A retrospective case-control study of modifiable risk factors and cutaneous markers in Indian patients with young coronary artery disease

Amitesh Aggarwal • Sourabh Aggarwal • Ashish Goel • Vishal Sharma • Shridhar Dwivedi
Division of Preventive Cardiology, Department of Medicine, University College of Medical Sciences and GTB Hospital, University of Delhi, Delhi, India
Correspondence to: Amitesh Aggarwal. Email: dramitesh@gmail.com

Summary

Objective Indians have the highest risk rates for coronary artery disease (CAD) among all ethnic groups. There is a paucity of data on the risk factors and clinical markers associated with premature CAD. We aimed to determine whether young CAD is due to preventable lifestyle-related factors and cutaneous clinical markers are useful in identifying at-risk patients.

Design Single-centre retrospective study.

Setting Tertiary care center.

Participants A total of 292 patients (age ≤40 years) who presented with acute CAD between January 2005 and June 2009 and 92 age, and gender-matched controls.

Major outcome measures Details of smoking, family history of premature CAD, waist size, blood sugar and lipid profile. Clinical evidence of arcus juvenilis, premature greying of hair and premature baldness sought.

Results Dyslipidaemia (91%), smoking (74.3%), low high-density lipoprotein cholesterol (HDL-C) (68.9%), central obesity (47.7%) and greying of hair (34.9%) were the most commonly associated factors. Compared with male patients, females had greater prevalence of dyslipidaemia, low HDL-C, central obesity, hypertension, diabetes and family history of premature CAD. The presence of cutaneous markers was significantly associated with premature CAD.

Conclusions CAD in young Indian people is multifactorial; dyslipidaemia, low HDL-C, smoking, hypertension, central obesity and family history of premature CAD are the most common risk factors. Smoking in men and central obesity in women are the most prevalent factors. Clinicians should be highly suspicious of patients with presence of cutaneous markers, and they should be followed intensively for lifestyle modifications.
Introduction

Coronary artery disease (CAD) is a leading cause of morbidity and mortality in both developing and developed countries. Approximately, one-sixth of the world’s population lives in India. CAD is the most common cause of mortality in India.1 The South Asian population, especially that of the Indian subcontinent, is believed to have a higher risk and prevalence of CAD compared with other ethnic groups.2 India has 29.8 million symptomatic patients with CAD, 19.3 million diabetics and 118 million hypertensive individuals, who are at risk of developing metabolic syndrome, thus potentiating the risk for CAD.3–5 CAD in the Indian subcontinent has been reported to manifest almost a decade earlier than in the West.5 Moreover, deaths related to CAD occur 5–10 years earlier in the Indian subcontinent than in Western countries.6

The association of smoking, dyslipidaemia, hypertension, diabetes, central obesity and a positive family history with CAD is well established, and recent studies have also associated these risk factors with premature CAD.7–10 More recently, various reports have indicated the potential association of different cutaneous markers with premature CAD so that the population at risk can be identified early.11–14 However, well-defined studies analysing such an association in India are lacking. This retrospective case-control study was done to establish the association of the above mentioned modifiable risk factors and identify the association of cutaneous markers like premature greying of hair, premature baldness and arcus juvenilis and further analyse the pattern of distribution of these risk factors in both males and females with premature CAD in India.

Methods

The present retrospective case-control study was conducted at the Guru Teg Bahadur Hospital, a 1200-bed teaching hospital in New Delhi. Ethical approval for the study was obtained from the Institutional Ethical Review Committee. The case records of all patients presenting acutely with premature CAD (age ≤40 years) and hospitalized to the coronary care unit of our hospital between January 2005 and June 2009 were analysed retrospectively. In order to obtain an adequate control population, records were searched for age and gender-matched patients who presented to hospital with non-cardiac complaints during the same time period. Data was obtained and selected for all patients who presented to outpatient clinics with acute conditions like viral rhinitis, sore throat, diarrhea, etc. All patients with a previous history of CAD and those who were admitted during acute presentation were excluded to remove elements of confounding bias. After very carefully reviewing all the available data, 92 patients were selected as controls.

