

UNIVERSITY OF ZAMBIA

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**The incidence and outcome of rhabdomyolysis among
musculoskeletal trauma patients at the University
Teaching Hospital, Lusaka**

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DECLARATION

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ABSTRACT

Introduction: Rhabdomyolysis is a frequent occurrence among trauma patients, with studies reporting an incidence of as high as 85% (Heurta-Aladin et al. 2004). Other studies however reported an incidence of as low as 6.7 % (Lawrence 2004). The incidence of Acute Kidney Injury (AKI) most studies is about 10 % (Carlos 2004; Ashish 2009, Essam 2010). The syndrome is mostly asymptomatic. Diagnosis is made by measuring creatinine kinase levels in the blood (Huerta-Alardin et al, 2004).

Objectives: To determine the incidence and outcome of rhabdomyolysis among trauma patients at UTH.

Methods: This was an observational prospective study, conducted in the male and female surgical wards at the University Teaching Hospital. There were a total of 151 trauma patients enrolled. The pattern and extent of injury was recorded and compared to the primary outcome, rhabdomyolysis, which was estimated by measuring the level of serum creatinine kinase. Serum creatine was used as a measure of kidney function.

Results: 81.5% of the patients were male and 18.5% were female. The age range was from 19yrs to 75yrs, with a mean age of 34.7years. Motor vehicle accidents accounted for 66.9% of the trauma cases with majority of the injuries occurring in the lower limbs. Rhabdomyolysis was present in 35% of the patients and acute kidney injury in 6%. Rhabdomyolysis was associated with risk of developing renal failure.

Conclusion: The incidence of rhabdomyolysis in trauma patients at UTH is 33.6% while that of renal failure was 6%. The greater the injury severity score, the higher the chance of developing rhabdomyolysis and renal failure. With early treatment, trauma induced rhabdomyolysis and renal failure lead to complete recovery.

DEDICATION

To my wife Bwembya, this is an indirect work of your patience and support during all those hours I spent working on this dissertation. Thank you very much for understanding and according me a chance to have it completed in its best form.

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ABBREVIATIONS

AKI	Acute Kidney Injury
CK	Creatinine Kinase
ICU	Intensive Care Unit
MESS	Mangled Extremity Severity Score
RTA	Road Traffic Accident
USA	United States of America
UTH	University Teaching Hospital

CHARTER ONE

1.1. INTRODUCTION

By definition, rhabdomyolysis is a syndrome that results from the breakdown of skeletal muscle (Bosch et al, 2009). This results in the leakage of cellular contents into the circulation. With muscle injury, large quantities of potassium, phosphate, myoglobin, creatinine kinase (CK) and urate leak into the circulation. The circulating myoglobin is filtered by the kidneys, where it can precipitate and cause renal tubular obstruction, causing kidney injury (Bosch et al, 2009).

Muscle bulk makes up approximately 40% of total body mass. A force large enough to cause a fracture in a limb always leads to crushing of muscles and other soft tissues (Ashish et al, 2009).

Clinical features can range from asymptomatic, to the most serious complication being acute kidney injury (AKI). Early diagnosis of rhabdomyolysis and intervention are important to prevent AKI.

It's a potentially lethal condition and as such, it must be suspected in all patients with a history of circumstances that can lead to muscle damage. Patients who develop rhabdomyolysis induced AKI have a mortality rate of approximately 20% (Huerta-Alardin et al, 2004).

Many cases of rhabdomyolysis are subclinical and are only detected by elevated CK enzyme levels. The rise in serum CK is preceded by a rise in serum myoglobin. Myoglobinuria occurs when the levels of myoglobin in urine exceeds 250micrograms per ml, well above the normal limit of 5 nanogrames per ml (Thompson, 2002). The half-life of myoglobin is short, 2 to 3 hours, and is cleared from the blood within 6 to 8 hours by renal filtration (Sahjian and Frakes, 2007).

CK on the other hand, has a half-life of 1.5days and so remains longer in serum. It is a more sensitive test for rhabdomyolysis than myoglobin (Sahjian and Frakes, 2007). Levels rise within 12hours of onset of muscle injury, peak in 1-3 days, and declines

from 3 – 5 days. Normal values of CK is 45 – 260U/l. levels above 5000U/l where associated with renal failure (Huerta-Alardin, 2004).

