Prevalence and Risk Factors of Peripheral Vascular Disease in a Selected South Indian Population

The Chennai Urban Population Study

GOPAL PREMALATHA, MBBS, FDIAB
SUBRAMANIAM SHANTHIRANI, MSC
RAJ DEEPA, MPHIL, PHD
JEROME MARKOVITZ, MD, MPH
VISWANATHAN MOHAN, MD, PHD, DSC

OBJECTIVE — The epidemiology of peripheral vascular disease has rarely been studied in non-European populations. The purpose of this study was to determine the prevalence and risk factors of peripheral vascular disease (PVD) among South Indians.

RESEARCH DESIGN AND METHODS — The Chennai Urban Population Study is an epidemiological study involving 2 residential areas in Chennai in South India. Of the 1,399 eligible subjects (≥20 years of age), 1,262 (90.2%) participated in the study. All of the study subjects underwent an oral glucose tolerance test and were categorized as having normal glucose tolerance (NGT), impaired glucose tolerance (IGT), or diabetes. Peripheral Doppler studies were performed on 50% of the study subjects, and PVD was defined as an ankle-brachial index (ABI) <0.9.

RESULTS — The prevalence rates of PVD were 2.7, 2.9, and 6.3% in individuals with NGT, IGT, and diabetes, respectively. The overall prevalence rate was 3.2%. Known diabetic subjects had a higher prevalence of PVD (7.8%) compared with newly diagnosed diabetic subjects (3.5%). PVD was uncommon until middle-age and then the prevalence rate increased dramatically. Univariate regression analysis showed age >50 years (odds ratio [OR] 6.3, 95% CI 2.1–20.6, $P < 0.001$) and hypertension (OR 2.7, 0.9–7.3, $P = 0.08$) to be associated with PVD, whereas smoking and serum lipid levels showed no association. Multivariate regression analysis identified age as the most significant risk factor for PVD. Of the 90 subjects who had coronary artery disease (CAD), only 6 had PVD, and the positive predictive value of the ABI for CAD was only 30%.

CONCLUSIONS — The prevalence of PVD in this urban South Indian population is considerably lower than that reported in European and U.S. studies and is in marked contrast to the high prevalence rate of CAD reported in this population.

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Peripheral vascular disease (PVD) is a major cause of morbidity and mortality especially affecting the elderly population (1–3). The prevalence of PVD is multifold higher in patients with diabetes compared with age- and sex-matched nondiabetic subjects (4), and this may be because of hyperglycemia, hypertension, hyperlipidemia, platelet factors, and other factors that are increased in diabetic subjects.

Recent estimates by the World Health Organization show that India already has the largest number of diabetic patients in any given country, and this trend will continue in the future (5). Several studies have shown that the prevalence of coronary artery disease (CAD) is very high among Asian Indians (6–9). Unfortunately, there is very little epidemiological data on PVD in either migrant Indians or individuals from the Indian subcontinent. Earlier clinic-based reports suggested that PVD is less common among Indian diabetic patients in the U.K. (10), South Africa (11), and Southern India (12). Because clinic-based reports are subject to referral bias, epidemiological data are needed to assess the burden posed by PVD. In this study, we report on the prevalence of PVD in a population-based study in urban Southern India.

RESEARCH DESIGN AND METHODS

Population description

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 ~6 million people. The methodological details of the study are described elsewhere (13). Briefly, 2 residential colonies in Chennai (Tirumangalam and T. Nagar), which represent the middle- and lower-income groups, respectively, were chosen for the study. These colonies were chosen for their geographic convenience, social differences, and the local support available, which would facilitate future incidence studies. In both colonies, all of the adults ≥20 years of age were invited to participate in a screening program for diabetes, hypertension, and other components of the insulin resistance syndrome (metabolic syndrome). The overall response rate

From the Madras Diabetes Research Foundation (G.P., S.S., R.D., V.M.), Gopalapuram, Chennai, India; and the University of Alabama at Birmingham (J.M.), Birmingham, Alabama.

