THE METABOLIC SYNDROME AMONG PATIENTS WITH CARDIOVASCULAR DISEASE IN ACCRA, GHANA

J. AKPALU¹, A. AKPALU¹ and F. OFEI¹,²
¹Department of Medicine, Korle Bu Teaching Hospital, PO Box KB 77, Korle Bu, Accra, Ghana and Department of Medicine & Therapeutics, University of Ghana Medical School, PO Box 4236, Accra, Ghana

Author for correspondence: Dr Josephine Akpalu
E-mail: janduah@yahoo.com
Conflict of interest: None declared

SUMMARY
Background: There is evidence linking the Metabolic Syndrome with an increased risk of developing cardiovascular disease, previously thought to be rare in Africa but now a major public health concern.

Objectives: To determine the frequency of occurrence of the Metabolic Syndrome among patients presenting with cardiovascular disease at the Korle Bu Teaching Hospital, Ghana.

Methods: This was a case-control study of 100 consecutive cardiovascular disease patients and 100 age- and sex- matched controls who underwent an interview and physical examination. Anthropometric measurements and fasting blood samples for plasma glucose and lipids were taken. The National Cholesterol Education Programme: Adult Treatment Panel III criteria were used for the diagnosis of the Metabolic Syndrome.

Results: The prevalence of Metabolic Syndrome among cases and controls was 54% and 18% respectively, with the prevalence increasing with advancing age. Hypertension and central obesity were the two components with the highest frequency among individuals with Metabolic Syndrome. The Metabolic Syndrome was associated with the development of cardiovascular disease (OR = 5.35, 95% CI: 2.81 – 10.18, p= 0.0001), with the odds ratio increasing with the number of components present.

Conclusion: The Metabolic Syndrome is prevalent among cardiovascular disease patients attending the Korle Bu Teaching Hospital, with a significant association between the number of components of the Metabolic Syndrome present and the probability of developing a cardiovascular disease. A policy to institute routine screening in clinical practice and provision of appropriate interventions for Metabolic Syndrome components among Ghanaian adults is needed.

Keywords: Metabolic Syndrome, cardiovascular disease, Syndrome X, Ghana

INTRODUCTION

The Metabolic Syndrome (MetS), which connotes the clustering of known cardiovascular disease (CVD) risk factors including abdominal obesity, dyslipidaemia, hyperglycaemia and systemic hypertension, is a major public health challenge worldwide.¹ The syndrome, which has been described variously as Insulin Resistance Syndrome², Deadly Quartet¹, and Syndrome X³ was recognized at least 80 years ago.⁴ However, it was not until 1998 that an attempt was made by the World Health Organization (WHO) Diabetes Expert Group⁵ to provide an internationally recognized definition. Subsequently, several definitions have been proposed. Among these, the National Cholesterol Education Program: Adult Treatment Panel III (NCEP: ATPIII) criteria⁶ which was proposed in 2001, has good clinical relevance and application while avoiding sophisticated laboratory investigations, and is therefore the most practical for use in our setting in Ghana.

In earlier studies, using the WHO definition in the same population tended to give a higher prevalence rate of the MetS than the rate obtained with the NCEP: ATPIII definition.² Using one criterion alone (the NCEP: ATPIII) in different parts of the world has demonstrated a variable prevalence of MetS from place to place. Prevalence rates of between 9.8%⁸ and 26.2%⁹ have been obtained for some European and Asian countries, while 24% of adult north Americans meet the diagnostic criteria for MetS.¹⁰ Very few population-based studies have been conducted in Africa to determine the prevalence of the MetS. However, studies conducted among Nigerian¹¹,¹² and Zimbabwean¹³ type 2 diabetes mellitus(DM) patients, using the WHO definition, puts the prevalence of MetS between 25.2% and 59.1%. The first population-based study in sub-Saharan Africa on the MetS using multiple criteria, namely, the WHO, NCEP: ATPIII as well as the International Diabetes Federation definitions, was recently undertaken in Cameroun.¹⁴ The highest prevalence (7.9% for men, 5.9% for women) was obtained with the WHO definition and the lowest (0.5% for men, 0.2% for women) with the NCEP: ATPIII criteria.
Insulin Resistance (IR) has been identified as the primary underlying cause for the MetS and it is currently recognized that visceral adiposity (central obesity) is a major contributor to the development of both IR and MetS through the production of large numbers of adipokines. There is also evidence to suggest a genetic basis for the MetS.

