# **ORIGINAL ARTICLE**

## Prevalence of metabolic syndrome among Psychiatric Patients in the Kumasi Metropolis, Ghana

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This cross-sectional study seeks to find the prevalence of the metabolic syndrome (MetS), its individual components and oxidative stress in psychiatric patients on antipsychotic medication compared to newly diagnosed patients attending the Psychiatric Department of the Komfo Anokye Teaching Hospital (KATH), Kumasi, Ghana, between February 2009 and July 2010. A total of 200 psychiatric patients comprising 100 newly diagnosed antipsychotic-naïve patients and 100 patients on antipsychotic medication were sampled for the study. MetS was diagnosed using the World Health Organization (WHO), International Diabetes Federation (IDF) and the National Cholesterol Education Programme, Adult Treatment Panel III (NCEP ATP III) criteria. The overall prevalence of MetS was 11.5%, 13.5% and 15.5% using NCEP ATP III, WHO and IDF criteria respectively. The prevalence was significantly higher among psychiatric patients on treatment as compared to treatment-naïve group using NCEP ATP III (21.0% vs. 2.0%; p < 0.0001) and IDF (29.0% vs. 2.0%; p < 0.0001) criteria but not WHO (13.0% vs. 14.0%; p = 0.8372). These overall prevalence rates were higher compared to the general Ghanaian population prevalence rates of 3.9%, 2.2% and 7.8% determined with the NCEP ATP III, WHO and IDF criteria respectively. Regular monitoring of metabolic parameters should be considered as a standard part of their medical care. Journal of Medical and Biomedical Sciences (2012) 1(2), 38-49

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#### **INTRODUCTION**

Within individuals in the general population as well as those with psychiatric illnesses such as schizophrenia, MetS is known to be a leading cause of cardiovascular disease (CVD)-related deaths and morbidity (Eckel *et al.*, 2005; Meyer *et al.*, 2005). Current studies based on the general population in Ghana have established that MetS, determined with the three definition criteria was 3.9% (NCEP ATP III), 2.2% (WHO), and 7.8% (IDF) predominant (Owiredu et al., under review).

The contributions that led to studies on MetS within

psychiatric individuals include the current invigoration of concern in medical comorbidity in mentally deranged individuals (Holt *et al.*, 2004; Lambert and Chapman, 2004) as well as the release of viable MetS definitions that are physician-friendly (NCEP, 2001; Alberti *et al.*, 2006). MetS prevalence rates of 28% to 37% in psychiatric subjects has been reported in diverse research works in Europe (De Hert *et al.*, 2006; Bobes *et al.*, 2007) but in the United States and Canada, more elevated rates of 43% and 46% respectively have been reported (Cohn *et al.*, 2004; McEvoy *et al.*, 2005).

In Ghana, psychiatric disorders occur more frequently due to the apparent adverse use of psychoactive substances like cannabis, heroin etc. (Turkson, 1998). In an earlier research by Owiredu

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et al., (2009), an interrelation between diabetes, dyslipidaemia and mental disorders was established. Within a research which analyzed ensuing dyslipidaemia after antipsychotic treatment, there was not only the correlation between hypertriglyceridaemia, reduced HDL cholesterol and the newly diagnosed psychiatric subjects but these factors became more pronounced among those on antipsychotic treatment (Owiredu *et al.*, 2009). Abnormalities in other factors, including blood pressure, body mass index and waist-to-hip ratio have also been associated with mental illness.

Globally, the MetS predominance has been poorly investigated. Several factors of lifestyle related to CVD like poor diet, inactive lifestyle, substance abuse and smoking, are common within individuals with psychotic illnesses (Taylor and MacQueen, 2006; Suvisaari *et al.*, 2007). Furthermore, contemplations are rising about the effect of some atypical antipsychotic drugs at the onset of MetS (Holt *et al.*, 2004; Lambert and Chapman, 2004).

Due to paucity of studies on MetS as a whole in psychiatric patients in Ghana, this study seeks to find the prevalence of MetS and associated co-morbid conditions in psychiatric patients on antipsychotics (conventional and atypical) compared to newly diagnosed psychiatric patients using the World Health Organization (WHO), International Diabetes Federation (IDF) and the National Cholesterol Education Programme, Adult Treatment Panel III (NCEP ATP III) criteria for defining MetS.

## MATERIALS AND METHODS Study population and setting

This case related study was carried out at the Psychiatric department of the Komfo Anokye Teaching Hospital, (KATH), Kumasi, Ghana. Patients attending the psychiatric department between February 2009 and July 2010 were eligible for recruitment. A total of 200 psychiatric patients comprising 100 newly diagnosed antipsychotic-naïve patients and 100 patients on antipsychotic medication were invited through a written informed consent to participate in the study.

## Sampling

About 5 ml of venous blood sample was collected from the antecubital fossa of the study participants after an overnight fast (12 – 16 hours). One milliliter (1 ml) of the blood sample was dispensed into fluoride oxalate tube and the other 4 ml into vacutainer plain tubes. The sera and plasma were obtained as supernatants after centrifugation at 500 g for 15 minutes. With the aid of Pasteur pipettes, the sera and plasma were transferred into well-labelled cryotubes and stored at -80°C until assay was performed. Assay parameters include: fasting blood glucose (FGB), total cholesterol (TC), triglycerides (TG), high density lipoprotein (HDL) cholesterol and uric acid. Serum low density lipoprotein (LDL) cholesterol was estimated with the Friedewald equation. Reagent manufacturer's protocol was adopted for the estimation of analytes. Malondialdehyde (MDA) concentration was determined by the method described by Kamal et al., (1989).

