Prevalence of Coronary Artery Disease and Its Relationship to Lipids in a Selected Population in South India

The Chennai Urban Population Study (CUPS No. 5)

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OBJECTIVES

The aim of this study was to assess the prevalence and risk factors for coronary artery disease (CAD) in a native urban South Indian population.

BACKGROUND

High prevalence rates of premature CAD have been reported in migrant Asian Indians. There are very few studies on CAD in native Indians living in the Indian subcontinent.

METHODS

The Chennai Urban Population Study (CUPS) is an epidemiological study involving two residential areas in Chennai in South India. Of the total of 1,399 eligible subjects (age ≥20 years), 1,262 (90.2%) participated in the study. All the study subjects underwent a glucose tolerance test and were categorized as having normal glucose tolerance (NGT), impaired glucose tolerance (IGT) or diabetes. Twelve-lead electrocardiogram (ECG) was performed in 1,175 individuals (84%). Coronary artery disease was diagnosed based on previous medical history or Minnesota coding of ECGs.

RESULTS

The overall prevalence rate of CAD is 11.0% (age standardized, 9.0%). The prevalence rates of CAD were 9.1%, 14.9% and 21.4% in those with NGT, IGT and diabetes, respectively. Prevalence of CAD increased with an increase in total cholesterol (trend chi-square: 26.2, p < 0.001), low-density lipoprotein (LDL) cholesterol (trend chi-square: 24.5, p < 0.001), triglycerides (trend chi-square: 9.96, p = 0.002) and total cholesterol/high-density lipoprotein ratio (trend chi-square: 6.14, p = 0.0132). Multiple logistic regression analysis identified age (odds ratio [OR]: 1.05, p < 0.001) and LDL cholesterol (OR: 1.009, p = 0.051) as the risk factors for CAD.

CONCLUSIONS

The prevalence of CAD is rising rapidly in urban India. Lifestyle changes and aggressive control of risk factors are urgently needed to reverse this trend. (J Am Coll Cardiol 2001;38: 682–7) © 2001 by the American College of Cardiology

Asian Indians have considerably higher prevalence of premature coronary artery disease (CAD) and standardized mortality rates for CAD compared with Europeans, Chinese and Malays (1–4). A recent report from the Study of Health Assessment and Risk in Ethnic Groups (SHARE) indicates a significantly higher risk of cardiovascular events among South Asians compared with Europeans and Chinese (3). Within the Indian subcontinent, a dramatic increase in the prevalence of CAD has been predicted in the next 20 years due to rapid changes in demography and lifestyle consequent to economic development (5,6). Earlier studies in Asian Indians have shown that classical risk factors do not explain the excess of CAD seen in this ethnic group (7–13). It is also possible that the risk factors for CAD could differ considerably between native and migrant Indians because of differences in diet, physical activity, body weight and lifestyle changes consequent to affluence and cultural changes consequent to migration. Studies on the prevalence and risk factors of CAD in native Indians within the subcontinent are, therefore, urgently needed, particularly since the population of India has just reached one billion. In this paper, we report on the prevalence of CAD in an urban South Indian population and look at its relationship with serum lipids.

METHODS

The Chennai Urban Population Study (CUPS) is an ongoing population-based study on diabetes and its complications in Chennai (formerly Madras) in Southern India, a city with a population of approximately six million people. This study was approved by the institutional ethical committee. The methodological details of the study have been published recently (14). Briefly, two residential colonies in the urban Chennai city were selected for the study. All individuals age ≥20 years were eligible for the study. Of the total 1,399...
Abbreviations and Acronyms
ACE = angiotensin-converting enzyme
BMI = body mass index
BP = blood pressure
CAD = coronary artery disease
CUPS = Chennai Urban Population Study
ECG = electrocardiogram or electrocardiography
HDL = high-density lipoprotein
IGT = impaired glucose tolerance
LDL = low-density lipoprotein
MI = myocardial infarction
OR = odds ratio
SHARE = Study of Health Assessment and Risk in Ethnic Groups
UKPDS = United Kingdom Prospective Diabetes Study
WHR = waist-hip ratio

individuals, 1,262 (response rate 90.1%) underwent a screening program for diabetes, hypertension and other components of the insulin resistance syndrome (metabolic syndrome). Informed consent was obtained from all the participants. Ninety-one individuals had diabetes before the survey, and 61 were detected to have diabetes after the survey, and thus, there were a total of 152 diabetic subjects living in the two colonies. Additionally, 74 subjects with impaired glucose tolerance (IGT) were also identified based on the World Health Organization consultation group criteria (15).