Address correspondence and reprint requests to Viswanathan Mohan, MD, MNAMS, PhD, DSc, Madras Diabetes Research Foundation, 35 Conran Smith Rd., Gopalapuram, Chennai, 600 086, India. E-mail: drmohan@giasmd01.vsnl.net.in.

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Abbreviations: ABI, ankle-brachial index; CAD, coronary artery disease; CUPS, Chennai Urban Population Study; FPG, fasting plasma glucose; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; NFG, normal fasting glucose; NGT, normal glucose tolerance; OR, odds ratio; PG, plasma glucose; PVD, peripheral vascular disease; WHR, waist-to-hip ratio.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

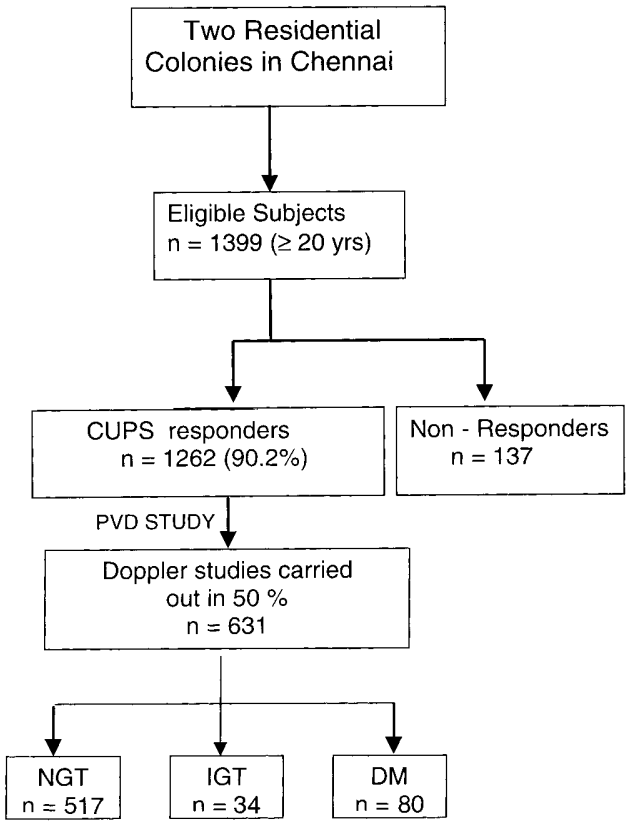

Figure 1—*Flow chart showing subject selection. DM, diabetes.*

was 1,262 of 1,399 eligible participants (90.2%).

A structured interview was used by a trained epidemiological team to record details of hypertension, diabetes, CAD, smoking, alcohol intake, and physical activity. Anthropometric measurements included height and weight measurements, and BMI was determined according to kilogram per meter squared. Waist and hips were measured using standard techniques, and the mean of 2 measurements was taken for calculating the waist-to-hip ratio (WHR). The blood pressure was recorded using a mercury sphygmomanometer in the right arm in the sitting position. Two readings were taken 5 min apart, and the mean was taken. Individuals were classified as nonsmokers (never smoked) and smokers (ex-smokers and current smokers). Alcohol intake was categorized as none and alcohol (social and regular).

Biochemical investigations

A fasting blood sample was taken, 75 g glucose was given orally with 200 ml water to all of the individuals excluding known diabetic subjects, and a 2-h postglucose sample was then collected. All of the blood samples were transported in ice boxes within 2–3 h to the M.V. Diabetes Specialities Centre, Chennai, India, for analysis.

All of the biochemical parameters were carried out on a Corning Express Plus Auto Analyzer (Corning, Medfield, MA.) using kits supplied by Boehringer Mannheim (Mannheim, Germany). Fasting and 2-h plasma glucose (PG) (glucose oxidase method), serum cholesterol (cholesterol oxidase method), serum triglycerides (glycerol phosphate oxidase method), and serum creatinine (modified kinetic method of Jaffé) were measured. HDL cholesterol was estimated by the cholesterol oxidase method after precipitating LDL and chylomicron fractions by the addition of phosphotungstic acid in the presence of magnesium ions and VLDL. LDL cholesterol was calculated using the Friedewald formula (14).

