9 in AKI group vs 13.8 in no-AKI group, p value, 0.317)

III-Injury severity score (ISS)

Similarly, our study showed highly significant difference between both groups regarding ISS; patients who developed AKI had higher ISS than those who didn't develop, (40.33 in AKI group vs 25.34 in Non-AKI group)

Our data were in concordance with data collected by **Mikael Eriksson et al. 2013** found that ISS has highly significant impact on AKI, as the ISS in patients with AKI was higher than in patients without AKI (29 in AKI group and 24 in No-AKI group).

Also study done by **Wei-Hung Lai 2016** showed significant impact of ISS on developing AKI within range 16-24 (19.2 in AKI group vs 11.1 in non-AKI group) and when ISS >25 it had highly significant impact on developing AKI (29.5 in AKI group vs 4.9 in non-AKI group).

On the other hand, Study done by **D.L. Skinner et al. 2013** showed non significant correlation between AKI and ISS as median ISS was 22 in non-AKI group vs 25 in AKI group, p-value 0.665.

Also data collected by **John P. et al. 2015** showed non significant difference between patients with AKI and patients without AKI regarding ISS (25 in AKI group vs 22 in non-AKI group, p-value 0.17).

IV-Laboratory data

1-Creatine kinase (CK)

Our study revealed a significant impact of creatine kinase on developing AKI in as patients with AKI had CK levels more than those without AKI (median CK 2468.5 U/L, 4344 U/L and 3661.5 U/L for D1, D2 and D3 respectively in AKI group vs 783 U/L, 1489 U/L and 733.5 U/L in non-AKI group, p-value 0.013, 0.000 and 0.000 for D1, D2, and D3 respectively).

Our data were in concordance with the data collected by **Arulselvi Subramanian et al. 2013** and showed higher CK levels in patients with AKI than those without AKI (median CK 620 U/L, 1360 U/L and 1280.5 U/L for D1, D3 and D5 respectively in AKI group vs 287.5 U/L, 636.5 U/L and 416 U/L in non-AKI group, p-value 0.00, 0.006 and 0.03 for D1, D3, and D5 respectively).

We also calculated the cutoff values of serum CK for development of AKI on the D1, D2 and D3 by ROC analysis which came out to be ≥1385 IU/L, ≥3114 IU/L, and ≥1723 IU/L, respectively.

The sensitivity in D1 was 91% and 100% in D2 and D3. The specificity of serum CK on the 1st, 3rd, and 5th days was 60.5%, 89.47%, and 84.21%

respectively. So, trauma patients with serum CK values above these cutoffs are more liable to develop AKI.

These data were in agreement with data collected by **Arulselvi Subramanianand et al. 2013** revealed cutoff values of serum CK for development of renal failure on the 1st, 3rd, and 5th days by ROC analysis which came out to be ≥1320 IU/L, ≥1146 IU/L, and ≥1754 IU/L, respectively, and serum creatinine was also found to be highly correlated with CK. The sensitivity on the 1st, 3rd, and 5th day was 70%, 55.5%, and 75%, respectively. The specificity of serum CK on the 1st, 3rd, and 5th days was 69%, 55.5%, and 71%, respectively. Hence, trauma patients with serum CK values above these cutoffs are more prone to develop renal failure.

2-Renal function tests:

A-BUN

Our study showed a significant difference between both groups in day 1(22 in AKI group vs 16.5 in non-AKI group), in the second and third day there was highly significant difference between both groups (31mg/dL in AKI group vs 15mg/dL in non-AKI group in the second day and 39.5mg/dL in AKI group vs 15mg/dL in non-AKI group in the third day).

Our data were in concordance with data collected by **Wei-Hung Lai et al. 2016** and revealed highly significant relation between AKI and BUN (28.9mg/dL in AKI group vs 15.5 mg/dL in non-AKI group, p-value 0.000).

Also data collected by **Kisoon Ryu et al. 2015** showed highly significant difference between both groups regarding BUN as patients with AKI had higher levels than patients without AKI (14.7mg/dL in non-AKI group vs 32.3mg/dL in AKI group, p-value <0.001.

On the contrary, data collected by **Sang Heon Suh et al. 2013** showed non significant difference between both groups regarding BUN (19.4mg/dL in AKI group vs 19.3 in non-AKI group, p-value 0.696).

Also **Maria Plataki et al. 2011** showed non significant difference between both groups (29mg/dL in AKI group vs 28mg/dL in non-AKI group, p-value 0.32).

