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Gender differences in the prevalence of impaired fasting glycaemia and impaired glucose tolerance in Mauritius. Does sex matter?

Gender differences in impaired glucose categories

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Abstract

Objective. To examine gender differences in the characteristics and prevalence of various categories of glucose tolerance in a population study in Mauritius.

Research Design and Methods. In 1998 a community-based cross-sectional survey was conducted in Mauritius. Categories of glucose metabolism were determined in 5,388 adults, with an oral glucose tolerance test given to those who did not have previously diagnosed diabetes (n=4036). Other cardiovascular risk factors were assessed among those without known diabetes.

Results. For men and women the prevalence of diabetes (22.0% vs. 21.8% respectively) and the prevalence of co-existing impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) (3.2% vs. 2.9%) were similar. However, men were twice as likely as women to have isolated IFG (5.1% (4.2-6.0) vs. 2.9% (2.3-3.5)), despite being younger, thinner and with lower plasma insulin but higher lipids. Conversely, the prevalence of isolated IGT was lower in men (9.0% (7.9-10.2) vs. 13.9% (12.6-15.1)). Among non-diabetic individuals, fasting glucose was higher in men than women, whereas 2-hour glucose was higher in women. In people without diabetes, women had significantly higher body mass index, beta cell function (HOMA-B), fasting and 2-hour insulin than men and significantly lower waist-hip ratios, waist circumference, insulin sensitivity (HOMA-S) and triglycerides.

Conclusion. In Mauritius the distribution of impaired glucose metabolism differs by sex. The observation that IFG is more prevalent in men and IGT more prevalent in women raises important questions about their underlying aetiology and the ability of the current glucose thresholds to equally identify men and women at high-risk of developing diabetes. IFG should be seen as a complimentary category of abnormal glucose tolerance, rather than a replacement for IGT.
Key Words: Gender, Impaired Fasting Glucose, Impaired Glucose Tolerance, Mauritius, Diabetes.

Abbreviations Used:

ADA – American Diabetes Association
WHO – World Health Organization
IFG – Impaired Fasting Glucose
IGT – Impaired Glucose Tolerance
FPG – Fasting Plasma Glucose
2hPG – 2-hour Plasma Glucose
OGTT – Oral Glucose Tolerance Test
NGT – Normal Glucose Tolerance
BMI – Body Mass Index
WC – Waist Circumference
WHR – Waist-Hip Ratio
UK – United Kingdom
**Introduction**

The most recent reports from the American Diabetes Association (ADA)\(^1\) and World Health Organization (WHO) consultation\(^2\) on diagnosis and diagnostic criteria for diabetes include categories of impaired glucose metabolism. These categories identify persons with elevated fasting and/or post-load blood glucose concentrations which have been shown to be associated with high risk of progression to diabetes\(^3\text{-}^6\) as well as risk of future cardiovascular disease\(^6\text{-}^{10}\).

It is already apparent that there are significant differences between impaired fasting glucose (IFG) and impaired glucose tolerance (IGT), both in their respective prevalence within a population, and in the classification of individuals\(^5\text{-}^{11}\). Furthermore, it also appears that there might be some sex differences, with IGT being more common in women and IFG more common in men. We set out to explore this sex difference further, as it may have important implications both for the understanding of the pathogenesis of abnormal glucose metabolism and for the methods of screening men and women for this condition. The implications for screening are highly pertinent, especially since the ADA proposes the use of fasting plasma glucose (FPG) alone, which cannot identify IGT.
Research design and methods

Background and subjects

Data collected in a population-based study conducted in Mauritius in 1998 were used to
determine the prevalence of impaired glucose metabolism in men and women and to
compare the phenotypic characteristics of the different categories. Mauritius is an
Indian Ocean island nation approximately 800km east of Madagascar. The population
consists of 70% Asian Indians (both Hindus and Muslims), 2.1% Chinese and 27.9%
“general population” who are predominantly people of African ancestry (Creoles) with
varying amounts of European, Malagasy and Indian admixture. We have previously
reported the high prevalence of diabetes, (almost universally type 2) in Mauritius\textsuperscript{12}. All
persons over 24 years of age living in selected areas, which have been described in detail
elsewhere\textsuperscript{12, 13}, were invited to attend the survey and the response rate was 80%. In
addition, individuals who no longer resided in the selected areas but who had
participated in similar surveys in 1987 and 1992 were invited to participate. The survey
protocol was reviewed and approved by the local ethics committee (Melbourne,
Australia) as well as the Ministry of Health, Mauritius.

