Metabolic syndrome components in Indian migrants with type 2 diabetes
A matched comparative study

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SUMMARY
Objective: To study the metabolic syndrome (MS) in Indian subjects with type 2 diabetes (T2D) in comparing them with controls from the Indian community and from the general population.
Method: An adapted definition of MS by the Third report of the National Cholesterol Education Program's Adult Treatment Panel III was used. We defined three groups matched for sex and age (+/-5 years). Non parametric tests for comparison of matched samples and conditional logistic regression were used.
Results: We selected 71 Indians with T2D (group 1) and two control groups with fasting blood glucose <6.1 mmol/L: 71 Indians (group 2) and 213 subjects from the general population (group 3). Patients were 24 to 76 years-old and each group contained 56% men. Globally, MS was identified in 77% of the group 1 when diabetes was taken into account. When diabetes was excluded there were 47% of MS in group 1, 18% in group 2 and 16% in group 3. The clusters of four factors (hypertension, large waist circumference, hypertriglyceridemia and Low HDL-C) were more common in Indians. The most frequent factors were hypertriglyceridemia and large waist circumference in Indians. Indians with T2D had a 5-fold higher risk of MS than the general population group, OR (95% CI): 4.93 (2.71 - 8.97); P<0.001.
Conclusion: The high frequency of MS and of hypertriglyceridemia in Indians with T2D highlights the need for screening and management of MS in this population facing a high cardiovascular risk.

Key-words: Indians migrants · Type 2 diabetes · Metabolic syndrome · Hypertriglyceridemia · Guadeloupe.


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RéSUMÉ
Composantes du syndrome métabolique chez des sujets diabétiques de type 2, descendants de migrants indiens. Étude comparative

Objectif : Étudier le syndrome métabolique (SM) chez des indiens atteints de diabète de type 2 (DT2) en les comparant à des témoins issus de la communauté Indienne et de la population générale.
Méthode : Une définition adaptée du SM par le National Cholesterol Education Program’s Adult Treatment Panel III a été utilisée. Trois groupes de sujets apparisés pour le sexe et l’âge (± 5 ans) ont été définis. Des tests non paramétriques pour la comparaison d’échantillons apparisés et la régression logistique conditionnelle ont été utilisés.
Résultats : La population de l’étude comportait 71 indiens avec un DT2 (groupe 1) et deux groupes sélectionnés avec une glycémie à jeun < 6,1 mmol/L : 71 sujets indiens (groupe 2), et 213 sujets de la population générale (groupe 3). Les sujets étaient âgés de 24 à 76 ans et il y avait 56 % d’hommes dans chaque groupe. Le SM était identifié chez 77 % du groupe 1 quand le diabète était pris en compte. En excluant le diabète, les fréquences du SM étaient : 47 % (groupe 1), 18 % (groupe 2) et 16 % (groupe 3). Les combinaisons de quatre facteurs (hypertension, large tour de taille, hypertriglycéridémie et HDL-C bas) étaient fréquentes chez les Indiens. Il en était de même pour l’hypertriglycéridémie et l’obésité abdominale. Les Indiens avec un DT2 avaient un risque de SM 5 fois plus élevé que la population générale OR (95 % CI) : 4, 93 (2,71 - 8,97) ; P < 0,001.
Conclusion : Les fréquences élevées de SM et d’hypertriglycéridémie chez les Indiens avec un DT2 mettent en exergue la nécessité du dépistage et de la prise en charge du SM dans cette population à haut risque cardiovasculaire.

Mots-clés : Migrants · Indiens · Diabète de type 2 · Syndrome métabolique · Hypertriglycéridémie · Guadeloupe.

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Introduction

The metabolic syndrome (MS), also called insulin resistance syndrome [1] is constituted by the clustering of several cardiovascular risk factors. This syndrome associated with an increased risk of cardiovascular disease [2] includes the following factors: hypertension, central obesity, high fasting glucose and dyslipidemia. These risk factors are used in the definition of the MS by the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) guidelines [3].