## Anthropometric variables

Height to the nearest centimetre without shoes was measured against a wall-mounted ruler and weight to the nearest 0.1 kg in light clothing on a bathroom scale (Zhongshan Camry Electronics Co. Ltd. Guangdong, China). The body mass index (BMI) was calculated by dividing weight (kg) over the height squared (m<sup>2</sup>). Waist circumference (to the nearest centimetre) was measured with a Gulick II spring-loaded measuring tape (Gay Mill, WI) midway between the inferior angle of the ribs and the suprailiac crest. Hip circumference was measured as the maximal circumference over the buttocks in metres and the waist to hip ratio (WHR) calculated by dividing the waist circumference (m) by the hip circumference (m).

## **Definitions for MetS**

MetS was diagnosed using three sets of criteria as stated below:

National Cholesterol Education Program, Adult Treatment Panel III (NCEP ATP III) Criteria: The NCEP ATP III criteria mandates that individuals with MetS should have three or more of the following five components of MetS: (1) Abdominal obesity (waist circumference >102 cm for men or >88 cm for women); (2) Raised triglyceride ( $\geq$ 1.7 mmol L<sup>-1</sup>); (3) Low HDL-cholesterol (<0.9 mmol L<sup>-1</sup> in men or <1.0 mmol L<sup>-1</sup> in women); (4) High Blood Pressure (systolic BP  $\geq$ 130 mmHg or diastolic BP  $\geq$ 85 mmHg or treatment of hypertension) and (5) Raised fasting glucose ( $\geq$ 6.1 mmol L<sup>-1</sup>) (NCEP, 2002).

International Diabetes Federation (IDF) Criteria: The IDF criteria mandates that MetS be diagnosed if Central obesity (waist circumference >90 cm for men or >80 cm for women) is accompanied by any two (2) of the following four (4) factors: (1) Triglyceride level  $\geq$ 1.7 mmol L<sup>-1</sup>; (2) HDL cholesterol <1.03 mmol L<sup>-1</sup> for men or <1.29 mmol L<sup>-1</sup> for women; (3) Blood pressure  $\geq$ 130/85 mmHg or treatment of previously diagnosed hypertension and (4) Fasting blood glucose (FBG)  $\geq$ 5.6 mmol L<sup>-1</sup> or previously diagnosed type 2 diabetes (Alberti *et al.*, 2006).

World Health Organization (WHO) Criteria: The WHO criteria mandates the presence of diabetes mellitus, impaired glucose tolerance or insulin resistance and any two (2) of the following: (1) Body mass index (BMI)  $\geq$ 30 kg m<sup>-2</sup> and/or waist to hip ratio >0.90 for males or >0.85 for females; (2) Blood pressure  $\geq$ 140/90 mmHg or on medication; (3) Triglyceride  $\geq$ 1.7 mmol L<sup>-1</sup> and (4) HDL cholesterol <0.91 mmol L<sup>-1</sup> in males or <1.01 mmol L<sup>-1</sup> in females (World Health Organization, 1999).

All three study definition criteria were used to assess the relationship between MetS and patient variables.

#### **Statistical Analysis**

Results are presented as Means  $\pm$  SD. Unpaired *t*-test was used to compare the means of all continuous variables. The Chi-square test statistic was used to assess the statistical significance of categorical variables. Logistic regression test statistic was used to estimate the crude (c) and adjusted (adj) odds ratio (OR) for risk factors of MetS. A p-value < 0.05 was considered to be statistically significant. All sta-

MetS in psychiatric patients *Owiredu et al.,* 

tistical analyses were performed using MedCalc® version 10.2.0.0 (www.medcalc.be) for windows.

### RESULTS

#### **General Characteristics**

Table 1 presents the general characteristics of the study population stratified by treatment. Patients on antipsychotic (AP) medication were significantly older (37.9  $\pm$  1.4 years) and heavier (66.1  $\pm$  1.4 kg) than the newly diagnosed antipsychotic-naïve patients (26.2  $\pm$  1.0 years and 61.9  $\pm$  1.3 kg respectively) (p < 0.000). The mean waist circumference in patients on AP medication (85.2  $\pm$  1.3 cm) as a marker of central obesity was significantly higher compared to the newly diagnosed AP-naïve patients  $(76.7 \pm 1.0 \text{ cm}) \text{ (p} < 0.000)$  likewise the body mass index of 24.7  $\pm$  0.5 kg m<sup>-2</sup> and 22.7 $\pm$  0.6 kg m<sup>-2</sup> respectively (p = 0.009). The mean systolic (125.2  $\pm$ 2.0 mmHg) and diastolic (79.5  $\pm$  1.0 mmHg) blood pressure in patients on treatment was also significantly higher in comparison to the newly diagnosed AP-naïve patients (117.8  $\pm$  1.8 mmHg, 75.3  $\pm$  0.9 mmHg respectively).

