Diabetes & coronary artery disease

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Over 20 million people are affected by diabetes in India. These numbers are expected to increase to 57 million by 2025. Diabetic patients are at increased risk of atherosclerosis and its clinical sequelae, particularly coronary artery disease (CAD). CAD remains the most important cause of mortality among diabetic patients. The pathophysiological process of atherosclerosis in diabetic subjects is accelerated by several factors such as hyperglycaemia, insulin resistance, abnormal lipid profile, oxidative modification of lipoproteins, increased blood pressure, altered rate of fibrinolysis, etc. These changes in diabetes render the dormant atherosclerotic plaque vulnerable precipitating an early clinical event. Thus CAD in diabetic subjects carries a worse prognosis than in non-diabetic subjects. This review focuses on the potential role of various risk factors contributing to atherosclerosis in diabetic patients.

Key words Chennai urban population study (CUPS) - coronary artery disease - diabetes - dyslipidaemia - fibrinogen - homocysteine - intimal medial thickness (IMT) - lipoprotein (a)

The prevalence and severity of atherosclerosis is higher among diabetic patients, particularly coronary artery disease (CAD) which is a major contributor to mortality and morbidity among type 2 diabetic subjects. In spite of the wide ethnic and geographical variation in the prevalence of both diabetes and CAD, the association between these two disease entities remains strong. Diabetic subjects have been shown to have a higher risk for CAD compared to the non-diabetic population. Further, independent of the cardiovascular risk factors seen among non-diabetic subjects, diabetes specific factors also contribute to the increased CAD risk and also to vulnerability of plaque rupture.

Epidemiological evidence of CAD in diabetic subjects

The Framingham study was the first to demonstrate that diabetic men and women have a 3.5 to 4 fold higher risk of CAD mortality compared to their non-diabetic counterparts. Follow up data after 24 yr showed greater mortality among the diabetic subjects reflecting the cumulative effect of age and diabetes. This was further confirmed by the Multiple Risk Factor Intervention Trial (MRFIT) study. It was also demonstrated that the mortality increased markedly among diabetic subjects compared to non-diabetic subjects due to the co-existence of multiple risk factors. The protective effect seen among non-diabetic pre-menopausal women disappeared in those who had diabetes. Indeed diabetic women had a higher risk for CAD than diabetic men. A study by Haffner et al clearly suggested a two-fold higher risk for CAD among diabetics compared to non-diabetic subjects. A recent publication suggested that diabetes decreased
the life expectancy of an individual by eight years. The Cardiovascular Health Study reported that diabetic subjects have increased incidence of CAD, stroke and myocardial infarction. Haffner et al elegantly showed that the risk for CAD starts from the stage of impaired glucose tolerance itself i.e., even before overt diabetes sets in.

Rising prevalence of diabetes & CAD among Indians

India is the world's second largest country with a population of 1 billion. The health profile of India in the 21st century is rather disturbing, as it is currently facing a triple health burden. The first is the still unconquered existing communicable diseases; second, the newly emerging infectious diseases and finally the man made degenerative or non-communicable diseases (NCDs). Of the NCDs, diabetes and CAD appear to be the major threat to Indians.

The Global Burden of Disease Study projects a CAD epidemic world-wide with a greater impact on developing countries. Further, this study estimates that India would face the greatest burden due to CAD. Projection of the mortality rates due to CAD in India predict a 100 per cent increase in the rates from 1985-2015. Industrialized countries show a trend towards a decline in CAD mortality, while the epidemiological transition in developing countries triggers a reverse trend with an increase in CAD mortality. Indeed, the total number of CAD deaths from China and India is expected to equal that of the CAD deaths contributed by all developed countries put together. A marked ethnic diversity has been also well documented in the prevalence of CAD with Indians having an increased propensity for developing premature CAD. This has been shown consistently in epidemiological studies on migrant Indians in UK, Trinidad, Singapore and other countries. Projections based on current Indian data reveal that India would lead the world in the number of CAD deaths in the next 15 yr. This is further confirmed by the recent Jaipur Heart Watch Study and the subject has been elegantly reviewed recently.

In India, the CAD epidemic almost appears to overlap with the epidemic of diabetes. Recently the World Health Organization (WHO) has declared India as the country with the largest number of diabetic subjects in the world. Current estimates suggest that India presently has approximately 20 million diabetic people, which is expected to increase to 57.2 million in 2025 and by that time, approximately 20 per cent of the total diabetic patients world-wide would be from India.