The causes of rhabdomyolysis are diverse. The most common are direct muscle injury (Thompson, 2002), alcohol abuse, muscle overexertion, muscle compression, and the use of certain medications or illicit drugs (Sauret, 2002).

The Mangled Extremity Severity Score (MESS) is a good indicator of the extent to which a muscle is crushed, and it has been shown that there is a correlation between the extent of injury and probability of developing rhabdomyolysis (Ashish et al, 2009).

The MESS estimates the limb viability and is a predictor of likelihood of limb amputation after trauma. It is based on four clinical criteria; skeletal and soft-tissue injury, ischemia, shock, and age. Each parameter is assigned a score according to severity and how old an individual is (the older an individual is, the higher the score). A summation or total score of the individual parameters is the patient's total MESS. The criteria is as shown below

Table 1: **Mangled Extremity Severity Score**

FACTOR	SCORE
Skeletal/soft-tissue injury	
• Low energy (stab, fracture, civilian gunshot wound)	1
• Medium energy (open or multiple fracture)	2
• High energy (shotgun or military gunshot wound, crush)	3
• Very high energy (above plus gross contamination)	4
Limb ischemia	
• Pulse reduced or absent but perfusion normal	1
• Pulseless, diminished capillary refill	2
• Patient is cool, paralyzed, insensate, numb	3
Shock	
• Systolic blood pressure always >90 mm Hg	0
• Systolic blood pressure transiently <90 mm Hg*	1
• Systolic blood pressure persistently <90 mm Hg	2
Age, yr.	
• <30	0
• 30-50	1
• >50	2

*transient blood pressure refers to a systolic blood pressure which improves to above 90mmHg after fluid resuscitation

The clinical syndrome of rhabdomyolysis comprises acute muscle necrosis with swollen and tender muscle, and associated limb weakness. This may be accompanied by the voiding of dark, tea coloured- urine indicating myoglobinuria (increased urinary excretion of myoglobin) which is the most significant consequence of muscle breakdown.

Earliest cases on record of rhabdomyolysis can be found in the bible, in the book of numbers, where it is reported that the Israelites during the exodus, became ill and died after eating quail thought to have consumed hemlock seeds. Epidemics of rhabdomyolysis, reported in the Balkans, in the 1930s, are thought to have been due to

eating contaminated fish. Interest in rhabdomyolysis was stimulated in 1941 by Beall and Bywaters, when they studied patients with crush injuries with acute myoglobinuric renal failure in the London bombings during the Second World War (Yiannis 2008).

Principle of treatment of rhabdomyolysis is the prevention of the progression to AKI by aggressive administration of intravenous fluid. Up to 10L of fluid per day maybe needed with addition of 100mmol of sodium bicarbonate to each liter of fluid to alkalinize the urine. This intervention is theoretically aimed at preventing precipitation of myoglobin in the renal tubules as some studies have shown that alkalization of urine does not have any proven efficacy (Meijer, 2003; Carlos, 2004). Once renal failure is established, dialysis is the only reliable therapeutic modality (Vanholder, 2002).

The incidence of rhabdomyolysis in trauma at UTH is not documented. The serum levels of CK are not routinely measured. From the admission records in the surgical admission wards over the past 12months, no patient was admitted nor treated for trauma induced rhabdomyolysis.

In the management of the acutely injured patient, fluids resuscitation is one of the main interventions; which medical staff at UTH surgical departmentis good at. Therefore, prompt administration of intravenous fluids may account for the fact that myoglobinuric AKI is not seen in trauma patients admitted at UTH. In treating the haemorrhagic shock which accompanies trauma, the fluid resuscitation serves to prevent myoglobin from accumulating into the renal tubules thus preventing AKI.

1.2. LITERATURE REVIEW

1.2.1 Rhabdomyolysis and AKI in Trauma patients

A number of studies show that rhabdomyolysis is common among trauma patients, and that the incidence of AKI disease is high among these patients.

Ashish et al. (2009) in a prospective study involving 55 patients in India reported that 80% of musculoskeletal trauma was as a result of road traffic accidents. 9.1% of these developed AKI.

Two other studies reported a higher incidence of rhabdomyolysis among trauma patients. Heurta-Aladin et al. (2004) and Poznanovic (2007) found that 85% and 96.3% of trauma patients had rhabdomyolysis and elevated CK respectively. The incidence of AKI was 10 and 7.4% respectively.

