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Nephrology

# THE STUDY OF RHABDOMYOLYSIS IN VIPER BITE AND OUTCOME

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**ABSTRACT**

**Aim:** The aim of this study is to study the prevalence of rhabdomyolysis in viper bite and the outcome of rhabdomyolysis associated renal failure.

**Methods:** A prospective observational study was done in snake bite victims admitted in Government Mohan Kumaramangalam Medical college Hospital, Salem.

**Results:** The total number of patients included in the study was 143. The total number of patient with acute kidney injury was 110. Rhabdomyolysis was noted in 52 (36.36%) patients. Nine patients underwent fasciotomy. The mean peak serum creatinine in the fasciotomy group was 2.3±1.46, when compared to 5.38±3.37 in those who did not underwent fasciotomy which was significant (P=0.01).

**Conclusion:** The manifestation of AKI in snake bite victims with rhabdomyolysis is similar to those without rhabdomyolysis. Fasciotomy should be used judiciously in snake bite victims with compartment syndrome to salvage renal function.

**KEYWORDS :** Acute kidney injury, Compartment syndrome, Fasciotomy, Rhabdomyolysis, Viper bite.

## Introduction

Snake bite is an occupational hazard of farmers in India. Envenomation due to viperidae group of snake commonly leads to renal failure.[1] Factors contributing to acute kidney injury (AKI) in snake bite are bleeding, hypotension, circulatory collapse, intravascular hemolysis, rhabdomyolysis, disseminated intravascular coagulation, microangiopathic hemolytic anaemia and the direct nephrotoxicity of venom.[2] The Russell's viper is considered a highly venomous snake throughout its range in Asia.[3] Russell's viper venom contains phospholipaseA2, which causes rhabdomyolysis and due to local effect of toxin causes diffuse limb swelling.[4] The pathogenesis of rhabdomyolysis is toxin causing increase in sarcoplasmic influx of sodium, chloride, and water, resulting in cell swelling and auto destruction. The release of necrotic muscle constituents, results in altered plasma concentrations of several compounds, which are responsible for toxic and sometimes life threatening complications including acute kidney injury (AKI).[5] The early volume resuscitation can prevent renal injury in rhabdomyolysis.

**Objectives:** To study the prevalence of rhabdomyolysis in viper bite and the outcome of rhabdomyolysis associated renal failure.

## Materials and methods

Study design is a prospective observational study. The study period was one year from2016 to 2017. The permission from hospital ethics committee obtained. The snake bite victims admitted in medial wards of Government Mohan Kumaramangalam Medical college Hospital, Salem, with history of viper bite and cellulitis crossing atleast one large joint were included in the study. Patients with pure neurotoxic bite, cellulitis not crossing large joint, patient with pre existing chronic kidney disease, epilepsy, recent myocardial infarction, trauma and patients with history of drug intake like statins and fibrates were excluded from the study.

All patients underwent detailed history, physical examination, biochemical investigation, hematological test, coagulation profile and creatinine phosphokinase (CPK).

**Creatinine phosphokinase**: Since extreme quantities of CPK are released during rhabdomyolysis and its overall degradation and removal are slow, CPK remains longer in the circulation than myoglobin in assessing presence and intensity of muscle damage. So, CPK was measured to assess muscle damage. The CPK level more than 1000 IU/L were taken as evidence of significant muscle damage. Collected data were analyzed using SPSS software.

## Result

The total number of patients included in the study was 143. The number of male patients was 93. The number of female patient was 50. The mean age in the male cohort was 42.48±14.55. The mean age in the female cohort was 48.36±13.94. The total number of patient with acute kidney injury was 110. The number of male patients with acute kidney injury was 70. The number of female patients with acute kidney injury was 40. The number of patients who needed renal replacement therapy was 84.

Rhabdomyolysis was noted in 52 (36.36%) patients. Rhabdomyolysis with creatinine phosphokinase (CPK) more than 1000 IU/L occurred in 38 patients with AKI and 14 patients without AKI. Two patients with rhabdomyolysis died of capillary leak syndrome within 72 hours.