The MetS is associated with an increased risk of developing CVD, and it serves as a simple clinical tool for identifying individuals with a relatively high long-term risk of CVD. While non-communicable diseases (NCD) are relatively more prevalent in developed countries, their impact is far more devastating in developing countries since they represent a significant burden on the already under-resourced public health service. A recent WHO report identifies CVDs as accounting for 9.2% of total deaths in the African region in 2001, and it is estimated that by the year 2015 the number of deaths in Africa due to NCDs in general will exceed that due to communicable diseases. This looming epidemic is adequate reason for the early institution of appropriate interventions to reduce the risk factors for CVD, including that related to MetS.

In Ghana and West Africa, the prevalence of hypertension, DM, IR, hyperlipidaemia and obesity that are individual components of MetS are on the increase. There has also been a documented increase in CVD morbidity and case fatality in Ghana. Whereas these disorders have been reported on separately in Ghana, studies are yet to be done to ascertain the occurrence and collective impact of features of MetS on CVD morbidity. This study aimed at determining the frequency of occurrence of MetS and its relation to cardiovascular events at Korle Bu Teaching Hospital (KBTH), Accra, Ghana.

METHODS

This case-control study was undertaken at the department of Medicine, (KBTH), Accra, Ghana, over a 12-month period. A case was any patient who was admitted to the medical ward with a stroke, acute coronary syndrome, peripheral arterial disease or heart failure related to hypertensive or ischaemic heart disease. Controls were apparently normal age (+2 years) - and sex-matched individuals, 65% of whom had come to the hospital to undergo routine pre-employment medical examination. The remaining 35% were attendants at general internal medicine out-patient clinics at the KBTH. Participants (cases and controls) with chronic kidney disease, cancer, connective tissue disease, rheumatic heart disease, infective endocarditis and sepsis were excluded from the study after history and clinical examination.

Sample size was calculated using the formula for hypothesis test of odds ratio for a case-control study (Power 80%, two-sided type 1 error 5%). Assuming an estimated prevalence for controls of 20% and Odds ratio of 2.5, a minimum sample size of 94 was obtained for both cases and controls. Consecutive patients meeting the inclusion criteria were recruited into the study after informed consent was obtained. The University of Ghana Medical School Research and Ethics Committee approved the study.

Data were collected through a questionnaire, clinical examination and the taking of anthropometric measurements. The questionnaire was administered to each participant (cases and controls) to obtain information on demographic characteristics and CVD risk factors (personal or family history of hypertension, DM or dyslipidaemia, tobacco use and physical activity). Physical activity was defined as being engaged in leisure time exercise at least 3 times a week for a minimum of 30 minutes. Waist circumference was measured using a flexible measuring tape at the mid-point between the lower border of the rib cage and the iliac crest. The average of two blood pressure (BP) measurements taken 30 minutes apart on the day of examination was recorded. Venous blood samples were taken following a 12-hour overnight fast for measurement of glucose, total cholesterol, HDL cholesterol and triglycerides. Plasma glucose levels were measured using the glucose hexokinase method. Lipid levels were generated using ATAC 8000 random access clinical chemistry autoanalyzer (Elan Diagnostics, USA) and LDL cholesterol levels were estimated using the Friedewald formula.

MetS was defined using the NCEP: ATPIII criteria of 3 or more of the following:

- Abdominal/central obesity (waist circumference \( > 102 \) cm in men, \( > 88 \) cm in women)
- Hypertriglyceridaemia \( \geq 1.7 \) mmol/L
- (Low) HDL cholesterol (men \( \leq 1.036 \) mmol/L, women \( \leq 1.295 \) mmol/L)
- (High) blood pressure \( \geq 130/85 \) mmHg or documented use of anti-hypertensive medication(s)
- (High) fasting plasma glucose \( > 6.1 \) mmol/L or documented use of anti-diabetic medication(s)

Statistical analysis

Analysis of the data was done with SPSS 12.0 software. The Chi-square test and Student t-test were used respectively for comparison of categorical and continuous variables between the two groups. The odds ratio (OR) was used to determine the association between MetS and CVD.
Determination of the strength of association between MetS components and CVD was by multivariate multiple logistic regressions analysis. All statistical tests were two-sided and the level of significance was set at p< 0.05.