Records of all subjects less than 40 years of age presenting with acute coronary syndrome were included for analysis. The diagnosis of acute coronary syndrome was made on the basis of symptoms, electrocardiogram (ECG) abnormalities, cardiac injury enzymes and/or echocardiography as described by Luepker et al.15 The case sheets were scrutinized for historical features, smoking and family history of premature CAD. Records were screened for presence or absence of arcus juvenilis, premature greying of hair and premature balding. Incomplete case records (with missing data on smoking history, family history of CAD, diabetes mellitus, hypertension, premature arcus, balding or greying of hair), subjects who presented as brought dead to the hospital or those who had unexplained deaths were excluded from the study.

Waist size, fasting and postprandial blood sugar, fasting lipid profile (total cholesterol, high-density lipoprotein cholesterol [HDL-C], low-density lipoprotein cholesterol [LDL-C] and triglycerides) and measurement of carotid intima media thickness (CIMT) was also noted. The grading of smoking was assessed by calculating the smoking index (SI), which was based on the number of cigarettes/day multiplied by total duration in years of active smoking. The guidelines used for diagnosis of dyslipidaemia, hypertension, diabetes mellitus, obesity, premature greying of hair and baldness in this study have been described elsewhere.4
The intima media thickness (IMT) of the carotid artery, determined by a high-resolution B mode USG System having an electronic linear, high-frequency broadband transducer for superficial scanning with a mid-frequency of 7.5 MHz, was measured at three areas along the vessel wall including (1) the posterior aspect of the common carotid artery, (2) common carotid artery bifurcation and (3) anterior wall of internal carotid artery. IMT measurements were quantified as the average of arterial wall thickness (excluding segments involved with plaque) as per protocol followed by the trained physician who had done the measurements. Note was also made of the presence of any plaque.

Statistical analysis was done using SPSS v.17 (SPSS South Asia, New Delhi, India). Continuous variables were expressed as mean ± standard deviation (SD) and percentage was calculated for categorical variables. Comparison of continuous and categorical variables was done in both male and female groups using unpaired two-tailed t-test and chi-squared test and any statistically significant difference was noted. Odds ratio (OR) was calculated for risk factors with discrete variables. For the purpose of the study, P value < 0.05 was considered statistically significant.

Results

A total of 292 young patients (age ≤40 year) of acute coronary syndromes were admitted to our hospital during the study period from January 2005 to June 2009. Mean age of patients was 36.3 ± 4.1 years with 261 (89.4%) being men and 31 (10.6%) being women. Ninety-two controls were selected from the same time period with mean age of 35.6 ± 3.26 years with 81 (88.0%) being men and 11 (12%) being women. There was no significant difference between the case and control groups with regard to age and gender (P > 0.05). ST elevation myocardial infarction was seen in 79.4% patients in CAD group with anterior wall involvement as the most common ECG diagnosis (48.6%). Risk factor profile of young CAD patients is shown in Table 1. Dyslipidaemia, smoking, low HDL-C and central obesity were the most commonly associated risk factors in young CAD patients. Smoking (OR, 17.6; 95% confidence interval [CI], 9.2–33.4; P < 0.0001), hypertriglyceridaemia (OR, 2.58; 95% CI, 1.43–4.66; P = 0.0021), hypertension (OR, 2.2; 95% CI, 1.14–4.31; P = 0.0235) and central obesity (OR, 1.91; 95% CI, 1.13–3.22; P = 0.0217) were more significantly associated with the patient group as compared with the control group. The presence of cutaneous markers namely arcus juvenilis (OR, 17.46; 95% CI, 2.37–128.39, P = 0.0003), premature balding (OR, 12.89; 95% CI, 3.09–53.74; P < 0.0001) and premature greying of hair (OR, 3.95; 95% CI, 2.01–7.76; P < 0.0001) were also found to be more significantly associated with young CAD patients as compared with controls. Mean CIMT was found to be 0.62 ± 0.12 mm. In all, 11.7% of patients had a CIMT value of more than 0.80 mm and 9.9% had presence of plaque in carotids.