Rhabdomyolysis and renal replacement therapy

Renal replacement therapy was needed in 34 out of 50 patients with rhabdomyolysis and 50 out of 91 patients without rhabdomyolysis. There was no association in snakebite AKI patients between the occurrence of rhabdomyolysis and the need for RRT (P=0.15). (table1)

**Table1. Rhabdomyolysis and renal replacement therapy**

| Snake bite | RRT | No RRT |
|---|---|---|
| Rhabdomyolysis | 34 | 16 |
| No rhabdomyolysis | 50 | 41 |

P =0.15

RRT – renal replacement therapy

### Rhabdomyolysis and Oliguric AKI

Oliguric acute kidney injury occurred in 41 out of 72 in snakebite AKI patients without rhabdomyolysis and 25 out of 38 patients with rhabdomyolysis. There was no association in snakebite AKI patients between the occurrence of rhabdomyolysis and oliguric renal failure (P= 0.42).

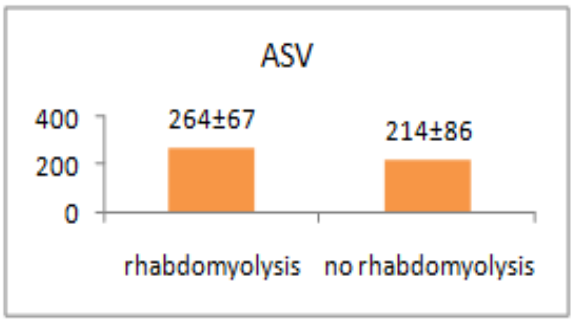
### Rhabdomyolysis and anti snake venom (ASV) initiation

Anti snake venom was initiated in more than 6 hours of bite in 25 out of 72 in snakebite AKI patients without rhabdomyolysis and 4 out of 38 patients with rhabdomyolysis. Early initiation of ASV was noted in most snakebite AKI patients (90%) with rhabdomyolysis (P=0.006).

### Anti snake venom dose and rhabdomyolysis

Mean ASV dose needed by snake bite victim, with rhabdomyolysis was 264±67ml and those without rhabdomyolysis was 214±86ml. Snake bite victim with rhabdomyolysis need significantly more ASV (P=0.002). (figure1)

**Figure 1: Mean ASV dose needed in ml**



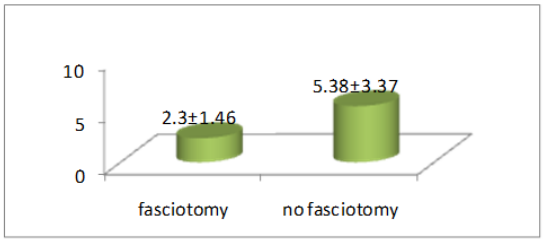

P=0.002
ASV – anti snake venom

The average peak serum creatinine in snakebite AKI patients with rhabdomyolysis was 6.19±2.93 when compared to those without rhabdomyolysis 5.67±2.61 which was not significant (P= 0.35).

**Rhabdomyolysis and fasciotomy**

Among 50 snakebite patients with rhabdomyolysis and AKI, 9 patients underwent fasciotomy. Two patients had cellulitis involving whole unilateral upper limb and the remaining 7 had cellulitis involving the whole unilateral lower limb. The mean peak serum creatinine in the fasciotomy group was 2.3±1.46 when compared to 5.38±3.37 in those who did not underwent fasciotomy which was significant (P= 0.01). (figure2)

**Figure2. Fasciotomy and peak serum creatinine (mg/dl)**




P= 0.01

**Discussion**

Snake bite envenomation produces local and systemic effects. Venom systemic effects result in hemorrhage and coagulopathy.[6] Locally, there is increased vascular permeability allowing fluid accumulation. The phospholipase A2 of Russell's viper cause myolysis and cell swelling leading to myoglobinemia, hyperkalemia, and acute kidney injury.[7] The pathogenesis of myoglobinuric AKI are renal vasoconstriction, intraluminal cast formation, and direct heme-protein induced cytotoxicity. The cast formation and direct heme toxicity are favored by dehydration and renal vasoconstriction, which decrease tubular flow and enhance water reabsorption. The other factor favoring precipitation of uric acid and myoglobin is a low pH of tubular urine, which is due to underlying acidosis.[8]