The mean concentrations of the lipid profile including total cholesterol (4.7  $\pm$  0.1 mmol L<sup>-1</sup>, p = 0.003), low density lipoprotein cholesterol (2.9  $\pm$ 0.1 mmol L<sup>-1</sup>, p < 0.000) and very low density lipoprotein (0.3  $\pm$  0.0 mmol L<sup>-1</sup>, p = 0.012) in patients on treatment was significantly higher than in the newly diagnosed AP-naïve patients with mean concentrations of 4.3  $\pm$  0.1, 2.4  $\pm$  0.1 and 0.2  $\pm$  0.0 mmol L-1 respectively. Conversely, the mean concentrations of high density lipoprotein (1.2  $\pm$  0.0 mmol L<sup>-1</sup>, p = 0.001) and MDA (0.8 ± 0.0 mmol L<sup>-</sup> <sup>1</sup>, p < 0.000) in patients on treatment were significantly lower compared to that in newly diagnosed AP-naïve patients (1.4  $\pm$  0.0 mmol L<sup>-1</sup> and 0.9  $\pm$  0.0 mmol L<sup>-1</sup> respectively) while the mean triglyceride, fasting blood sugar concentrations and waist to hip ratio showed no statistically significant differences (Table 1).

#### **Co-morbid conditions**

Odds analysis to evaluate the risk of developing certain physical co-morbidities and lifestyle associated with MetS in psychiatrics patients based on

	Total	On Treatment	Newly Diagnosed	
Variables	(n = 200)	(n = 100)	(n = 100)	P value
Age (yrs)	$32.0 \pm 1.0$	$37.9 \pm 1.4$	$26.2 \pm 1.0$	< 0.000
Weight (kg)	$64.0 \pm 1.0$	$66.1 \pm 1.4$	$61.9 \pm 1.3$	0.028
Height (m)	$1.6 \pm 0.0$	$1.6 \pm 0.0$	$1.6 \pm 0.0$	0.054
WC (cm)	$81.2 \pm 0.9$	$85.7 \pm 1.3$	$76.7 \pm 1.0$	< 0.000
HC (cm)	$98.7 \pm 1.0$	$100.3 \pm 1.4$	$97.1 \pm 1.1$	0.073
WHR	$1.1 \pm 0.2$	$1.3 \pm 0.5$	$0.8 \pm 0.0$	0.268
BMI (kg m <sup>-2</sup> )	$23.7 \pm 0.4$	$24.7 \pm 0.5$	$22.7 \pm 0.6$	0.009
SBP (mmHg)	$121.5 \pm 1.4$	$125.2 \pm 2.0$	$117.8 \pm 1.8$	0.006
DBP (mmHg)	$77.4 \pm 0.7$	$79.5 \pm 1.0$	$75.3 \pm 1.0$	0.002
FBS (mmol L-1)	$5.4 \pm 0.2$	$5.5 \pm 0.3$	$5.3 \pm 0.2$	0.426
Uric acid (µmol L-1)	$236.3 \pm 5.1$	$255.3 \pm 7.9$	$217.4 \pm 5.8$	0.000
TC (mmol L-1)	$4.5 \pm 0.1$	$4.7 \pm 0.1$	$4.3 \pm 0.1$	0.003
TG (mmol L <sup>-1</sup> )	$1.4 \pm 0.1$	$1.4 \pm 0.1$	$1.3 \pm 0.1$	0.138
HDL-C (mmol L-1)	$1.3 \pm 0.0$	$1.2 \pm 0.0$	$1.4 \pm 0.0$	0.000
LDL-C (mmol L-1)	$2.6 \pm 0.1$	$2.9 \pm 0.1$	$2.4 \pm 0.1$	< 0.000
VLDL (mmol L-1)	$0.3 \pm 0.0$	$0.3 \pm 0.0$	$0.2 \pm 0.0$	0.012
MDA (µmol L-1)	$1.0 \pm 0.0$	$0.8 \pm 0.0$	$0.9 \pm 0.0$	< 0.000

Results are presented as mean  $\pm$  SD. P value defines the level of significance when study population on treatment was compared to the newly diagnosed. WC = waist circumference, HC = hip circumference, WHR = waist to hip ratio, BMI = body mass index, SBP = systolic blood pressure, DBP = diastolic blood pressure, FBS = fasting blood sugar, TC = total cholesterol, HDL-C = high density lipoprotein cholesterol, LDL-C = low density lipoprotein cholesterol, VLDL = very low density lipoprotein, MDA = malondialdehyde.

treatment classification (AP naïve and those on AP) are shown in Table 2. Patients on treatment are approximately 12 times at risk of indulging in alcoholism (p=0.024) and 26 times at risk of developing hyperuricaemia (p = 0.0001) when compared to the newly diagnosed patients. The odds of being obese (2.5 times), developing hypercholesterolaemia (3 times), having low high density lipoprotein (HDL) cholesterol (3 times), developing high low density lipoprotein (LDL) cholesterol (3 times) in patients on treatment were all statistically significant compared to the newly diagnosed AP-naïve patients. Being on treatment however conferred some level of protection against oxidative stress (p = 1.000) while sex, smoking, hypertension, diabetes and hypertriglyceridaemia showed no statistical significance when patients on treatment were compared to the newly diagnosed AP-naïve patients.

