Microalbuminuria and the metabolic syndrome in non-diabetic black Africans

IKECHI G OKPECHI, MICHAEL D PASCOE, CHARLES R SWANEPOEL, BRIAN L RAYNER

Abstract

It is recognised that the metabolic syndrome promotes the development of cardiovascular disease. Although several studies have shown a relationship between the metabolic syndrome and kidney disease, few of these have used non-diabetic subjects, especially in the African population.

This was a cross-sectional study of subjects of African origin, using the metabolic syndrome (MS) criteria of the National Cholesterol Education Program (NCEP) third Adult Treatment Panel (ATP III). Subjects with impaired fasting glucose, with two-hour glucose > 11.1 mmol/L after a glucose tolerance test, were excluded. Spot urine for albumin-to-creatinine ratio (ACR) was measured and the glomerular filtration rate (GFR) was estimated using the Modification of Diet in Renal Disease (MDRD) equation. Microalbuminuria was defined as ACR between 3–30 mg/mmol.

There was a significant decline in GFR and a significant increase in ACR with increasing number of MS traits. ACR increased four-fold between subjects with no MS traits and those with four or more traits. In subjects with the metabolic syndrome, there was a significant correlation between ACR and systolic blood pressure (SBP), diastolic blood pressure (DBP) and fasting glucose. Estimated GFR correlated significantly and inversely with body mass index (BMI) and serum leptin.

These observations raise major clinical and public health concerns for developing countries, where both the metabolic syndrome and kidney disease are being reported more and more frequently. The potential economic impact is huge.

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Key words: leptin, metabolic syndrome, microalbuminuria, obesity.

Introduction

A number of epidemiological studies have linked the metabolic syndrome with an increased risk for microalbuminuria, an early marker of kidney injury. Chen et al. reported statistically significant associations between the metabolic syndrome and microalbuminuria and also significant correlations between the number of metabolic syndrome traits and a glomerular filtration rate (GFR) < 60 ml/min. Although black Africans have a higher prevalence of chronic kidney disease (CKD) from diabetes and hypertension, it remains unclear whether the metabolic syndrome contributes significantly to the cause of kidney disease in black Africans in the absence of diabetes mellitus, especially as there are currently no relevant data from Africa. We conducted this cross-sectional study in a homogenous black African population to examine the relationship between early kidney disease and the metabolic syndrome in non-diabetic black (Xhosa) South Africans.

Materials and methods

The study was approved by the research ethics committee of the University of Cape Town and was conducted between May 2005 and July 2006 in the black township of Gugulethu in the Western Cape, where 334 subjects were recruited. Subjects with severe or malignant hypertension, diabetes mellitus, established renal disease or a family history of renal disease were excluded, as were pregnant women. Although testing for infection with the human immunodeficiency virus (HIV) was not performed, all subjects on highly active antiretroviral treatment (HAART) were also excluded.

A questionnaire was used to collect relevant demographic data. Weight, height and waist circumference were measured and recorded to the nearest 0.1 cm. Blood pressure (BP) was measured twice, using a validated and standard mercury sphygmomanometer, after the subject had been seated for five minutes and the average of the two readings was taken. Hypertension was defined as systolic BP of ≥ 130 mmHg or a diastolic BP of ≥ 85 mmHg or subjects reporting to be currently taking antihypertensive medications.

Blood was drawn in the fasting state for estimation of lipids, creatinine, glucose, insulin, C-reactive protein (CRP) and leptin. Spot urine was collected to measure the urine albumin-to-creatinine ratio (ACR); microalbuminuria was defined as urine ACR of 3–30 mg/mmol. An oral glucose tolerance test (OGTT) was performed using 75 g of glucose in 300 ml of water for subjects with impaired fasting glucose (IFG); those with a two-hour glucose level ≥ 11.1 mmol/L were classified as diabetic and excluded from the study. Glomerular filtration rate (GFR) was determined using the...
abbreviated Modification of Diet in Renal Disease (MDRD) equation. The metabolic syndrome (MS) was defined by the National Cholesterol Education Program (NCEP) third Adult Treatment Panel (ATP III) guidelines. All samples were analysed at the National Health Laboratory Services of the Groote Schuur Hospital.

Statistical analysis was performed using SPSS statistical software version 10.1 (SPSS Inc., US). One-way analysis of variance (ANOVA) was used to analyse data from subjects with varying components of MS traits. A p value <0.05 was taken as significant.

**Results**

The prevalence of the metabolic syndrome and microalbuminuria was 33.5% and 19.5%, respectively. Traditional metabolic risk factors such as body mass index (BMI), waist circumference (WC), fasting blood glucose (FBG) and lipids increased significantly (p<0.0001) as the number of MS traits increased and this trend persisted after the p value was adjusted for age, gender, duration of hypertension and number of antihypertensive medications (table 1). Serum leptin also increased significantly with increasing number of metabolic syndrome traits (p<0.0001).

Importantly, there was a four-fold increase of urine ACR between those subjects without MS traits and those with four or more traits; estimated GFR also significantly decreased as the number of MS traits increased (p<0.0001). Urine ACR positively and significantly correlated with SBP (β=0.255, p = 0.002), DBP (β=0.206, p=0.037 ) and fasting glucose (β=0.230, p=0.008) in subjects with MS while estimated GFR inversely and significantly correlated with BMI (β=-0.223, p = 0.024 ) and serum leptin concentration (β=-0.272, p<0.0001) in the same subjects.

