SERUM URIC ACID LEVEL AS AN INDEPENDENT COMPONENT OF THE METABOLIC SYNDROME IN TYPE 2 DIABETIC BLACKS.

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ABSTRACT
Context: No consensus has been achieved on the components included in the definition of Metabolic Syndrome (MS). Uric acid and Gamma glutamyl transpeptidase are however newer markers not included in previous studies.

Objectives: This study was carried out to determine the prevalence of MS in Diabetes Mellitus, the correlation between hyperuricaemia and MS as well as make a case for the inclusion of serum Uric acid level as a new marker for MS.

Methodology: Fasting venous sample from the cubital vein of 77 females and 44 males diagnosed NIDDM patients for enzymatic determination of serum lipids, glucose and uric acid using QCA kits. The demographic records were obtained from the folders. Metabolic syndrome was diagnosed using the WHO criteria

Result: The prevalence of the new component hyperuricaemia among the study subjects was 10.7%. Thirty-eight (31.6%) of the subjects who had high blood pressure, hypertriglyceridaemia, low HDL-C and BMI > 30 kg/m² diagnostic of MS also had hyperuricaemia as against the 29 (23.9%) subjects who had MS only. About 23.7% of the 38 subjects who had MS and hyperuricaemia had serum uric acid values above 0.38mmol/l recommended as the cut off value. There was a significant correlation (r = 0.301, p<0.01) between serum uric acid level, BMI, total cholesterol, LDL-C and HDL-C/TC, among the female subjects while the male subjects showed significant correlation (p<0.05) between their BMI and serum HDL-C level only. There was a significant difference (p<0.001) in the CHD risk ratio between the male and the female MS subjects.

Conclusion: The correlation between hyperuricaemia and other components of MS as demonstrated in this study may suggest a common etiological factor between the MS components as suggested in other studies. Insulin resistance has been implicated as a common denominator. Thus a further investigation in this direction would be needed.

Keywords: Serum, Uric Acid, Metabolic Syndrome, Diabetes Mellitus. (Accepted 28 August 2006)

INTRODUCTION
Uric acid is a by product of the continual process in the body where old cells are broken down and new ones formed. It is the major product of purine metabolism formed from Xanthine by the action of Xanthine oxidase. The serum level of uric acid varies with height, body weight, blood pressure, kidney function (eliminated from the body in urine,) and alcohol intake in adults. It value also increases in women after menopause suggesting an interaction with sex hormones. There is evidence also to suggest an association or correlation between serum uric acid and metabolic syndrome with all its components such as obesity, hypertension, reduced high density lipoprotein (HDL) cholesterol, hypertriglyceridaemia, hyperinsulinemia and recently associated with insulin resistance and reduced sensitivity. Serum uric acid has been demonstrated to have an independent, significant association with MS, showing a consistence relation to insulin resistance. This relationship persisted when the differences in age, sex, overall obesity, abdominal obesity were taken into account. Facchini et al. found that urinary uric acid clearance decreases in proportion to increases in insulin resistance in normal volunteers, leading to an increase in the serum uric acid concentration. In a previous study, a strongest correlation was found between serum lipids and BMI, serum lipids And uric acid level, BMI and uric acid

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Fasting plasma glucose was determined by the glucose oxidase method while serum lipids and lipoproteins were assayed by enzymatic methods (QCA kit, Spain). Serum HDL cholesterol was also determined by enzymatic method after precipitation of low-density and very-low-density lipoproteins with dextran sulfate MgCl₂ (QCA kit, Spain). Elevated levels were defined according to the WHO guidelines as cholesterol (>5.2 mmol/L), triglyceride (1.8 mmol/L), HDL-C (>0.9 mmol/L) and LDL-C (4.65 mmol/L) respectively. Serum uric acid was measured with use of an enzymatic method (QCA kit, Spain).

Blood pressure was measured with the patients in a sitting position after a 5-minute rest with use of a mercury sphygmomanometer and read to the nearest 5 mm Hg. Subjects were classified as having hypertension if they had systolic blood pressure of above 140 mm Hg or diastolic blood pressure of above 90 mm Hg independent of each other on two clinic visits at three weeks interval. Body mass index (BMI)-Kg/m² was derived in the subjects as weight (Kg) divided by the square of height in meter (m²). BMI of <20 was regarded as under weight, 20-24.9 as normal weight, 25-30 as overweight and >30 as obese.