Anthropometric measurements included height and weight measurements, and the body mass index (BMI) was calculated using the formula weight (kg)/height (m²). Waist and hip were measured using standard techniques, and the mean of two measurements was taken for calculating the waist-hip ratio (WHR). The weight/height ratio was also calculated. Individuals were classified as nonsmokers (never smoked) and smokers (ex-smokers plus current smokers). Alcohol intake was categorized as nil and yes (social drinking and regular drinking). Blood pressure (BP) was recorded in the sitting position in the right arm with a mercury sphygmomanometer (Diamond Deluxe BP apparatus, Pune, India). Two readings were taken 5 min apart, and the mean of the two was taken as the BP. Blood pressure was recorded by a trained physician who was unaware of the clinical status of the study subjects. Systolic pressure was recorded at the first appearance of sounds, and diastolic pressure was measured at the disappearance of sounds.

A fasting blood sample was collected after an overnight fast of at least 10 h for biochemical investigations. All biochemical parameters were carried out on Corning Express Plus Auto Analyser (Corning, Medfield, Massachusetts) using kits supplied by Boehringer Mannheim, Germany. Fasting and 2-h plasma glucose estimations (glucose oxidase method), serum cholesterol (CHOD-PAP method) and serum triglycerides (GPO-PAP method) were measured. High-density lipoprotein (HDL) cholesterol was estimated by CHOD-PAP method after precipitating low-density lipoprotein (LDL) and chylomicron fractions by the addition of phosphotungstic acid in the presence of magnesium ions and very low-density lipoprotein. Low-density lipoprotein cholesterol was calculated using the Friedewald formula (16). Hypertension was diagnosed based on a past medical history or if the BP was > 140/90 mm Hg (17).

CAD. A resting 12-lead electrocardiogram (ECG) was carried out on 1,175 subjects (response rate: 84%). Minnesota coding was used to grade the ECGs by a single trained grader (G. P.) who was blinded to the clinical status of the patient.

Definition of CAD for prevalence studies. Coronary artery disease was diagnosed based on a past history of documented myocardial infarction (MI) or ECG changes suggestive of ST-segment depression (Minnesota codes 1-1-1 to 1-1-7) or Q-wave changes (Minnesota codes 4-1 to 4-2) or T-wave changes (Minnesota codes 5-1 to 5-3) (15). Documented MI was diagnosed if an individual had a positive history of MI in the medical records (a summary report after discharge from a hospital). Medical records were verified wherever possible, and drug treatment for CAD (aspirin or nitrates) was also diagnosed as CAD.

Definition of CAD for analysis of risk factors. For analysis of cardiovascular risk factors, CAD was diagnosed based on documented MI or the presence of Q-waves or ST-segment changes on ECG.

Statistical analysis. All the data were computed on FoxPro database, and statistical analyses were done using SPSS PC + 4.0.1 version. The crude prevalence rates obtained from the study were age-adjusted based on the 1991 Chennai population census. Student t tests were used for comparison of means, and chi-square tests and Fisher exact tests were used for comparison of frequencies. Univariate regression analysis was performed using CAD as a dependent variable and age, gender, BMI, WHR, total, LDL and HDL cholesterol, triglycerides, systolic and diastolic BP, fasting and 2-h plasma glucose and pack years of smoking as independent variables. The independent variables that had a p value <0.2 on univariate analysis were used for risk factor analysis in multiple logistic regression analysis.

RESULTS

Table 1 shows the prevalence of CAD in the population. The overall prevalence of CAD is 11%, while the age standardized prevalence is 9.0%. The prevalence of Q-wave changes and ST-segment depression are similar among men and women, while the prevalence of T-wave abnormalities is higher among women (p < 0.001). The age standardized prevalence rate of overall Q-wave abnormalities among men is 2.1%, while in women it is 1.3%. The prevalence of CAD is also higher in those with IGT and diabetes compared with the normal glucose tolerance group.

It is possible that subjects with T-wave changes (Minnesota codes 5-1 to 5-3) may not have CAD but could have
left ventricular hypertrophy or other nonspecific causes. Hence, for the rest of the paper, to look at risk factors for CAD, only those with documented MI or those who had Q-wave or ST-segment changes were included (n = 47).