#### Prevalence of MetS

Table 3 presents a general overview of the prevalence of MetS and its score in the study population defined by the three different classification criteria. When defined by the National Cholesterol Education Program, Adult Treatment Panel III (NCEP ATP III) criteria, 21.0% of the patients on treatment compared to 2.0% of the newly diagnosed AP-naïve patients are at risk of developing MetS (score  $\geq$  3) with an odds ratio of 13.0 (p < 0.000). On using the International Diabetic Federation (IDF) criteria, 29.0% of the patients on treatment compared to 2.0% of the newly diagnosed APnaïve patients were at risk of developing MetS (OR = 20.0, p < 0.000). Contrary to the results from the two criteria stated above, the World Health Organization (WHO) criteria gave percentage prevalence of 13.0% and 14.0% for patients on AP

		On	Newly		
	Total	Treatment	Diagnosed		
Variables	(n = 200)	(n = 100)	(n = 100)	OR(95% CI)	P value
Females	121(60.5%)	63(63.0%)	58(58.0%)	1.2(0.7-2.2)	0.563
Smokers	1(0.5%)	1(1.0%)	0(0.0%)	3.0(0.1-75.3)	1.000
Alcohol	5(2.5%)	5(5.0%)	0(0.0%)	11.6(0.6-212.3)	0.024
Hypertension	28(14.0%)	17(17.0%)	11(11.0%)	1.7(0.7-3.7)	0.308
Diabetes	53(26.5%)	27(27.0%)	26(26.0%)	1.1(0.6-2.0)	1.000
Obesity	33(16.5%)	16(16.0%)	7(7.0%)	2.5(1.0-6.5)	0.046
Hypercholesterolaemia	43(21.5%)	30(30.0%)	13(13.0%)	2.9(11.4-5.9)	0.006
Hypertriglyceridaemia	58(29.0%)	28(28.0%)	30(30.0%)	0.9(0.5-1.7)	0.876
Low HDL-cholesterol	51(25.5%)	36(36.0%)	15(15.0%)	3.2(1.6-6.3)	0.001
High LDL-cholesterol	168(84.0%)	91(91.0%)	77(77.0%)	3.0(1.3-6.9)	0.011
Hyperuricaemia	11(5.5%)	11(11.0%)	0(0.0%)	25.8(1.5-444.9)	0.000
Oxidative stress	189(94.5%)	90(90.0%)	99(99.0%)	0.1(0.0-0.7)	1.000

Table 2: Co-morbid conditions stratified by treatment among the studied population

Percentage values represent variables expressed as a proportion over their respective total (n), Obesity is defined as BMI  $\geq$  30 kg m<sup>-2</sup>, Hypertension = blood pressure  $\geq$  140/90 mmHg, Diabetes = fasting blood sugar greater or equal to 7.0 mmol L<sup>-1</sup>, Hypercholesterolaemia = total cholesterol > 5.2 mmol L<sup>-1</sup>, Hypertriglyceridaemia = triglyceride > 1.8 mmol L<sup>-1</sup>, Low HDL-Cholesterol = HDL-C < 1.0 mmol L<sup>-1</sup>, High LDL-cholesterol = LDL-C > 1.8 mmol L<sup>-1</sup>, and Hyperuricaemia = uric acid > 416.4 µmol L<sup>-1</sup> (for men) and 356.9 µmol L<sup>-1</sup> (for women), oxidative stress = MDA > 0.7 µmol L<sup>-1</sup>.

treatment and newly diagnosed AP-naïve patients respectively with an odds ratio of 0.9 but the difference was not statistically significant (p = 0.837).

#### Prevalence of components of MetS

Assessment of the percentage prevalence of the individual components of MetS per the classification criteria for the study population is presented in Table 4. Patients on treatment are more prone to being obese when classified by the NCEP ATP III, IDF and WHO criteria with percentage prevalence of 32.0% (p = 0.001), 47.0% (p < 0.000) and 40.0% (p = 0.015) respectively. Twenty-three percent (23%) of the patients on treatment are more likely to develop significantly raised blood pressure compared to 11.0% of the newly diagnosed patients when classified by the NCEP ATP III and IDF criteria (p = 0.038). However, no statistically significant difference was observed when raised blood pressure was assessed in patients on treatment and newly diagnosed AP naïve patients using the WHO criteria (p = 0.308). No significant difference in the prevalence of raised fasting blood sugar was observed in the study population when evaluated with the three classification criteria and likewise in the prevalence of raised triglyceride levels. The prevalence of low HDL cholesterol in patients on treatment as determined by the NCEP ATP III and WHO criteria showed no statistical significance but when classified by the IDF criteria, 50.0% of the patients on treatment were at risk of developing reduced HDL levels compared to 11.0% in newly diagnosed AP naïve patients and the difference was statistically significant.

#### **Risk factors of MetS**

Table 5 shows univariate analysis of the risk factors of MetS evaluated by the three classification criteria for the study population. In using the NCEP ATP III criteria as a dependent variable for the presence