Survey procedures

Each survey participant who had not previously been diagnosed with diabetes was asked
to complete a 75gm oral glucose tolerance test (OGTT) (75g dextrose monohydrate in
250ml water, replicating the procedure used in both the 1987 and 1992 Mauritius
surveys\textsuperscript{12, 13}) after an overnight fast. Blood was centrifuged, separated and the plasma
was frozen on-site. Plasma glucose was measured using a YSI2300 analyzer (Yellow
Springs, OH) approximately four months later in Newcastle upon Tyne, UK at the
reference laboratory, which is a member of the Wellcome quality assurance scheme. In
the 2 previous surveys (1987 and 1992), glucose was measured on-site, with quality
controls measured several months later in Newcastle upon Tyne using a YSI analyzer (Yellow Springs, OH). This showed a small, but consistent and systematic fall in glucose over time. Therefore, the 1998 values were adjusted upwards using an equation based on the difference between on-site values and quality controls from the 1987 and 1992 surveys (n=2328 paired samples; adjusted glucose = 0.0288 + 1.037 x measured glucose; r²=0.981). Glucose tolerance status was determined according to 1999 WHO criteria². Of the 6291 participants 154 were of Chinese origin, 38 were pregnant and 3 were aged under 25 years. These people were excluded from the analyses. Of the 6096 remaining study participants, 1352 had diabetes and a further 708 had missing FPG or 2hPG results. Analyses of the glucose categories of those without diabetes include the remaining 4036 people. Demographic data, physical measurements and questionnaires about lifestyle, medical history and health knowledge and attitudes were completed for each person. Prevalences, age and gender standardized to the 1998 Mauritius population¹₄ for those aged over 30 years (age standardization was only performed on the population aged over 30 years because of the very low numbers of people in the 25-29 year age group), were calculated for normal glucose tolerance (NGT), isolated IFG, isolated IGT, coexisting IFG/IGT and diabetes by sex. The characteristics of men and women in each category of impaired glucose metabolism were compared to determine if the conditions being described are consistent across sexes.

As IFG and IGT are not mutually exclusive categories, persons with IGT may or may not have IFG. In this study comparisons were made between individuals with isolated IFG and those with isolated IGT. Persons defined as having isolated IFG had a FPG concentration ≥ 6.1 and < 7.0 mmol/l and a 2hPG < 7.8 mmol/l and those with isolated IGT had a 2hPG ≥ 7.8 and < 11.1 mmol/l and a FPG < 6.1 mmol/l. Subjects with FPG ≥ 6.1 and < 7.0 mmol/l and a 2hPG ≥ 7.8 and < 11.1 mmol/l were designated as having co-
Persons were defined as having diabetes if they were taking either insulin or oral medication for the control of diabetes or if they had a FPG ≥ 7.0 mmol/l and/or a 2hPG ≥ 11.1 mmol/l. The difference between individual fasting and 2-hour glucose values was calculated as 2hPG (mmol/l) – FPG (mmol/l).

Total cholesterol and triglycerides were determined on fasting blood by manual enzymatic methods. Blood pressure was measured with a standard mercury sphygmomanometer in the right arm of participants who had been seated for 5-minutes. Using the first and fifth Korotkoff sounds, blood pressure was recorded twice to the nearest 2 mmHg and the mean value was calculated. Hypertension was diagnosed on the basis of WHO criteria (systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg) or on self reported antihypertensive medication taken in the past week. Height and weight were measured in light clothing without shoes, and BMI was calculated as weight(kg)/height(m)². Waist circumference (WC) was measured at the horizontal level between the xiphisternum and umbilicus yielding the minimum measurement. Hip circumference was taken as the horizontal measure around the pelvis at the point of maximal protrusion of the buttocks. Waist and hip circumference were measured twice, and the mean calculated. If duplicate waist or hip measurements differed by >2 cm, a third was taken. The mean of the closest two measurements was subsequently used. Waist-hip ratio (WHR) was calculated as the mean waist measurement divided by mean hip measurement. Both WC and WHR were investigated as measures of central obesity. The modified homeostatic model was used to estimate beta cell function (HOMA-B) and insulin sensitivity (HOMA-S).