In another prospective study conducted in Rome, Italy, 153 trauma patients consecutively admitted to the general Intensive Care Unit (ICU) were enrolled from December 1991 to May 1994. Incidence of rhabdomyolysis was 43% (Vivino, M. and Antonelli, M. (1998).

Essam and Robert, F. (2010) in a review article reported that 7% of cases of AKI in the United States were as a result of rhabdomyolysis.

Carlos et al. (2004) reported an 85% incidence of rhabdomyolysis in trauma patients. They reviewed medical records of 2,083 trauma patients admitted to surgical ICU of Los Angeles County Medical center, in the United States between January 2007 and September 2002. The overall incidence of AKI was 10%. Overall mortality was 16% and 39% deaths in the group with AKI.

Bocsh et al. (2009) in a review article reported a varying incidence of acute kidney injury among rhabdomyolysis patients (13 – 50%).

Melli et al (2005), which found an incidence of AKI of 46% among 475 hospitalized patients with rhabdomyolysis in Baltimore, USA.

In contrast, a few studies have shown that rhabdomyolysis is an infrequent occurrence among trauma patients.

Lawrence (2003) reported an incidence of 6.7% among 154 patients with musculoskeletal trauma.

Siagan, M. and Frakes, M. (2007) reported the incidence of rhabdomyolysis secondary to trauma being 0.1 per 10 000 population.

1.2.2 Rhabdomyolysis in Non Trauma patients

The other causes of rhabdomyolysis listed in different studies include ischaemia, polymyositis, drug overdose, seizures, burns, sepsis and viral illnesses (Craig 2008).

Vigorous exercise has also been reported as a cause of rhabdomyolysis (Boland et al. 2009).

Few studies or none at all have looked at rhabdomyolysis in Africa including Zambia. The only study was in South Africa that looked at mob justice victims which found 98% of rhabdomyolysis and 11% of AKI (Wood and Rosadale, 2012).

Therefore, there was need to do a study to determine the incidence of rhabdomyolysis in trauma patients at UTH.

1.3. STATEMENT OF THE PROBLEM

1.4. JUSTIFICATION OF THE STUDY

Admission records in the surgical admission wards indicate that trauma accounts for 66%. A number of studies have reported high incidences of rhabdomyolysis and AKI among trauma patients.

Unfortunately, the incidence of rhabdomyolysis in trauma patients has not been studied in Zambia including UTH, and as such it is not considered as part of work up in trauma patients; therefore, its contribution to mortality and morbidity in trauma is unknown.

of all admissions. Literature has shown that the incidence of rhabdomyolysis in trauma to be as high as 85% in some studies and as low as 6.7%. Left untreated, rhabdomyolysis can lead to AKI.

There is, therefore, every need to know the incidence of rhabdomyolysis and AKI in trauma patients at UTH.

Findings of this study will serve to fill this information gap, and most likely influence the way trauma is managed and possibly lower the mortality rate.

1.5. HYPOTHESIS

The incidence of rhabdomyolysis is more than 50% among patients admitted with trauma at UTH.

CHAPTER TWO

2.1. GENERAL OBJECTIVE

To determine the incidence, severity and outcomes of rhabdomyolysis among trauma patients at UTH.

2.2. SPECIFIC OBJECTIVES

- To grade the severity of injuries using the MESS in patients admitted for trauma at UTH.
- To measure the levels of creatinine kinase in trauma patients at UTH.
- To measure the kidney function in trauma patients at UTH.
- To determine the course of rhabdomyolysis.

CHAPTER THREE

3.1. METHODOLOGY

The study was an observational prospective clinical cohort study conducted at UTH department of surgery, Lusaka, conducted from February 2014 to January 2015. All patients with musculoskeletal trauma were considered for enrolment into the study. Only those that met the inclusion criteria were recruited. A total of 151 patients were recruited. The study did not interfere with the management of trauma patients.

At enrolment, the patients' demographics, severity of injury, blood pressure, mechanism of injury, serum creatinine and creatinine kinase levels were entered onto a data collection sheet. The MESS was calculated for each patient. CK and serum creatinine levels were repeated on day 3 and on day 5 for all patients. For those with normal values of CK and creatinine kinase, day 5 was the end of the follow up period.

3.2. INCLUSION CRITERIA

- All patients presenting with musculo-skeletal trauma with a Mangled Extremity Severity Score (MESS) of 2 and above.

