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Title: Serum FCN-3 protein as a potential biomarker in assessing Rheumatic Heart Disease

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Background & Aims: Acute rheumatic fever (ARF) and rheumatic heart disease (RHD), sequelae of group A Streptococcus infection, are significant contributors to morbidity and mortality worldwide, especially in Africa. Ficolins, of which Ficolin-3 (FCN3) represents the most abundant circulating type, are a group of proteins capable of activating the complement system via the lectin pathway. Previous reports indicate an association of FCN3 gene polymorphisms and autoimmune diseases, such as systemic lupus erythematosus and more recently, RHD. Understanding the pathogenesis of RHD, which currently is poorly understood, may provide guidance towards prompt diagnosis and treatment to prevent progression to severe states of disease.

Methods: We aimed to examine the serum FCN-3 protein levels in patients with severe RHD, using an enzyme-linked immunosorbent assay (ELISA). The protein levels were compared to those in controls. We further sought to corroborate findings from the machine learning-derived predictions from our earlier SWATH-MS analysis. Lastly, we sought to genotype FCN3 gene polymorphisms, if any, in a subset of the cohort (50 patients and 50 controls) by direct cycle sequencing of genomic regions of interest. Baseline phenotypic characteristics were compared between case and control groups using Mann-Whitney U tests for continuous variables.

Results: In total, 215 patients of severe RHD and 230 controls were included in the current study. A negative association of FCN-3 with severe RHD was observed on ELISA (fold change 0.41, p-value 0.02839), aligning with our prior in-silico predictions. Genotyping analysis of possible FCN-3 gene polymorphisms is underway, the results of which will be presented.

Conclusions: This study's observation of a lower abundance of FCN-3 in sera of suspected RHD cases may be a useful biomarker for disease progression and patient outcomes. Assessments of whether polymorphisms in the FCN-3 gene are responsible for the lack of FCN-3 in RHD cases, are pending.