Summary of the study

Coronary artery disease is currently the most prevalent non-communicable disease, and Indians reported to have a higher incidence and prevalence of CAD at a younger age compared with other populations, leading to a greater social and economic impact. Immune dysregulation has been attributed to the chronic inflammation associated with atherosclerosis, which is now accepted to have an autoimmune etiology. The circulating immune cells provide a reflection of the immune system of an individual and abnormalities in the peripheral blood cells have been noticed in coronary artery disease patients. The main objective of the present study was to understand the immune system of coronary artery disease in this high-risk population. The peripheral immune cell profile, their functional activity, and possible mechanisms associated with the dysregulation were explored in CAD patients, healthy control subjects, patients having recurrent cardiac events and those showing an improvement after posttreatment. The proportion of inflammatory cells (Th17 and Tc17), classical monocytes, IL6 and IL17A and the inflammatory score were high in patients with compromised regulatory T cells compared to control. An increase in inflammation and deficient immune regulation could be observed with disease severity and in patients having recurrent cardiac events. The pro-inflammatory gene expression as well as circulating Th17 cells reduced as the patients showed clinical improvement. Our preliminary results suggest that classical monocytes and Th17 cells could be a predictive biomarker for systemic inflammation and hyperglycemia is a major factor which increases these cell numbers. Functional studies with Treg and Th17 showed that Tregs from controls were able to suppress the Th17 proliferation and foam cell formation while Tregs from patients were compromised in
their functional activity, suggesting that loss of regulatory function could be a cause of immune dysregulation in CAD patients. Interestingly, young or premature CAD patients (<45 years), without any known classical risk factors were found to have a higher level of serum glucose levels, although their Hb1Ac levels were normal. In these patients, who are probably prediabetic an association was observed between glucose levels and inflammatory Th17 cells. Further, hyperglycemia could trigger the expansion of Th17 and apoptosis in regulatory cells, suggesting a link between stress and loss of function of regulatory cells.

The level of subclinical infection was not differentiating patient and control population but CMV and CPN infection level show a correlation to inflammatory cells. Contrary to earlier reports, we observed a lower level of antibodies to HSP60 and ApoB proteins in patients with the acute coronary syndrome, compared to healthy individuals, while circulating antigen levels to HSP60 were significantly higher in these patients. An inverse correlation was observed between antibody levels and Th17 cells and IL17 concentration in serum.

The results from our study suggest that there is a progressive loss of regulatory T cells and expansion of inflammatory cells with the severity of CAD. Stress induced by hyperglycemia is an important factor which can activate autoimmune response, inflammation and loss of Treg function, leading to the expansion of inflammatory cells. This also results in loss of protective antibodies which can sequester the autoantigens and reduce the exacerbation of autoimmune response. Controlling stress and early detection and prevention of hyperglycemia will be beneficial in controlling the high prevalence of CAD in India.