3.3. CASE DEFINITION

- **Rhabdomyolysis**

Serum creatinine kinase levels of 1000 IU and above (Heurta-Aladin et al (2004).

- **Acute kidney Injury**

Serum creatine of 160 μ mol/L (raise in creatinine from upper limit of 110 μ mol/L as defined by RIFLE classification)

3.4. EXCLUSION CRITERIA

- MESS < 2
- Those that refuse to consent.

3.5. VARIABLE DESCRIPTIONS

- **Dependent variables**
Primary outcome: Rhabdomyolysis
Secondary outcome: Acute kidney injury
- **Independent variables**
 - age
 - sex
 - MESS
 - Mechanism of trauma
 - Pattern of injury
 - Blood pressure at admission.

3.6. SAMPLE SIZE

All patients fitting the inclusion criteria were enrolled until desired sample size (150) was reached.

An estimated prevalence of 50% of rhabdomyolysis was used to calculate the sample size as follows:

$$n = \frac{Z^2 \times P(1 - P)}{m^2}$$

n – Required sample size

Z – 1.96 at 95% confidence level

p – Estimated prevalence (50%)

m – 8%

n – 150.

3.7. DATA ANALYSIS

Epi info 7 was used to analyze the data collected for analysis. Results were presented in form of Frequency tables and graphs. Chi square was used to test for associations for categorical variables and t-test was used for continuous variables where p value of < 0.05 was considered statistically significant. Univariate logistic regression was used to determine factors associated with rhabdomyolysis and AKI and multivariate logistic regression to adjust for confounders at confidence level of 95% (p value =0.05).

3.8. ETHICAL CONSIDERATIONS

Ethical clearance was obtained from the University of Zambia Biomedical Research Ethics Committee (**UNZABREC**). Permission to conduct this research was obtained from the Head, Clinical Care at UTH.

This was an observational study and as such we did not interfere with the current management of patients with musculoskeletal trauma. Participation in this study was by informed consent. Patient information was kept confidential. No patient identifying markers were used on the data collecting sheet.

CHAPTER FOUR

RESULTS

4.1. Baseline demographic and lab data.

Table 2: Table showing Baseline demographic and lab data.

Variable	Value
Mean Age in yrs. (range)	34.6(19 – 75)
Male sex (%)	123 (81)
Creatinine in $\mu\text{mol/l}$ (%)	
• 120 – 160	13(8.6)
• 160 – 250	9(6)
• >250	0(0)
MESS	
Mean	3.4
• 2 – 4(%)	119(78.8)
• 5 – 7(%)	28(18.5)
• >7(%)	4(2.6)
Creatinine Kinase(%)	
• 500	71(47.0)
• 501 – 1000	29(19.2)
• >1000	45(33.8)
Systolic BP in mmHg (%)	
1. <90	39(25.8%)
2. \geq 90	112(74.2%)

151 patients were enrolled in this study with a male predominance of 123 (81.5%) and a mean age of 34.6 (19-75). 134 (88.7%) of patients were between the ages of 15 and 45 years age. 9(6%) had serum creatinine above $160\mu\text{mol/L}$. The mean MESS was 3.4 with the majority of patients having a MESS score of ≤ 4 (78.8%). 45(33.8%) of patients had CK levels above 1000U/L . The proportion of patients presenting with systolic blood pressure $\leq 90\text{mmHg}$ was 25.8%.

4.2. Mechanism and Pattern of Injury

Table 3: Table showing mechanism of injury

Incident Causing Injury	n (%)	MESS		
		(2-4)	(5-7)	(>7)
ASSAULT	17(11.26)	15	2	0
Bp<90	2	2	0	0
Bp>90	15	13	0	0
FALL	25(16.56)	25	0	0
Bp<90	0	0	0	0
Bp>90	25	25	0	0
INDUSTRIAL ACCIDENTS	8(5.3)	8	0	0
Bp<90	1	1	0	0
Bp>90	7	7	0	0
RTA	101(66.89)	71	26	4
Bp<90	36(35.6)	21	12	3
Bp>90	65	50	14	1

101(66.89%) of the trauma cases were due to RTA, 25(16.56%) falls, and 8(5.3%) industrial accidents. 36 of the 39 patients with hypovolaemia (92.3%) were RTA victims. Of the 32 patients with a MESS above 4, 30(88.2%) were also RTA victims and 2(11.8%) were assault group. All patients with falls and industrial accidents had a MESS of 4 or less. All four patients who had a MESS ≥ 7 , were RTA victims, had crush injuries and three (75%) of these had hypovolemic shock.

