CARBONYL STRESS REVISITED IN ACUTE KIDNEY INJURY IN TROPIC

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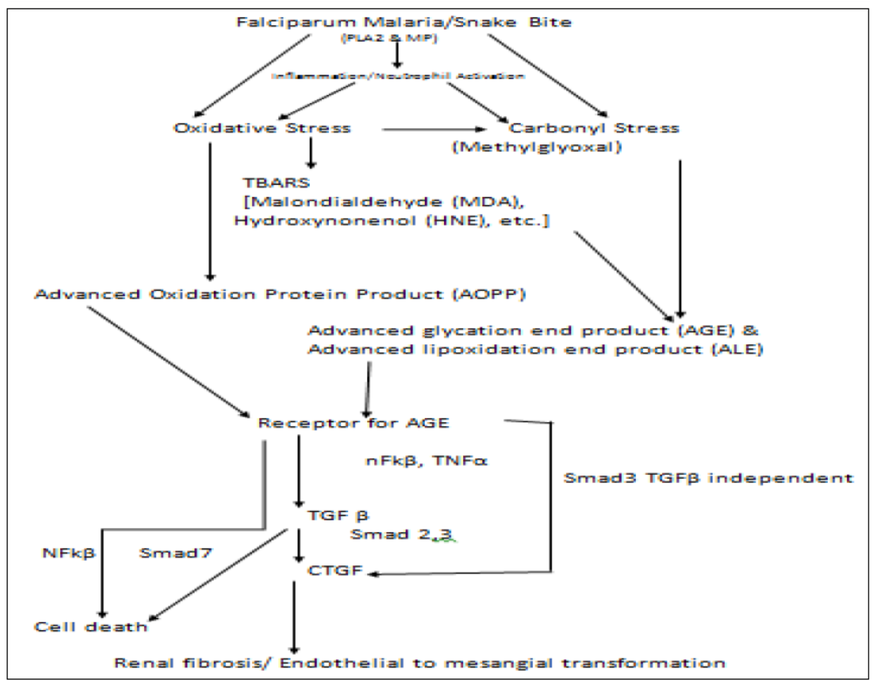
OBJECTIVES

- Malaria and snake bite are two common causes of AKI in tropics with lot of morbidity and mortality.
- The aims of this study was
  1.To evaluate the carbonyl and oxidative stress in these group and their pathogenesis link.
  2.Prognostic predictability of carbonyl and oxidative stress marker in this AKI.

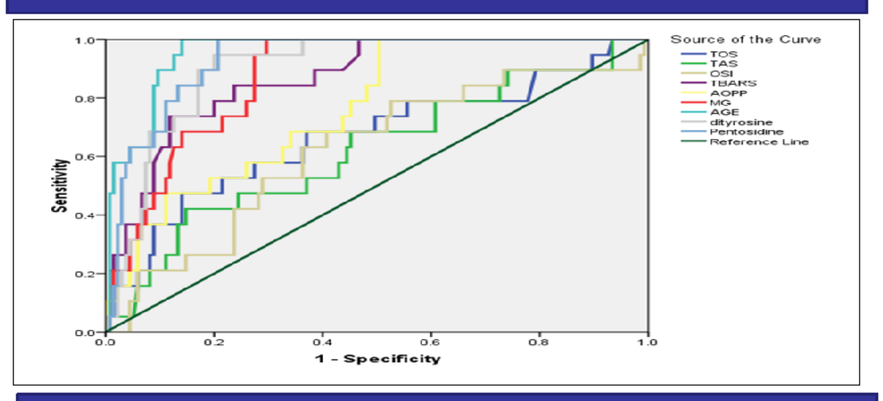
METHODS

- All cases of falciparum malaria mediated AKI (FMAKI)(n=50), confirmed by antigen and/or in peripheral blood smear and snake bite mediated AKI(SAKI)(n=58) were included.
- AKI was calculated as per RIFLE criteria. Demographical, clinical and biochemical data were analyzed and they are followed from hospitalization to discharge/death.
- Oxidative and carbonyl stress markers [Advanced oxidation protein product (AOPP), Advanced Glycation End product (AGE), Pentosidine, Dityrosine, Thioberbituric acid reactive substance (TBARS) and Methyl glyoxal (MG)] were measured consecutively according to standard protocol.
- Predictive importance was assessed from trend analysis, ROC curve analyses and multiple logistic regression with AKI as positive response.

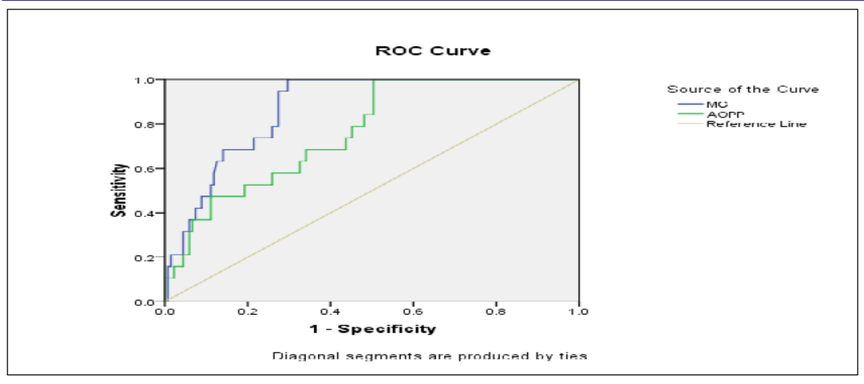
Proposed Pathway of FMAKI/SAKI



ROC CURVE FOR DIFFERENT OXIDANT IN FMAKI PATIENTS



ROC CURVE FOR AOPP AND MG IN MAKI PATIENTS



RESULTS

- The Oxidative stress index(OSI) of FMAKI patients were 1.89 higher than normal control .
- The TBARS, MG level were 6.49 and 5.56 times higher indicating a significant carbonyl stress in these patients.
- AOPP level the marker of protein modification was also 2.33 times higher than normal control indicating that proteins are highly insulted in FMAKI.
  - Areas under the curves for AOPP and MG were (0.735, p= 0.001),(0.691, p= 0.005) respectively.
- Similarly in SAKI. Significantly elevated total oxidant stress (TOS) (p=0.002) with decreased total anti oxidant stress(TAS) (p=0.048) leads to net oxidative stress in the patients of SAKI which was depicted by increased oxidative stress index(OSI) values (p<0.001).
- MG, was found to be increased by 3.48 times (p<0.001). When the level of oxidative and carbonyl stress markers and protein modifications where compared among the survived and expired only AOPP (248.64±17.4 vs. 168.75±12.56, p=0.001) and MG (39.93±2.11 vs. 28.89±2.41, p=0.004) were found to be significantly elevated in expired patients than the survived.
- Area under the curve (AUC) of receiver operated curve for AOPP (AUC 0.822 CI 0.699-0.945, p<0.001) and MG (AUC 0.83 CI 0.714-0.946, p<0.001) were significant higher than the reference line (AUC 0.5) indicate their predictive power for the adverse outcome. At univariate level all the parameters can differentiate between AKI and the non-AKI group (Area under the ROC curve> 0.5; p<0.05). At multivariate level, methylglyoxal, AOPP and dityrosine appeared to be independent predictor of AKI in snake bite and malaria infected patients (p<0.05).

CONCLUSIONS

1. MG, the carbonyl stress marker along with oxidative stress are significantly raised and possibly linked to the pathogenesis of AKI.
2. MG and AOPP can be used as a surrogate marker in these tropical AKI.

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