Though Indians have long been shown to have a high degree of predilection for CAD, not many epidemiological studies have analyzed the extent of the problem in diabetic patients. We took up an epidemiological study called the Chennai Urban Population Study (CUPS) to determine the prevalence of diabetes and CAD in urban south Indians. The study subjects were categorized as having normal glucose tolerance (NGT), impaired glucose tolerance (IGT) or diabetes based on oral glucose tolerance test (OGTT). CAD was diagnosed using medical history and Minnesota coding of using 12 lead ECGs. The overall CAD prevalence was 11 per cent in the total population. This represents a ten-fold increase in prevalence of CAD in urban India during the last 40 yr and the figures are now approaching those reported in migrant Indians (Fig. 1) and also confirm the findings of an earlier south Indian study.

The prevalence of diabetes in this study population was 12 per cent, and an additional 5.9 per cent of subjects had impaired glucose tolerance. This means that 1 out of every 6 individuals in urban Chennai above the age of 20 yr has either diabetes or impaired glucose intolerance. These results are supported by a similar population-based-study conducted in six urban areas in India, where the overall prevalence rate of diabetes was 12.1 per cent.

In the CUPS study, the prevalence of CAD was higher among diabetic subjects. 21.4 per cent (known diabetes- 25.3%, newly diagnosed diabetes - 13.1%) of the diabetic subjects had CAD compared to 9.1 per cent of subjects with normal glucose
tolerance\textsuperscript{26}. Indeed, the risk for CAD seemed to increase even at the stage of impaired glucose tolerance and was similar to that noted among newly diagnosed diabetic subjects (Fig. 2).

**Studies on preclinical atherosclerotic markers**

CAD is one of the clinical end points of atherosclerosis, which in its earlier stages involves both functional and structural changes in the arteries. These changes can be studied using sophisticated non-invasive techniques like high-resolution ultrasound. Structural changes can be assessed by studying the carotid intimal medial thickness (IMT)\textsuperscript{36} while functional changes can be assessed by studying endothelial dysfunction by flow mediated dilatation or by arterial stiffness studies\textsuperscript{36}. These pre-clinical atherosclerotic markers have

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**Fig. 1. Rising prevalence of CAD - Comparison of Indian surveys.**

<table>
<thead>
<tr>
<th>Reference</th>
<th>State, Country</th>
<th>Sample size (age in yr)</th>
<th>Year</th>
<th>Prevalence of CAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gupta et al\textsuperscript{32}</td>
<td>Haryana, India</td>
<td>1504 (&gt;30)</td>
<td>1975</td>
<td>4.5%</td>
</tr>
<tr>
<td>Gupta et al\textsuperscript{33}</td>
<td>Uttar Pradesh, India</td>
<td>2212 (≥20)</td>
<td>1995</td>
<td>7.6%</td>
</tr>
<tr>
<td>CUPS\textsuperscript{26}</td>
<td>Tamil Nadu, India</td>
<td>1175 (≥20)</td>
<td>2000</td>
<td>11.0%</td>
</tr>
</tbody>
</table>

**Fig. 2. Prevalence of CAD in subjects with different degrees of glucose intolerance CUPS data.**

Source: Mohan et al\textsuperscript{26}.
gained wide recognition in the field of cardiology, as they are useful surrogate markers for CAD and can also be used in studies on prevention of CAD.

Earlier studies on carotid IMT clearly demonstrated that atherosclerosis manifests two to three decades earlier among diabetic subjects compared to non-diabetic subjects. The Cardiovascular Health Study showed that preclinical cardiovascular disease predicts subsequent clinical events. It has also been shown that increase in glucose levels even in the non-diabetic range leads to increased IMT of the common carotid artery.

In the CUPS study we examined the carotid IMT in diabetic and non-diabetic subjects. The mean IMT values among diabetic subjects were higher compared to normal subjects. Carotid atherosclerosis (defined as IMT >1.1 mm) was present in 20 per cent of diabetic subjects compared to 1 per cent of non-diabetic subjects. We also observed that the diabetic subjects had increased IMT at every age point compared to their non-diabetic counterparts. Further, the newly diagnosed diabetic subjects had significantly higher IMT values compared to non-diabetic subjects, but significantly lower compared to known diabetic subjects. Further analysis of the data revealed that diabetes per se was an important risk factor for increase in IMT.