In the multi-ethnic population of Guadeloupe, a French Caribbean island, there are about 80% of subjects of African descent and 8% of Indian migrant descent who came, most often, from South India. The overall prevalence of diabetes in Guadeloupe was evaluated at 6.6% (vs 3.6% in mainland France) whereas the standardized prevalence, for sex and age, was 22.5% in the Indian community [4]. Patients with type 2 diabetes (T2D) are often insulin resistant and are characterized by the existence of clustering of cardiovascular disease (CVD) risk factors [5]. Moreover, Indian diabetic subjects are considered at high risk of cardiovascular complications. The MS definition of the NCEP is an interesting and simple tool for clinicians but, the clusters of MS components vary between countries and between ethnic groups. Knowledge of the distribution of components of this syndrome is needed in our population.

Our aim was to study the MS in Indian subjects with T2D in comparing them with controls from the Indian community and from the general population.

Methods

Population

Data of two previous studies conducted in 1997 [6] and 2000 [7] were used for a new analysis. In one of these previous studies, all the subjects (n=429) came from the Indian community located in one city of Guadeloupe. The Indian ethnic origin was defined on name, physical appearance and/or when the patient defined him/herself as Indian. In the other previous study, the consecutive subjects (n=1010) were selected during one month in a Health Centre that performs medical examination for the general population.

Study Population

Our study population was thus constituted of three patient groups.

Group 1 were Indian subjects who were known T2D taking oral hypoglycaemic treatment or had T2D diagnosed at the time of the initial epidemiological study [6]. Subjects receiving insulin treatment were excluded.

The subjects in group 2 and group 3 were randomly selected among those without diabetes or blood glucose abnormality (fasting blood glucose <6.1 mmol/L) and matched for sex and age (+5 years) on the Indian T2D subjects.

Group 2 were Indian subjects controls matched on the basis of one control for one diabetic.

Group 3 were controls from the general population and matched on the basis of three controls for one diabetic.

Data collection

For this analysis, we selected subjects with complete data for age, sex, diabetic status, body size measures (height (m), weight (Kg), waist circumference (WC in cm), blood pressure measurements, laboratory data (fasting glucose, triglycerides, high density lipoprotein cholesterol (HDL-C)).

Systolic (SBP) and diastolic (DBP) blood pressure were assessed with automated monitors. WC was taken, with participants standing, above the iliac crests and below the lowest rib margin at minimal respiration. The measurements were made by trained nurses. Body mass index (BMI) was calculated as weight/height² (Kg/m²). The same methods were used for physical measures in the original studies.

In both original studies, blood samples were obtained after an overnight fast. The biochemical analyses were performed in two different laboratories but with the same methods.

Glycaemia were assessed by glucose oxydase method. Cholesterol, HDL-cholesterol (HDL-C) and triglycerides were measured enzymatically.

Definition of clinical Factors

Obesity was defined as a BMI ≥ 30 Kg/m².

The metabolic syndrome (MS) defined by the National Cholesterol Education Program’s Adult Treatment Panel III (NCEP: ATP III) includes three or more of the following abnormalities: SBP ≥ 130 mmHg and/or DBP ≥ 85 mmHg, WC ≥ 102 cm in men or >88 cm in women, HDL-C < 1.04 mmol/L (40 mg/dL) in men or <1.29 mmol/L (50 mg/dL) in women, triglycerides ≥ 1.69 mmol/L (150 mg/dL) and fasting glucose ≥ 6.1 mmol/L (110 mg/dL) [3].

We used an adapted definition of the NCEP syndrome and, using of anti-hypertensive treatment or hypolipemic drugs was considered as hypertension or hypertriglyceridemia for the purpose of our study. In addition, since subjects did not have a glucose abnormality in groups 2 and 3, the MS was evaluated in group 1 (T2D) with and without taken into account diabetes.

Statistical analysis

Data for categorical variables are presented as numbers (percentages) and for continuous variables as means (standard deviations). Non parametric tests to compare more than two matched samples were used for the overall comparison between the three groups and for comparison between
Results

Overall, 335 subjects were included, 71 Indians with T2D (group 1), 71 Indians without blood glucose abnormality (group 2) and 213 subjects from the general population without blood glucose abnormality (group 3).

There were 56.3% of men in each group. Although subjects were matched on age (±5 years), the mean age of the Indian diabetic subjects was greater than that of the two other groups, in both genders. Among the component factors of the metabolic syndrome, means WC and triglyceride levels were also greatest in men and women in the diabetic group. Indian normoglycemic subjects (group 2) had greater mean triglyceride levels in men and greater mean triglyceride levels and mean WC in women than normoglycemic controls from the general population (group 3), (table I).

