Dear Editor,

Atherosclerotic coronary artery disease (CAD) affects both men and women and accounts for approximately >4.5 million deaths annually in the developing countries.\(^1\) Atherogenic lipoproteins namely, low density lipoprotein (LDL) and lipoprotein remanants promote atherosclerosis, and high density lipoprotein (HDL) prevents it. However, in some instances increased plasma HDL concentrations can result from reduced catabolism due to blockade in the dynamic flow of HDL lipids from peripheral tissues to the liver. In such a scenario, measuring HDL concentration alone may not be accurate in assessing the cardio vascular risk. With literature review, Framingham study (HDL concentrations predicting cardiovascular risk) reveals that 40% of coronary events occurred in subjects with normal HDL levels.\(^2\) This has fueled our search in which measuring HDL Quality, rather than Quantity, would help in a better prediction of atherosclerotic coronary artery disease.

High density lipoprotein is believed to have two important functions affecting the occurrence of atherosclerosis. One function is called reverse cholesterol transport, which may be conceptualized in terms of cholesterol efflux from the arterial macrophages. The lipid deposited at the site of atherosclerotic lesions are removed and transported to the liver or other cholesterol metabolizing tissues for catabolism. This involves specific transporters like ABC transporter A1 (ABCA1) and ABCG1.\(^3\)

The other function of HDL is antioxidant/anti inflammatory property. Apo A1 is important in determining the antioxidant role of HDL by protecting against oxidation of LDL. The presence of antioxidant enzymes on HDL such as paraoxonase and acetyl hydrolase platelet activating factor were found to prevent the formation of oxidized LDL. It has been suggested that HDL has evolved as part of the innate immune system. High density lipoprotein also stimulates endothelial nitric oxide synthase (eNOS), diminish endothelial dysfunction, and thereby retard the process of atherosclerosis.\(^4\) In addition, HDL stimulates glucose uptake and fatty acid oxidation, decrease insulin resistance, and increase the insulin secretion by the pancreas.

Dodani and colleagues have reported that 70% of south Asian immigrants with subclinical CAD has dysfunctional HDL compared to controls.\(^5\) Cell based assay which require endothelial cells, smooth muscle cells and monocytes were originally used for the measurement of dysfunctional HDL. Recently, cell-free assay, which is a rapid diagnostic test for the detection of dysfunctional HDL has been developed. The test measures the ability of HDL in preventing the formation of oxidized phospholipids. The HDL inflammatory index can be calculated by normalizing the cell-free assay values. According anti-inflammatory index, HDL can be classified into proinflammatory or anti inflammatory one. Studies have documented in subjects with high HDL an inflammatory index to classify it as pro inflammatory i.e dysfunctional and this assay allows the identification of individuals at high risk.\(^6\)

Concentration of HDL in plasma is an individual risk predictor. However, the association of atherosclerotic coronary artery disease with dysfunctional HDL has been proven in many studies. The measurement of HDL alone might be a true predictive of coronary artery diseases. The association of HDL concentration and the disease seem to depend on whether or not HDL is proinflammatory. Further large scale research is required to establish such an association.

Balasubramaniam Gayathri MD,
Department of Biochemistry, PSG Institute of Medical Sciences and Research, Coimbatore, No.55, Ashok Nagar II Avenue, M.K.P Colony, Tamilnadu, India.
Tel: +91 944 4547482
Email: drgayukv@yahoo.co.in
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