We also looked at functional markers of atherosclerosis by studying endothelial dysfunction and arterial stiffness. Endothelial dysfunction was measured as flow mediated dilatation (FMD) of the brachial artery using high resolution B mode ultrasonography. Flow mediated dilatation (FMD) was found to be reduced in diabetic patients (2.1±2.95%) compared to age and sex matched non-diabetic subjects (6.64±4.38%, P<0.0001). Arterial stiffness was measured by the Augmentation index of the radial artery by the SphygmoCor machine and was found to be significantly greater in diabetic subjects (Augmentation index - 27.48±7.41%) compared to age and sex matched non-diabetic subjects (19.10±8.19%, P<0.0001).

**Link between diabetes & CAD**

While a strong association between diabetes and CAD has been well established, it is still not clear whether these disease entities occur in parallel or in series. If it is in series i.e., one is a consequence of the other, then control of one might help to prevent the other. On the other hand, if they occur in parallel, disease management will be more complicated and will need separate approaches for both entities. The common soil hypothesis suggests these two entities could have a common genetic abnormality. The Barker hypothesis suggests that these two diseases could be related to low birth weight. According to this hypothesis low birth weight followed by obesity in adolescence or early adulthood would lead to insulin resistance and hence to diabetes and CAD. In the sections below we examine the role of individual factors in increasing the risk of CAD in diabetic patients.

**Role of hyperglycaemia & advanced glycation end products**

Evidence for the association of hyperglycaemia with CAD comes from the Whitehall Study, Honolulu Heart Study, Bedford survey, Pathobiological Determinants of Atherosclerosis in Youth (PADY) study and several others. The Whitehall study followed up 18,403 individuals for 7.5 yr and suggested that subjects with glucose intolerance had 1.5 to 2.5 fold high risks for CAD mortality. The Honolulu study based on 12 yr data revealed that the subjects with base-line glucose values in the fifth quintile had higher risk for CAD compared to the lowest quintile. The Bedford survey demonstrated a stepwise increase in CAD mortality from normal to diabetes during a 10 yr follow up period. A 10 per cent increase in CAD was shown among type 2 diabetic subjects with 1 per cent increase in glycosylated haemoglobin (HbA1c) in the Wisconsin Epidemiologic study. The PADY study examined coronary arteries in youth and observed an increase in fatty streaks in subjects with HbA1c greater than 8 per cent.

In the CUPS study, the odds ratio for CAD increased with increase in quartiles of fasting plasma glucose and 2 h post glucose load plasma glucose indicating a strong association with CAD (Fig. 3). A similar association has been shown in another Indian study conducted at Bangalore.
It is well known that hyperglycaemia contributes to the development of micro and macrovascular complications in diabetes and the chief promoters are the advanced glycosylated end products (AGEs)\(^{48}\). AGEs are formed due to irreversible non-enzymatic reaction between the aldehyde group of glucose (in circulation) and the free epsilon amino group of N-terminal amino acids of proteins. These molecules once formed undergo oxidation and glycoxidation leading to conformational changes in the proteins. Certain AGEs that contribute to a greater propensity to develop micro and macrovascular complications among diabetics are carboxy methy lysine (CML), pentosidine and pyrraline\(^{49,50}\). These products stimulate several pathways like oxidative stress and inflammation and thus predispose to atherosclerosis.

**Role of hypertension**

It has been well documented that the prevalence of hypertension is higher among diabetic compared
to non-diabetic subjects. Similarly the prevalence of diabetes among hypertensive subjects is higher compared to normotenstive subjects. This clearly indicates that these two diseases co-exist. However, it is still not clear whether diabetes precedes hypertension or vice versa. A higher prevalence of CAD among hypertensives is well documented.