Table 4: Table showing the pattern of injuries sustained.

PatternOfInjury	n (%)	MESS		
		2-4	5-7	>7
Crush Injury	4(2.65)	0	0	4
Bp<90	3	0	0	3
Bp>90	1	0	0	1
Femur Fracture	23(15.23)	18	5	0
Bp<90	6	1	5	0
Bp>90	17	17	0	0
Forearm Fracture	20(13.25)	19	1	0
Bp<90	2	1	1	0
Bp>90	18	18	0	0
Humerus Fracture	6(3.97)	5	1	0
Bp<90	6	5	1	0
Bp>90	0	0	0	0
Multiple Fractures	22(14.57)	12	10	0
Bp<90	7	2	5	0
Bp>90	15	10	5	0
Soft Tissue Injury	29(19.21)	25	4	0
Bp<90	5	5	0	0
Bp>90	24	20	4	0
Tibia Fracture	47(31.13)	40	7	0
Bp<90	10	10	0	0
Bp>90	37	30	7	0

Figure 1: Scatter graph showing the relationship between ck and MESS

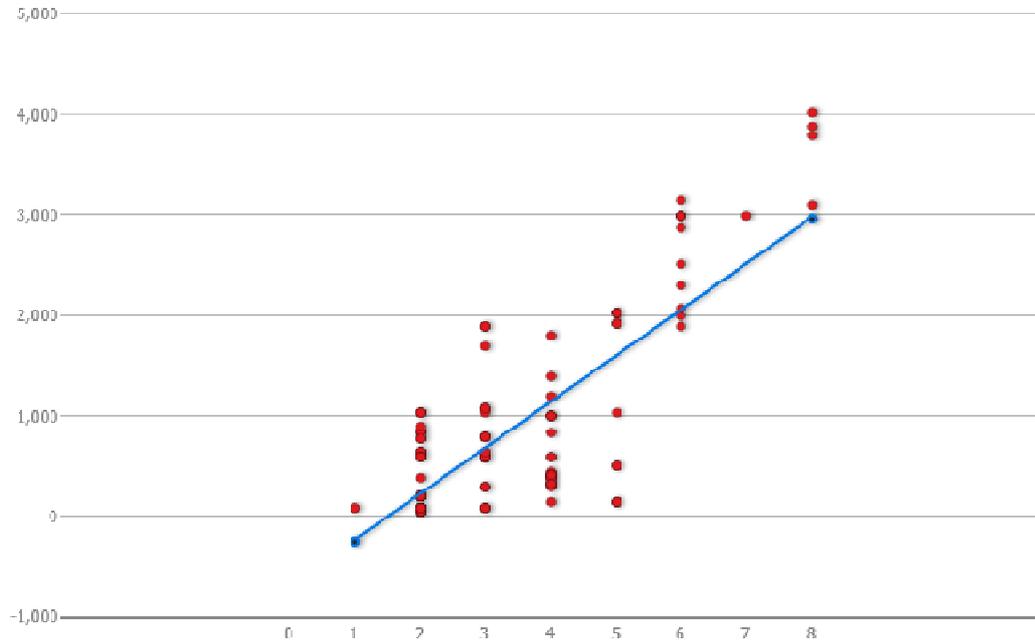


Figure 1 shows a scatter graph of MESS plotted against CK. It shows a positive linear relationship between MESS and CK levels, the higher the MESS the higher the degree of rhabdomyolysis. A linear regression analysis showed a significant correlation ($p < 0.0001$).

4.3. Logistic regression model for determinants of rhabdomyolysis

Table 5.

Term	Odds Ratio	95% C.I.	P-Value
Fall	0.2657	0.0698 – 0.9439	0.0407
Industrial Accidents	0.0779	0.0077 – 0.7921	0.0310
RTA	0.2768	0.0943 – 0.8126	0.2324
MESS	11.2640	4.1714 – 30.4159	<0.0001
Femur Fracture	0.2618	0.0600 – 0.9123	0.9973
Forearm Fracture	0.0081	0.0200 – 0.0421	0.9904
Humerus Fracture	0.0004	0.0000 - 1.012	0.9844
Multiple Fractures	0.0001	0.0020 - 1.012	0.9813
Crush Injury	0.0822	0.1000 - 1.120	0.9950
Tibia Fracture	0.0040	0.0040 - 1.012	0.9890

The MESS and not the mechanism of injury and pattern of injury were associated with developing rhabdomyolysis, with a p value of < 0.0001.