Statistical analyses
All analyses were conducted using SPSS version 10.0.5 (SPSS Inc., Chicago). Triglycerides, glucose, weight and insulin values were log transformed before calculating (geometric) means. Chi-squared tests were used to compare proportions and means were compared using Student’s t-tests. Both unadjusted glucose values, and values adjusted for the difference between QC and on-site glucose measurements from the 1987 and 1992 surveys were used to examine the difference in the relationship between fasting and 2-hour glucose values in men and women. Univariate general linear models were applied to calculate and compare mean FPG and 2hPG levels for each sex adjusted for fasting and 2-hour insulin, triglycerides and either BMI or WHR. Various other parameters were included in the models to see if they could explain sex differences in the glucose values.
Results

Table 1 shows the prevalence of different states of glucose intolerance in Mauritius by sex. There were no significant differences in mean age or age distribution across decades for men compared with women. The distribution of the population over the glucose categories differed significantly by ethnic group ($\chi^2$ (4 d.f.) = 9.5, p=0.049) with Indians more likely to have diabetes and Creoles more likely to have IFG or IGT. Within each of the ethnic groups there were similar sex differences in the percent in each glucose category (Indians p=0.0001, General Population p=0.001). The prevalence of diabetes and co-existing IFG/IGT was similar in men and women, however, men were more likely than women to have isolated IFG (5.3% vs 3.1% p<0.001). Conversely, the prevalence of isolated IGT was lower in men (9.3%) than in women (13.9%) (p<0.0001). These findings were the same when either adjusted or unadjusted glucose values were used (data not shown).

Comparisons of the characteristics of non-diabetic men and women within different categories of glucose tolerance are shown in Table 2. With the exception of females being slightly older than males among those with IFG, there were no significant differences between the sexes for age or prevalence of hypertension within the four non-diabetic glucose categories. Men and women with NGT differed significantly from each other on all other characteristics, with women having significantly higher 2hPG, fasting and 2-hour insulin, BMI and HOMA-B and significantly lower FPG, WC, WHR, weight, HOMA-S, triglycerides and total cholesterol than men. With the exception of FPG and 2hPG (which are used as the basis for categorization), similar patterns were seen in each of the other glucose tolerance categories.
When men with isolated IFG were compared with men with isolated IGT their FPG and 2hPG, 2-hour insulin, WC, BMI and HOMA-B differed significantly (each with p-value at least <0.05). Comparison between women in the isolated IFG and IGT groups showed they did not differ significantly for WC, or BMI but were significantly different for the other factors that differed in men i.e. FPG, 2hPG, 2-hour insulin and HOMA-B (p<0.001), as well as WHR (p = 0.02).

Men had significantly higher mean FPG (p<0.001) and significantly lower 2hPG (p<0.001) than women. These differences remained highly significant (p<0.01) even after adjusting for all other variables in Table 2.

Figure 1 shows the mean 2hPG value for any given FPG in the non-diabetic range for men and women. When grouped into 0.5 mmol/l categories of FPG, the mean 2hPG was significantly higher in women than men for each group (p<0.05). The mean difference between FPG and 2hPG was greater for women than for men (1.41 mmol/l vs. 0.65 mmol/l, p<0.001). It remained significantly greater for women both after adjustment for age, 2-hour and fasting insulin, HOMA-B, HOMA-S, triglycerides, obesity and weight (1.15mmol/l vs. 0.99mmol/l, p<0.01), and adjustment for age and weight only (1.47 vs. 0.57, p<0.0001).

When only FPG values were considered irrespective of diabetes status based on the 2hPG, the proportion with a FPG in the range 6.1 to 6.9 mmol/l was 13.4% in men and 9.7% in women (p<0.0001). Also, when only 2hPG was considered irrespective of diabetes status based on the FPG, the proportion with a value between 7.8 and 11.1 mmol/l was 16.1% in men and 21.0% in women (p<0.0001).
Discussion

Data from this population-based survey show distinct sex differences in the prevalence of IFG and IGT, with IGT being more common in women and IFG more common in men. Other recent epidemiological studies\textsuperscript{17-24} have also reported similar sex differences in the prevalence of IFG and IGT, and the majority of IGT studies reviewed by the WHO showed that IGT was more common in men than women\textsuperscript{25}. Furthermore, we have now described a difference in the relationship between FPG and 2hPG in men and women that may contribute to this phenomenon.