The group with CAD was older than the group without CAD (p < 0.001). Body mass index (p = 0.006), waist circumference (p = 0.039), waist-to-height ratio (p = 0.012), systolic and diastolic BP (p = 0.02) and hypertension (p < 0.001) were higher among the group with CAD compared with the group without CAD (p < 0.05) (Table 2).

Of the 11 CAD subjects who were receiving antihypertensive therapy, six were receiving beta-adrenergic blocking agents alone; two were receiving angiotensin-converting enzyme (ACE) inhibitors; one was receiving a calcium channel blocking agent, and two subjects were receiving a combination therapy of beta-blockers and ACE inhibitors. Among the 41 subjects who were receiving antihypertensive therapy in the non-CAD group, 14 were receiving beta-blockers; 12 were receiving calcium channel blockers; seven were receiving alpha receptor agonists; two were receiving ACE inhibitors, and six subjects were receiving a combination of beta-blockers and calcium channel blockers.

Only one subject in the CAD group (statin) and six subjects in the non-CAD group (3: statins, 3: fibrates) were receiving lipid lowering drugs.

The prevalence of CAD is 1.4% in subjects with cholesterol ≤4.0 mmol/l (154 mg/dl), 3.3% in those with cholesterol between 4.01 to 5 mmol/l (155 to 192 mg/dl), 6.9% in those between 5.01 mmol/l to 6.0 mmol/l (193 to 231 mg/dl), 11.3% in the 6.01 to 7.0 mmol/l group (232 to 269 mg/dl) and 12.5% in subjects with cholesterol levels >7.0 mmol/l (269 mg/dl). This increase is statistically significant (trend chi-square: 26.2, p < 0.001).

The prevalence of CAD in subjects with triglycerides ≤1 mmol/l (88 mg/dl) is 2.1%, 4.8% for triglycerides 1.01 to 2.0 mmol/l (89 to 177 mg/dl), 6.3% for those between 2.01 and 3.0 mmol/l (178 to 265 mg/dl) and 9.6% for those with triglycerides >3.0 (265 mg/dl). This increase is statistically significant (trend chi-square: 9.96, p = 0.002).

The prevalence of CAD is 7.6% in individuals with HDL cholesterol lower than 0.7 mmol/l (27 mg/dl), 2.5% in those between 0.71 and 0.90 mmol/l (28 to 35 mg/dl), 3.9% in those between 0.91 to 1.1 mmol/l (36 to 42 mg/dl), 6.1% for 1.11 to 1.3 mmol/l group (43 to 50 mg/dl) and 4.3% for those with HDL cholesterol for >1.3 mmol/l (50 mg/dl) (trend chi-square: 0.10, p = NS).

The prevalence of CAD is 2.2% in subjects with LDL cholesterol ≤3.0, 5.4% for LDL cholesterol between 3.01 to 4.0, 11.5% for LDL cholesterol between 4.01 to 5.0 and 11.8% for LDL cholesterol >5.0. There is a significant increase in the prevalence of CAD with an increase in LDL cholesterol levels (trend chi-square: 24.5, p < 0.0001).

The prevalence of CAD is 2.6% in subjects with total cholesterol to HDL ratio ≤3.5, 2.4% for a ratio between 3.5 and 4.5, and 5.9% for a ratio ≥5.5. The increase in the prevalence of CAD with an increase in total cholesterol to HDL ratio was significant (trend chi-square: 33.9, p < 0.0001).
lipoprotein; LDL is considered to be important risk factors for CAD (29,30) in other reports. Other reports show that microalbuminuria (33), small dense LDL (34), lipoprotein(a) (29), homocysteine (35), fibrinolytic and thrombogenic risk factors like tissue plasminogen activator, plasminogen activator inhibitor and fibrinogen are associated with CAD (13,36–38).

This study confirms that subjects with glucose intolerance have a greater risk of CAD (Table 1). It is well known that patients with type 2 diabetes have a two-fold to three-fold increased risk of developing CAD (39). Recent findings from the United Kingdom Prospective Diabetes Study (UKPDS) (40) show that among type 2 diabetic subjects, a quintet of potentially modifiable risk factors, namely increased concentration of LDL cholesterol, decreased concentration of HDL cholesterol, hypertension, hyperglycemia and smoking confer the risk of CAD.

Smoking, a well-established risk factor (41), had no association with CAD in this study. However, earlier case control studies have shown smoking to be a risk factor in Indians (9). The absence of association with smoking in this study can be attributed to small sample size or the under-reporting of smoking due to cultural and other barriers. Unfortunately, we could not perform serum nicotine estimations to quantify smoking habits in this study.