Blood pressure is by far the most important factor contributing to endothelial dysfunction and this was also seen in the CUPS study. Once endothelial dysfunction sets in, this leads to structural changes in the arteries, which manifest as increased intimal-medial thickness. Intervention studies have demonstrated that treatment of hypertension reduces CAD mortality more among diabetic subjects compared to non-diabetics. The Hypertension Optimal Treatment (HOT) trial, Systolic Hypertension in the Elderly Program study (SHEP), the United Kingdom Prospective Diabetes Study (UKPDS) and the Heart Outcomes Prevention Evaluation (HOPE) Study have demonstrated the beneficial effect of blood pressure control in preventing CAD. The SHEP study demonstrated a 22 per cent reduction in CAD among diabetic subjects. The UKPDS study also amply demonstrated that blood pressure control decreased the risk of CAD. The HOPE study suggested that controlling blood pressure with Ramipril may even delay the onset of diabetes, confirming the common link between diabetes and hypertension.

**Role of dyslipidaemia**

The Framingham study showed that hypertriglyceridaemia and low high density lipoprotein (HDL) cholesterol are commonly associated with diabetes. The specific features of diabetic dyslipidaemia are raised serum triglycerides and low levels of HDL cholesterol and alterations in the low density lipoprotein (LDL) phenotype with a preponderance of the small dense LDL pattern (phenotype B).

The association of serum cholesterol with CAD has been convincingly shown in clinical trials and in epidemiological studies. The Scandinavian Simvastatin Survival Study (4S), Cholesterol and Recurrent Events (CARE) and Heart Protection Study are the successful intervention trials that demonstrated reduction in CAD risk at par with cholesterol reduction in diabetic subjects. The 4S trial results showed a 55 per cent reduction in CAD mortality with simvastatin among diabetics versus 32 per cent among non-diabetic subjects, while the CARE trial demonstrated a 27 per cent risk reduction in diabetic subjects compared to 22 per cent among non-diabetic subjects with pravastatin. These studies confirm the beneficial effect of cholesterol lowering in reducing CAD mortality in diabetic patients.

The co-existence of other risk factors with hypercholesterolaemia increases the risk for CAD among diabetic subjects as shown by the MRFIT study. In the CUPS study the prevalence of CAD was higher among diabetic subjects for any given cholesterol level compared to non-diabetic subjects (Fig. 4).

The link between hypertriglyceridaemia and CAD has been shown in several studies. Overproduction of very low density lipoprotein (VLDL) in response to hypertriglyceridaemia leads to an abnormal lipoprotein profile that contributes to atherosclerosis. Moreover, the presence of triglyceride-rich lipoproteins in the human atheroma, provides ample evidence that triglyceride (TG) plays a pathophysiologic role in atherogenesis. A meta-analysis of 17 population-based prospective studies, showed increased plasma TG concentrations to be associated with a 32 per cent increase in risk of CAD in men and a 76 per cent increase in risk in women. However, it is still not clear whether it is hypertriglyceridaemia per se or the associated low HDL cholesterol that is more important as a risk factor for CAD as hypertriglyceridaemia is invariably associated with low HDL cholesterol levels.

Low levels of HDL cholesterol was first identified as a risk factor by the Framingham study. Studies on subfractions of HDL revealed HDL 2 cholesterol to be more reduced than HDL 3 cholesterol in diabetic subjects. Moreover, the catabolic rate of HDL seems to be increased among diabetic subjects. Recently the Veterans Affairs High
Density Lipoprotein Intervention Trial (VA-HIT) showed that an increase in HDL cholesterol was associated with reduction in the incidence of fatal and nonfatal myocardial infarction\textsuperscript{66}.

LDL cholesterol levels have been reported to be associated with CAD\textsuperscript{26}. Very recently, the small dense LDL has been shown to be most atherogenic\textsuperscript{67}. A recent study reports an increase in the prevalence of small dense LDL in migrant Asian Indians compared to Europeans\textsuperscript{68}.

In the CUPS study, it was observed that prevalence of CAD increased with increase in total cholesterol, LDL cholesterol, triglycerides and total cholesterol/HDL ratio. Risk factor analysis using multiple logistic regression analysis identified age and LDL cholesterol as the main risk factors for CAD\textsuperscript{26}.

**Role of oxidised LDLs in diabetes & cardiovascular disease**

The oxidative modification of lipids in vivo has been proposed to play a central role in atherogenesis and to contribute to the diverse vascular disease and ageing. The enhanced endocytosis of oxidised LDL by vascular wall macrophages transforms them into lipid-laden foam cells that characterize early atherosclerotic lesions\textsuperscript{69}. LDL also gets glycosylated and this further propagates damage to the vascular wall\textsuperscript{70}.