#### MetS in psychiatric patients Owiredu et al.,

	Total	On Treatment	Newly Diag-					
Variables	(n=200)	(n =100)	nosed (n= 100)	OR(95% CI)	P value			
National Cholesterol Education Programme Adult Treatment Panel III criteria								
MetS	23(11.5%)	21(21.0%)	2(2.0%)	13.0(3.0-57.3)	< 0.000			
MetS Score								
0	52(26.0%)	19(19.0%)	33(33.0%)	0.5(0.3-1.0)	0.056			
1	81(40.5%)	34(34.0%)	47(47.0%)	0.6(0.3-1.0)	0.061			
2	44(22.0%)	26(26.0%)	18(18.0%)	1.8(0.9-3.5)	0.087			
$\geq 3$	23(11.5%)	21(21.0%)	2(2.0%)	13.0(3.0-57.3)	< 0.000			
	, í v	Vorld Health Organ	nization criteria	· · · ·				
MetS	27(13.5%)	13(13.0%)	14(14.0%)	0.9(0.4-2.1)	0.837			
MetS Score	· · · ·							
0	102(51.0%	42(42.0%)	60(60.0%)	0.5(0.3-0.8)	0.011			
1	47(23.5%)	24(24.0%)	23(23.0%)	1.1(0.6-2.0)	0.869			
2	22(11.0%)	19(19.0%)	3(3.0%)	7.6(2.2-76.6)	0.000			
≥3	19(9.5%)	15(15.0%)	4(4.0%)	4.2(1.4-13.3)	0.008			
	Inte	rnational Diabetic	Federation criteria	1				
MetS	31(15.5%)	29(29.0%)	2(2.0%)	20.0(2.6-26.7)	< 0.000			
MetS Score								
0	58(29.0%)	22(22.0%)	36(36.0%)	0.5(0.3-0.9)	0.029			
1	70(35.0%)	32(32.0%)	38(38.0%)	0.8(0.4-1.4)	0.374			
2	50(25.0%)	26(26.0%)	24(24.0%)	1.1(0.6-2.1)	0.744			
$\geq 3$	22(11.0%)	20(20.0%)	2(2.0%)	12.3(2.8-54.0)	< 0.000			

Table 3: Prevalence of MetS and its score among the studied population stratified by treatment

OR = odds ratio, CI = confidence interval, MetS = Metabolic syndrome

or absence of MetS: treatment (cOR = 13.0, p = 0.001), obesity-WC<sup>1</sup> (cOR = 3.2, p = 0.011), obesity -WC<sup>2</sup> (cOR = 2.6, p = 0.037), obesity BMI (cOR = 1.8, p = 0.026), raised BP<sup>1</sup> (cOR = 3.1, p = 0.020), hyperuricaemia (cOR = 5.1, p = 0.015), hypercholesterolaemia (cOR = 2.5, p = 0.048) and raised TG (cOR = 3.1, p = 0.012) turned out to be significant risk variables and predictors of MetS. However, when the risk variables were further assessed with adjustment for age (Table 6), only treatment (adjOR = 6.8, p = 0.015), obesity-WC<sup>1</sup> (adjOR = 2.5, p = 0.048), obesity BMI (adjOR = 4.8, p = 0.009) and raised TG (adjOR = 4.4, p = 0.004) turned out as true significant predictor variables for MetS when classified by the NCEP ATP III criteria.

When the IDF criteria was applied, female gender (cOR = 2.5, p = 0.041), treatment (cOR = 20.0, p < 0.001), obesity-WC<sup>1</sup> (cOR = 3.8, p = 0.001), obesity

-WC<sup>2</sup> (cOR = 3.6, p = 0.001) and reduced HDL-C<sup>2</sup> (cOR = 2.6, p = 0.016) were significant risk variables and predictors of MetS with the exception of oxidative stress (cOR = 0.2, p = 0.034) which appeared to confer some level of protection against the development of MetS. Upon adjusting for age, the above mentioned risk variables turned out as true significant predictors of MetS in addition to obesity BMI (adjOR = 3.1, p = 0.045) with adjusted odds ratio of 2.9, 9.5, 3.3, 3.2 and 2.3 respectively. Furthermore, oxidative stress turned to be a significant protector from the development of MetS (Tables 5 & 6). No statistically significant differences were observed in the risk variables when classified by the WHO criteria in both univariate analyses and age-adjusted analyses (Tables 5 & 6).

	Total	On Treatment	Newly Diagnosed	
Variables	(n = 200)	(n = 100)	(n = 100)	P value
OBESITY				
NCEP ATP III Criteria				
> 102 cm (men)/> 88 (women)	43 (21.5%)	32 (32.0%)	11 (11.0%)	0.001
IDF Criteria				
> 90 (men)/> 80 (women)	64 (32.0)	47 (47.0%)	17 (17.0%)	< 0.000
WHO Criteria				
> 0.9  (men) /> 0.85  (women)	63 (31.5)	40 (40.0%)	23 (23.0%)	0.015
<b>BLOOD PRESSURE</b>				
NCEP ATP III/IDF Criteria				
$\geq 130/85$	34 (17.0)	23 (23.0%)	11 (11.0%)	0.038
WHO Criteria				
$\geq 140/90$	28 (14.0%)	17 (17.0%)	11 (11.0%)	0.308
FASTING BLOOD SUGAR				
NCEP ATP III/WHO Criteria				
$\geq 6.1$	55 (27.5%)	29 (29.0%)	26 (26.0%)	0.752
IDF Criteria		24 (24 00/)		0 5 2 4
$\geq 5.6$	57 (28.5%)	31 (31.0%)	26 (26.0%)	0.531
	FQ (20 00/)	20.(20.00)	20(20,00/)	0.074
≥ 1.7 HDL-C	58 (29.0%)	28 (28.0%)	30 (30.0%)	0.876
NCEP ATP III/WHO Criteria				
	36(19.00%)	22(22.00/)	12 (12 00/)	0.098
< 0.9 (men)/< 1.0 (women) IDF Criteria	36 (18.0%)	23 (23.0%)	13 (13.0%)	0.096
< 1.03 (men)/< 1.29 (women)	61 (30.5%)	50 (50.0%)	11 (11.0%)	< 0.000

Table 4: Prevalence of MetS components among the study populations stratified by treatment

NCEP ATP III = National Cholesterol Education Program, Adult Treatment Panel III, IDF = International Diabetes Federation, WHO = World Health Organization, HDL-C = High Density Lipoprotein Cholesterol.