**Discussion**

Microalbuminuria, a sign of endothelial dysfunction, may herald impending and serious renal impairment. Yudkin proposed that the clustering of risk factors attributed to insulin resistance and microalbuminuria may all be features of damage to different aspects of endothelial function. In this study, the four-fold rise in ACR in subjects without MS traits compared to those with four or more MS traits clearly shows that additional metabolic risk factors, even in the absence of diabetes, increase the risk for cardiovascular disease.

An important aspect of this study may relate to the adequacy of blood pressure control in black Africans, who suffer more from kidney disease resulting from hypertension. A study from Nigeria showed that microalbuminuria is seen in about 37% of newly presenting hypertensives, while in another study from South Africa, the prevalence of microalbuminuria was significantly higher in hypertensive blacks compared to white, Asian and Indian subjects.

Some of our results, particularly the significant inverse correlation of GFR with BMI and serum leptin, may imply obesity as a factor for renal disease in this population. Chen et al. showed that the risk for being affected by CKD was more than twice as high in patients with an increased waist circumference compared to those without, suggesting that obesity may be an independent risk factor for CKD. Although the exact mechanisms that link obesity and renal damage have not yet been made clear, it has been suggested that at least some of the many adipocytokines, including

<p>| Table 1. Characteristics of the participants by number of metabolic syndrome traits |
|-------------------------------------------------------------|----------------|----------------|----------------|----------------|----------------|</p>
<table>
<thead>
<tr>
<th>Variable</th>
<th>0 (n=334) (%)</th>
<th>1 (n=334) (%)</th>
<th>2 (n=334) (%)</th>
<th>3 (n=334) (%)</th>
<th>≥ 4 (n=334) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>36 (10.8)</td>
<td>56 (16.8)</td>
<td>130 (38.9)</td>
<td>73 (21.9)</td>
<td>39 (11.6)</td>
</tr>
<tr>
<td>Males (%)</td>
<td>18 (50.0)</td>
<td>34 (58.6)</td>
<td>32 (28.0)</td>
<td>24 (33.8)</td>
<td>6 (15.9)</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>124.5 (2.4)</td>
<td>138.4 (3.3)</td>
<td>148.2 (1.8)</td>
<td>153.2 (2.2)</td>
<td>161.1 (1.7)</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>81.7 (1.5)</td>
<td>86.8 (1.6)</td>
<td>93.4 (1.0)</td>
<td>95.0 (1.4)</td>
<td>100.5 (6.8)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.9 (0.9)</td>
<td>27.4 (0.8)</td>
<td>35.4 (0.8)</td>
<td>36.3 (0.8)</td>
<td>37.7 (1.1)</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>80.9 (1.5)</td>
<td>92.8 (2.0)</td>
<td>109 (1.3)</td>
<td>114.2 (1.5)</td>
<td>115.8 (2.0)</td>
</tr>
<tr>
<td>FBG (mmol/L)</td>
<td>4.7 (0.1)</td>
<td>4.7 (0.1)</td>
<td>5.0 (0.1)</td>
<td>5.5 (0.1)</td>
<td>5.8 (0.1)</td>
</tr>
<tr>
<td>HOMA</td>
<td>1.5 (0.1)</td>
<td>1.6 (0.2)</td>
<td>3.9 (0.7)</td>
<td>7.2 (1.4)</td>
<td>14.4 (3.5)</td>
</tr>
<tr>
<td>TG (mmol/L)</td>
<td>0.7 (0.1)</td>
<td>1.0 (0.1)</td>
<td>1.2 (0.1)</td>
<td>1.6 (0.1)</td>
<td>2.1 (0.1)</td>
</tr>
<tr>
<td>HDL (mmol/L)</td>
<td>1.7 (0.1)</td>
<td>1.7 (0.1)</td>
<td>1.5 (0.1)</td>
<td>1.3 (0.1)</td>
<td>1.2 (0.1)</td>
</tr>
<tr>
<td>Leptin (ng/ml)</td>
<td>14.3 (2.5)</td>
<td>18.7 (2.6)</td>
<td>35.8 (2.3)</td>
<td>34.9 (2.8)</td>
<td>36.9 (3.4)</td>
</tr>
<tr>
<td>GFR (ml/min/1.73 m²)</td>
<td>133.9 (6.1)</td>
<td>112.9 (3.5)</td>
<td>100.6 (2.6)</td>
<td>103.9 (2.6)</td>
<td>94.4 (3.0)</td>
</tr>
<tr>
<td>ACR (mg/mmol)</td>
<td>1.4 (0.5)</td>
<td>1.2 (0.2)</td>
<td>2.8 (0.6)</td>
<td>3.3 (0.6)</td>
<td>4.7 (1.8)</td>
</tr>
</tbody>
</table>

Key: SBP = systolic blood pressure; DBP = diastolic blood pressure; BMI = body mass index; WC = waist circumference; HOMA = homeostasis model assessment; TG = triglycerides; HDL = high-density lipoprotein cholesterol; CRP = C-reactive protein; GFR = glomerular filtration rate; ACR = albumin-to-creatinine ratio; FBG = fasting blood glucose

P* - P value adjusted for age, sex, duration of hypertension and antihypertensive medications

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leptin, interleukin-6 (IL-6) and tumour necrosis factor-α (TNF-α), may be partly involved in promoting renal impairment.

Our observations raise major clinical and public health concerns, especially for developing countries where both the metabolic syndrome and kidney disease are becoming common. The potential economic impact is huge. Given the nature of this problem, clinical trials with renal end points aiming to clarify the mechanisms of kidney disease in the metabolic syndrome should be considered a research priority. Physicians in developing countries, especially in Africa, need to reiterate those lifestyle measures which, if modified, would reduce cardiovascular diseases arising from the epidemics of obesity and the metabolic syndrome.

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Conflicts of interest statement
None declared.

References