A resting 12-lead electrocardiogram was carried out on all of the subjects, and Minnesota coding was performed.

Peripheral Doppler studies

Because of logistical reasons, it was decided to restrict the Doppler studies to 50% of the participants of the study, i.e., every alternate individual. Figure 1 shows a flow chart of the selection of the study subjects. Thus, of the 1,262 responders in the main CUPS, Doppler studies were performed on 631 individuals by an operator who was blinded to subject conditions. All of the Doppler studies were performed by a single observer using the Kody Vaslab machine (Kody Labs, Chennai, India). Blood pressure recordings were made of the brachial pulses in the upper limb. Similar recordings were made of the dorsalis pedis and posterior tibial pulses in the lower limb by inflating the cuff proximal to the ankle, and the mean of these 2 readings was taken as the ankle pressure. The ankle-brachial index (ABI) ratio was calculated in every subject. A criterion for diagnosis of PVD was an ABI <0.9.

Definitions and diagnostic criteria

Diabetes was diagnosed in the study participants based on past medical history, drug treatment for diabetes (insulin or oral hypoglycemic agents), and/or criteria outlined by the World Health Organization (15). Diabetes was diagnosed if fasting PG (FPG) level was $\geq$126 mg/dl (7.0 mmol/l) and/or the 2-h PG level was $\geq$200 mg/dl (11.1 mmol/l). IGT was diagnosed if the FPG level was $<$126 mg/dl (7.0 mmol/l) and the 2-h PG level was between 140 and 199 mg/dl (7.7–11.0 mmol/l). Individuals with diabetes and impaired glucose tolerance (IGT) were considered together as having glucose intolerance for some of the calculations.

Hypertension was diagnosed based on history of drug treatment for hypertension or if blood pressure was $>$140/90 mmHg (16). Hypercholesterolemia and hypertriglyceridemia were diagnosed if serum cholesterol or triglycerides were $>$5.2 mmol/l (200 mg/dl) and $>$2.26 mmol/l (200 mg/dl), respectively, according to National Cholesterol Education Program guidelines (17). CAD was diagnosed according to documented history of myocardial infarction or Minnesota codes 1-1-1 to 1-1-7, 4-1, 4-2, or 5-1 to 5-3 (18).

Statistical analysis

All of the data were computed on a FoxPro database, and statistical analyses were done using SPSS PC version 4.0.1. Student's *t* tests were used for comparison of means, and χ^2 tests and Fisher's exact test were used for comparison of frequencies. Multi-

Table 1—*Baseline characteristics of the study population*

Men	253 (40)
Age (years)	46 ± 15
BMI (kg/m^2)	22.9 ± 4.6
Waist-to-hip ratio	0.84 ± 0.09
FPG (mmol/l)	4.9 ± 2.3
Systolic BP (mmHg)	125 ± 16
Diastolic BP (mmHg)	79 ± 9
Serum cholesterol (mmol/l)	4.7 ± 1.0
Serum triglycerides (mmol/l)	1.3 ± 0.80
Serum creatinine (μmol/l)	75.1 ± 21.2
Smokers (ex-smokers and current smokers)	72 (11.4)
Alcohol (regular and social)	113 (17.9)
Hypertension	111 (17.6)

Data are *n* (%) or means ± SD. BP, blood pressure.

ple logistic regression analyses were performed using PVD as the dependent variable and age, sex, smoking, BMI, WHR, hypertension, glucose intolerance, serum cholesterol, serum triglycerides, HDL cholesterol, LDL cholesterol, and serum creatinine as independent variables.

RESULTS

Study population

The study population was divided into the following glucose tolerance categories: *1*) NGT (*n* = 517), *2*) IGT (*n* = 34), *3*) newly diagnosed diabetes (i.e., diagnosed after the survey) (*n* = 29), and *4*) known diabetic subjects (*n* = 51).

