Coronary Heart Disease Risk Factors: Known and the Less Known

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Primordial prevention strategy for coronary heart disease (CHD) involving control of three lifestyle related risk factors - smoking, physical inactivities and aberrant diet, the most cost-effective method\(^1\) could be considered rather crude. As one looks, it will be noticed that major coronary risk factors-smoking, hypertension, high low density lipoproteins (LDL) cholesterol, diabetes mellitus, and those peculiar to South Asians-truncal obesity, low HDL cholesterol and high triglycerides are secondary manifestations of these deviant lifestyles and explain more than 90\% of the incidence of CHD worldwide.\(^2\)

CHD increases with age in both men and women. The risk factors have been classified into modifiable (related to lifestyle, habits, stress) and partially modifiable/immodifiable (diabetes mellitus, positive family history, age, gender).

The term ‘risk factor’ is generally used to describe those characteristics found in individuals that have been shown in observational studies, epidemiological studies, autopsy studies, metabolic studies and genetic studies to relate to subsequent occurrence of CHD. It is necessary to differentiate between risk and uncertainty: risks are future outcomes to which it is possible to attach probabilities, whereas ‘uncertainty’ is a situation where a probability cannot be ascribed.

CHD risk factor assessment is concerned with the nature of risk, where probabilities can be ascribed to outcome and where modification of the factors can have a beneficial effect on outcome.

Coronary heart disease does not begin with chest pain, dyspnoea or an arrhythmia but rather with the more subtle signs like poor coronary risk profile or silent myocardial ischaemia (ischaemia is relatively mild and therefore does not stimulate the pain receptors or patients are less sensitive to painful stimuli because of defect of the sensory nerves as in diabetics).

Atherosclerosis is a result of aging process per se as well as the cumulative effect of the known risk factors exerting their effect over time. Diabetes mellitus and hypertension both tend to cause accelerated atherosclerosis. When the pathological basis of all the three acute coronary syndromes -unstable angina, acute myocardial infarction and sudden ischaemic death is considered, it is the association of thrombosis with atherosclerosis that is paramount.\(^3\) It is important to understand the concepts of ‘plaque’ burden; the average number of plaques in the coronary arteries and the nature of plaques appear to determine the incidence of CHD. The level of inflammatory activity in the plaque makes it vulnerable and may lead to precipitation of thrombotic episode. The plaque disruption involves the mechanical tearing of the fibrous cap of the plaque that has a lipid core. Endothelial erosion is simply a continuation of endothelial denudation that occurs over many plaques and is an important mechanism in diabetic subjects.

It will thus be realised that the spontaneously occurring coronary atherosclerosis, accelerated by the risk factors mentioned above appear to be preparing a ground upon which is superimposed the triggering event now known to be an occlusive thrombus often associated with platelet/fibrin emboli. Angiographic studies have revealed that plaques that underlie thrombotic lesions and infarction are not necessarily those that have previously caused stenosis. Plaque rupture, disruption or fissuring exhibit a wide spectrum of severity.

Emotional and physical stress may be identified as triggers to acute MI through mechanisms of increased adrenergic activation and characterised by

1. An increased heart rate and contractility that increase the oxygen demand (MVO) and precipitates ischemia
2. Increased arterial blood pressure that is associated with increased cardiac output and increased alpha adrenergic-mediated peripheral vascular resistance exaggerates ischemia and damages the vascular endothelium
3. Increased circulating free fatty acids have harmful effects on membranes and promote platelet aggregation.

Many and multiple risk factors have been identified; the weightage attributable to a given factor can vary. There have been papers in which it has been pointed out that not all conventional factors may have an equally decisive role to play in our geographico-ethnic and social diverse cultural conditions.

In the Indian context it is important that the role of lesser known factors is studied and understood well. There is a high incidence of prevalence of insulin resistance, diabetes and central obesity in Indians. Among the emerging risk factors are high levels of lipoprotein (a), homocysteine, Apo B, triglycerides, ferritin, fibrinogen and PAI-I found in Indians.
Some factors which are atheroprotective like HDL and HDL 2b are found in low levels in Indians. The impact of nurture appears to be greater in Indians than in other populations due to genetic predispositions. Elevated levels of Lp(a) in childhood is a better predictor of premature CHD than any other risk factor and this correlates with premature CHD in parents and grandparents. Elevated levels of Lp(a) along with high homocysteine levels explains epidemic of CHD in Indians.

Observations in large clinical and epidemiological studies have suggested that elevated homocysteine levels are a risk factor for atherosclerosis. Moreover, moderate and intermediate hyperhomocysteinemia is present in 12% to 47% of patients with coronary, cerebral, or peripheral arterial occlusive disease. Homocysteine is said to have a direct toxic effect on endothelial cells. It is also proposed that homocysteine induced endothelial injury exposes the subendothelial matrix, which in turn leads to platelet activation. Various epidemiological studies have evaluated a number of haemostatic factors. Of these, fibrinogen, plasminogen activator inhibitor type I (PAI-I) and Factor VII (FVII) have shown significant independent association with arterial vascular disease, most consistently for fibrinogen and PAI-I; platelet hyperactivity has also been observed.

Several studies have examined whether a relatively common polymorphism mutation (PIA2) of the platelet glycoprotein IIIa gene, has been associated with MI risk. The recognition that as many as 30-50% of patients with established CAD lack the traditional risk factors has led to the search for additional risk factors that may predispose individuals to CAD.

Wilma D, et al in their article have studied the role of ferritin as a potent threat for acute myocardial infarction. The role of ferritin has been long debated and particularly appears to be relevant in the Indian context where there is high prevalence of anaemia. The statistical tests applied and the conclusion drawn do indicate that endorsement of the finding by more studies from other parts of the country can throw more light on the issue.

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REFERENCES