While there may be some overlap between IFG and IGT, it is now quite apparent that they identify different sub-populations\textsuperscript{5, 11, 26, 27}. This is understandable in the context that IFG reflects the basal fasting state while IGT signals postprandial abnormalities. Even though it is now clear that IFG and IGT encompass different sub-populations, using glucose measurements alone it is difficult to differentiate between the precise underlying abnormalities of insulin resistance and ß-cell dysfunction which lead to the conditions\textsuperscript{28, 29}. Therefore, although the new category of IFG may broaden the description of intermediate abnormal states in glucose metabolism, it should be seen as complementary to IGT rather than its replacement. Screening programs aimed at identifying people at risk of developing diabetes that rely solely on the FPG, chance missing a considerable proportion of the at-risk population, and if our observations are further confirmed, may result in a sex-biased selection of individuals.

Previous studies looking at insulin resistance and beta cell function in IFG and IGT have produced conflicting results. Data from the Pima Indian studies suggest that IFG and
IGT are associated with similar abnormalities of insulin action, and that IFG is also associated with reduced insulin secretory capacity\textsuperscript{30, 31}. This finding was supported in a recent paper from the United Kingdom\textsuperscript{28}. However, the Botnia study reported the opposite, with the IFG group displaying insulin resistance, whereas subjects with IGT had impaired secretory capacity\textsuperscript{19}. Our data are in keeping with the findings from the Pima and UK populations, and show that both categories are insulin resistant, and that beta cell function is reduced in those with IFG, but not those with IGT. In Mauritius we found that men have lower levels of beta cell function and higher rates of IFG than women, and women have lower insulin sensitivity than men and higher rates of IGT.

The 2hPG associated with any given FPG is higher in women than men in this population. This remained true even after adjusting for a range of factors, including body weight. Thus, these male-female differences are not simply a consequence of giving the same glucose load to smaller individuals (i.e. women). This contributes to the explanation of why there are differences in the proportion of men and women classified as having isolated IFG or isolated IGT. By definition, people with isolated IFG must have a relatively small difference between their FPG and 2hPG, which can now be seen to be more likely to occur in men than women. Conversely, isolated IGT requires a relatively large difference between the glucose values – a situation more likely to occur in women. These differences are partially a consequence of the cut-off values of the classification criteria and the relationship between FPG and 2hPG in each of the sexes. However, in addition to the apparent difference in the relationship between FPG and 2hPG by sex, we found significant differences in the proportion of men and women with a FPG in the range 6.1 to 6.9 mmol/l or a 2hPG between 7.8 and 11.1 mmol/l regardless of the other respective glucose value. Adjusting for obesity using BMI or WHR did not explain the sex differences in either FPG or 2hPG. The importance of these sex
differences lies not only in the number of persons classified into each category but also in whether or not men and women in a particular glucose category are at similar risk of developing diabetes and its associated complications. Despite the majority of studies showing a preponderance of IGT among women, it is true that a number of studies identify men as having a higher prevalence of IGT than women. It is not clear what factors might be influencing these results, with a number of geographically and ethnically diverse populations represented among the studies showing a male predominance.

The sex difference in the prevalence of different glucose categories raises the possibility that the classifications as currently defined have different prognostic implications for men and women. Further studies are required to elucidate the sex differences in glucose metabolism, and to determine longitudinally whether the rates of adverse outcomes associated with IFG and IGT are similar in both sexes.
Acknowledgments

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Table 1 Percent of population aged ≥30 years in each glucose category by sex*