The WHO criteria on diagnosis and classification of diabetes mellitus, was used in determining MS in our study group. Data analyses were done with the Epi Info ver.6.1 software.

RESULT

Of the 121 diabetic subjects studied, 77 (63.6%) were females while 44 (36.4%) were male. The age range was 37-78 years (mean 57.3±10 years) in both sexes. The mean age of the female subjects was 56.1±9.3 years while that of the male was 59.3±10.2 years. The age and sex distribution is as shown on table 1.

As outlined in table 2, Thirty one (25.6%) of the subjects were obese (BMI>30Kg/m²) while 47 (38.9%) were overweight. Among the obese were 17(22%) female while only 14 (31.8%) were males. About forty-two (34.7%) of the subjects was found to have hypercholesterolemia with 37 (48.1%) and 15 (34.1%) of the female and male subjects respectively having hypercholesterolemia. The overall prevalence of hypertriglyceridemia was 21%, though hypertriglyceridemia was commoner among the female (23.4 %) than the male (22.7%) subjects. HDL-C below recommended level was observed in 64.9% and 72.7% of the female and male subjects respectively. The mean total subjects respectively. The mean total cholesterol and the LDL-C were higher among the obese compare to the other weight status, while the Mean TG was highest

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amongst normal weight subjects (BMI>18.5-24.9kg/m²).
Thirty-eight (31.6%) of the subjects who had high blood pressure, hypertriglyceridemia, low HDL-C and BMI > 30 kg/m² diagnostic of MS also had hyperuricaemia as against the 29 (23.9%) subjects who had MS only. About 23.7% of the 38 subjects who had MS and Hyperuricaemia had serum uric acid values above 0.38mmol/l recommended as the cut off value, while the mean serum uric acid level of the subjects studied was 0.30mmol/L.
There was a significant correlation (r = 0.301, p<0.01) between the BMI and total cholesterol, LDL-C and HDL-C/TC, among the female subjects while the male subjects showed significant correlation (p<0.05) between the BMI and the HDL-C.
The pattern of combination of various components of metabolic syndrome in subjects with serum uric acid level greater than 0.38 is as displayed on table 3. Only

<table>
<thead>
<tr>
<th>Component</th>
<th>Total No of subjects MS Components (n)</th>
<th>Male (%)</th>
<th>Female (%)</th>
<th>TOTAL (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DM + HBP</td>
<td>28(23.1%)</td>
<td>2 (40)</td>
<td>3 (60)</td>
<td>5 (17.9)</td>
</tr>
<tr>
<td>DM +OB</td>
<td>31(25.6%)</td>
<td>7 (77.8)</td>
<td>2 (22.2)</td>
<td>9 (29.0)</td>
</tr>
<tr>
<td>DM + HL</td>
<td>25(20.7%)</td>
<td>1 (20.0)</td>
<td>4 (80.0)</td>
<td>5 (20.0)</td>
</tr>
<tr>
<td>DM +HU</td>
<td>18(14.8%)</td>
<td>7 (77.8)</td>
<td>2 (22.2)</td>
<td>9 (50.0)</td>
</tr>
<tr>
<td>HBP + OB</td>
<td>10(8.3%)</td>
<td>2 (0)</td>
<td>0 (0)</td>
<td>2 (13.6)</td>
</tr>
<tr>
<td>HBP + HL</td>
<td>22(18.2%)</td>
<td>3 (100)</td>
<td>0 (0)</td>
<td>3 (11.8)</td>
</tr>
<tr>
<td>HL + OB</td>
<td>17(14.1%)</td>
<td>2 (0)</td>
<td>2 (100)</td>
<td>2 (23.7)</td>
</tr>
<tr>
<td>HBP + HU</td>
<td>6(5)</td>
<td>1 (16.7)</td>
<td>5 (83.3)</td>
<td>6 (100)</td>
</tr>
<tr>
<td>HL + HU</td>
<td>7(57.9)</td>
<td>5 (71.4)</td>
<td>2 (28.6)</td>
<td>7 (100)</td>
</tr>
<tr>
<td>OB + HU</td>
<td>9(7.4)</td>
<td>7 (77.8)</td>
<td>2 (22.2)</td>
<td>9 (100)</td>
</tr>
<tr>
<td>DM+HL+HBP+OB</td>
<td>29(23.9%)</td>
<td>7 (77.8)</td>
<td>2 (22.2)</td>
<td>9 (31.1)</td>
</tr>
<tr>
<td>DM+HL+HBP+OB+HU</td>
<td>38(31.4%)</td>
<td>7 (77.8)</td>
<td>2 (22.2)</td>
<td>9 (13.6)</td>
</tr>
</tbody>
</table>

