URINARY NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN IS AN EARLY BIOMARKER OF ACUTE KIDNEY INJURY FOLLOWING RUSSELL'S VIPER ENVENOMING

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Objectives: Snake envenoming is a major public health problem in Sri Lanka. Russell's viper (*Daboia russelii*) is responsible for 30–40% of all snake envenomings. Acute kidney injury (AKI) is an important complication of Russell's viper envenoming. Currently, AKI is diagnosed based on creatinine, which does not increase immediately with AKI. This study aims to assess the diagnostic utility of a panel of renal injury biomarkers in diagnosing AKI following Russell's viper envenoming.

Methods: Patients admitted to Polonaruwa hospital with definite Russell's viper bites were recruited to the study. Serial blood and urine samples were collected on admission (usually within the first 4h post-bite), between 4-8h, 8-16h and 16-24h and at 1 month and 3 months post-bite. Russell's viper envenoming was confirmed by enzyme linked immunosorbent assay (ELISA). The Acute Kidney Injury Network (AKIN) criteria were used to define AKI and categorise patients by severity (stage 1, 2 and 3). Novel urinary biomarkers, albumin, beta2-microglobulin (uβ2M), cystatin C, neutrophil gelatinase-associated lipocalin (uNGAL), osteopontin (uOPN) and trefoil factor-3 (uTFF3) were quantified using conventional ELISA and by a bioplex system. The diagnostic performance of biomarkers to detect patients with AKI at each time interval was assessed by area under the receiver operator characteristic curve (AUC–ROC).

Results: Of 40 consenting patients [median age: 39 (range: 15-71 years) 32 males (80%)], 30 developed AKI (AKIN stage 1, n=17, AKIN stage 2, n=5, AKIN stage 3, n=8). Most biomarker concentrations were above the normal range in patients who developed AKI within 8h post-bite. Peak biomarker concentrations were associated with AKI severity. Serum creatinine was a poor early marker of AKI with an AUC-ROC of 0.51 (95% CI: 0.24-0.78), within 4h which increased to 0.84 (0.68-0.99) between 4-8h post-bite. Among the urinary biomarkers tested, uNGAL showed good AUC-ROC profile within 4h of the bite with an AUC-ROC of 0.82 (0.58-1.0), an excellent one between 4-8h post-bite, with an AUC-ROC of 0.93 (0.83-1.0). Urinary cystatin C and serum cystatin C were also reasonable early markers of AKI with AUC-ROCs of 0.77 (0.51-1.0) and 0.78 (0.58-0.97) respectively within 4h of the bite. However, neither was better than serum creatinine between 4-8h post-bite. Urinary TFF3, urinary albumin, uβ2M and uOPN all had AUC-ROCs <0.7 within 4h post-bite and less then serum creatinine between 4-8h post-bite, so were not early diagnostic markers of AKI.

Conclusions: Urinary NGAL is the earliest biomarker of AKI following Russell's viper envenoming with a rapid increase in the first 4h post-bite. Urinary Cystatin C and serum cystatin C were relatively good within 4h post-bite and alternative early biomarkers. Increase in the structural injury biomarkers such as uNGAL, urinary cystatin C and TFF3 confirmed Russell's viper envenoming causes both tubular and glomerular injury.