Subgroup analysis of CAD patients showed 261 men with a mean age of 36.1 ± 4.1 years and 31 women with a mean age of 37.1 ± 3.6 years. Risk factor profile and comparison of young CAD male and female patients is shown in Table 2. As compared with women, men were more likely to be smokers, have increased total cholesterol, LDL-C, triglycerides, CIMT, arcus juvenilis and premature greying of hair. Dyslipidaemia, low HDL-C, central obesity, hypertension, diabetes and family history of premature CAD were more commonly associated with female gender. However, only the difference in smoking (more in men) and hypertension and central obesity (more in women) were statistically significant.

A majority of patients had between four and five concurrent risk factors among those studied, including smoking, family history of premature disease, hypertension, dysglycaemia, central obesity, increased LDL-C, increased triglycerides and low HDL-C (Figure 1).

Discussion

In this retrospective study, we found a statistically significant association of smoking, hypertension, hypertriglyceridaemia and central obesity in Indian patients with premature CAD as compared with controls; smoking was more predominantly associated with men and hypertension and central obesity were more commonly associated with women. Among cutaneous markers the patients had a significantly higher occurrence of
arcus juvenilis, premature greying of hair and premature baldness.

CAD has been known to be a disease in which multiple factors like smoking, dyslipidaemia, hypertension, diabetes, central obesity and hereditary factors play a major role. Smoking has been shown to be a major dominant modifiable risk factor associated with young CAD. It has been observed that health awareness campaigns in the developed world have resulted in a decline in smoking and it has become socially less acceptable than it was a decade ago. In contrast, developing countries like China and India are witnessing an increase in the incidence of smoking, especially among adolescents and a rise in the use of smokeless tobacco. We noted a high incidence (74.3%) of smoking in our study subjects, with a stronger association with men. Similar findings have been reported by Achari and Thakur. The results indicate that greater efforts are needed to control smoking among the young.

The importance of dyslipidaemia in the pathogenesis of CAD is well known. Elevated levels of cholesterol, LDL-C and triglycerides have been found in young Indian subjects with CAD and been postulated to be of particular importance even in the younger variant of the disease. In a study done between 1998 and 2002 in a North Indian population, Goel et al. showed that CAD occurs at much lower levels of total cholesterol and LDL-C than other populations, and high triglyceride and low HDL levels are more of a universal phenomenon in this population. Our study revealed a high prevalence of dyslipidaemia (91%), especially low HDL-C (68.9%), in our study population and significantly higher triglyceridaemia in the patient population. It can be postulated that metabolic profile of patients have deteriorated over time and a possible explanation could be degradation of lifestyle habits with greater consumption of junk foods by the young population.

