Cardiovascular disease (CVD) covers all diseases that affect the heart and circulation which clinically referred as coronary heart disease (angina and heart attack) and stroke. Despite the significant improvement which has been achieved in the management of cardiovascular diseases, atherosclerosis remains the leading cause of illness, disability and death in present era¹ (Fig 1.1). Coronary artery disease (CAD) has emerged as a staggering health burden in India. Recent analysis of the data pertaining to native Indians has clearly indicated, India is on the verge of CAD epidemic. It is presumed that by the year 2015, CAD mortality is going to increase in the order of 103% in males and 90% in women. In India the prevalence of CAD reported from the studies performed in the last decade range between 7.6% to 12.6% for urban population and 3.1% to 7.4% for rural population respectively.²

![Fig 1.1: PREVALENCE OF CVD](image)

Multiple genetic, environmental, physiological and metabolic functions may contribute to the multifactorial cardiovascular disease. A large number of studies have demonstrated an association of family history with CVD, suggesting that inherited genetic factors may play an important role in disease progression. Recent studies conducted on candidate genes have evaluated that genetic risk data with environmental risk factors has led to a promising improvement in the prediction of CAD.³
INTRODUCTION

The sequence of events leading to CVD includes endothelial dysfunction, atherosclerotic plaque formation, and rupture of atherosclerotic lesion. Atherosclerosis is an inflammatory disease of the large arteries which is characterized by the formation of atherosclerotic plaque. In majority of cases, atherosclerosis related clinical events, such as myocardial infarction or ischemic stroke, are caused by rupture of a vulnerable atherosclerotic lesion.

The risk factors for CVD could be classified as conventional or traditional risk factors, which have been shown to be causally associated with CVD like smoking, diabetes etc, and the emerging or novel risk factors, which have been shown to be associated with CVD, but their usual role in development of CVD is still debated. Conventionally, the traditional risk markers as LDL-C were widely renowned as an established cardiovascular risk marker. Results of numerous clinical trials demonstrate the capability of LDL-C to independently predict development and progression of coronary heart disease. However, there are subsets of patients who do not have raised lipid profile and normal LDL-C values but still they develop CVD. Extensive researches have been done to determine the underline causes of CVD and risk markers exclusively related to the group of these patients.

Several inflammatory molecules have been put forward as biomarkers for plaque vulnerability. Biomarkers are biochemical features that can be used to measure the presence of certain disease, the disease progress, or the effect of treatment. In the context of atherosclerosis, concentrations of C-reactive protein (CRP), fibrinogen and leukocyte count in blood have been investigated most extensively. However, large meta-analysis has demonstrated that their prognostic value for assessing risk of CVD or adverse outcomes is limited. Therefore, there is continuous search for novel, more powerful biomarkers which are able to predict the occurrence of future cardiovascular complications.

Recent studies have drawn attention towards myeloperoxidase (MPO), one of the enzymes of the innate immune system, as a potential marker of cardiovascular disease (CVD) and a potential target for treatment. Traditionally, MPO was considered as a bactericidal agent, but recent studies have emphasized the importance of MPO in CVD progression. The principal sources of MPO are activated neutrophils and monocytes. Myeloperoxidase has been identified in human plaques and exerts potent proatherogenic effects. These include oxidation of low-density
lipoprotein (LDL), rendering it atherogenic, as well as oxidative modification of apolipoprotein (apo) A1, attenuating its capacity to promote cholesterol efflux.\textsuperscript{14} Myeloperoxidase activity also diminishes nitric oxide bioavailability, which leads to endothelial dysfunction.\textsuperscript{15} This combination of detrimental effects has culminated in the concept that MPO may be an active mediator of atherogenesis.\textsuperscript{11}

MPO has been shown to provide prognostic value in the setting of chest pain and acute coronary syndromes.\textsuperscript{16} Recent studies of the community-based European Prospective Investigation of Cancer (EPIC)/Norfolk population reported that systemic MPO independently predicted risk of development of incident cardiovascular disease and death in apparently healthy middle-aged subjects. Moreover role of -463G/A genetic polymorphism of myeloperoxidase is involved in the occurrence and severity of CVD is suggested by different scientist.\textsuperscript{17}

Patients who were deficient in MPO were less susceptible to cardiovascular diseases.\textsuperscript{18} A functional MPO promoter polymorphism −463G/A, which altered MPO expression levels, was associated with increased incidence of CAD and severity of atherosclerosis.\textsuperscript{19} It has been reported that \textit{MPO} gene -463G/A polymorphism is related to changes in lipid levels,\textsuperscript{20} that may be involved in the oxidation of low-density lipoprotein, the high levels of MPO increasing the brittleness of artery plaques, thereby converting the plaque from the stable to the unstable state, thus increasing the risk of acute coronary syndrome.\textsuperscript{21}

The intensity of the MPO expression influences and alters both the diagnostic accuracy and prognostic value of MPO. The genotype GG for MPO is present in 60 - 66\% of the western population and is associated with higher levels of Myeloperoxidase than the genotypes AG or AA.\textsuperscript{22} Genetic polymorphism has identified different individual abilities of expression, observing that patients with low expression present fewer cardiovascular events and higher susceptibility for severe infections.\textsuperscript{23} On the other hand, GG homozygotic individuals for MPO submitted to elective coronary angiographies present strong expression and lower survival rates.\textsuperscript{24}

Thus with the realization that Asian Indians are highly susceptible to CVD and India is at the verge of CVD epidemic, there is an all round effort to identify risk prone individuals to adopt effective strategies for the prevention and management of CVD. Several candidate metabolic and genetic factors had been suggested as the risk factors for CVD. Reports pertaining to their association with CVD and its
pathophysiology, however, are not uniform from different parts of world, suggest different milieu of gene-environment– metabolic interactions. Related studies on the Indian subjects in India and abroad are relatively recent and preliminary. Since, levels of MPO and oxidized LDL along with oxidative stress are some of the emerging risk factors of CVD in Asian Indians.

It is important to elucidate the role of MDA, Catalase, oxidized LDL, non-HDL cholesterol and MPO in the pathophysiology and biochemical aspects of CVD and the genetic determinants of the same. Also the factors which influence LDL oxidation hence need to be elucidated and subjects with higher than acceptable levels of oxidized LDL as well as those predisposed to the same need to be investigated or studied. Moreover the question arises that how the association between -463G/A genetic polymorphism in Myeloperoxidase influence the risk and severity of CVD as well as its independent association with CVD needs to be investigated. There is paucity of such published reports / studies from India. Hence, it is worth exploring whether these variants of MPO are genetic determinant for predisposition to CVD.