**Table 3. Multiple Logistic Regression of Determinants of CAD**

<table>
<thead>
<tr>
<th>Variables</th>
<th>$\beta$</th>
<th>S. E.</th>
<th>$p$ Value</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.053</td>
<td>0.0119</td>
<td>$&lt;0.0001$</td>
<td>1.05 (1.03–1.08)</td>
</tr>
<tr>
<td>Body mass index</td>
<td>0.030</td>
<td>0.04</td>
<td>0.43</td>
<td>1.03 (1.0–1.1)</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>$-0.0019$</td>
<td>0.015</td>
<td>0.90</td>
<td>1.0 (0.97–1.03)</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>0.0126</td>
<td>0.022</td>
<td>0.57</td>
<td>1.01 (0.9–1.06)</td>
</tr>
<tr>
<td>Fasting plasma glucose</td>
<td>0.004</td>
<td>0.003</td>
<td>0.87</td>
<td>1.004 (1.0–1.006)</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>$-0.014$</td>
<td>0.020</td>
<td>0.49</td>
<td>1.0 (0.95–1.03)</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>0.0090</td>
<td>0.0046</td>
<td>0.051</td>
<td>1.009 (1.0–1.02)</td>
</tr>
<tr>
<td>Serum triglycerides</td>
<td>0.004</td>
<td>0.003</td>
<td>0.17</td>
<td>1.004 (1.0–1.09)</td>
</tr>
</tbody>
</table>

Dependent variable: coronary artery disease; independent continuous variables: age, body mass index, systolic blood pressure, diastolic blood pressure, fasting plasma glucose, HDL cholesterol, LDL cholesterol, serum triglycerides.

**DISCUSSION**

**Prevalence of CAD.** Earlier studies on Asian Indians, mostly in migrant populations, have reported on the high prevalence of CAD and its occurrence at a young age (premature CAD) (1,3,12). This paper reports on the prevalence of CAD in an urban South Indian population and shows that the prevalence of CAD in urban Indians is now approaching the figures reported in migrant Indians, which range between 7% to 17% (18–22). The overall figure of 11% of CAD in the population represents approximately a 10-fold increase in the prevalence of CAD in urban India during the last 40 years (23–27).

Bhatnagar et al. (12) compared migrant Indians living in West London with native Indians living in Punjab. The migrant Indians had higher BMI, systolic BP and significantly higher lipid levels. However, both the migrant and native Indians had elevated lipoprotein(a) levels, suggesting that genetic influences may predispose Indians to premature CAD (3,11,28). It is of interest that, in the SHARE study, while atherosclerosis (carotid intimal medial thickness) was actually higher among Europeans, thrombosis was significantly higher in South Asians, suggesting that a thrombogenic risk factor profile predisposes the latter group to CAD (3).

**Risk factors for CAD.** Total and LDL cholesterol are considered to be important risk factors for CAD (29,30) in some studies, while hypertriglyceridaemia is reported to be the major risk factor in others (31,32). Other reports show that HDL ratio is statistically significant (trend chi-square: 6.14, $p = 0.013$).

Multiple logistic regression analysis was performed using CAD as the dependent variable and the risk factors, which had a significant association with CAD in the univariate analysis, namely age, BMI, systolic and diastolic BP, HDL and LDL cholesterol, triglycerides and fasting plasma glucose, as the independent variables. Only age (odds ratio [OR]: 1.05, $p < 0.001$) and LDL cholesterol (OR: 1.009, $p = 0.051$) had a significant association with CAD (Table 3).
many could have died at a young age due to CAD or other complications of diabetes. The second limitation of the study is that treatment with hypertensive drugs among the CAD group could have resulted in lower BP, which could be one of the reasons for the lack of association of BP with CAD. Moreover, hypertension was assessed using a conventional sphygmomanometer. This could have introduced observer bias. However, as all readings were taken by the same observer and two readings were taken and averaged, we believe this would have reduced this bias to some extent. Prospective longitudinal follow-up studies are required to throw light on the true risk factors for various cardiovascular end points including mortality. We intend to follow-up this cohort to obtain such data in the future.

Conclusions. The prevalence of CAD among urban South Indians is increasing rapidly and is now approaching the figures reported in migrant Asian Indians. Urgent steps are needed to modify lifestyle by increasing physical activity, modifying diet and perhaps making aggressive use of statins as part of the preventive strategy to reduce risk factors and, thus, the burden of CAD in this population.

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