Moreover the LDLs that get sequestered inside the arterial compartment get modified and become proatherogenic augmenting the expression of several cytokines and growth factors that help smooth muscle cells to proliferate and migrate from the media to the intima of the artery\textsuperscript{71}. Extensive in vitro and in vivo studies have shown that modified (oxidised) LDL could initiate atherogenesis and thus be regarded as a potent risk factor.

**Novel risk factors**

The conventional risk factors like diabetes, lipids, blood pressure, obesity and smoking only explain 50 to 60 per cent of the total CAD risk of an individual. This indicates the necessity for identifying new risk factors to improve clinical risk stratification. Newer risk factors like lipoprotein(a), plasminogen activator inhibitor - 1, tissue plasminogen activator, fibrinogen, vascular cell adhesion molecule and integrins like fibronectins have been studied to find a possible association with diabetes and CAD. A recent study showed that most of the above mentioned risk factors are increased among South Asians compared to other ethnic groups indicating that South Asians have a vulnerable atherothrombogenic cardiovascular risk profile particularly among diabetic subjects\textsuperscript{72}.
Lipoprotein (a)

Lipoprotein (a) [Lp(a)] is a LDL-like lipoprotein that greatly increases the risk of atherosclerosis. Individuals with elevated levels of this lipoprotein are most prone to premature strokes and myocardial infarction\(^ {73,74}\). Lp (a) has homology with plasminogen and thus blocks fibrinolysis \textit{in vitro}. It may also interact with the endothelium to stimulate the growth of atherosclerotic plaques or promote thrombotic complications of atherosclerosis. Studies on native Indians have clearly shown Lp(a) to have a contributory role in CAD\(^ {75-78}\). Our study\(^ {76}\) on Lp(a) revealed high levels among subjects with CAD compared to normal subjects (Table I). We also found Lp (a) to be an independent risk factor for CAD in patients with type 2 diabetes even after correcting for LDL cholesterol and other lipid fractions\(^ {73,76}\). We further demonstrated that increased Lp(a) to be associated with increase in carotid IMT\(^ {78}\).

Homocysteine

Homocysteine, a sulphur-containing amino acid has been shown to be atherothrombogenic and thus is a potent risk factor for CAD\(^ {79}\). Retrospective and prospective studies have reported hyperhomocysteinaemia to be a risk factor for cardiovascular disease, independent of classic risk factors such as smoking, hypercholesterolaemia, diabetes mellitus and hypertension\(^ {80}\). Cell culture studies showed that homocysteine triggers platelet adhesion\(^ {81}\). Studies on migrant Indians have shown higher levels of homocysteine compared to the native population\(^ {82}\). However, studies on its association with CAD among native Indians have been consistently negative\(^ {83,84}\).

We found no difference in the mean homocysteine values in south Indian diabetic patients and non-diabetic patients with and without CAD\(^ {83}\). Hyperhomocysteinaemia is common in the elderly population and this is attributed to low intake of the B vitamins like folate, vitamin B\(_{6}\), and vitamin B\(_{12}\)\(^ {85}\). Intake of folate, is the most important dietary determinant of serum homocysteine levels and this may be an effective means of decreasing cardiovascular risk. It is possible that the decreased levels of homocysteine observed among the native Indians could be due to increased folate intake. However, it must be emphasized that all Indian studies were based on small numbers and all had measured homocysteine levels in the fasting state. Larger studies, perhaps using methionine loaded homocysteine levels, are needed to throw further light on the association of homocysteine and CAD in Indians.

Coagulation risk factors

The prothrombotic state is believed to be accelerated in diabetic subjects and this has been attributed to increased levels of fibrinolytic factors, which include tissue plasminogen activator (tPA) and plasminogen activator inhibitor (PAI-1). Diabetes is associated with various abnormalities of the haemostatic and fibrinolytic system. Indeed, diabetes is considered to be a hypocoagulable and hypofibrinolytic state. Increased levels of fibrinogen and PAI-1 have been shown to be present in diabetic subjects\(^ {86,87}\). Reduced fibrinolysis may predispose diabetic patients to deposit fibrin and this may exacerbate accumulation of LDL, as dyslipidaemia is a common phenomenon among these subjects. This is followed by vascular smooth muscle cell migration predisposing to a coronary event.