<table>
<thead>
<tr>
<th>Glucose Category</th>
<th>Men (N = 2358)</th>
<th></th>
<th>Women (N = 3030)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>95% CI</td>
<td>N</td>
</tr>
<tr>
<td>Normal</td>
<td>1320</td>
<td>60.7</td>
<td>58.7 – 62.7</td>
<td>1666</td>
</tr>
<tr>
<td>Isolated IFG</td>
<td>125</td>
<td>5.1</td>
<td>4.2 – 6.0</td>
<td>95</td>
</tr>
<tr>
<td>Isolated IGT</td>
<td>219</td>
<td>9.0</td>
<td>7.9 – 10.2</td>
<td>421</td>
</tr>
<tr>
<td>IFG and IGT</td>
<td>90</td>
<td>3.2</td>
<td>2.4 – 3.9</td>
<td>100</td>
</tr>
<tr>
<td>Diabetes</td>
<td>604</td>
<td>22.0</td>
<td>20.3 – 23.8</td>
<td>748</td>
</tr>
</tbody>
</table>

* Age and gender standardized to the 1998 Mauritius population aged ≥30 years
### Table 2 Mean values or percent prevalence for characteristics of non-diabetic men and women within different glucose categories.

<table>
<thead>
<tr>
<th>Glucose category</th>
<th>NGT</th>
<th>I-IFG</th>
<th>I-IGT</th>
<th>IFG/IGT</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>F</td>
<td>M</td>
<td>F</td>
<td>M</td>
</tr>
<tr>
<td>N</td>
<td>1320</td>
<td>1666</td>
<td>125</td>
<td>95</td>
<td>219</td>
</tr>
<tr>
<td>Age (years)</td>
<td>46.4</td>
<td>46.7</td>
<td>49.3</td>
<td>54.1‡</td>
<td>50.0</td>
</tr>
<tr>
<td>FPG (mmol/l)*</td>
<td>5.2</td>
<td>5.1‡</td>
<td>6.4</td>
<td>6.4</td>
<td>5.45</td>
</tr>
<tr>
<td>2hPG (mmol/l)*</td>
<td>5.3</td>
<td>5.9‡</td>
<td>5.7</td>
<td>6.3‡</td>
<td>8.6</td>
</tr>
<tr>
<td>Fasting insulin (mmol/l)*</td>
<td>6.9</td>
<td>8.1‡</td>
<td>8.7</td>
<td>10.4†</td>
<td>9.7</td>
</tr>
<tr>
<td>2-hour insulin (mmol/l)*</td>
<td>28.4</td>
<td>46.5‡</td>
<td>30.7</td>
<td>52.5‡</td>
<td>91.3</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>23.8</td>
<td>25.0‡</td>
<td>24.0</td>
<td>26.8‡</td>
<td>25.4</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>84.9</td>
<td>77.5‡</td>
<td>86.7</td>
<td>81.9‡</td>
<td>89.6</td>
</tr>
<tr>
<td>Weight (kg)*</td>
<td>66.0</td>
<td>57.9‡</td>
<td>66.5</td>
<td>61.6‡</td>
<td>68.7</td>
</tr>
<tr>
<td>Waist-Hip ratio</td>
<td>0.89</td>
<td>0.79‡</td>
<td>0.91</td>
<td>0.80‡</td>
<td>0.92</td>
</tr>
<tr>
<td>HOMA-B (%)*</td>
<td>98.0</td>
<td>113.4‡</td>
<td>77.8</td>
<td>87.4†</td>
<td>113.9</td>
</tr>
<tr>
<td>HOMA-S (%) *</td>
<td>55.2</td>
<td>47.5‡</td>
<td>41.1</td>
<td>34.7†</td>
<td>39.1</td>
</tr>
<tr>
<td>Triglycerides (mmol/l)*</td>
<td>1.4</td>
<td>1.1‡</td>
<td>1.5</td>
<td>1.2‡</td>
<td>1.6</td>
</tr>
<tr>
<td>Total Cholesterol (mmol/l)</td>
<td>5.1</td>
<td>4.6‡</td>
<td>5.3</td>
<td>4.8‡</td>
<td>5.4</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>22.5</td>
<td>21.3</td>
<td>37.9</td>
<td>38.9</td>
<td>40.4</td>
</tr>
</tbody>
</table>

NGT – normal glucose tolerance; I-IFG – isolated IFG; I-IGT – isolated IGT; IFG/IGT – co-existing IFG and IGT.

* geometric mean
†p<0.05   ‡p < 0.01. p-values are for comparison with men within the same glucose category.
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23. Zargar AH, Khan AK, Masoodi SR, Laway BA, Wani AI, Bashir MI, et al. Prevalence of type 2 diabetes mellitus and impaired glucose tolerance in


