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SERUM LACTATE DEHYDROGENASE AS A PREDICTOR OF OUTCOMES IN RUSSELL'S VIPER ENVENOMATION

Short Running Title: Serum LDH and outcomes in Russell's viper envenomation

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ABSTRACT

Russell's viper (*Daboia russelii*) envenomation is a major cause of morbidity and mortality in Myanmar, often complicated by acute kidney injury (AKI), disseminated intravascular coagulation (DIC), and shock. Serum lactate dehydrogenase (LDH), a marker of tissue injury and hemolysis, shows promise as an indicator of envenomation severity. The objective of this study is to determine the association between serum LDH levels and clinical outcomes in patients with Russell's viper envenomation. A hospital-based cross-sectional study was conducted at Mandalay General Hospital, Myanmar, from January to December 2018. Patients admitted within 72 hours of confirmed Russell's viper bite were included. Serum LDH was measured 18–72 hours after the bite, and outcomes recorded included AKI, DIC, shock, and mortality. Statistical analysis was performed using *t*-tests and one-way ANOVA, with $p < 0.05$ considered significant. Serum samples of 98 patients were analyzed (62.2% male; median age 35 years, range 12–64 years). AKI occurred in 49 (50.0%), DIC in 23 (23.5%), shock in 20 (20.4%) and only 5 (5.1%) patients died. Mean serum LDH was significantly higher among patients with complications: AKI 902.7 vs 389.5 IU/L ($p < 0.001$), shock 1004.5 vs 554.2 IU/L ($p < 0.001$), DIC 1100.0 vs 506.9 IU/L ($p < 0.001$), and death 1146.8 vs 619.2 IU/L ($p = 0.012$). Elevated serum LDH was strongly associated with AKI, DIC, shock, and mortality in Russell's viper bite patients. LDH is an inexpensive and widely available biomarker and is useful for early risk stratification to guide clinical management.

Keywords: acute kidney injury; disseminated intravascular coagulation; envenomation; lactate dehydrogenase; snake bites.

INTRODUCTION:

Snakebite envenomation is a significant public health issue in Myanmar, where the Russell's viper (*Daboia russelii*) accounts for 90% of snake bites, with a case fatality of 8.2% [1]. Complications from Russell's viper bites include acute kidney injury (AKI), disseminated intravascular coagulation (DIC) and shock, which contribute to morbidity and mortality, especially in rural agricultural regions where delayed presentations and limited access to healthcare are common [2,3].

Early identification of patients at risk of severe envenomation is crucial for the timely management and effective use of anti-snake venom (ASV). Clinical parameters, such as prolonged bite-to-injection time and uncoagulable blood status have been associated with poor outcomes [4,5]. However, laboratory markers that can be rapidly and inexpensively measured are needed to improve prognostication. Serum lactate dehydrogenase (LDH), a widely available enzyme marker of tissue injury and hemolysis has been proposed as a potential indicator of envenomation severity [6]. Elevated LDH levels have been associated with hemolysis, rhabdomyolysis and organ dysfunction in viper bite victims [7,8].

This study aimed to evaluate the association between serum LDH levels and clinical outcomes, including AKI, shock, DIC and mortality among patients with Russell's viper bites admitted to Mandalay General Hospital, Myanmar. This hospital is a major tertiary referral center that receives snakebite cases from the Mandalay, Sagaing and Magway regions.

METHODOLOGY

This was a hospital-based cross-sectional study conducted at Mandalay General Hospital, Myanmar from 1st January to 31st December 2018. All patients admitted within 72 hours of a Russell's viper bite were included. Snake identification was based on the description provided by the patient or eyewitnesses, inspection of the dead snake (if available), and/or the presence of clinical features consistent with systemic envenomation.

Patients were excluded if they had pre-existing medical conditions known to elevate serum LDH, such as hemolytic anemia, pancreatitis, chronic hepatitis, lymphoma, leukemia, carcinoma, recent myocardial infarction or pulmonary embolism. Patients who were already presented with AKI, shock or DIC on admission were also excluded.

The following details were obtained from the hospital records:

demographic data, time of the snake bite, time of hospital admission, and time of administration of ASV, as well as clinical manifestations and complications, such as AKI, shock, DIC and mortality. Serum LDH was measured between 18 and 72 hours after viper bite using the kinetic method (ABX Pentra LDH CP reagent, Pentra C400 automatic chemistry analyzer). Serum creatinine was measured daily for the first three days of admission.

The platelet count, the activated partial thromboplastin time (APTT), and prothrombin time (PT) were measured in patients with spontaneous bleeding manifestations.

Acute kidney injury (AKI) was defined as a rise in serum creatinine of at least 1.5 times the baseline or urine output below 0.5mL/kg/hr for at least 6 hours. Patients were considered in shock if the systolic blood pressure was below 80 mm Hg or inotropic support was needed, while DIC was diagnosed in patients with spontaneous bleeding, prolonged PT or APTT and low platelet count.

