CARDIOVASCULAR RISK FACTORS ASSOCIATED WITH DIABETES IN AN INDIAN COMMUNITY OF GUADELOUPE. A CASE CONTROL STUDY

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SUMMARY
- Indians of Guadeloupe have an especially high prevalence type 2 diabetes mellitus and a particular susceptibility to coronary heart disease. This case-control study conducted from September 15 to 24, 1997, analysed cardiovascular risk factors associated with diabetes and particularly dyslipidaemia in the Indian community of Guadeloupe. The 172 subjects included 86 diabetic patients of Indian origin and 86 age- and sex-matched non-diabetic controls. All subjects underwent a physical examination by the same observer. Obesity and hypertension were assessed, and fasting lipid concentrations were measured. The body mass index and waist-to-hip ratio were higher among patients than controls: 27.8 vs 25.1 Kg/m² (p < 0.001) and 0.94 vs 0.90 (p < 0.001). Mean arterial systolic and diastolic pressures were higher for patients than controls (p < 0.001). Median HDL-cholesterol was 1.23 mmol/L for patients vs 1.4 mmol/L for controls (p < 0.001), and median triglycerides were 2.0 vs 1.3 mmol/L (p < 0.001). Mean apolipoprotein B was 1.40 ± 0.36 g/L for patients vs 1.23 ± 0.35 g/L for controls (p < 0.001). Our results show slight hypertension, central obesity, a lower plasma HDL-cholesterol concentration, a higher triglyceride concentration, and a higher apolipoprotein B concentration for diabetics. These data would appear to have important implications for the prevention of cardiovascular disease in this population.

Key-words: type 2 diabetes mellitus, cardiovascular disease, risk factors, indians.

RÉSUMÉ - Facteurs de risque cardio-vasculaires associés au diabète dans une population d’Indiens de la Guadeloupe
Les Indiens de Guadeloupe ont une prévalence particulièrement élevée de diabète de type 2 et une susceptibilité particulière pour les maladies coronaires. Cette étude cas-témoins menée du 15 au 24 Septembre 1997 a analysé, dans une communauté indienne de Guadeloupe, les facteurs de risque cardio-vasculaires associés au diabète et surtout les dyslipidémies. Les 172 sujets d’origine indienne inclus comprenaient 86 diabétiques et 86 non diabétiques appariés sur l’âge et le sexe. Tous subirent un examen clinique par le même observateur. L’obésité et l’hypertension furent pris en compte et les valeurs à jeun des paramètres lipidiques. L’indice de masse corporelle (IMC) et le rapport taille sur hanches étaient plus élevés chez les diabétiques que chez les témoins: 27.8 vs 25.1 Kg/m² (p < 0.001) and 0.94 vs 0.90 (p < 0.001), ainsi que la tension artérielle systolique et diastolique (p < 0.001). La médiane de l’HDL-cholestérol était 1.23 pour les patients vs 1.4 mmol/l pour les témoins (p < 0.001), et la médiane des triglycérides était de 2.0 vs 1.3 mmol/L (p < 0.001). La moyenne d’apo B était de 1.4 ± 0.36 g/L pour les diabétiques vs 1.2 ± 0.35 g/L pour les témoins (p < 0.001). Nos résultats montrent une hypertension artérielle modérée, une obésité centrale, un taux plus bas de HDL-cholestérol, une concentration plus élevée de triglycérides et d’apo B chez les diabétiques. Ces données pourraient avoir des implications importantes pour la prévention des maladies cardiovasculaires dans cette population.

Mots-clés : diabète type 2, maladies cardiovasculaires, facteurs de risque, indiens.
INTRODUCTION

From 1853 to 1889, 42,000 people migrated to Guadeloupe from the southeastern Indian subcontinent, mainly from Pondicherry, Karikal and Mahe [1]. Data show that vascular diseases have been the leading cause of mortality among this Indian population [2], which has a particular susceptibility to coronary heart disease (CHD). In fact, many studies have found a higher prevalence of CHD among Indians than other ethnic groups in Trinidad [3], Jamaica [4], England [5-7], Singapore [8] and Africa [9-11]. In the Caribbean, some differences in CHD prevalence have been reported among ethnic groups [12].