### Table 1

| Profile of risk factors in young CAD patients and young control population |
|--------------------------------------------------|
| **CAD group (n = 292)** | **Control group (n = 92)** | **P value** | **OR (95% CI)** |
| Age (years ±SD) | 36.3 ± 4.11 | 35.6 ± 3.26 | 0.1737 | |
| Smokers* | 217 (74.3) | 13 (14.1) | <0.0001 | 17.6 (9.2–33.4) |
| Smoking index* | Range 0–1500 | Range 0–600 | <0.0001 | |
| Hypertension* | 73 (25.0) | 12 (13.0) | 0.0235 | 2.2 (1.14–4.31) |
| Family history of premature CAD | 88 (30.1) | 25 (27.1) | 0.6799 | 1.16 (0.69–1.95) |
| Diabetes mellitus | 43 (14.7) | 7 (7.6) | 0.1115 | 2.10 (0.91–4.84) |
| Prediabetes | 16 (5.4) | 4 (4.3) | 0.8753 | 1.28 (0.42–3.92) |
| Central obesity* | 113/236 (47.7) | 27/83 (32.5) | 0.0217 | 1.91 (1.13–3.22) |
| Premature arcus* | 47 (16.1) | 1 (1.1) | 0.0003 | 17.46 (2.37–128.39) |
| Premature balding* | 65 (22.3) | 2 (2.2) | <0.0001 | 12.89 (3.09–53.74) |
| Premature greying* | 102 (34.9) | 11 (11.9) | <0.0001 | 3.95 (2.01–7.76) |
| Dyslipidaemia | 172/189 (91.0) | 73/83 (87.9) | 0.5787 | 1.39 (0.61–3.17) |
| High total cholesterol | 36/189 (19.0) | 17/83 (20.5) | 0.9134 | 0.91 (0.48–1.74) |
| Low HDL-C | 122/177 (68.9) | 47/99 (59.5) | 0.1838 | 1.51 (0.97–2.62) |
| High triglycerides* | 81/185 (43.8) | 19/82 (23.2) | 0.0021 | 2.58 (1.43–4.66) |
| High LDL-C | 73/173 (42.2) | 28/80 (35.0) | 0.3427 | 1.36 (0.78–2.35) |
| Mean carotid intima media thickness (mm)* | (n = 111) 0.62 ± 0.12 | (n = 74) 0.54 ± 0.08 | <0.0001 | – |
| Increased CIMT (>0.80 mm)* | 11 (9.9) | 1(1.1) | 0.3447 | 3.56 (0.46–27.97) |
| Plaque* | 13/111 (11.7) | 0/74 (0.0) | 0.0058 | – |

* IQ, interquartile range

Figures in parentheses denote percentages

*P < 0.05
Enas et al.\textsuperscript{18} showed that Indian emigrants to Western states have a high prevalence of dyslipidaemia and insulin resistance, thereby increasing risk of CAD. A modest increase in body fat with central distribution has been shown to increase the risk of CAD.\textsuperscript{19} We found that a high prevalence (80.7\%) and a statistical significant association (OR, 1.91; 95\% CI, 1.13–3.22; \(P = 0.0217\)) of central obesity in patients with premature CAD (80.7\%).

Jain \textit{et al.}\textsuperscript{20} showed that a family history of premature CAD in first-degree relatives is associated with development of CAD. Gambhir \textit{et al.}\textsuperscript{21} further showed that low-molecular-weight isoforms of lipoprotein (a) were prevalent in Indian subjects with a positive family history of premature CAD. Interleukin-6 gene polymorphisms have also been described to be important genetic factors in premature CAD, and in the regulation of key atherogenic markers in Asian Indian families.\textsuperscript{22} We found that a positive family history was present in 30.1\% of our subjects. The family history not only indicates the genetic predisposition to disease but may also represent the sum total of the interaction of the individual with his environment, expressed in several ways including diabetes, thrombotic disorders, as well as a behavioural predilection to smoking. However, since it was a retrospective study, we could not assess association of low-molecular-weight isoforms of lipoprotein (a) due to the unavailability of data. Prevalence of an increasing number of risk factors in patients with premature CAD is also crucial since it has been shown that as the number of cardiovascular risk factors increases, so does the severity of asymptomatic coronary and aortic atherosclerosis in young people.\textsuperscript{23}

There has been increased interest regarding the usefulness of cutaneous markers in identifying people at high risk for CAD.\textsuperscript{12–14,24–26} We analysed the association of arcus juvenilis, premature greying of hair and premature baldness in this study and found a statistically significant association between these cutaneous markers and the presence of young CAD. Recent studies