Table II presents the distribution of the MS components in the three groups. Globally, when diabetes was taken into account, MS was identified in 77% of group 1. When diabetes was taken aside in group 1, the frequency of MS was 47% in group 1. In group 2 and 3, both without blood glucose abnormality, frequencies of MS were respectively 18% and 16%. MS was more frequent in women than in men in the three groups. The association of a large WC and elevated triglycerides was more frequent in group 1. P values for comparisons of group 1 vs group 2 and group 2 vs group 3 are given in table I and table II.

In considering only four factors (hypertension, large waist circumference, hypertriglyceridemia and Low HDL-C), the greatest proportions of clusters of these four factors were found in Indian subjects with T2D. The distributions of different associations of factors by gender are shown in table III.

Table IV shows the results of the conditional logistic regression analysis of MS. The general population control group was considered as the reference group. At step 1, the Indian controls had no excess of risk of MS. At step 2, risk factors for MS were: female gender, 10-years increase in age and being in group 1. Indian with T2D had a 5-fold higher risk of MS than the general population group; adjusted OR: 4.93 (2.71-8.97); P<0.001.

Table I

<table>
<thead>
<tr>
<th></th>
<th>Indian descents</th>
<th>Normoglycaemic General population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group 1</td>
<td>Group 2</td>
</tr>
<tr>
<td>Age (y)</td>
<td>49.8 (10.7)</td>
<td>48.2 (11.7)</td>
</tr>
<tr>
<td>Waist circumference, mmol/l</td>
<td>96.9 (9.6)</td>
<td>88.9 (10.2)</td>
</tr>
<tr>
<td>Body mass index, Kg/m²</td>
<td>27.7 (3.9)</td>
<td>25.5 (4.4)</td>
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<tr>
<td>Systolic blood pressure, mmHg</td>
<td>138.8 (22.5)</td>
<td>122.3 (21.2)</td>
</tr>
<tr>
<td>Diastolic blood pressure, mmHg</td>
<td>81.6 (9.9)</td>
<td>73.1 (9.5)</td>
</tr>
<tr>
<td>Cholesterol, mmol/L</td>
<td>5.7 (1.1)</td>
<td>5.3 (1.0)</td>
</tr>
<tr>
<td>HDL, cholesterol, mmol/L</td>
<td>1.3 (0.3)</td>
<td>1.4 (0.3)</td>
</tr>
<tr>
<td>Triglycerides, mmol/L</td>
<td>2.8 (2.4)</td>
<td>1.3 (0.6)</td>
</tr>
<tr>
<td>Fasting blood glucose, mmol/L</td>
<td>10.1 (4.3)</td>
<td>5.3 (0.4)</td>
</tr>
</tbody>
</table>

Group 1: Indian T2D subjects.
Group 2: Indian normoglycaemic controls.
Group 3: normoglycaemic controls from the general population.
In this study where we defined MS with adapted NCEP/ATP III criteria, we found a very high prevalence of MS in Indians with T2D. Frequencies of MS in the group from the general population (9% in men, 21% in women) were lower than those previously observed in African Americans (16% in men, 26% in women) [8]. This is not surprising since controls were selected in our study as not having fasting blood glucose abnormality which is one of the five components of MS as defined by the NCEP/ATP III. The most frequent MS risk factors were not similar in the three groups with enlarged WC and hypertriglyceridemia more frequently found in the diabetic and non-diabetic Indian individuals. Conversely, hypertriglyceridemia was not a frequent finding in the general population mainly of African descent.

### Hypertension and metabolic syndrome

Hypertension was highly prevalent in Indians with T2D and in the general population group. In this latter group, the more common combinations were those including hypertension. It has been shown that insulin resistance has a modest contribution in the increasing of the prevalence of hypertension in the MS [9] and the link between blood pressure and insulin sensitivity is related to obesity. Fat distribution influence blood pressure and changes in BMI are accompanied by reciprocal changes in peripheral vascular resistance [10]. Increased sympathetic nervous activity and stimulation of the renin-angiotensin system have been suggested to explain the changes observed in obese hypertensive subjects [11].