A research unit (INSERM U21) and the Endocrinology Department of the University Hospital in Guadeloupe had previously found a high prevalence of non-insulin-dependent diabetes mellitus in the Indian population: 22.6% in Indian men vs 5% in Africans and 8.5% in others, and 22.4% in Indian women vs 7.3% in Africans and 2% in others [13, 14]. Thus, it seemed important to analyse the cardiovascular risk factors (hypertension, obesity, dyslipidaemia) associated with diabetes in this population. Moreover, lipid parameters, which had not been assessed until now, were studied according to ARCOL thresholds [15, 16]. This work should have important implications for the prevention of cardiovascular disease in the Indian community.

MATERIALS AND METHODS

In a previous study [17], 429 subjects (age range 25-85 years) had been recruited for a genetic and prevalence study in an Indian community of Guadeloupe from September 15 to 24, 1997. This study was performed in collaboration with the European Centre of Diabetes Disease (Strasbourg) and the Department of Endocrinology of the University Hospital in Guadeloupe.

The present paper concerns a case control study (172 subjects) conducted from this sample. The subjects (male and female) were of Indian origin as determined by family name and appearance, at least 25 years old, and showed three generations with the same ancestry. The 86 patients were diabetic and age- and sex-matched with 86 non-diabetic controls. Individuals were classified as diabetic according to World Health Organization (WHO) criteria [18] if they were taking insulin or oral antidiabetic medication or had a fasting glucose concentration above 7.8 mmol/L or a 2-h glucose concentration greater than 11.1 mmol/L after a 75 g oral glucose tolerance test. Individuals under 25 years of age were excluded as well as those who did not correspond to Indian criteria, who were not fasting, or who had excessive alcohol consumption. All subjects gave their informed consent to participate.

Procedure – After an overnight fast, subjects attended between 6 and 8:30 a.m. when two fasting (venous) blood samples were taken on a standard assay and on fluoride oxalate to measure glucose. A second specimen on fluoride oxalate was obtained 2 h after administration of a 75 g glucose equivalent load for all patients except those with insulin treatment or on oral hypoglycaemic agents. A clinical examination was conducted by questionnaire using physicians who spoke French and Creole. It included questions on medical history (family history of hypertension and dyslipidaemia, course and treatment of the disease for diabetic patients), smoking, alcohol intake, diet, physical activity, occupation and demographic background.

Anthropometry – Three consecutive anthropometric measurements were performed by a single observer, which were obtained when participants were wearing light clothing and no shoes. Weight was measured to the nearest 1 Kg, and height to the nearest 1 cm, with the head parallel to the floor. The body mass index (BMI) was calculated as the ratio of weight (Kg) to height squared (m²). The waist was measured as the smallest circumference between the costal margin and the iliac crest.Hip measurements were made at the level of the most lateral point on the great trochanter. The ratio of waist-to-hip circumferences (WHR) was used as a measurement of body fat distribution. After the participants had been seated at rest for 10-15 minutes, two consecutive blood pressure measurements were made using an automatic Dinamap sphygmomanometer [19]. The mean of the two measurements was used to estimate blood pressure, which was compared to the WHO classification [20] and that of the Joint National Committee [21].

Laboratory measurements – Samples were transported in an insulated refrigerated box to the laboratory of the University Hospital in Guadeloupe. All analyses were performed within 24 h of sampling, and apolipoproteins were measured before serum was stored at -20°C.

Serum creatinine was measured using the standard method of Jaffe, serum total cholesterol and triglycerides were assayed enzymatically, and HDL-cholesterol was separated by dextran sulphate/magnesium precipitation and measured in supernatant. These biochemical measurements were performed on an Axon analyzer (Bayer Diagnostic, France). Glucose concentrations were measured by the glucose oxidase method (Cobas-Bio, Roche Diagnostics). Serum Apolipoprotein A1 (apo A1) and serum Apolipoprotein B (apo B) were quantified by laser immunonephelometry using reagents supplied by Behring Instruments (France).