Baseline characteristics of the whole population are presented in Table 1. Men comprised 40% of the population, 12% were smokers, and the mean BMI was 22.9 ± 4.6 kg/m^2.

Prevalence of PVD

Table 2 shows the prevalence of PVD. PVD was present in 20 of 631 subjects studied (3.2%). The age-standardized prevalence rate in the population was 2.0% (95% CI 1.0–3.3). The breakdown of PVD in relation to glucose tolerance showed that 14 of 517 (2.7%) subjects with NGT, 1 of 34 (2.9%) subjects with IGT, and 5 of 80 (6.3%) subjects with diabetes had evidence of PVD. Prevalence of PVD in newly diagnosed diabetic subjects was 3.5 vs. 7.8% in known diabetic subjects. If FPG alone is used as a criterion for the diagnosis of diabetes, 9 subjects had FPG ≥140 mg/dl, none of whom had PVD. If FPG ≥126 mg/dl is used for diagnosis, 13 subjects had diabetes, 1 of whom had PVD (7.7%)

Figure 2 shows the age-specific prevalence rates of PVD. In those subjects <30 years of age, the prevalence of PVD was 0%. In subjects 31–50 years of age with NGT, the prevalence was 1.5% and with glucose intolerance was 2.1%. In subjects 51–70 years of age with NGT, the prevalence was 3.4% and in those with glucose intolerance was 6.3%, and in subjects >70 years of age with NGT, the rates were 12.5 and 17.6%, respectively. The trend χ^2 (19.4) for the increase with age was statistically significant ($P = 0.001$) in the NGT patients, but it was not significant in the glucose-intolerant group, which could be because of small numbers resulting in broad CIs.

The mean age of the PVD group was higher than the non-PVD group ($P < 0.001$). The PVD group also had significantly higher systolic blood pressure compared with the non-PVD group ($P = 0.002$). None of the other clinical or biochemical parameters showed any significant difference between individuals with and without PVD. The prevalence of CAD among the PVD group was significantly higher than the non-PVD group ($P = 0.09$).

Univariate regression analysis revealed an odds ratio (OR) of 1.4 for hypercholesterolemia (>5.2 mmol/l), 0.6 for hypertriglyceridemia (>2.26 mmol/l), 0.7 for low HDL cholesterol (<0.9 mmol/l), 1.5 for high LDL cholesterol (>3.9 mmol/l), 2.6 for smoking, and 2.4 for diabetes. None of these risk factors had a significant association with PVD. Hypertension (OR 2.7, 95% CI 0.9–7.3, $P = 0.08$) had a weak association with PVD, and age >50 years (OR 6.3, 2.1–20.6, $P < 0.001$) had a strong association with PVD.

The relative OR in relation to FPG levels divided according to the recent American Diabetes Association classification as normal fasting glucose (NFG), impaired fasting glucose (IFG), and diabetes (19) were analyzed. There was a linear increase in the ORs for PVD with an increase in FPG levels (IFG OR 2.7, 95% CI 0.3–13.4; diabetes OR 4.4, 1.2–15.3); the NFG group was taken as the reference.

The multivariate logistic regression analysis using PVD as the dependent variable showed that only age (OR 2.6, 1.5–4.3, $P < 0.001$) had a significant association with PVD.

Table 3 shows the comparison of prevalence rates of PVD reported in various studies that have used similar techniques and criteria for the diagnosis of PVD. It can be seen that the prevalence rates of PVD in our study appear to be considerably lower than those reported among Europeans.

Relationship of PVD with CAD

The prevalence of CAD among the PVD group was not significantly greater than the non-PVD group. Because PVD (as measured by the ABI) has been found to be an independent predictor of CAD in other studies (2,20), we calculated the sensitivity and specificity of the ABI in predicting CAD in this population. The sensitivity was extremely low (7%), whereas the specificity was high (97%). The positive predictive value was 30%, and the negative predictive value was 86%.

