STUDY OF BIOMARKERS PREDICTIVE IN SNAKEBITE AKI (SAKI) TO CHRONIC KIDNEY DISEASE

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INTRODUCTION: Snake bite is a significant occupational health hazard, leading to high mortality and morbidity in tropical country. Snake venom-induced acute kidney injury (SAKI) and the comprehensive evaluation of the risk factors leading to progression from SAKI to chronic kidney disease (CKD) remains inadequately studied and explored.

AIMS: To evaluate the risk of progression from snake venom-induced acute kidney injury (SAKI) to chronic kidney disease (CKD).

METHOD: A prospective longitudinal follow-up study was conducted to investigate the potential progression from snake bite-induced acute kidney injury to chronic kidney disease. The study included snake bite patients admitted to NRS Medical College from July 2018 to March 2020. Clinical histories were examined, and blood and urine samples were collected with the patients' consent. Follow-up visits were scheduled at 1 month (1MFU), 3 months (3MFU), and 6 months (6MFU) post-hospital discharge, during which samples were collected. Renal injury and functional markers such as plasma and urinary NGAL, Cystatin C, KIM-1, and TGFβ1 were assessed alongside CRP, methylglyoxal (MG), advanced oxidation protein product (AOPP), and CPK levels at each time point. Data were presented as mean ± standard error of mean. Statistical analyses, including ANOVA following Tukey post hoc analysis were performed to detect any significant differences between the parameters of the studied groups. Nonparametric populations were assessed using the Man-Whitney U-test or Kruskal-Wallis ANOVA. Additionally, Pearson correlation and chi-square tests along with Univariate and multivariate logistic regression models were employed for further analysis.

RESULT: 67 SAKI patients were enrolled for biomarker study. M:F was 2.7:1.About 80% age between 18-60 years. Patients received 22.12 ± 1.13 vials of anti-snake venom with a median requirement of 3 hemodialysis sessions. 47.76% of SAKI patients experienced . AKIN stage 3 group.

Significant alterations were observed in all renal functional parameters, including plasma and urinary NGAL, Cystatin C, KIM-1 and TGFβ1 in the snake venom-induced acute kidney injury group (SAKI) when compared to both the control and the group without kidney injury (NSAKI).

Additionally, CRP, MG, and AOPP levels exhibited a significant increase in the order of SAKI > NSAKI > Control. NGAL, KIM1 and Cystatin C were found to be a good predictor of the disease at univariate level ($p<0.001$). These markers did not show a significant reduction toward normal levels during subsequent follow-ups. Furthermore, at the 1st, 3rd, and 6th-month follow-ups, 38%, 32.3%, and 61.2% of patients, respectively, exhibited moderately higher plasma creatinine values (1.2-1.5 mg/dl).

GFR was lower (<90 ml/min/1.73m2) in 29.1%, 29.86%, and 45.1% of patients at 1, 3, and 6 month, respectively.

Plasma creatinine demonstrated a strong association with inflammation, stress, and injury markers.

Hematuria/hemoglobinuria was observed in 38.12% of patients at different follow-up time points, and urinary protein was present in 60%, 75.4%, and 82.85% of patients at 1, 3, and 6 month, respectively.

Table 1: Area under the ROC curve for the studied parameters

Test Result Variable(s)	Area	Standard Error	Asymptotic Significance	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
Plasma KIM1	0.872	0.048	0.001	0.778	0.966
Urinary KIM1	0.905	0.038	0.001	0.831	0.979
Plasma to Urine KIM1 ratio	0.247	0.065	0.002	0.12	0.274
Plasma Cystatin C	0.864	0.054	0.001	0.758	0.959
Urinary Cystatin C	0.836	0.054	0.001	0.730	0.942
Plasma to Urine Cystatin C ratio	0.373	0.074	0.112	0.228	0.518
Plasma NGAL	0.558	0.074	0.480	0.413	0.704
Urinary NGAL	0.844	0.056	0.001	0.734	0.953
Plasma to Urine NGAL ratio	0.799	0.063	0.001	0.676	0.923
Plasma IL6	0.773	0.061	0.001	0.654	0.892
Urinary IL6	0.919	0.042	0.001	0.837	1.000
Plasma to Urine IL6 ratio	0.701	0.077	0.017	0.550	0.853

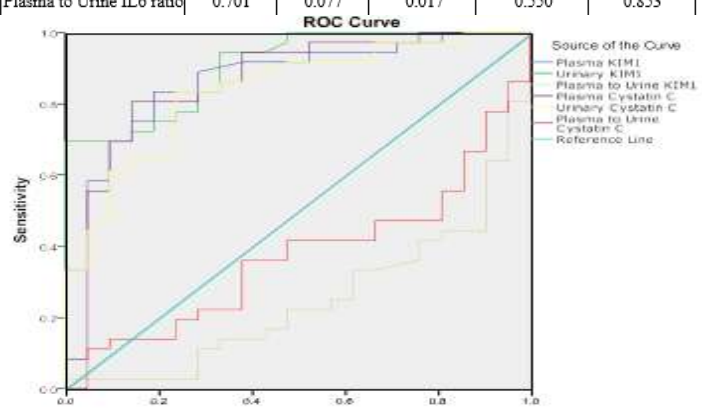

Figure 1 ROC CURVE

CONCLUSION: There is a discernible risk of progression from snake bite-induced acute kidney injury to chronic kidney disease. The follow-up data indicates that patients exhibiting low glomerular filtration rate (GFR), elevated plasma creatinine, proteinuria, hematuria, and high levels of SAKI predictors including KIM1, NGAL, Cystatin C, and TGFβ1 are particularly prone to the development of chronic kidney disease .

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