KEY
DM - Diabetes Mellitus HBP - Hypertension HU - Hyperuricaemia HL - Hyperlipidemia OB - Obesity

Table 4 Characteristics of Serum Uric Acid in MS subjects

<table>
<thead>
<tr>
<th>Variables</th>
<th>High uric acid (N=8)</th>
<th>Low uric acid (n=30)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>60.2±7.6</td>
<td>56.5±9.2</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>29.8±1.1</td>
<td>30.1±4.0</td>
<td>p&gt;0.8</td>
</tr>
<tr>
<td>Total triglyceride (mmol/L)</td>
<td>1.98±0.2</td>
<td>1.3±0.5</td>
<td>p=0.1</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>3.8±0.7</td>
<td>5.7±1.8</td>
<td>p=0.9</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/L)</td>
<td>0.7±0.2</td>
<td>0.8±0.3</td>
<td>p=0.7</td>
</tr>
<tr>
<td>LDL cholesterol (mmol/L)</td>
<td>2.0±0.3</td>
<td>3.4±0.3</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Plasma glucose (mmol/L)</td>
<td>6.9±3.7</td>
<td>8.9±4.3</td>
<td>p=0.1</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>140.0±10.7</td>
<td>141.3±16.1</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>87.5±8.0</td>
<td>87.3±10</td>
<td>p=1</td>
</tr>
</tbody>
</table>

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The prevalence of a new component named hyperuricaemia among the NIDDM subjects studied was 10.7%. This finding further support earlier conclusion that hyperuricaemia as a finding in NIDDM. A previous study has observed an increasing evidence that NIDDM associated with hyperuricaemia is closely related to an increase oxidative stress response in NIDDM with its antecedent vascular complications. Thus, the hyperuricaemia may be an indicator of an increased endogenous water-soluble antioxidant of the body.

However, like the other components of MS, hyperuricaemia as an independent risk factor for cardiovascular disease is now well established even though the mechanism(s) via which hyperuricaemia is associated with CVD remain unexplained. This may suggest that hyperuricaemia might be an 'innocent bystander,' a non specific marker of adverse pattern of risk factors. The significant difference (p<0.001) in the average CHD risk ratio of 0.20 among male MS subjects and the high CHD risk ratio (0.18) in the females may suggest that hyperuricaemia could be an independent MS component especially in females.

The relationship of uric acid with other components of MS was demonstrated in this study by a significant correlation (r = 0.301, p<0.01) between the BMI and total cholesterol, LDL-C and HDL-C/TC among the female subjects, while the male subjects showed significant correlation (p<0.05) between serum uric acid, BMI and the HDL-C is similar to earlier study. Even though many studies has suggested that insulin resistance may be a common aetiological factor for both the WHO components as well as the newer individual components of MS, interestingly, consensus concerning the components included in the definition rom MS may not be over or far frombeen achieved. Recently, several other components of MS such as raised PAL-1, gamma glutamyl transpeptidase have been described and are now becoming new markers included in the most frequently proposed metabolic abnormalities for MS. However, as earlier suggested a clear description of the essential components of the syndrome is needed with more studies to correlate to the existing WHO components with emerging ones because the association between hyperuricaemia and other components of MS as demonstrated in this study may suggest a common etiological factor between the components Many studies have suggested insulin resistance as the common denominator. Thus a further investigation in this direction would be needed especially in this environment where there are very scanty existing literature and studies on the WHO criteria.

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