Hypotension in snake bite is due to increased kinin production, blood loss, myocardial depression and hemorrhage into adrenals. Necrosis of the muscles results in the accumulation of substantial amounts of fluid in the affected limbs (up to 10 L per limb). Unless large amounts of volume are administered, shock and deterioration of renal function will occur. Hypovolemia must be prevented by the aggressive administration of intravenous fluids.[9] The preferable fluid is 1L isotonic saline alternating with 1 L of glucose 5% + 100 mmol bicarbonate. The only drawback of alkaline rehydration is the fall in serum ionized calcium.[10] If muscles recover faster than the kidneys, fluid is released into the circulation at a later stage. Poor diuresis may then result in expansion of the extracellular and plasma volume and pulmonary edema.

According to Woodrow G et al, the majority of patients with rhabdomyolysis and acute kidney injury recover renal function. The creatinine/urea ratio is higher in AKI due to rhabdomyolysis than in an unselected group of patients with other causes of AKI. The prognosis of rhabdomyolysis-associated AKI is relatively benign.[11]

In our study, the occurrence of oliguric AKI was similar in snake bite patients with or without rhabdomyolysis. The serum creatinine in patients with rhabdomyolysis AKI was higher when compared those without rhabdomyolysis, which was not significant. About 90% of snake bite victims with rhabdomyolysis AKI had ASV initiated in less than 6 hour in our study, when compared to those without rhabdomyolysis. In snake bite victims with rhabdomyolysis, there was a trend towards more need of RRT. So, early aggressive hydration for first 48 hours in addition to ASV, in snake bite victim with substantial limb swelling can salvage the kidney function from both exogenous snake toxin and endogenous muscle toxin.

The limb muscles are contained within rigid compartments formed by fasciae and bones. There is increase in local tissue pressure within a closed fascial compartment due to muscle cell swelling. High intracompartmental pressure provokes additional damage and necrosis, which if not treated can compromise vascularity leading to ischemic contracture and the worst outcome, amputation.[12] The key signs of compartment syndrome are pain that is out of proportion to clinical findings, pain with passive stretch of involved muscles, pain with palpation of involved compartment and pressure increase within the compartment (>30mm of Hg) as measured.[13] A pulseless extremity is a very late finding in compartment syndrome and may not develop at all despite protracted elevated pressures.

According to Gold BS et al, in snake bite victims, antivenom administration reduces limb swelling and improves elevated compartment pressures. The dose of antivenom needed is at least 4 to 6 vials, repeated as necessary until the patient is stable.[14] Therefore, antivenom administration is indicated in all cases of compartment syndrome, and also for all cases involving substantial progressive limb swelling.[15]

According to Hardy et al, fasciotomy is needed even in antivenom treated patients. Because compartments are noncommunicating closed systems, the only way to decrease the pressure is to decompress the fascial system surgically by fasciotomy.[16] Complications of fasciotomy include wound infection, hematoma, ulceration, and muscle herniation.[11] In a series of open fasciotomies, Rush et al, found that the only complications relating to fasciotomy are easily treated superficial wound infections.[17]

In our study, the peak serum creatinine in those who underwent Fasciotomy was significantly lower when compared to those without fasciotomy. So, fasciotomy is beneficial in snake bite victims. Even though fasciotomy may not be needed to salvage the limb function, early fasciotomy is helpful in snake bite victims with compartment syndrome to salvage the renal function.

**Conclusion**

Rhabdomyolysis is common in snake bite victims. The spectrum of rhabdomyolysis range from subclinical rise in CPK to a medical emergency, manifested as compartment syndrome and AKI. The manifestation of AKI in snake bite victims with rhabdomyolysis is similar to those without rhabdomyolysis. The snake bite victims with rhabdomyolysis need more anti snake venom. The renal failure in snake bite with rhabdomyolysis is often oliguric. Early volume replacement should be used in snake bite victim with rhabdomyolysis in addition to ASV to prevent renal failure. After 48 hours of bite, fluid should be administered cautiously. Fasciotomy should be used judiciously in snake bite victim with compartment syndrome to salvage renal function.

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