Statistical analyses – Data were recorded and analysed with Epi Info 6 statistical software. Categorical variables were compared using the chi-square test. Variables were tested for skewness. For skewed variables, non-parametric tests were used for comparisons between groups (Kruskal-Wallis U test). Student’s t-test was used for normally distributed variables. Values are expressed as the mean (± standard deviation) for normally distributed data and the median (25th and 75th percentile) for skewed data.

RESULTS

The general characteristics of the population are shown in Table I. Patients and controls were age- and sex-matched; there were no significant differences in smoking habits between the two groups. Among the
patients, 37 (43%) new diabetic cases were discovered during the investigation. For known diabetics (n=49) mean fasting plasma glucose was 11.7 mmol/L, and all had treatment in the form of: diet (n=10), oral antidiabetic medication (n=34), insulin (n=4) or associations of these (n=1). There were no significant differences in physical activity between the two groups. However, 15% of patients had no physical activity. A family history of diabetes was found for 76 patients (88%) vs 55 controls (64%). In the control group, 11 subjects (12%) had previous hypertension vs 27 (31.3%) among patients. Seven (8.1%) of the controls vs 20 (23.2%) of the patients received treatment. Dyslipidaemia was observed in 27 (31.3%) subjects in the control group vs 40 patients (46.5%), and 13 (15.1%) subjects received treatment as compared to 14 (16.2%) patients. BMI and WHR were higher for patients than controls, respectively 27.8 vs 25.1 kg/m² (p<0.001) and 0.94 vs 0.90 (p<0.001). Mean arterial systolic pressure was 136.5 ± 23.2 mmHg for patients vs 125.8 ± 22.3 mmHg for controls (p<0.001), and mean arterial diastolic pressure was 80.1 ± 11.4 mmHg for patients vs 74.6 ± 9.6 mmHg for controls (p<0.001). HDL-cholesterol, triglycerides, and apo B were significantly different between the two groups (Table II). Median HDL-cholesterol was 1.23 mmol/L for patients vs 1.4 mmol/L for controls (p<0.001), and median triglycerides were respectively 2.0 mmol/L vs 1.3 mmol/L (p<0.001). Mean apo B was 1.40 ± 0.36 g/L for patients vs 1.23 ± 0.35 g/L for controls (p<0.001). When lipid parameters were analysed according to ARCOL (1989) thresholds [15, 16], which correspond to a high cardiovascular risk, two parameters appeared important (Table III): Firstly, for a triglyceride concentration >2.3mmol/L, there were 40.6% of patients vs 9% of controls, and the significant odds ratio was 6.69 (p<0.001). Secondly, for apo B >1.3 g/L, there were 54.6% of patients vs 37.2% of controls, and the significant odds ratio was 2.03 (p<0.02).

### DISCUSSION

In this analysis, non-insulin-dependent diabetic Indians showed a characteristic pattern of cardiovascular risk factors: slight hypertension, central obesity, decreased plasma HDL-cholesterol, raised plasma triglycerides, and increased apo B. Blood pressure for patients was indicative of slight hypertension according to the classification of JNC VI [21]. These results are in agreement with those of Knight et al. [22], who found limited evidence of an increased tendency to higher blood pressure in an Asian Indian group. In their prospective hospital-based case-control study of 200 Indian patients with a first acute myocardial infarction (AMI), Prem Pais et al. [23] found that the most important predictor of AMI was current smoking. However, there were few smokers in our study (only 6.9% of patients), and no significant differences were found between the two groups. BMI was higher for patients, and WHR was particularly higher relative to values defined by other authors [24]. These results are indicative of central obesity. Two population studies [22, 25] in the United Kingdom, in which most of the subjects were native to the Punjab region of the Indian subcontinent, showed a similar striking tendency to central obesity. Central obesity is generally regarded as a more important predictor of ischaemic heart disease than generalised obesity [26]. In our study, although some diabetic patients had been receiving treatment, their fasting plasma glucose level was not satisfactory enough to prevent CHD. With respect to dyslipidaemia, there were no significant differences between the two groups for total cholesterol, which is in agreement with the findings of Prem Pais et al. in their case-control study [23]. HDL-cholesterol was lower for patients. Studies of Indian populations in other countries have found that Indians generally do not have higher total cholesterol than Caucasians or Afro-Caribbean populations, but have lower HDL-cholesterol and higher triglyceride concentrations [27-29]. Triglyceride concentrations were particularly high for patients. Dhawan et al. [24] and Prem Pais et al. [23], in their case-control studies in which patients were referred for diagnostic angiography for chest pain or for AMI, also found higher triglyceride concentrations among Asian Indians. These results are consistent with the effects of central obesity and insulin resistance on triglyceride production. Apo A1 is the