#### DISCUSSION

#### Prevalence of MetS and Associated Disorders

The prevalence of MetS in psychiatric patients on AP medication calculated in this study using the IDF criteria was 29% compared to 2% in AP-naïve patients. This prevalence rate is slightly higher than the 20 - 25% prevalence rate of MetS in the world's population reported in the IDF consensus statement (Alberti *et al.*, 2006). In using the NCEP ATP III criteria, the prevalence of MetS in patients on AP medication was 21%. This finding is close to the MetS prevalence rate of approximately 22% estimated in the United States using the NCEP ATP III criteria (Ford *et al.*, 2002). The WHO criteria on the

other hand gave a lower rate of MetS in patients on AP medication (13.0%) and a higher rate in the AP -naïve patients (14%) when generally compared to prevalence rates in patients on AP medication and AP-naïve patients respectively determined by the IDF and NCEP ATP III criteria.

A number of publications have mentioned the potential relationship between antipsychotic drugs and hyperglycaemia (Sernyak *et al.*, 2002; Taylor *et al.*, 2005). Ryan *et al.*, (2003) in their study found that first episode and drug naïve patients may show insulin resistance which complicates the underlying mechanisms in this regard. Fasting blood glucose

MetS in psychiatric patients Owiredu et al.,

Table 5: Univariate anal	vsis of risk factors	s for MetS among	the study p	opulation ( $N = 200$ )

	NCEP ATP III		WHO	WHO		IDF	
Variables	cOR(95% CI)	P value	cOR(95% CI)	P value	cOR(95% CI)	P value	
Female	2.0(0.7-5.3)	0.168	1.7(0.7-4.0)	0.263	2.5(1.0-6.2)	0.041	
Treatment	13.0(3.0-57.2)	0.001	0.9(0.4-2.1)	0.836	20.0(4.6-86.6)	0.000	
Obesity-WC1	3.2(1.3-8.0)	0.011	1.0(0.4-2.7)	0.976	3.8(1.7-8.6)	0.001	
Obesity-WC <sup>2</sup>	2.6(1.1-6.1)	0.037	0.9(0.4-2.1)	0.732	3.6(1.6-7.9)	0.001	
Obesity-WHR	1.4(0.6-3.6)	0.443	1.6(0.7-3.8)	0.264	1.8(0.8-4.0)	0.152	
Obesity-BMI	1.8(1.2-9.6)	0.026	0.6(0.1-2.6)	0.478	2.1(0.8-6.0)	0.143	
Raised BP1	3.1(1.2-8.0)	0.020	1.5(0.5-4.0)	0.440	1.9(0.8-4.7)	0.161	
Raised BP <sup>2</sup>	1.9(0.6-5.5)	0.262	1.5(0.5-4.3)	0.469	1.6(0.6-4.3)	0.353	
Raised FBS <sup>1</sup>	1.5(0.6-3.7)	0.408	1.4(0.5-3.3)	0.467	0.9(0.4-2.2)	0.818	
Raised FBS <sup>2</sup>	1.4(0.6-3.5)	0.479	1.3(0.5-3.1)	0.551	0.9(0.4-2.0)	0.718	
Hyperuricaemia	5.1(1.4-19.1)	0.015	0.6(0.1-5.1)	0.663	2.2(0.5-8.6)	0.277	
Hypercholesterolaemia	2.5(1.0-6.3)	0.048	1.2(0.5-3.2)	0.647	1.8(0.8-4.2)	0.161	
Raised TG	3.1(1.3-7.5)	0.012	1.8(0.8-4.3)	0.152	1.4(0.6-3.2)	0.388	
Reduced HDL-C1	1.7(0.6-4.7)	0.288	1.4(0.5-3.7)	0.540	1.8(0.7-4.3)	0.223	
Reduced HDL-C <sup>2</sup>	1.7(0.7-4.1)	0.236	1.0(0.4-2.5)	0.921	2.6(1.2-5.7)	0.016	
High LDL-C	2.1(0.5-9.6)	0.320	0.8(0.3-2.3)	0.702	1.3(0.4-4.1)	0.610	
Oxidative stress	0.6(0.1-5.7)	0.689	0.8(0.1-6.9)	0.818	0.2(0.0-0.9)	0.034	

Obesity-WC<sup>1</sup> = NCEP ATP III criteria, Obesity-WC<sup>2</sup> = IDF criteria, Raised BP<sup>1</sup> = NCEP ATP III/IDF criteria, Raised BP<sup>2</sup> = WHO criteria, Raised FBS<sup>1</sup> = NCEP ATP III/WHO criteria, Raised FBS<sup>2</sup> = IDF criteria, Reduced HDL-C<sup>1</sup> = NCEP ATP III/WHO criteria, Reduced HDL-C<sup>2</sup> = IDF criteria, cOR = crude odds ratio, CI = confidence interval.

showed no statistical significance when compared in the two study groups but as a mandatory component in the WHO definition, the absence of a statistically significant difference could be a major reason in the inability of the WHO criteria to well define the presence of MetS in the study population. Furthermore, glucose dysregulation in patients on AP in this study might not be explained exclusively on the individual drugs themselves but the contribution of these drugs for other components of MetS including cardiovascular risks and dyslipidaemia might certainly contribute to such predisposition as related in the study of Jin et al., (2004). The relationship between age and MetS has long been documented. Ford et al., (2002) and Alexander et al., (2003) reported increases in the prevalence of MetS with increase in age. A high prevalence rate of MetS was observed in patients on AP medication who were

significantly older when compared to the AP-naïve patients.