B- Serum creatinine

Our study showed that there was non significant difference between both groups regarding creatine levels in the first day (1mg/dL in AKI group vs 0.9mg/dL in non-AKI group, p-value 0.297), but in the second and third day there was highly significant difference between both groups (2.05mg/dL in AKI group vs 0.8 in non-AKI group, p-value 0.000 in the second day and 3.15mg/dL in AKI group vs 0.8mg/dL in non-AKI group, p-value 0.000 in the third day).

Our results are in concordance with data collected by **Wei-Hung Lai et al. 2016** and revealed highly significant difference between both groups, patients with AKI showed higher levels than patients without AKI (2.1mg/dL in AKI group vs 1.1mg/dL in non-AKI group, p-value 0.000).

Also data collected by **Kisoon Ryu et al. 2015** showed highly significant difference between both groups as patients with AKI showed higher levels than patients without AKI (1.59 mg/dL in AKI group vs 2.04 p-value <0.001).

Also **Laura E. White et al. 2013** showed highly significant difference between both groups regarding creat. level as patients with AKI showed higher levels than patients without AKI (0.8mg/dL in non-AKI group vs 1.5mg/dL on non-AKI group, p-value 0.000).

3-Potassium (K^+) level

Our study showed that patients with AKI showed higher levels of K^+ and there was significant difference between both groups in day 1 (4.26mEq/dL in AKI group Vs 3.92mEq/dL in non-AKI group, P-value 0.017) and highly significant difference between both groups in day 2 and day 3 (5.11mEq/dL in AKI group Vs 3.85±0.48mEq/dL in non-AKI group, P-value 0.003) and (4.31±0.67mEq/dL In AKI group Vs 3.64±0.29mEq/dL in non-AKI group, p-value 0.000)

Our results were in concordance with data collected by **Hamid Reza Samimagham et al. 2011** who revealed that patients with AKI had higher K^+ levels than patients without AKI (4.56mEq/dL in AKI group vs 4.12mEq/dL in non-AKI group, p-value 0.002).

On the contrary, data collected by **Laura E. White et al. 2013** showed non significant difference between patients with AKI and those without AKI (4.7mEq/dL in non-AKI group vs 4.1mEq/dL in AKI group, p-value > 0.05).

Further analysis of K^+ levels in our study revealed 50% of patients with AKI developed hyperkalemia during first three days of stay in ICU.

Similarly data collected by **Shahid Behesht et al. 2016** showed 53.2% of patients developed hyperkalemia in first day of admition.

4- Haemoglobin

Our results showed highly significant difference between both groups regarding haemoglobin, day 1 (9.11gm/dL in AKI group vs 11.64gm/dL in non-AKI group, p-value 0.000), day 2 (7.83gm/dL in AKI group vs 10.56 in non-AKI group, p-value 0.000) and day 3 (8.81gm/dL in AKI group vs 10.23gm/dL in non-AKI group, p-value 0.007).

Our results were in agreement with data collected by **Wei-Hung Lai et al. 2016** Showed lower haemoglobin levels in patients with AKI than patients without AKI (12.1gm/dL in AKI group vs13.2gm/dL in non-AKI group, p-value 0.001)

On the contrary data collected by **Laura E. White et al. 2013** showed non significant difference

between both groups regarding haemoglobin (10.2 in AKI group vs 10.0gm/dL in non-AKI group, p-valcentral >0.05).

5-Total leukocytic count

Our results showed non significant difference between both groups as day 1 (4.26/mcL in AKI group vs3.92 in non-AKI group, p-value 0.403), day 2 (5.11/mcL in AKI group vs 3.85/mcL in non-AKI group, p-value 0.688) and day 3 (4.31/mcL in AKI group vs 3.64/mcL in non-AKI group, p-value 0.523).

Our results were in concordance with data collected by **Laura E. White et al. 2013** showed non significant difference between both groups (17.54/mcL in non-AKI group vs 14.7/mcL in AKI group, p-value >0.05).

Also data collected by **Maria Plataki et al. 2011** showed non significant difference between patients with AKI and those without AKI (12.5/mcL in non-AKI group vs 13.9/mcL in AKI group, p-value 0.18).

V-ICU management

1-mechanical ventilation

Our results showed that mechanical ventilation had a highly significant impact on AKI (83.3% in AKI group Vs only 26.3% in non-AKI group were mechanically ventilated. P-value 0.000).

Our results were in concordance with data collected by **Luis Alberto et al. 2015** showed that patients with AKI were more likely to be ventilated than patients without AKI (72% of patients in AKI group were mechanically ventilated vs 42.3% of patients in non-AKI group, p-value 0.000).