### TABLE I. General characteristics of the population.

<table>
<thead>
<tr>
<th>Parameters (n=172)</th>
<th>Controls (n=86)</th>
<th>Patients (n=86)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>49.3 (10.4)*</td>
<td>49.2 (9.3)</td>
<td>NS</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>40/46</td>
<td>40/46</td>
<td>NS</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>5 (5.8)</td>
<td>6 (6.9)</td>
<td>NS</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.1 (3.9)*</td>
<td>27.8 (4.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>WHR</td>
<td>0.90 (0.05)*</td>
<td>0.94 (0.06)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ASP (mmHg)</td>
<td>125.8 (22.3)*</td>
<td>136.5 (23.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ADP (mmHg)</td>
<td>74.6 (9.6)*</td>
<td>80.1 (11.4)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* means (standard deviation)
BMI: Body mass index
WHR: Waist-to-hip ratio
ASP: arterial systolic pressure
ADP: arterial diastolic pressure
NS: not significant
p: degree of significance
Major apolipoprotein in HDL and plays various structural and functional roles in HDL metabolism [30]. Many studies have found that apo A1 levels were substantially lower in patients with coronary artery disease [31-34]. However, only a few investigators have tried to determine the relative predictive value of apo A1 levels compared to HDL-cholesterol levels, and the results are contradictory. Although some studies concluded that apo A1 concentration is a better predictor of coronary artery disease risk than HDL-cholesterol concentration [31, 32], others reported that HDL-cholesterol is as good as or better than apo A1 in discriminating persons with coronary artery disease from controls [33, 34]. In our study, apo A1 concentrations were not different between the two groups.

Apo B, the major apolipoprotein of LDL, plays an essential structural role among these lipoprotein particles. Many studies have found that apo B levels are better correlated with the presence of coronary artery disease than are total or LDL-cholesterol levels [32, 34]. Kwiterovitch et al. [32, 35] indicated that apo B was a particularly differential characteristic for ischaemic cardiovascular accidents among high triglyceride patients. In our Indian population, singularly higher triglyceride concentrations (up to 17.6 mmol/L) were found for patients. The lower HDL concentrations, marginally higher triglyceride values, and higher apo B concentrations for patients are in agreement with the observations of McKeigue et al. [36] and Knight et al. [37], who related lipid patterns observed in

**Table II. Biological parameters.**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Controls (n = 86)</th>
<th>Patients (n = 86)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine (µmol/L)</td>
<td>63 (53-74)**</td>
<td>58.5 (49-71)</td>
<td>NS</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>5.4 (1.1)*</td>
<td>5.7 (1.1)</td>
<td>NS</td>
</tr>
<tr>
<td>HDL-cholesterol (mmol/L)</td>
<td>1.40 (1.05-1.58)**</td>
<td>1.23 (1.05-1.40)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>1.30 (0.9-1.7)**</td>
<td>2.00 (1.5-2.8)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Fasting plasma glucose (mmol/L)</td>
<td>5.6 (5.1-6.1)**</td>
<td>8.9 (6.9-13.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Apolipoprotein A1 (g/L)</td>
<td>1.47 (0.30)*</td>
<td>1.46 (0.27)</td>
<td>NS</td>
</tr>
<tr>
<td>Apolipoprotein B (g/L)</td>
<td>1.23 (0.35)*</td>
<td>1.40 (0.36)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

