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Clinical significance of markers of collagen metabolism in rheumatic mitral valve disease - A chronic acquired disorder that seeks greater attention

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Background: Rheumatic heart disease (RHD) results from acute rheumatic fever. It is a major public health concern in low and middle income countries (LMICs). In general, mitral valve is affected and show thickening and fibrosis with or without calcification. It is predicted that RHD would continue to cause high mortality and morbidity in LMICs and hence requires improved diagnosis and treatment strategies.

Objective: The present study was conducted to investigate whether extracellular matrix re-modeling in rheumatic valve leads to altered levels of collagen metabolism markers and if such markers can be clinically used to diagnose or monitor disease progression.

Methods: The study included the subjects with rheumatic heart disease before and after valve replacement surgery and age and sex matched controls in Indian sub-population. Periodic clinical monitoring was performed with echocardiography. Circulating levels of markers of collagen turnover were monitored by immunoassay. Histopathology studies were performed on excised mitral valve leaflets. A p-value <0.05 was considered statistically significant.

Results: Plasma PICP and PIIINP concentrations increased significantly ($p < 0.01$) in MS and MR subjects compared to controls but decreased gradually over a one year period post mitral valve replacement ($p < 0.05$). In MS, PICP level and MMP-1/TIMP-1 ratio strongly correlated with mitral valve area ($r = -0.40$; $r = 0.49$ respectively) and pulmonary artery systolic pressure ($r = 0.49$; $r = -0.49$ respectively); while in MR they correlated with left ventricular internal diastolic ($r = 0.68$; $r = -0.48$ respectively) and systolic diameters ($r = 0.65$; $r = -0.55$ respectively). Receiver operating characteristic curve analysis established PICP as a better marker (AUC = 0.95; 95% CI = 0.91-0.99; $p < 0.0001$). A cut-off >459ng/mL for PICP provided 91% sensitivity, 90% specificity and a likelihood ratio of 9 in diagnosing RHD. Histopathological studies were done on excised mitral valve leaflets to examine tissue architecture, altered abundance of fibrillar collagens, inflammation, scarring, neo vascularization and extensive leaflet fibrosis in diseased mitral valve. It has been found that circulating levels of interleukin (IL-6) is increased whereas IL-10 act as an anti-inflammatory marker in RHD.

Conclusions: Levels of collagen metabolism markers correlated with echo cardiographic parameters for RHD diagnosis. Therefore, progressive fibrosis in rheumatic valve could be monitored by a robust increase in collagen metabolism markers particularly PICP. They also determined disease prognosis.

Biography

Tanima Banerjee has completed her Bachelor of Science & Master degree from Vinoba Bhawe University, Hazaribag, India. Currently she is pursuing PhD in Cardiovascular disease at CSIR-Indian Institute of Chemical Biology, Kolkata, India. Her primary objective of research is to understand the extracellular matrix remodeling in Rheumatic Heart Disease. Part of the work is already published in a peer-reviewed journal and presented at various national and international meetings. She has publications in, *International Journal of Cardiology*, *Plos One* and *Clinical Proteomics* etc and has also two patents in her name.

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