#### **Co-morbidities**

There is growing evidence that severe mental illnesses are associated with significant physical comorbidities (Davidson *et al.*, 2001; Mitchell and Malone, 2006) that may lead to increased risk of premature mortality in many psychiatric patients (Dembling *et al.*, 1999; Saha *et al.*, 2007). Weight gain is an established side effect of most of the antipsychotic drugs (including typical and atypical antipsychotics) which association is well documented for the first generation (typical) antipsychotics and more recently newer or second generation (atypical) antipsychotic drugs (Klett and Caffey, 1960; Taylor and McAskill, 2000). Excessive weight gain has many adverse clinical consequences includ-

MetS in psychiatric patients *Owiredu et al.,* 

Table 6: Age adjusted	l odds ratio of the	risk factors for	MetS among th	ne study population	(N = 200)
					· /

	ATP II	Ι	WHO		IDF	
Variables	aOR(95% CI)	P value	aOR(95% CI)	P value	aOR(95% CI)	P value
Female	1.9(0.7-5.5)	0.216	1.6(0.7-4.0)	0.292	2.9(1.0-7.8)	0.041
Treatment	6.8(1.5-31.4)	0.015	0.5(0.2-1.3)	0.137	9.5(2.1-43.2)	0.003
Obesity WC <sup>1</sup>	2.5(1.0-6.8)	0.048	0.8(0.3-2.3)	0.697	3.3(1.3-8.5)	0.014
Obesity WC <sup>2</sup>	2.0(0.8-5.3)	0.140	0.7(0.3-1.8)	0.451	3.2(1.3-8.0)	0.011
Obesity WHR	1.0(0.3-2.7)	0.940	1.4(0.6-3.3)	0.463	1.2(0.5-3.1)	0.720
Obesity BMI	4.8(1.5-15.4)	0.009	0.6(0.1-2.7)	0.500	3.1(1.0-10.0)	0.045
Raised BP1	1.9(0.6-5.5)	0.250	1.1(0.4-3.1)	0.860	0.9(0.3-2.7)	0.803
Raised BP2	1.0(0.3-3.6)	0.960	1.1(0.4-3.5)	0.815	0.7(0.2-2.6)	0.632
Raised FBS <sup>1</sup>	1.9(0.7-5.2)	0.223	1.5(0.6-3.7)	0.354	1.1(0.4-2.9)	0.889
Raised FBS <sup>2</sup>	1.8(0.7-5.1)	0.238	1.5(0.6-3.6)	0.399	1.1(0.4-2.9)	0.914
Hyperuricaemia	3.2(0.8-13.6)	0.108	0.4(0.1-3.6)	0.437	1.0(0.2-4.7)	0.984
Hypercholesterolaemia	2.0(0.7-5.3)	0.183	1.0(0.4-2.7)	0.957	1.3(0.5-3.3)	0.641
Raised TG	4.4(1.6-12.1)	0.004	2.0(0.8-4.7)	0.114	1.8(0.7-4.7)	0.223
Reduced HDL <sup>1</sup>	1.9(0.6-5.6)	0.273	1.4(0.5-3.7)	0.554	2.0(0.7-5.9)	0.184
Reduced HDL <sup>2</sup>	1.3(0.5-3.4)	0.600	0.9(0.4-2.2)	0.785	2.3(1.0-5.6)	0.043
High LDL-C	1.9(0.4-5.6)	0.422	0.7(0.3-2.2)	0.582	1.1(0.3-3.8)	0.921
Oxidative stress	0.6(0.1-6.0)	0.655	0.8(0.1-7.2)	0.834	0.1(0.0-0.7)	0.018

#### aOR = adjusted odds ratio

ing predisposition to a number of physical illnesses like cardiovascular disorders, diabetes, stroke, osteoarthritis and sleep apnoea in addition to low self esteem, decreased quality of life and reduced adherence to treatment. Clinical manifestations of increased lipid profiles are also among the main causes of morbidity and mortality for cardiovascular diseases with increases in serum cholesterol being considered as a major risk factor for such diseases (Austin *et al.*, 1998). A Finish study reported that individuals treated with antipsychotic medications were three times more likely to have high cholesterol or high triglyceride than those who were not taking the drugs (Saari *et al.*, 2004).

Patients on AP medication from this study were three times more likely to have high cholesterol, high LDL-cholesterol and low HDL-cholesterol; two and half times more likely to be obese and twelve times more likely to indulge in alcoholism. These findings explain the high prevalence rate of MetS in patients on AP medication and their significant risk of developing cardiovascular disease (CVD) compared to the AP naïve patients as determined with the IDF and NCEP ATP III criteria which could likely be worsened if the patient indulges in alcoholism. Alexander et al., (2009) in a study on the prevalence of MetS among Australians with severe mental illness found no difference in the prevalence of MetS between the gender and Mackin et al., (2007) in their study also found that differences in smoking behaviour did not account for excess metabolic and cardiovascular risk in people with mental illness who smoked compared with controls. Female gender, smoking, hypertension, diabetes and hypertriglyceridaemia did not show

significant differences in patients on treatment with AP compared to AP-naïve patients in this study. Furthermore, diabetes did not present as a significant physical co-morbidity which reason could further explain the inability of the WHO criteria to define MetS in this study group as it mandates individuals to be diabetic.