** medians (25th-75th percentile)
* means (standard deviation)
NS : not significant
p : degree of significance

**Table III. Evaluation of lipid parameters using ARCOL (1989) thresholds.**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Controls</th>
<th>Patients</th>
<th>OR (CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>T. cholesterol &gt; 6.5 mmol/L</td>
<td>20</td>
<td>21</td>
<td>1.07 (0.5-2.29)</td>
<td>NS</td>
</tr>
<tr>
<td>HDL-cholesterol &lt; 0.9 mmol/L</td>
<td>4</td>
<td>5</td>
<td>1.27 (0.26-6.61)</td>
<td>NS</td>
</tr>
<tr>
<td>Triglycerides &gt; 2.3 mmol/L</td>
<td>8</td>
<td>35</td>
<td>6.69 (2.68-17.25)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Apo A1 &lt; 1.2g/L</td>
<td>18</td>
<td>11</td>
<td>0.55 (0.22-1.36)</td>
<td>NS</td>
</tr>
<tr>
<td>Apo B &gt; 1.3g/L</td>
<td>32</td>
<td>47</td>
<td>2.03 (1.05-3.95)</td>
<td>&lt; 0.02</td>
</tr>
</tbody>
</table>

T. cholesterol: Total cholesterol
Apo A1: Apolipoprotein A1
Apo B: Apolipoprotein B
OR: Odds ratio
CI: Confidence interval (95%)
NS: not significant
p: degree of significance
Asians to their higher risk of atherosclerosis and diabetes, which suggests an underlying mechanism for both.

Miller et al. [29], who compared fasting serum lipoprotein concentrations and CHD prevalence rates in Trinidad men of various ethnic origins (Indian, African, European, Chinese, Semitic and mixed), found a higher prevalence rate for CHD among Indian men than in other ethnic groups. Men with CHD tended to have higher LDL-cholesterol and lower HDL-cholesterol concentrations than men without CHD. In this respect, our results were similar. Our findings in relation to cardiovascular risk factors are consistent with those of previous studies in Indians and other south Asian ethnic groups as compared to other ethnic groups in countries to which members of these communities have migrated [25, 27, 38]. Genetics may account for this tendency. In our study, 88% of patients had a diabetic parent. In a previous study, a parental link was found for 50% of diabetic Indian subjects vs 26% in other groups [13]. Among five gene candidates for non-insulin-dependent diabetes and obesity, a case-control study conducted in our population found a significant association of the type 2 fatty acid transport protein (FABP2) with hypertriacylglyceridaemia >2 g/L and arterial hypertension in a multivariate model [17]. The authors concluded that the FABP2 gene might be linked to the metabolic syndrome of insulin resistance. Other unmeasured behavioural factors, including dietary components, may contribute to ethnic differences. Although Indians in Guadeloupe had long resisted cultural assimilation, changes in dietary fat from traditional sources to polyunsaturated vegetable oils are now apparent. Nevertheless, some traditions persist within the family and home, and many Indians have retained dietary customs of Hindu origin. Thus, the role of dietary factors cannot be excluded. Fifty percent of the subjects had no physical activity. The enhancement of their socioeconomic and cultural level is certainly responsible for a more sedentary way of life.

These disturbances in our Indian population correspond to the insulin-resistance syndrome, which includes hyperglycaemia, hypertriglyceridaemia, elevated concentrations of apo B and a reduced concentration of HDL-cholesterol [39-41], associated with a striking tendency to central obesity. The only known environmental influences on insulin resistance are dietary energy intake [42] and physical activity [43]. If the insulin-resistance hypothesis is correct, control of obesity and greater physical activity offer the best chances for prevention of diabetes and CHD [25].

CONCLUSIONS

Our study of an Indian community of Guadeloupe with a particularly high prevalence of non-insulin-dependent diabetes, found slight hypertension, central obesity, a lower plasma HDL-concentration, a higher triglycerides concentration, and a higher apo B concentration in diabetic patients. Strategies for preventing heart disease in this community require greater emphasis on increased physical activity and the control of diabetes and central adiposity.

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