### Overall obesity, abdominal obesity and MS

WC is a measure of visceral obesity also called abdominal obesity. In our study, the Indian non diabetic subjects,
had non significant trends of lower BMI in women and higher WC in both genders than did the non diabetic from the general population. The predominance of visceral rather than subcutaneous adipose tissue has been previously noted in Asians and Asian Indians [12,13] whereas in African-American, abdominal subcutaneous fat was found predominant [14]. Insulin resistance is correlated with total visceral fat and not with subcutaneous adipose tissue [13]. Some authors have suggested that the definition of abdominal obesity in Asian populations should be based on lower WC cut-offs, perhaps 80 and 90 cm for women and men, respectively [15,16]. This lower cut-offs should, most probably, increase the frequency of abdominal obesity in our Indian groups. This abnormal obesity is a strong cardiovascular risk factors. In fact, in a case-control study of acute myocardial infarction in 52 countries, representing every inhabited continent, the authors showed that abdominal obesity accounts for the risk of myocardial infarction worldwide in both sexes and at all ages in all regions. The association of abdominal obesity to myocardial infarction and its population attributable risks (PAR) was 1.12 for top vs lowest tertile and 1.62 for middle vs lowest tertile, PAR 20.1% for top two tertiles vs lowest tertile) [17].

Dyslipidemia

Indian populations are known to show a high cardiovascular risk and a high triglyceride concentration compared to Caucasians [18,19]. The risk associated with hypertriglyceridemia was quantified in a meta-analysis of prospective studies in which the results found that for each 1-mmol/l increase in plasma triglyceride there was a 32% increase in coronary disease risk for men and a 76% increase for women [20]. In addition, a high triglyceride level was identified as a risk factor for cardiovascular disease for both women and men in the general population, independent of HDL cholesterol [20]. Previous studies have also suggested that plasma triglycerides in diabetes was related to hyperglycaemia and that control of postprandial glucose excursion reduced the postprandial triglyceride increase [21,22]. The cluster of a large WC and hypertriglyceridemia was found in about half of the Indians with T2D in our study and was more prevalent in Indian controls than in the general population. This “triglycerides waist” phenotype has been estimated as an inexpensive screening tool to identify men at high risk for CVD [23]. The body composition of Asian Indians (excess truncal subcutaneous fat and intra abdominal fat) and the associated dyslipidemia might explain their high tendency to develop insulin resistance, more than the other ethnic groups [24].

Diabetes

The Indian population has an ethnic and genetic susceptibility for diabetes. Prevalence of diabetes in the island of Guadeloupe is three-time higher in Indian subjects than in the overall population and similar trends are noted for the incidence rate of T2D in Trininad, another Caribbean island [25,26].

With this combination of high genetic predisposition and an environmental susceptibility, the Indian population faces a high risk for diabetes and its associated complications [27]. We found a four-times higher percent of cluster of MS components (equal to four) in the Indian control group compared to general population control group. This clustering of risk factors and the metabolic disturbances related to insulin resistance might also explain the high cardiovascular morbidity observed in this population.

Limitations of the study

Selection bias might have occurred related to the fact that subjects were recruited from two different previous studies. Because lower WC cut-offs than those of the NCEP/ATPIII are proposed for the definition of abdominal obesity in Asian populations [15,16,28], frequencies of MS in the Indian groups might be higher, showing that the difference between Indian controls and the general population are underestimated.
Concerning the ethnic specificities, our Indian subjects were compared with the general population which also includes Indian subjects. This situation may also lead to a decrease in the differences of frequencies of MS between controls groups.

Despite these limitations, to our knowledge, this is the first study examining the MS components in the island of Guadeloupe. The strengths of this study also lie in the comparative design and in our results on subjects of Indian descent which are consistent with those of previous studies on Indians.

Therapeutic implications

Lifestyle changes such as diet and exercise, focusing on waist circumference cut-offs, are important recommendations for individuals with MS. Ethnic specificities should be taken into account. Pharmacological therapy is often necessary, particularly in patients with type 2 diabetes exhibiting other components of the MS and, as shown by clinical trials [29], priority should be given to antihypertensive [29] and lipid-lowering treatment [30].

In summary, the high prevalence of the metabolic syndrome in Indians with T2D and the magnitude of clustering of multiple factors confirm that this population is at high risk to develop cardiovascular morbidity and mortality. Intervention programs with tight control of the different MS components are needed to reduce cardiovascular risk in the Indian population.

References