\begin{table}[h]
\centering
\caption{Comparative risk factors profile of young male and female CAD patients}
\begin{tabular}{|l|c|c|c|c|}
\hline
 & \textbf{Males (n = 261)} & \textbf{Females (n = 31)} & \textbf{\(P\) value} & \textbf{OR (95\% CI)} \\
\hline
\textbf{Age (years \pm SD)} & 36.1 \pm 4.1 & 37.1 \pm 3.6 & 0.1572 & \\
\textbf{Smokers*} & 211 (80.8) & 5 (16.1) & <0.0001 & 21.94 (8.03–59.98) \\
\textbf{Smoking index*} & Range 0–1500 & Range 0–112 & <0.0001 & \\
 & Median 140 & Median 0 & & \\
 & IQ range 284 & IQ range 0 & & \\
\hline
\textbf{Hypertension*} & 59 (22.6) & 14 (45.1) & 0.0116 & 0.35 (0.17–0.76) \\
\textbf{Family history of premature CAD} & 76 (29.1) & 12 (38.7) & 0.3717 & 0.65 (0.30–1.41) \\
\textbf{Diabetes mellitus} & 35 (13.4) & 8 (25.8) & 0.1156 & 0.45 (0.18–1.07) \\
\textbf{Prediabetes} & 14 (5.3) & 2 (6.4) & 0.8014 & 0.82 (0.18–3.80) \\
\textbf{Central obesity*} & 91/210 (43.33) & 22/26 (84.61) & 0.0002 & 0.14 (0.05–0.42) \\
\textbf{Premature arcus} & 44 (16.8) & 4 (12.9) & 0.7600 & 1.37 (0.46–4.11) \\
\textbf{Premature greying} & 95 (36.3) & 8 (25.8) & 0.3330 & 1.65 (0.71–3.82) \\
\textbf{Dyslipidaemia} & 159/170 (93.5) & 19/19 (100) & 0.9681 & – \\
\textbf{High total cholesterol} & 35/170 (20.5) & 1/21 (4.7) & 0.1460 & 5.19 (0.67–39.98) \\
\textbf{Low HDL-C} & 113/159 (71.0) & 17/18 (94.4) & 0.0648 & 0.14 (0.01–1.12) \\
\textbf{High triglycerides} & 72/164 (43.9) & 9/21 (42.8) & 0.9276 & 1.04 (0.42–2.61) \\
\textbf{High LDL-C} & 67/155 (43.2) & 6/18 (33.3) & 0.5807 & 1.52 (0.54–4.27) \\
\hline
\textbf{Mean carotid intima media thickness (mm)} & 0.62 \pm 0.14 & 0.59 \pm 0.06 & 0.1829 & – \\
\textbf{Increased CIMT (\(\geq 0.80\) mm)} & 11/96 (11.4) & 0/15 (0.0) & 0.3593 & – \\
\textbf{Plaque} & 13/96 (13.5) & 0/15 (0.0) & 0.2779 & – \\
\hline
\end{tabular}

\text*{IQ, interquartile}
\text*{Figures in parentheses denote percentages}
\text*{\(P < 0.05\)}
\end{table}
in Singapore by Wu et al.\textsuperscript{13} and Ang et al.\textsuperscript{24} have demonstrated a significant association of arcus with cardiovascular risk factors. Our study highlights the importance of this marker in young CAD patients as well. Premature greying of hair has been shown to predispose one for CAD, and Pomerantz\textsuperscript{27} showed that premature greying of hair occurs in patients with CAD under 35 years of age. Trueb\textsuperscript{28} suggested that scalp ageing is subject to intrinsic and extrinsic factors including ultraviolet radiation and smoking. Usefulness of baldness as a marker of underlying CAD is still controversial. Recently, Mansouri et al.\textsuperscript{14} reported a significant association of androgenetic alopecia with CAD in women under the age of 55. We also reported a significant association of premature greying of hair and baldness in patients with premature CAD.

CIMT has been proposed to identify preclinical disease and it has been shown that a 0.1-mm increase in thickness augments the likelihood of acute myocardial infarction by 11%.\textsuperscript{29} Ward et al.\textsuperscript{30} showed that an increase in CIMT by 0.80 mm correlated with an enhanced risk of carotid atherosclerosis. We found that 11.7% of our study subjects had CIMT value more than 0.80 mm and 9.9% showed plaques. Measurement of CIMT could be used as a reliable non-invasive tool for early detection of CAD. Further prospective studies in the Indian population may be needed to establish its use.