RESULTS

One hundred cases were studied. These included 60 (60%) stroke patients (31 cases of haemorrhagic stroke, 29 cases of infarctive stroke), 22 (22%) heart failure patients, 17 (17%) acute coronary syndrome patients and 1 (1%) patient with peripheral arterial disease. An equal number of age- and sex-matched controls were recruited.

Fifty-four (54) of the cases were male and 46 were female with a male to female ratio of 1.2:1. Similarly, a male to female ratio of 1:2:1 was obtained for the controls. The mean age of the cases and controls were 55.6 ± 11.6 years and 54.9 ± 11.0 years respectively, with the difference not statistically significant. (p= 0.682).

The frequency of cardiovascular risk factors for cases and controls is illustrated in Figure 1. Majority of both cases (89%) and controls (75%) were not engaged in any leisure-time physical activity. There was however a significant difference between cases and controls with respect to the engagement in leisure-time physical activity. Significant differences were also noted between cases and controls regarding the past medical history of hypertension, DM and CVD (p< 0.05).

The frequency of cardiovascular disease risk factors among cases and controls

![Graph showing the frequency of cardiovascular disease risk factors among cases and controls](image)

PMH Past medical history; FH Family history; *p<0.05

The anthropometric measurements and clinical chemistry parameters for cases and controls are shown in Table 1. The frequency of MetS components for cases and controls and the corresponding odds ratio are as shown in Table 2. Hypertension, the most frequently diagnosed component, was seen in 83% cases and 45% controls, followed by central obesity (54% cases and 33% controls). MetS components were found in significantly more cases than controls (p < 0.05).

The test of association between NCEP: ATPIII individual components and MetS resulted in central obesity having the highest Odds ratio of 5.38 (95% CI 3.22-8.98), followed by hypertension and low HDL. Hypertriglyceridaemia (OR= 3.30, 95% CI 2.33 – 4.66) and hyperglycaemia (OR=3.24, 95% CI 2.22 – 4.72) had the lowest values (p< 0.0001) Table 2.

Table 1 Comparison of anthropometric and biochemical measurements of study and control subjects.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cases Mean (SD)</th>
<th>Controls Mean (SD)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waist circumference (cm)</td>
<td>Males 98.6 (13.3)</td>
<td>Females 96.9 (11.8)</td>
<td>0.0001</td>
</tr>
<tr>
<td></td>
<td>100.5 (14.7)</td>
<td>100.5 (14.7)</td>
<td></td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>160 (26)</td>
<td>132 (15)</td>
<td>0.0001</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>99 (17)</td>
<td>84 (9)</td>
<td>0.0001</td>
</tr>
<tr>
<td>FPG (mmol/l)</td>
<td>7.0 (2.5)</td>
<td>5.2 (0.9)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Total Cholesterol (mmol/l)</td>
<td>5.89 (1.79)</td>
<td>5.39 (1.0)</td>
<td>0.016</td>
</tr>
<tr>
<td>HDL (mmol/l)</td>
<td>1.20 (0.42)</td>
<td>1.52 (0.53)</td>
<td>0.0001</td>
</tr>
<tr>
<td>TGL (mmol/l)</td>
<td>1.55 (0.82)</td>
<td>1.31 (0.71)</td>
<td>0.028</td>
</tr>
<tr>
<td>LDL (mmol/l)</td>
<td>3.99 (1.68)</td>
<td>3.38 (1.09)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Table 2 Frequency of metabolic syndrome components for cases and controls and corresponding odds ratios (OR)