Another study done by **Pavan K. Bhatraju et al. 2016** revealed highly significant impact of MV on AKI as (68% of patients in non-AKI group were mechanically ventilated vs 75% in AKI group, p-value <0.01).

Also data collected by **Paulo Roberto Santos et al. 2015** showed significant impact of mechanical ventilation on AKI as 70%of patients in AKI group were mechanically ventilated vs 59.9% of patients in non-AKI group, p-value 0.016.

2- Blood transfusion

Our results showed that blood transfusion has no significant effect on developing AKI (41.7% of patients in AKI group Vs 26.3% in non-AKI group received blood transfusion. P-value 0.312).

On the contrary data collected by **Wei-Hung Lai et al. 2016** showed highly significant difference between patients with AKI and those without AKI regarding blood transfusion as (16.7% in AKI group received blood transfusion vs 3.7% in non-AKI group, p-value 0.000).

Also data collected by **Paulo Roberto Santos et al. 2015** showed highly significant difference between both groups regarding blood transfusion as (78% of patients in AKI group received blood transfusion vs 55% in non-AKI group, p-value 0.001).

3-Vasoactive drugs

Our results revealed that Patients who received Vasopressor medications were at high risk for developing AKI (50% in AKI group Vs only 2.6% in non-AKI group, P-value 0.000)

These results were in concordance with data collected by **Paulo Roberto et al. 2015** revealed highly significant impact of Vasopressor medications on developing AKI as (19.2% of patients in non-AKI group vs 40.2% of patients in AKI group received Vasopressor medications, p-value 0.000).

On the contrary data collected by **Luis Alberto 2015** revealed non significant relation between AKI and Vasopressor medications as (10% of patients in AKI group vs 9.6% of patients in non-AKI group received Vasopressor medications, p-value 0.940).

VI-Length of stay in ICU (LOS)

Our results showed that AKI has no significant impact on length of stay in ICU (5 days in AKI group vs 7 days in non-AKI group, p-value 0.655).

Our results were in concordance with data collected by **Kisoon Ryu et al. 2015** and revealed non significant difference between both groups regarding LOS in ICU as (9 days in AKI group vs 8.5 days in non-AKI group, p-value 0.752).

Also data collected by **Maria Plataki et al. 2011** showed non significant difference between both groups regarding LOS in ICU as (3 days in AKI group vs 4 days in non-AKI group, p-value 0.34).

On the contrary data collected by **Paulo Roberto Santo 2015** showed patients with AKI had longer duration of stay in ICU than those without AKI (7.4 days in non-AKI group vs 9.2 days in AKI group, p-value 0.021).

Also data collected by **John P. Reilly 2015** showed highly significant impact of AKI on LOS in ICU as (20 days in AKI group vs 7 days in non-AKI group, p-value 0.001).

VII- outcome

A. Acute kidney injury

Our results showed that 12 patients out of 50 (24%) developed AkI, (41.7%) of them were in risk stage, (8.3%) were in the injury stage and (50%) were in the failure stage.

Our results were in concordance with data collected by **Mikael Eriksson et al. 2013** and revealed that 24.9% of patients developed AKI. Stages 1, 2, and 3 according to the KDIGO definition developed in 59%, 13%, and 28% respectively.

On the contrary data collected by **Arulselvi Subramanianand et al. 2013** and revealed that only 9.3% developed acute renal failure. In this study acute renal failure was defined as creatine level >2mg/dL.

B. Mortality

Our results showed that AKI had a significant effect on the mortality as 7 patients (58.3%) died in AKI group vs 3 patients (7.9%) in non- AKI group p-value=0.000).

Our results were in concordance with data collected by **Paulo Roberto Santo 2015** showed 71.7 % of patients in AKI group died vs only 14.4% of patients in non-AKI group, p-value 0.000).

Conclusion

Patients who suffer from severe traumatic injuries are prone to develop rhabdomyolysis and acute renal injury. The serum level of CK is a good prognostic indicator for renal outcome in rhabdomyolysis following a crush injury and correlates well with most biochemical parameters. Hence, screening via biomarkers such as serum CK is required.

Incidence of rhabdomyolysis in our study was 65% and incidence of AKI 24%. The cut off values of serum CK on the 1st, 2nd, and 3d days were >1385 U/L IU/L, >3114 U/L, and >1723 U/L, respectively.

Recommendation

Evaluating for serum CK in posttraumatic patients can help in early detection of AKI and improvement in prognosis.

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