

# Risk Factors for Coronary Artery Disease in Indians

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Cardiovascular disease (CVD) has emerged as a major health burden worldwide. CVD contributed to 15.3 million deaths in 1996, of which 5.5 million was from developed countries and 9.77 million from developing countries.<sup>1</sup> A rise in the prevalence of CVD in the early half of twentieth century and a subsequent decline in the latter half have been well documented in the industrialized countries. However, the scenario is reversed in developing countries especially India with a steady escalation in prevalence of CVD.<sup>2</sup>

Earlier studies on migrant Indians in the UK, USA, Canada and Trinidad showed that migrant Indians had higher rates of CAD compared to the indigenous population. It is consistently observed that Indians have premature CAD and that their risk for CAD was two to four times higher than the white European population.<sup>3</sup> The recent SHARE study showed a CAD prevalence of 10.7% among South Asians compared to 4.6% in Europeans.<sup>4</sup>

Within the Indian subcontinent also, there has been a rapid rise in CAD prevalence. In 1959, Padmavati<sup>5</sup> reported the prevalence of CAD to be 1.0% and this rose to 4.5% in the year 1975<sup>6</sup> and 7.9% in the year 1996 in subjects aged 20 years and above.<sup>7</sup> In a recent study of subjects aged 40 years and above, the prevalence was shown to be 14.3%.<sup>8</sup> The Chennai Urban Population Study (CUPS) carried out in 1262 individuals > 20 years of age showed the crude prevalence of CAD to be 11% while the age-adjusted prevalence rate was 9.0%.<sup>9</sup> Thus the prevalence of CAD appears to be ten times higher in India compared to that reported 40 years ago and the prevalence of CAD in urban Indians is fast approaching the figures reported in migrant Indians.<sup>9</sup>

Recent data from the Jaipur Heart Watch-2, on 1800 subjects based on a stratified sampling technique reported an escalation in the prevalence rates of conventional cardiovascular risk factors like obesity, diabetes and dyslipidemia among North Indians compared to the figures noted in 1990.<sup>10</sup>

CAD has a multi-factorial etiology, with many of the risk factors being influenced by lifestyle. Rapid change in dietary habits coupled with decreased physical activity in India as a consequence of urbanization may partly explain the escalation of CAD. India is at present experiencing an epidemiological transition with high rates of urbanization. This has led to

economic improvement the consequence of which is increased fast food consumption and tobacco usage and decreased physical activity. One of the effects of this transition is a shift in the disease spectrum from communicable to non-communicable diseases, particularly CAD and diabetes.

Given the high prevalence of CAD among Indians, studies on cardiovascular risk factors in native Indians are warranted as most risk factors for CAD have been derived from Western studies. In this issue, Achari and Thakur<sup>11</sup> report on a large retrospective study on 5748 CAD patients and 8103 healthy normals. Serum cholesterol levels, LDL cholesterol levels and total cholesterol to HDL ratio were higher among the CAD subjects compared to normals. The study also makes another interesting observation that there is a lack of association of serum triglycerides levels with CAD. Though the study results are of interest, regression analysis to identify the risk factor for CAD would have added more value to the article.<sup>11</sup> In the case-control study by Burman *et al*, again LDL cholesterol levels and total cholesterol/HDL cholesterol ratio and Lp(a) levels were higher in CAD patients compared to controls but there was no significant difference in serum triglyceride levels.<sup>12</sup>

In CUPS, we noted that LDL cholesterol and age were risk factors for CAD but serum triglyceride levels did not come out as an independent variable.<sup>9</sup>

Another large clinic-based study on 17,855 type 2 diabetic subjects looked at the association of isolated hypercholesterolemia and isolated hypertriglyceridemia with CAD.<sup>13</sup> The prevalence of CAD was significantly higher among patients with isolated hypercholesterolemia, isolated high LDL and isolated low HDL cholesterol compared with normal lipidemic individuals, but not in those with isolated hypertriglyceridemia.

There appears to be differences in lipid associations with CAD between native and migrant Indians. In migrant Indians, serum triglyceride levels have been consistently found to be associated with CAD.<sup>14</sup> However in native Indians, LDL cholesterol and total cholesterol/HDL cholesterol ratio appears to be more important. One factor which is common to all Indians is a low HDL cholesterol levels.<sup>14</sup> In the face of low HDL cholesterol levels, even moderate elevation of LDL cholesterol appears to be sufficient to produce an atherogenic profile.