<table>
<thead>
<tr>
<th>MetS components</th>
<th>Cases n*1 (%)</th>
<th>Controls n*2 (%)</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal obesity</td>
<td>54 (54)</td>
<td>33 (33)</td>
<td>5.38</td>
<td>3.22-8.98</td>
</tr>
<tr>
<td>Hypertension</td>
<td>83 (83)</td>
<td>45 (45)</td>
<td>4.50</td>
<td>2.29-8.85</td>
</tr>
<tr>
<td>Low HDL</td>
<td>48 (48)</td>
<td>26 (26)</td>
<td>3.63</td>
<td>2.42-5.43</td>
</tr>
<tr>
<td>Hypertriglyceridaemia</td>
<td>32 (32)</td>
<td>23 (23)</td>
<td>3.30</td>
<td>2.33-4.66</td>
</tr>
<tr>
<td>Hyperglycaemia</td>
<td>54 (54)</td>
<td>14 (14)</td>
<td>3.24</td>
<td>2.22-4.72</td>
</tr>
</tbody>
</table>

HDL=High density lipoprotein cholesterol; *n=100 for cases and controls

Fifty-four percent of cases and 18% of controls had 3 or more MetS components, making the prevalence of the MetS among cases and controls 54% and 18%, respectively. Significantly more females (cases 69%, controls 28.3%) than males (40.7% cases, 9.3% controls) had MetS (p= 0.004).
The most common combination of the MetS for cases was hypertension, central obesity and hyperglycaemia, while that for controls were hypertension, central obesity and hypertriglyceridaemia. The prevalence of the MetS was found to increase with age. Prevalence rates of 3.7% and 66.7% were obtained for individuals aged 30 - 39 years and those older than 70 years, respectively. However this finding was not statistically significant. (p= 0.227).

The number of MetS components for cases and controls is as shown in Table 3. For cases, 32% had 2 components and a similar percentage was also found to have 3 of the MetS components. Nine percent of cases had all 5 components. Among the control subjects 27% had no MetS component, while 32% and 23% of controls had either 1 or 2 components respectively. There was a statistically significant difference between cases and controls with regard to the number of MetS components (p < 0.05). The odds ratio for the MetS was 5.35 [95% CI 2.81-10.18, p= 0.0001]. As the number of components increases the odds ratio for MetS also increases (Table 3).

**Table 3 Number of MetS components for cases and controls and corresponding odds ratio**

<table>
<thead>
<tr>
<th>No. of MetS components</th>
<th>Controls</th>
<th>Cases</th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>27</td>
<td>2</td>
<td>0.06</td>
<td>0.01-0.24</td>
</tr>
<tr>
<td>1</td>
<td>32</td>
<td>11</td>
<td>0.26</td>
<td>0.12-0.56</td>
</tr>
<tr>
<td>2</td>
<td>23</td>
<td>32</td>
<td>1.65</td>
<td>0.88-3.08</td>
</tr>
<tr>
<td>3</td>
<td>11</td>
<td>32</td>
<td>3.81</td>
<td>1.79-8.10</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>13</td>
<td>2.84</td>
<td>0.97-8.29</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
<td>9</td>
<td>4.85</td>
<td>1.02-23.03</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

**Table 4 Association between MetS components and cardiovascular disease**

<table>
<thead>
<tr>
<th>MetS Components</th>
<th>p-value**</th>
<th>OR ††</th>
<th>95% C.I.</th>
</tr>
</thead>
<tbody>
<tr>
<td>TGL</td>
<td>0.707</td>
<td>0.863</td>
<td>0.400-1.862</td>
</tr>
<tr>
<td>FPG</td>
<td>0.000</td>
<td>6.555</td>
<td>3.039-14.139</td>
</tr>
<tr>
<td>HDL</td>
<td>0.076</td>
<td>0.523</td>
<td>0.256-1.071</td>
</tr>
<tr>
<td>HPT</td>
<td>0.000</td>
<td>5.755</td>
<td>2.708-12.230</td>
</tr>
<tr>
<td>WC</td>
<td>0.109</td>
<td>0.565</td>
<td>0.281-1.137</td>
</tr>
<tr>
<td>Constant</td>
<td>0.010</td>
<td>0.278</td>
<td></td>
</tr>
</tbody>
</table>

**Significance for the Wald test**

†† Predicted change in odds for a unit increase in covariate

Multivariate multiple logistic regression analysis done using NCEP: ATPIII cut-off values for the MetS components showed that hyperglycaemia (FPG ≥6.1mmol/L) and hypertension (BP≥130/85mmHg) were the only MetS components with a significant association with the development of CVD in this study (Table 4).

