Correlation of IL-6, IL-10, IL-18 and TNF-α Levels with Severity of Rheumatic Mitral Stenosis and Secondary Pulmonary Hypertension

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Purpose
Rheumatic heart disease (RHD) remains a serious public health problem in developing countries. The pattern of immune response after exposure to streptococcal infection is one of the main determinants of the rheumatic inflammatory process, making it essential to identify the patients who remains at higher risk of disease progression. We aim to give an insight into the pathophysiology of rheumatic afflicted valves and the role of IL-6, IL-10, IL-18 and TNF-α in the different stages of RHD, and their correlation with disease severity and pulmonary hypertension.

Methods
The study included 84 consecutive patients (62 females, mean age 34.6 ± 10.6 years) with symptomatic, severe chronic rheumatic mitral stenosis (Group-A). 79 age and gender matched normal healthy volunteers were enrolled as controls (Group-B). Patients with chronic rheumatic mitral stenosis were further divided into subgroups based on severity of mitral stenosis [MVA ≤ 1 cm² (Subgroup Aa) and MVA > 1 cm² (Subgroups Ab)] and presence or absence of pulmonary hypertension [RVSP ≥ 36 mm Hg (Subgroup Ac) and RVSP < 36 mm Hg (Subgroup Ad)]. IL-6, IL-10, IL-18, TNF-α and hs-CRP levels were assessed in both groups.

Results
The mean serum levels of IL-6, IL-10, IL-18, TNF-α and hs-CRP in Group-A and Group-B were 6.57 ± 3.53 pg/mL and 2.73 ± 1.01 pg/mL (p <0.001), 8.19 ± 2.80 pg/mL and 3.51 ± 0.86 pg/mL (p <0.001), 136.31 ± 89.02 pg/mL and 47.96 ± 9.76 pg/mL (p <0.001), 21.26 ± 18.59 pg/mL and 5.36 ± 3.57 pg/mL (p <0.001), 4.69 ± 6.31 pg/mL and 2.63 ± 2.22 pg/mL (p <0.008) respectively. On subgroup analysis mean TNF-α in subgroup Aa was 20.71 ± 16.84 pg/mL, while in subgroup Ab it was 7.56 ± 1.93 pg/mL (p <0.001). Mean IL-10 in subgroup Ac and Ad was 8.74 ± 3.29 pg/mL and 7.47 ± 1.82 pg/mL respectively (p <0.028). The differences in levels of other cytokines were not found to be significantly different in the subgroups studied.

Conclusions
Chronic rheumatic mitral stenosis patients have increased IL-6, IL-10, IL-18, TNF-α and hs-CRP levels suggesting a continuous ongoing inflammatory activity even in chronic phase. Further subjects having severe mitral stenosis had increased TNF-α levels in comparison to subjects with mild to moderate mitral stenosis suggesting its possible role in acceleration of rheumatic process.