CONCLUSIONS

— This article reports on the prevalence of PVD in an urban South Indian population and shows that the prevalence of PVD is low in this population. The overall prevalence of PVD in the whole population was 3.2%, and it was 6.3% in the diabetic population. In contrast, high prevalence rates of PVD have been reported from the Netherlands (21), the U.K. (22,23), and the U.S. (24). Thus, this study confirms our earlier clinic-based data that the prevalence of PVD is low among Indians if ABI is used as

Table 2—*Prevalence of PVD in the study population*

	n	Cases	95% CI
Overall	631	20 (3.2)	1.9–4.9
NGT	517	14 (2.7)	1.5–4.5
IGT	34	1 (2.9)	0.0012–15.7
Type 2 diabetes			
Overall	80	5 (6.3)	2.0–14.0
Newly diagnosed	29	1 (3.5)	0.0014–18.2
Known diabetic patients	51	4 (7.8)	2.1–19.0

Data for cases are *n* (%).

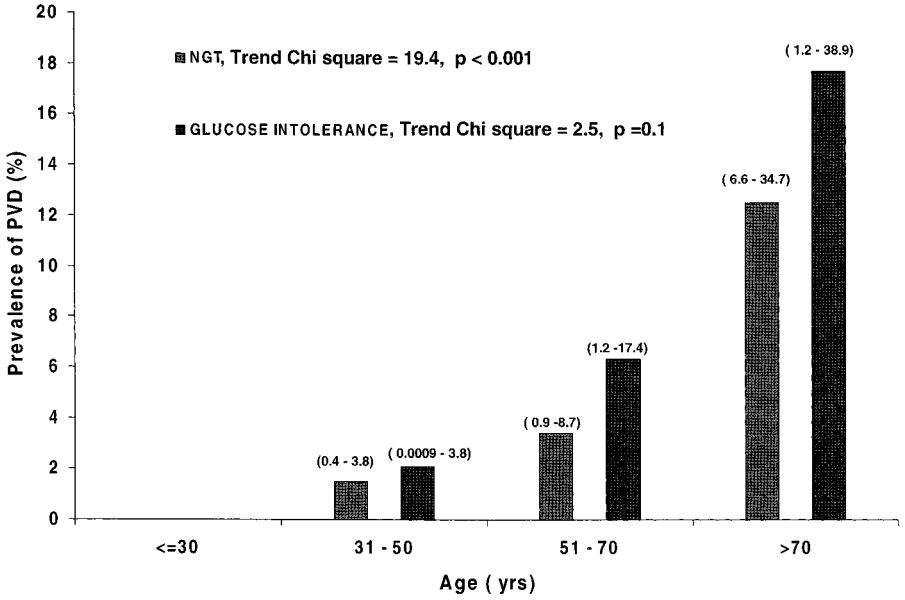

Figure 2—*The age-specific prevalence rates of PVD.*

the criterion for the diagnosis of PVD (12).

Prevalence of PVD among newly diagnosed diabetic patients was 3.5% in our study. This result is comparable to that in a recent report from Sri Lanka (25) but is considerably lower than that reported from Rochester (26) and the Hoorn Study (21). Whereas these differences in prevalence rates may be because of the differences in the subject selection, sample size, and other factors, they could also reflect true differences in prevalence of PVD in different ethnic groups (27). This suggests that different susceptibility factors may operate in different populations. Alternatively, it could also be because the prevalence of certain well-known risk factors, e.g., smoking, could be less common in certain populations. Finally, it could simply be a reflection of the younger age structure of the population, as shown by a steep increase in prevalence rates of PVD in those patients >70 years of age.

The differences between the prevalence rates of CAD and PVD in our population are quite striking. Thus, whereas CAD occurs with increased prevalence and at a younger age (premature CAD), PVD appears to show the opposite trend, i.e., lower prevalence and occurrence in older age-groups. This finding suggests that the pathogenic mechanisms for CAD and PVD could be different. In addition, our results suggest that screening for CAD using the ABI (2,20) is unlikely to be useful in a South Asian population.