4.4. Logistic regression model for determinants of developing acute kidney injury

Table 4.

Term	OR	95% CI	P value
Fall	17.0492	0.1217 – 238.5909	0.2607
Industrial Accidents	0.0000	0.0000 - 1.0912	0.9716
RTA	8.8570	0.1337 – 586.8723	0.3080
Femur Fracture	0.1095	0.0024 – 4.9663	0.2558
Forearm Fracture	0.9135	0.0094 – 88.4269	0.9690
Humerus Fracture	1.1183	0.0111 – 112.9464	0.9621
Multiple Fractures	1.2315	0.0167 – 91.0749	0.9244
Crush Injury	0.0441	0.0003 – 5.5921	0.2065
Tibia Fracture	0.1795	0.0020 – 16.0078	0.4535
Rhabdomyolysis	7.0745	1.416 – 60.0707	0.0182
Sex	0.6537	0.0483 – 8.8532	0.7492
Shock	12.061	2.373 – 60.946	0.0026

The factors associated with acute kidney injury were rhabdomyolysis and shock, with p values of 0.0182 and 0.0026 respectively.

4.5. Trend upon follow up

For patients with rhabdomyolysis and AKI, further blood samples were taken on day 3 and on day 5. In all affected cases, there was a reduction in the values of CK and serum creatinine. This showed that there was complete resolution for both rhabdomyolysis and AKI.

CHAPTER 5

DISCUSSION.

5.1. Descriptive Data

We enrolled 151 patients in this study the majority of which were males (81.5%) with a mean age of 34.6 ± 12.1 (see Table 2). 88.7% of the affected participants were between 15 and 45 years old; the most productive age group. Motor vehicle accidents accounted for 66.9% of all causes of injury.

This is in keeping with most studies from around the world which show that trauma is common in the young male population. Gomes et al (2010) reported 67% of trauma being as a result of road traffic accidents with predominance of males (80%) and a median age of 37. Vivino et al (1998) reported a male predominance of 79.7% and a mean age of 37.6 ± 19.6 . Ashish et al (2009) also reported 80% of trauma to be as a result of road traffic accidents, with a mean age of the participants being 37.4 year while Carlos et al reported an incidence of males (81%), with a mean age of 37 ± 17 . Therefore, our study only confirms the findings of other studies.

5.2. Mechanism and extent of injury

Fractures occurred more frequently in the lower limbs, a combined total of 46.5 % (tibia 31.3%, femur 15.2%), than in the upper limbs 17.22 % (Humerus 3.97%, forearm 13.25%). These findings are similar to what was reported by Douglas and Lawrence (1996), though they did not report the actual figures at which these injuries occurred.

The Mangled Extremity Severity Score was used as a measure of the extent of injury. Though this score is used as a predictor of limb salvage (Douglas and Lawrence, 1996), Ashish et al (2009) reported that it is also a good predictor of rhabdomyolysis, with a value of ≤ 7 being 100% predictive of limb salvage. The Mean MESS score in this study was 3.4 ± 1.5 , ranging from 2 to 8. As reported by Ashish et al (2009), we also found that the MESS had a positive linear relationship with levels of creatinine kinase. This

relationship is shown in figure 1, and the association was strong ($P < 0.0001$). Therefore, patients with $\text{MESS} \geq 7$ are more likely to develop rhabdomyolysis. Fortunately, in this study only 4 patients had a $\text{MESS} \geq 7$

5.3. Blood pressure.

Systolic blood pressure was measured on admission. Values $\leq 90\text{mmHg}$ were considered as hypovolaemic shock. 39 patients (25.83%) presented in hypovolaemic shock. This was higher than that reported by Ashish (2009), who reported an incidence of 18.2%. We could not account for these different figures, but we might speculate that we found a higher incidence of hypovolaemia because there is no pre hospital resuscitation in patients presenting to our surgical department; although this was not mentioned as an intervention by Ashish.