**DISCUSSION**

This is the first study on frequency of MetS among CVD patients in Ghana and the findings could serve as a backdrop for further research on the MetS in Ghana. High levels of known CVD risk factors such as hypertension, obesity, physical inactivity and dyslipidaemia were seen in this study. Low proportions of both cases and controls were engaged in physical activity. Regular and sustained physical activity has been shown to improve all the risk factors of MetS. Low levels of physical activity have been shown to be associated with high rates of obesity in a previous study conducted in Ghana. Studies conducted in Cameroon found central obesity to be the key determinant of MetS. The finding of central obesity, which had a high frequency of occurrence, as the component with the strongest association with MetS is in keeping with these observations.

From this study, cases had a higher number of clusters of MetS components than controls. This is similar to findings from studies on CVD patients in the Netherlands. The syndrome is thought to follow a progressive course with the development of one risk factor, usually abdominal obesity, followed later over time, by the development and worsening of other risk factors.

The prevalence of MetS among cases was three times higher than that for controls (54% vs 18%). Prospective studies on MetS and the risk of CVD have shown wide variations in the prevalence of the MetS among CVD patients, however, the prevalence ranged from 23% to 46% in majority of the studies. The prevalence of the MetS among the controls was comparable to rates in 'population-based' studies in Asia (15%- 18%) but lower than rates in Europe and USA.

In Africa, the prevalence rate of MetS in population-based studies in Tunisia is comparable to that found among controls in this study, while lower rates have been reported in Mauritius and Cameroun. The relatively high prevalence of MetS in this study could be due to the high prevalence of MetS components especially hypertension and central obesity as well as the low levels of physical activity. In addition, all study subjects lived in urban areas where the prevalence rate of MetS has been observed to be higher than in the rural areas. In this study, MetS had a strong association with CVD [OR=5.35 95%CI, 2.81-10.18] and this conforms to what has previously been demonstrated in other studies.
In one study, it was found that MetS was at least as powerful as high LDL cholesterol in predicting risk of CVD. Hypertension and hyperglycaemia were the two components of the MetS with a significantly strong association with the development of CVD in this study. However, hypertriglyceridaemia and low HDL cholesterol were found to be strong predictors of CVD in studies conducted among Caucasians. This brings to the fore the issue of racial differences with respect to the individual components of MetS. Indeed, it has been shown that hypertension carries a much greater CVD morbidity and mortality for people of African descent. In addition; preliminary studies have shown that people of African descent are more insulin resistant than their Caucasian counterparts.

In view of this, researchers have proposed a framework for the reclassification of MetS in people of African descent, including the identification of different thresholds for the MetS parameters. In addition, it is recommended that these parameters are weighted differently in terms of their greater risk to predict CVD in different racial and ethnic populations. However more prospective studies are needed especially in sub-Saharan Africa to affirm this hypothesis.

CONCLUSION
The presence of MetS is a significant predictor of CVD and serves as a simple clinical tool for identifying individuals with a relatively high risk of developing CVD. Individuals with MetS may have other metabolic risk factors that are not included in the standard diagnostic criteria. These risk factors, which impart independent risk for cardiovascular events, need to be identified and adequately treated to decrease CVD events.

A nationwide assessment of the impact of the MetS on adult morbidity and mortality is urgently needed together with a policy to institute routine screening in clinical practice and provision of appropriate interventions for MetS components among adults in Ghana.

ACKNOWLEDGEMENT
The authors wish to express their gratitude to the technicians of Central Laboratory, KorleBu Teaching Hospital and Reverend Tom Ndanu for their technical assistance. We acknowledge the contribution of the late Prof J.O.M. Pobee, who passed away after the supervision of this work and the initial review of this article.

REFERENCES
16. Hegele RA. Monogenic forms of insulin resistance: apertures that expose the common metabolic
28. A proposed method for determining blood glucose using Hexokinase and glucose-6-Phosphate dehydrogenase, Public Health Service, Center for Disease Control (1976)