Data was entered into Microsoft Excel and analyzed using Statistical Program for Social Science (SPSS). Continuous variables were expressed as mean (standard deviation, SD) and categorical variables as frequencies and percentages. Differences in mean serum LDH between two groups were assessed using the independent t-test or among three or more groups using one-way analysis of variance (ANOVA). Normality was assumed based on the sample size and data distribution. A p-value of <0.05 was considered statistically significant.

The study protocol was approved by the Postgraduate Academic Board of the University of Medicine, Mandalay. Patient data were anonymized prior to analysis, and all procedures complied with the principles of the Declaration of Helsinki [9].

RESULTS:

There were 98 patients with confirmed Russell's viper bites, of which 61 (62.2%) were male and 37 (37.8%) were female. The median age of all the patients was 35 years (range 12 to 64 years), with the highest proportion in the 31 to 40 years age group. Most patients were from the Mandalay region (59.2%), followed by Sagaing (37.8%) and Magway (3.1%).

All patients received ASV. The bite-to-needle time for administration of anti-snake venom was within 3 hours for 89 (90.8%),

between 3 and 6 hours in 7 (7.1%) and beyond 6 hours in 2 (2.0%). Nineteen patients (19.4%) received less than ten vials of ASV, 33 (33.7%) received 10 to 20 vials, 23 (23.5%) received 20 to 30 vials, and 23 (23.5%) required more than 30 vials. The mean total volume of ASV used per patient was 201 mL, increasing to 272 mL among patients who died.

Among the 98 patients, 42 (42.9%) had no complications, 26 (26.5%) developed one complication, while 30 (30.6%) had two or more complications. AKI occurred in 49 (50.0%), shock in 20 (20.4%), DIC in 23 (23.5%), while mortality occurred in 5 (5.1%) patients.

Serum LDH was measured in 91 patients; 56 (61.5%) had LDH levels above the normal range. LDH was significantly higher in patients with AKI (902.7±72.5 IU/L) than those without AKI (389.5±28.4 IU/L, $p < 0.001$). Patients with shock had a higher mean serum LDH (1004.5 ± 63.8 IU/L) compared to those without shock (554.2 ± 51.5 IU/L, $p<0.001$). Patients with DIC also had a higher mean serum LDH (1100.0 ± 137.5 IU/L) compared to those without DIC (506.9 ± 29.8 IU/L, $p < 0.001$). LDH increased progressively with the number of complications, where mean serum LDH was 331.9 ± 128.8 IU/L in patients with no complication, 651.2 ± 159.1 IU/L with one complication and 1081.5 ± 573.5 IU/L with two or more complications ($p < 0.001$, ANOVA). Patients who died also had a significantly higher LDH (1146.8 ± 148.9 IU/L) compared to 619.2 ± 47.0 IU/L ($p = 0.012$) in survivors.

DISCUSSION:

This study evaluated the association between serum LDH levels and clinical outcomes among patients with Russell's viper envenomation admitted to Mandalay General Hospital. LDH levels were significantly higher in patients with AKI, shock, DIC and mortality, compared to patients without these complications. The progressive rise in LDH with increasing number of complications also adds weight to support its role as a biochemical marker of disease severity. These findings are consistent with studies showing that elevated LDH reflects tissue injury, hemolysis, and rhabdomyolysis following viper envenomation [7,8, 10].

The mechanisms for these complications include phospholipase A2-mediated cellular damage, coagulopathy, and microangiopathic hemolysis, which has been described in detail previously [6]. LDH elevation likely represents a composite effect of direct venom toxicity and

secondary complications such as DIC and renal ischemia. As LDH rises within 18 hours of cell injury after Russell's viper bite, and remains elevated for several days, it offers a practical time window for clinical monitoring during the early phase of hospitalization.

The proportion of patients who developed AKI (50%), DIC (23.5%) and shock (20.4%) are similar to previous reported cases from Myanmar [11,12]. However, the mortality rate in this study was lower (5.1%) compared to the other studies, which exceeded 10% [11,12]. This may reflect improved ASV availability in this tertiary center. In addition, patients with delayed treatment beyond three hours, or requiring higher ASV doses tended to experience more severe complications. These findings support the continuing importance of timely anti-venom administration and supportive care.

From a clinical perspective, LDH is an inexpensive and widely available assay in Myanmar. Routine LDH measurement may aid early identification of patients at risk of systemic envenomation and guide triage decisions, especially where advanced laboratories or imaging facilities are unavailable. However, LDH is non-specific and may also be elevated in conditions such as myocardial infarction, sepsis or hemolytic anemia [13]. Thus, interpretation should be contextual and combined with clinical assessment and other laboratory indices.

The main limitations are that the study was conducted in a single tertiary center and may over-represent severe referred cases, leading to selection bias. The cross-sectional design limits causal inference, and LDH trends over time were also not measured. Future prospective studies with serial LDH measurements may help validate its prognostic utility.

CONCLUSION

Serum LDH showed a strong association with AKI, DIC, shock, and mortality in Russell's viper bite patients. As LDH is an inexpensive and widely available biomarker, LDH shows potential as a useful adjunct in assessing envenomation severity and guiding management in snake bite patients.

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