The importance of the study lies in the fact that our study brings out the distinct association of smoking in a large subgroup of obese young men and women suffering from CAD. This paper serves as a guide for policy-makers to

---

**Figure 1**

Distribution of the subjects by the number of conventional risk factors present among them ($n = 136$). Risk factors included are smoking, family history of premature CAD, hypertension, dysglycemia, central obesity, increased LDL-C, increased triglycerides and low HDL-C.

| Number of risk factors for CAD present in a patient out of those risk factors studied | Frequency |
|---|---|
| 0 | 10.0 |
| 1 | 10.0 |
| 2 | 20.0 |
| 3 | 30.0 |
| 4 | 40.0 |
| 5 | 50.0 |
| 6 | 60.0 |
| 7 | 70.0 |
| 8 | 80.0 |
| 9 | 90.0 |
| 10 | 100.0 |
help focus them on potential targets to develop strategies to prevent premature CAD. Our study highlights smoking, hypertension, central obesity and dyslipidaemia as potential targets. Also, we postulate that the presence of cutaneous clinical markers like arcus senilis, premature greying and baldness can be used as preliminary evidence by clinicians for classifying patients at risk for premature CAD and that these patients should then be monitored intensively for control of other modifiable risk factors. A large multicentre prospective study can help further substantiate our hypothesis and help devise a scoring system specific for Indian patients at higher risk for young CAD. As Figure 1 shows most of the patients had more than two risk factors, patients need to be managed intensively for control of multiple risk factors.

Our study has a few limitations. While it would have been desirable to determine the effect of serum homocysteine levels, lipoprotein (a), small LDL-C, C-reactive protein, psychological factors like stress, diet and lifestyle in the study subjects, it was not economically or logistically feasible for our study group. Since it was a retrospective study, many patient’s data had to be excluded due to the insufficiency of this data. Thus, the study sample may not be a true representation of the population of young CAD patients at large. Also, we could not get too many controls for more efficient comparison since we choose only patients who presented to outpatient clinics.

The rise in prevalence of premature CAD is a reality that is becoming increasingly evident in India. While men are still predominantly affected, young women may no longer be considered immune to its occurrence. Premature CAD in India is of a multifactorial causation and dyslipidaemia, low HDL-C, smoking, central obesity and family history of premature CAD play a crucial role in its development. While smoking in men and central obesity in women are prevalent modifiable associated factors, premature greying of hair may indicate an underlying CAD.

