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# Study of collagen metabolism markers in rheumatic heart valve disease: Indian sub-population

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Rheumatic Heart Disease (RHD), a chronic acquired heart disorder results from Acute Rheumatic Fever. The disease is primarily a hypersensitive reaction to streptococcal antigens and affects heart valves giving rise to an acute phase where there is fever, joint pain and features of frank heart failure like shortness of breath, palpitation and fatigue. Generally, mitral valve is affected and show thickening and fibrosis with or without calcification. Although RHD is prevalent in developing countries, thousands of new cases are being diagnosed worldwide every year. Many developing countries, as well as indigenous populations within developed countries, still carry a significant burden of rheumatic fever and rheumatic heart disease and there has been resurgence in efforts to eradicate the diseases in these populations. However, no biochemical markers are available for disease management. In India, rheumatic heart disease (RHD) is responsible for 30 to 40% of cardiovascular disease related hospital admissions. Whether structural remodelling of the rheumatic heart valve leads to altered level of collagen biomarkers are not yet examined. Thus it is required to investigate extracellular matrix remodelling which may help finding biomarkers of rheumatic heart disease subjects. Clinical examination was performed by trained physicians and the data recorded in a structured proforma. The study involved Indian subpopulation of rheumatic heart disease subjects with before and after valve replacement surgery which includes age and sex matched controls. Subjects were evaluated by 2-dimensional transthoracic echocardiography. Patients were classified into two groups- Mitral Stenosis (MS) and Mitral Regurgitation (MR). Immunoassays were assessed to monitor circulating levels of markers of collagen turnover and histopathology was conducted on excised mitral valve leaflets to examine tissue architecture, inflammation, neovascularisation and occurrence of fibrosis. Circulating Plasma PICP and PIIINP concentrations increased significantly ($p<0.01$) in MS and MR patients compared to controls but decreased gradually over a one year period post mitral valve replacement surgery ($p<0.05$). PICP was detected in urine of RHD Patients but found undetectable in control urine. 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 (ROC) was performed to establish PICP as a better marker (AUC = 0.95; 95% CI = 0.91 - 0.99; $p<0.0001$). A cut-off > 459 ng /mL for PICP provided 91% sensitivity, 90% specificity and a likelihood ratio of 9 in diagnosing RHD. Occurrence of fibrosis, inflammatory cells, extensive leaflet fibrosis was shown clearly from histopathological studies and arrangement and distribution pattern of collagen Type 1 was confirmed by immunofluorescence localization in mitral valve sections.The increased rate of collagen turnover is high in RHD groups suggesting the role of an ongoing chronic inflammation which results in significant elevation of collagen metabolism biomarkers of RHD and can be clinically used to diagnose or monitor disease progression.

## Biography

Tanima Banerjee has completed her Bachelor of Science & Master degree from Vinoba Bhave University, Hazaribag, India. Currently she is doing her 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 also have two patents on her name.

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