Of the 39 patients with hypovolaemia, 36 were as a result of road traffic accidents. Of the four patients with $\text{MESS} > 7$, 75% of these had hypovolaemia. The fact that RTA was associated with hypovolemia and a severe MESS, it is important that clinicians pay attention to RTA victims that present with severe MESS as they more likely to be in shock which may compound the problem of rhabdomyolysis.

5.4. Biochemical markers

5.4.1. Creatinine kinase

For this cohort, the case definition of rhabdomyolysis was CK level $\geq 1000\text{u/l}$. The incidence of rhabdomyolysis was 33.8%. This is in contrast to other studies which reported a higher incidence of rhabdomyolysis. This was mainly attributed to the differences in study populations and methodologies. These studies target population was from patients admitted to the intensive care units, while we recruited patients from the general admission wards. It can be inferred that they had a population of more severely injured patients. Vivino et al (1998) reported an incidence of 43% in his study, while Carlos et al (2004) and showed even higher incidence of 85%.

One study conducted outside the ICU setting by Ashish et al (1998) found an incidence of rhabdomyolysis of 85%. Like in our study, they used the MESS to measure the

severity of injury. The mean MESS in this study was 8.20, much higher than that of our study 3.4. There is however consistency with our findings which showed a linear relationship between the MESS and CK.

5.4.2. Serum creatinine

It was observed that despite the differences in the reported frequencies of rhabdomyolysis, the reported incidence of AKI was around 10%. (Ashish 2009; Carlos 2004). In this study, the incidence of AKI was 6%. Other studies reported a higher incidence of AKI. Vivino et al (1998) found an incidence of 31%, and Meijer et al (2003) found an incidence of 65%. These studies were conducted in the ICU on patients with a higher trauma score than ours and also other co morbidities like septic shock, requiring vasopressor support (Meijer 2003). This could explain why they had a higher incidence of AKI. MODS could also have been a contributing factor.

5.5. Relationship between Rhabdomyolysis and AKI.

Literature has shown that there is an association between Rhabdomyolysis and AKI (Vivino 1998; Carlos 2004; Heurta-Aladin 2004). Our findings were consistent with these observations. Of the 9 patients who developed AKI, seven (78%) had rhabdomyolysis. This was statistically significant. ($p=0.00031$). Patients with higher MESS were associated with higher rhabdomyolysis; it is thus patients with severe MESS should be screened for AKI and rhabdomyolysis as evidenced in this study.

CHAPTER SIX

6.1. Conclusion

1. Road traffic accidents account for the majority of patients seen with musculoskeletal trauma. Males in the reproductive age group are affected more than females. The MESS score was found to be a good indicator of the extent to which muscle is injured. The average mess score was 3.4.
2. Serum creatinine kinase levels are elevated in a predictable manner in trauma patients. There is a positive linear relationship between CK levels and MESS. The incidence of rhabdomyolysis was 33.6%.
3. The incidence of acute kidney injury was at 6%, and 78% of the cases were associated with rhabdomyolysis. This consistent with other studies
4. Although rhabdomyolysis is frequent amongst musculo-skeletal trauma patients, with prompt and adequate treatment, there is complete resolution.

6.2. Limitations

Written consent from the participants or their next of kin was needed in order for one to be enrolled in the study. This was not possible for a number of patients not in a position to consent on account of severity of their injuries. Most of these arrive at the hospital from the scene of accidents without any relations. The mortalities which occurred from trauma during the study period occurred in this cohort of patients. This is a limitation to this study as we were unable to investigate to what extent the MESS and AKI contributed to mortality.

6.3. Recommendations

From the findings in this study, we made the following recommendations

1. Measurement of serum Creatinine kinase levels should be made as part of the standard care of severe trauma patients or severe MESS to identify those with rhabdomyolysis early.
2. More research needs to be conducted to investigate the effect of rhabdomyolysis mortalities resulting from trauma, and also research is needed to investigate the long term effects of rhabdomyolysis on the rate of healing of fractures.
3. Prehospital resuscitation measures need to be instituted. A rapid response team trained evaluation and resuscitation of injured patients, especially the RTA victims with shock and severe MESS, needs to be set up as a matter of urgency.