References

1. Goyal A, Yusuf S. The burden of cardiovascular disease in the Indian subcontinent. Indian J Med Res 2006;124:235–44
2. Yusuf S, Reddy S, Oumpuu S, Anand S. Global burden of cardiovascular diseases: Part II: variations in cardiovascular disease by specific ethnic groups and geographic regions and prevention strategies. Circulation 2001;104:2855–64
3. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. Lancet 2005;365:217–23
4. Aggarwal A, Aggarwal S, Sharma V. Metabolic syndrome and coronary artery disease in Indians younger than 40 years. J Endocrinol Metab 2012;2:39–45
5. Gupta R. Burden of coronary heart disease in India. Indian Heart J 2005;57:632–8
6. Joshi P, Islam S, Pais P, et al. Risk factors for early myocardial infarction in South Asians compared with individuals in other countries. JAMA 2007;297:286–94
7. Achari V, Thakur AK. Association of major modifiable risk factors among patients with coronary artery disease – a retrospective analysis. J Assoc Phys India 2004;52:103–8
8. Tewari S, Kumar S, Kapoor A, et al. Premature coronary artery disease in North India: an angiography study of 1971 patients. Indian Heart J 2005;57:311–8
9. Goel PK, Bharti BB, Pandey CM, et al. A tertiary care hospital-based study of conventional risk factors including lipid profile in proven coronary artery disease. Indian Heart J 2003;55:234–40
10. Panwar RB, Gupta R, Gupta BK, et al. Atherothrombotic risk factors and premature coronary heart disease in India: a case-control study. Indian J Med Res 2011;134:26–32
11. Dwivedi S, Aggarwal A. The skin in general medicine. Clin Med 2010;10:306
12. Dwivedi S, Jhamb R. Cutaneous markers of coronary artery disease. World J Cardiol 2010;2:262–9
13. Wu R, Wang JJ, Tai ES, Wong TY. Cardiovascular risk factors, inflammation, and corneal arcus: the Singapore Malay eye study. Am J Ophthalmol 2010;150:581–7e1
14. Mansouri P, Mortazavi M, Eslami M, Mazinani M. Androgenetic alopecia and coronary artery disease in women. Dermatol Online J 2005;11:2
15. Lupeker RV, Apple FS, Christensen RH, et al. Case definitions for acute coronary heart disease in epidemiology and clinical research studies: a statement from the AHA Council on Epidemiology and Prevention; AHA Statistics Committee; World Heart Federation Council on Epidemiology and Prevention; the European Society of Cardiology Working Group on Epidemiology and Prevention; Centers for Disease Control and Prevention; and the National Heart, Lung, and Blood Institute. Circulation 2003;108:2543–9
16. Kumra V, Markoff BA. Who’s smoking now? The epidemiology of tobacco use in the United States and abroad. Clin Chest Med 2000;21:1–9, vii
17. Ray CS, Gupta PC. Bidis and smokeless tobacco. Curr Sci 2009;96:1324–34
18. Enas EA, Garg A, Davidson MA, Nair VM, Huet BA, Yusuf S. Coronary heart disease and its risk factors in first-generation immigrant Asian Indians to the United States of America. Indian Heart J 1996;48:343–53
19. Enas EA, Yusuf S, Sharma S. Coronary artery disease in South Asians. Second meeting of the International Working Group. 16 March 1997, Anaheim, California. Indian Heart J 1998;50:105–13
20. Jain P, Jain P, Bhandari S, Siddhu A. A case-control study of risk factors for coronary heart disease in...
urban Indian middle-aged males. *Indian Heart J* 2008;60:233–40

21 Gambhir JK, Kaur H, Prabhu KM, Morrisett JD, Gambhir DS. Association between lipoprotein(a) levels, apo(a) isoforms and family history of premature CAD in young Asian Indians. *Clin Biochem* 2008;41:453–8

22 Maitra A, Shanker J, Dash D, et al. Polymorphisms in the IL6 gene in Asian Indian families with premature coronary artery disease – the Indian Atherosclerosis Research Study. *Thromb Haemost* 2008;99:944–50

23 Berenson GS, Srinivasan SR, Bao W, Newman WP 3rd, Tracy RE, Wattigney WA. Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults. The Bogalusa Heart Study. *N Engl J Med* 1998;338:1650–6

24 Ang M, Wong W, Park J, et al. Corneal arcus is a sign of cardiovascular disease, even in low-risk persons. *Am J Ophthalmol* 2011;152:864–71e1

25 Shahar E, Heiss G, Rosamond WD, Szklo M. Baldness and myocardial infarction in men: the atherosclerosis risk in communities study. *Am J Epidemiol* 2008;167:676–83

26 Pandhi D, Gupta P, Singal A, Tondon A, Sharma S, Madhu SV. Xanthelasma palpebrarum: a marker of premature atherosclerosis (risk of atherosclerosis in xanthelasma). *Postgrad Med J* 2012;88:198–204

27 Pomerantz HZ. The relationship between coronary heart disease and the presence of certain physical characteristics. *CMAJ* 1962;86:57–60

28 Trueb RM. Aging of hair. *J Cosmet Dermatol* 2005;4:60–72

29 Salonen R, Salonen JT. Progression of carotid atherosclerosis and its determinants: a population-based ultrasonography study. *Atherosclerosis* 1990;81:33–40

30 Ward RP, Lammertin G, Vernich DE, Polonsky TS, Lang RM. Use of carotid intima-media thickness to identify patients with ischemic stroke and transient ischemic attack with low yield of cardiovascular sources of embolus on transesophageal echocardiography. *Stroke* 2008;39:2969–74