We found that PAI-1 antigen and tPA antigen levels were significantly elevated among subjects with CAD compared to those without CAD\(^ {88}\).
Patients with CAD were distributed more in the upper tertiles of these risk factors compared to those without CAD.

C-reactive protein

The inflammatory marker, C-reactive protein (CRP) has received a lot of attention recently in the field of cardiology. Several prospective studies have shown that high levels of high-sensitivity CRP identify increased risk of occurrence of CAD\(^9\). CRP, an acute phase reactant has long been considered as a classic marker for inflammation. Acute inflammation, infection, or tissue injury induces a marked increase in CRP. As atherosclerosis involves inflammation of the vascular endothelium, CRP levels tend to be raised. Given the lipoprotein binding and complement activation of CRP and its localization in atherosclerotic vessels, there is a strong likelihood that CRP may be involved in the atherosclerotic process\(^9\). Recent studies show that CRP enhances LDL aggregation and production of vascular cell adhesion molecules (VCAM) in cultured cells\(^91,92\).

Insulin resistance & clustering of risk factors

The higher mortality seen among type 2 diabetic patients is partly attributable to hyperglycaemia in association with an altered lipid profile. The altered composition of lipoproteins and lipids is preceded by hyperinsulinaemia resulting from insulin resistance\(^9\). Insulin resistance and the compensatory increase in insulin secretion bring about a state of chronically increased insulin and glucose levels in the blood (hyperinsulinaemia and hyperglycaemia) which is a predecessor for diabetes. The Helsinki Policeman Study, which followed up 982 individuals for 9.5 yr revealed fasting insulin level to be a predictor for CAD\(^9\). However, the role of hyperinsulinaemia per se in atherogenesis is still a debatable issue.

The terms ‘metabolic syndrome’ and ‘insulin resistance syndrome’ are used to describe a cluster of metabolic abnormalities (Fig. 5) comprising abdominal obesity, glucose intolerance/type 2 diabetes mellitus, dyslipidaemia and hypertension\(^9\). In the view of most experts, three of the four main

![Fig. 5. Clustering of cardiovascular risk factors or the components of metabolic syndrome. This cluster has factors which lead to atherosclerosis and thrombosis, thus insulin resistance syndrome precedes and predisposes to the atherothrombotic process leading to coronary artery disease.](image)
components are sufficient for defining the syndrome. The metabolic cluster seems to explain a major part of the pathogenesis of CAD.

We studied the prevalence of Insulin Resistance Syndrome (IRS) in the CUPS study using the European Group of Insulin Resistance (EGIR) criteria and found that IRS was present in 11.2 per cent of urban south Indians.

Hyperinsulinaemia, insulin resistance and other components of the metabolic syndrome have been shown to be more prevalent among Asian Indians. Studies have also shown low birth weight to be a contributor to insulin resistance among Indians. It has been hypothesized that low birth weight followed by a tendency to obesity in childhood or adolescence could lead to IRS during adulthood. Hyperinsulinaemia has been shown to have a potential role for CAD in Asian Indians. In addition, clustering of risk factors of the insulin resistance syndrome has also been shown among native Indians. In the CUPS study, subjects with more than one metabolic abnormality had higher prevalence of CAD compared to subjects with a single metabolic abnormality (Table II).

The decreased fibrinolysis, increased PAI-1 levels, increased tPA and increased fibrinogen levels are all considered to be features of the metabolic syndrome. Proinsulin and insulin have been shown to induce production of PAI-1 in experimental models. PAI-1 due to its acute phase reactant nature could increase during diabetes, due to inflammation. Further obesity, a component of the insulin resistance syndrome, has been shown to be related to increased PAI-1 synthesis. Conversely, marked weight loss has a beneficial effect on PAI-1. In our study on subjects with and without diabetes, fibrinogen levels were higher among diabetic subjects compared to non-diabetic subjects.

Conclusions

Numerous factors and pathways are involved in the increased predisposition of subjects with diabetes to CAD. With the emergence of newer risk factors, our understanding of the pathogenesis of CAD is improving. Though many of these may be genetically induced, behavioural changes or pharmacological interventions can modify many of them so as to prevent or postpone CAD. Lifestyle modifications which include dietary modification, regular physical activity, weight reduction and cessation of smoking along with control and prevention of diabetes, hypertension and hyperlipidaemia could eventually help to reduce the burden of CAD in our country.

References


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