However, the role of triglycerides cannot be completely ruled out as the link between hypertriglyceridemia and CAD has been shown in several studies. Triglyceride measurement

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per se is not that informative as some of the triglyceride-rich lipoproteins present in the plasma are not atherogenic like large VLDLs, while others like small VLDL are highly atherogenic. Increased production of small VLDL in response to hypertriglyceridemia could contribute to atherosclerosis. This is confirmed by the presence of triglyceride-rich lipoproteins in the human atheroma. Moreover, increase in triglyceride levels are associated with low HDL cholesterol and with small dense LDL molecules (Phenotype B).<sup>15</sup> Recently an increased prevalence of small dense LDL in migrant Asian Indians has been shown in a study conducted in USA.<sup>16</sup>

Prevalence of elevated LDL cholesterol defined by the NCEP guidelines levels is only 38.8% among CAD subjects in the study done by Achari.<sup>11</sup> This suggests that either the cut-off used for elevated LDL cholesterol is not appropriate among Indians or that more than 60% of the CAD is not explained by elevated LDL cholesterol levels. A similar finding was observed in the clinic study done on 17,855 type 2 diabetic patients that the prevalence of myocardial infarction was 2.9% in subjects with LDL levels below 100 mg/dl compared to 3.61% in subjects with LDL above 100 mg/dl. This could mean that in Indians, even those with LDL below the cut-off of NCEP<sup>13</sup> have a high risk for CAD suggesting that aggressive lipid lowering is justified in Indians.

In this regard the findings of Heart Protection Study are of great interest. This study demonstrated that the use of statins was beneficial even for subjects with LDL cholesterol levels below the threshold given by the NCEP guidelines. The main message from that study is to "treat high risk patients with high dose-statin irrespective of their baseline cholesterol levels".<sup>17</sup> This seems to be most applicable to Indians, where the threshold of LDL cholesterol for CAD appears to be lower than that demonstrated in Western populations. The main limiting factors of course would be the cost.

Recently, a number of newer cardiovascular risk factors have been identified. These factors are of great interest in native Indians where more than 60% of the CAD remains unexplained by conventional risk factors. Comparative studies on newer risk factors illustrated that Asian Indians have higher C-reactive protein, plasminogen activator inhibitor (PAI 1) and homocysteine levels.<sup>18</sup>

Lipoprotein (a) levels have been consistently shown to be elevated among Asian Indians compared to other ethnic groups suggesting a genetic predisposition to coronary artery disease.<sup>19,20</sup> A study of the cord blood of 542 male and 468 female newborns from three ethnic groups of Singapore correlated the racial profile of Lp(a) at birth with the CAD risk in adults. Elevated Lp (a) levels in Asian Indians parallel the three fold high risk of CAD compared to the Chinese.<sup>21</sup> The study by Burman, *et al*<sup>12</sup> done on 20 CAD patients and 20 healthy normals showed that Lp(a) level was associated with CAD. This confirms several earlier reports from India.<sup>22</sup> However, the point of interest in their study was that dietary fat intake was associated with higher Lp(a) levels in CAD patients but not in controls. This is a surprising finding

because traditionally Lp(a) levels are believed to be genetically inherited and not influenced by dietary factors. Though this association might be casual and not causal, one cannot rule out the role of environmental triggers in influencing genetic factors to produce detrimental effects such as the increase in Lp(a) levels.

Given that India is a large country with tremendous urban-rural differences and regional variations large, multicentre prospective long-term follow-up studies addressing non-communicable diseases like diabetes, hypertension and CAD are the urgent need of the hour. Several studies such as the Prospective Urban Rural Epidemiology (PURE) study, Industrial Cohort study and others are now in progress and should provide valuable incidence data in the years to come and thus throw significant light on the causative factors for CAD and thus pave the way for prevention of this silent killer.

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### *Announcement*

#### **Applications are invited from the members of API for**

1. Post of **Vice President** that has fallen vacant due to Dr. SB Gupta, who has been elected as President-Elect
2. Post of **Member/Faculty** that has fallen vacant due to Dr. AK Agarwal who has been elected as Vice Dean.

The contestant for the post of Vice President of API should fulfil the requirements of one continuous full term of 3 years in elected position in the Governing Body. The application should be duly proposed and seconded by the valid member of API.

To contest for member /faculty council of ICP, the contestant should be the member of API for 10 years and should be fellow or founder fellow of the college for 5 years standing. The application should be duly proposed and seconded by the valid member of ICP.

The application should reach **Hon. Secretary**, API, Laud Mansion, 3rd Floor, 21 Maharshi Karve Road, Opp. Charni Road Station (E), Mumbai 400004 latest by **28th February 2004**.

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The State/Local Chapters are invited to send their applications for **APICON 2006**. The application should be accompanied by a resolution of Governing body of the respective state/local chapter inviting for the conference and signed by Chairman and Secretary of that chapter. The application should reach **Hon. Secretary**, API, Laud Mansion, 3rd Floor, 21 Maharshi Karve Road, Opp. Charni Road Station (E), Mumbai 400004 latest by **15th March 2004**.