Indeed, the risk factors for PVD itself appear to differ in different populations. A study from China (28) reported that hypertension, diabetes, elevated serum cholesterol, LDL cholesterol, triglycerides, fibrinogen, and hyperglycemia are associated with PVD. A U.S. study showed diabetes to be the major risk factor for PVD (29). In Greece, serum triglycerides alone were found to be associated with PVD in diabetic subjects (30). A prospective study on type 2 diabetes showed triglycerides, HDL cholesterol, hypertension, and smoking as risk factors for PVD (31). Other reports showed microalbuminuria (32), homocysteine (33), and lipoprotein(a) (34) to be associated with PVD. However, the commonly known risk factors do not explain the high prevalence of PVD seen in some ethnic groups (35,36).

Although smoking provided a 2.7 times higher risk for PVD, this did not

Table 3—*Prevalence of PVD from various studies*

Reference	City, country	Age (years)	Category	Prevalence of PVD (%)	Diagnostic criteria
Beach et al. (31)	Washington, DC	50–70	Diabetes	22.0	ABI <0.95
			NGT	3.0	
Fowkes et al. (23)	Edinburgh, U.K.	55–74	General population	18.0	ABI <0.9 and/or intermittent claudication
Katsilambros et al. (30)	Athens, Greece	All age-groups	Diabetes	42.0	ABI <0.9 and/or intermittent claudication
Beks et al. (21)	Amsterdam, the Netherlands	50–74	NGT	7.0	ABI <0.9
			IGT	9.5	
			NDD	15.1	
			KD	20.9	
Present study	Chennai, India	≥20	NGT	3.5	ABI <0.9
			IGT	2.9	
			NDD	3.5	
			KD	11.8	
		>50	NGT	6.7	
			IGT	10.0	
			NDD	6.7	
			KD	9.1	

KD, known diabetes; NDD, newly diagnosed diabetes.

reach statistical significance. The absence of association with smoking can be attributed to a small sample size or to the underreporting of smoking because of cultural and other barriers. Unfortunately, we could not perform serum nicotine estimation to quantify smoking in this study. The weak association with serum lipids may also be because of the small sample size.

The higher ORs for PVD with FPG compared with 2-h PG suggests that diagnosis of diabetes based on an FPG of 126 mg/dl (7.0 mmol/l) probably identifies more severely diabetic patients in our population. This corroborates recent findings from our center that, in our population of relatively lean individuals, an FPG of 6.5 mmol/l (118 mg/dl) correlates better with a 2-h PG value of 11.0 mmol/l (200 mg/dl) (37). This is one of the first articles to report on the prevalence of PVD in a population setting in relation to the new diagnostic criteria for diagnosis of diabetes.

The criteria for assessment of PVD in this study was a decreased ABI measured using a peripheral Doppler. This method is considered to be a reliable method for detecting PVD (38). Earlier studies have suggested that an ABI <0.9 has a sensitivity of 95% for detecting angiogram-positive disease, whereas a ratio of ≥ 0.9 almost always excludes PVD (39). ABI is thus considered a suitable method to assess PVD for epidemiological and clinical studies. However, there are some limitations to the use of peripheral Doppler because calcified noncompressible arteries occur with increased frequency in patients with diabetes (40). One cannot rule out the possibility that, if angiography or duplex color Doppler studies had been done, the prevalence of PVD might have been higher.

In summary, this population-based study using the ABI shows that the prevalence of PVD is quite low among urban South Indians. One should, however, be cautious in interpreting these results. The population of India is steadily aging and the prevalence of diabetes is rising sharply. Thus, one cannot rule out the possibility that, in the future, PVD could emerge as a very significant cause of morbidity and mortality, even in India. Another limitation is that the sample size is small. However, the good response rate and the sensitive methods used are the strengths of the study.

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