REFERENCES

- Ashish, P. Bobby, J. Basant, P. Shalinder, S. (2009). Renal profile in patients with orthopedic trauma: A prospective study, *Acta Orthop. Belg.*75: 528-532.
- Boland, M. Heck, C. (2009). Acute exercise induced bilateral thigh compartment syndrome, *Orthop.* 32(3):218.
- Bosch, X. Esteban, P. and Josep, M. (2009). Rhabdomyolysis and Acute Kidney Injury, *N Engl J Med.* 361:62-72.
- Carlos, V. Peter, R. Linda, C. Kelly, E. Demetrios, D. George, C. (2004). Preventing Renal Failure in Patients with Rhabdomyolysis: Do Bicarbonate and Mannitol Make a Difference? *J Trauma.*56:1191–1196.
- Craig, S. (2008). Rhabdomyolysis in Emergency Medicine (ONLINE) (Updated 2010) available at <http://www.Medscape.com>. (Accessed Dec 2012)
- Douglas R and Laurence (1996). The Mangled Extremity: When Should It Be Amputated?*J Am Acad Orthop Surg*; 4:182-190
- Essam &Robert, F. (2010). Rhabdomyolysis: a review, with emphasis on the pediatric population, *Pediatr Nephrol* 25:7–18
- Huerta-Alardín, A. Varon, J. Marik, P. (2000). Bench-to-bedside review: Rhabdomyolysis – an overview for clinicians. *Crit Care*, 9:158-169doi:10.1186/cc2978
- Lawrence, B. and Allison, D. (2003) The Other Medical Causes of Rhabdomyolysis.*Am J Med Sci* 326(2):79–88.
- Meijer, A. Fikkers, B. Keijzer, M. Engelen, B. Drenth, J. (2003). Serum creatine kinase as predictor of clinical course in rhabdomyolysis: a 5-year intensive care survey. *Intensive Care Med*, 29:1121–1125
- Melli, G. Chaudhry, V. Cornblath, D. (2005). Rhabdomyolysis: an evaluation of 475 hospitalized patients. *Med. Bal.* 84:377-385.
- Poznanovic, M. (2007). Crush Syndrome in Severe Trauma. *Lijec Vjesn*; 129(5): 142-4
- Sahjian, M.and Frakes, M. (2007). Crush Injuries: Pathophysiology and Current Treatment. *Emergency Care*, 32(9):13-18.
- Sauret, J. George, M. Wang, G. (2002). Rhabdomyolysis. *American Family Physician*, 65(5).

Thompson, P. Warren, D. Blumbergs, P. (2002). Rhabdomyolysis: A review. *Muscle and Nerve*, 25(3):332-347.

Vanholder, R. Sever M. S (2000). Acute renal failure related to the crush syndrome: towards an era of seismo-nephrology? *Nephrol Dial Transplant*, 15:1517-1521

Vivino, M. Antonelli, M. Moro (1998). Risk factors for acute renal failure in trauma patients. *Intensive Care Med* 24:808-814

Wood, D. Rosedale, K. J. (2012). Traumatic rhabdomyolysis (crush syndrome) in the rural setting, *S Afr Med J*, 102:37-39.

Yiannis S. Gesthimani M. (2008) The Syndrome of rhabdomyolysis: Complications and Treatment, *Eur J. Intern. Med* 19(8): 568 – 574

APPENDIX

DATA COLLECTION SHEET

I. DEMOGRAPHIC DATA

1. Study number.....
2. Age.....
3. Sex.....

II. HISTORY

1. Drugs taken over the past 4 weeks
2. History of illness over the past month

III. INCIDENT CAUSING INJURY

1. Motor vehicle accidents =1
2. Fall from height =2
3. Assault =3
4. Industrial accidents =4

IV. PATTERN OF INJURY

1. Multiple fractures =1
2. Single limb fracture =2
3. Traumatic amputations =3
4. Crush injuries =4
5. Soft tissue injuries =5

V. Blood Pressure

1. on admission
2. upon resuscitation

VI. Limb Ischaemia

1. Pulse reduced or absent but perfusion normal =1
2. Pulseless, paraesthesias, diminished capillary refill =2
3. Cool, paralysed, insensate, numb =3

VII. Treatment received

1. Fluids given=1,YES; =2,NO
If yes, type and volume.....

VIII. SERUM CREATININE KINASE LEVELS

1. On admission.....
2. D3.....
3. D5.....
4. D7.....

IX. RENAL FUNCTION

Creatinine.....

1. On admission.....
2. D3.....
3. D5.....
4. D7.....

X. OUTCOME

1. Resolution
2. Renal failure
 - i. Death
 - ii. Resolution
 - iii. Progression to chronic kidney disease