### **Risk factors of MetS**

The outcome measures of the logistic regression shows the capability of AP medication to contribute to excess physical morbidity aside controlling the symptoms of psychiatric illness. Glucose dysregulation could not be explained exclusively by the individual drugs of AP medication but the contribution of the drugs for other components of MetS including cardiovascular risks and dyslipidaemia certainly contribute to such predisposition. Weight gain, especially visceral adiposity, as measured by waist circumference (IDF and ATP III criteria), BMI and dyslipidaemia pose attendant risks for the physical health of the patients.

## CONCLUSION

This study demonstrates a high prevalence of MetS (>20%) and the risk of CVD among Ghanaian psychiatric patients on antipsychotic medication. This therefore necessitates baseline and periodic medical evaluations as standard components in the on-going assessment and treatment plans for the patients.

## REFERENCES

- Alberti K.G., Zimmet P. and Shaw J. (2006) Metabolic syndrome--a new world-wide definition. A Consensus Statement from the International Diabetes Federation. *Diabet Med* 23, 469-480.
- Alexander C.M., Landsman P.B., Teutsch S.M. and Haffner S.M. (2003) NCEP-defined metabolic syndrome, diabetes, and prevalence of coronary heart disease among NHANES III participants age 50 years and older. *Diabetes* 52, 1210-1214.
- Austin M.A., Hokanson J.E. and Edwards K.L. (1998) Hypertriglyceridemia as a cardiovascular risk factor. *Am J Cardiol* 81, 7B-12B.

- Bobes J., Arango C., Aranda P., Carmena R., Garcia -Garcia M. and Rejas J. (2007) Cardiovascular and metabolic risk in outpatients with schizophrenia treated with antipsychotics: results of the CLAMORS Study. *Schizophr Res* 90, 162-173.
- Cohn T., Prud'homme D., Streiner D., Kameh H. and Remington G. (2004) Characterizing coronary heart disease risk in chronic schizophrenia: high prevalence of the metabolic syndrome. *Can J Psychiatry* 49, 753-760.
- Davidson S., Judd F., Jolley D., Hocking B., Thompson S. and Hyland B. (2001) Cardiovascular risk factors for people with mental illness. *Aust N Z J Psychiatry* 35, 196-202.
- De Hert M.A., van Winkel R., Van Eyck D., Hanssens L., Wampers M., Scheen A. and Peuskens J. (2006) Prevalence of the metabolic syndrome in patients with schizophrenia treated with antipsychotic medication. *Schizophr Res* 83, 87-93.
- Dembling B.P., Chen D.T. and Vachon L. (1999) Life expectancy and causes of death in a population treated for serious mental illness. *Psychiatr Serv* 50, 1036-1042.
- Eckel R.H., Grundy S.M. and Zimmet P.Z. (2005) The metabolic syndrome. *Lancet* 365, 1415-1428.
- Ford E.S., Giles W.H. and Dietz W.H. (2002) Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. *JAMA* 287, 356-359.
- Holt R.I., Peveler R.C. and Byrne C.D. (2004) Schizophrenia, the metabolic syndrome and diabetes. *Diabet Med* 21, 515-523.
- Jin H., Meyer J.M. and Jeste D.V. (2004) Atypical antipsychotics and glucose dysregulation: a systematic review. *Schizophr Res* 71, 195-212.
- Kamal A.A., Gomaa A., el Khafif M. and Hammad A.S. (1989) Plasma lipid peroxides among workers exposed to silica or asbestos dusts. *Environ Res* 49, 173-180.
- Klett C.J. and Caffey E.M., Jr. (1960) Weight changes during treatment with phenothia-

zine derivatives. J Neuropsychiatr 2, 102-108.

- Lambert T.J. and Chapman L.H. (2004) Diabetes, psychotic disorders and antipsychotic therapy: a consensus statement. *Med J Aust* 181, 544-548.
- Mackin P., Bishop D., Watkinson H., Gallagher P. and Ferrier I.N. (2007) Metabolic disease and cardiovascular risk in people treated with antipsychotics in the community. *Br J Psychiatry* 191, 23-29.
- McEvoy J.P., Meyer J.M., Goff D.C., Nasrallah H.A., Davis S.M., Sullivan L., Meltzer H.Y., Hsiao J., Scott Stroup T. and Lieberman J.A. (2005) Prevalence of the metabolic syndrome in patients with schizophrenia: baseline results from the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) schizophrenia trial and comparison with national estimates from NHANES III. Schizophr Res 80, 19-32.
- Meyer J., Koro C.E. and L'Italien G.J. (2005) The metabolic syndrome and schizophrenia: a review. *Int Rev Psychiatry* 17, 173-180.
- Mitchell A.J. and Malone D. (2006) Physical health and schizophrenia. *Curr Opin Psychiatry* 19, 432-437.
- NCEP (2001) Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). JAMA 285, 2486-2497.
- NCEP (2002) Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation* 106, 3143-3421.
- Owiredu W.K., Appiah-Poku J., Adusei-Poku F., Amidu N. and Osei Y. (2009) The impact of blood glucose and cholesterol levels on the manifestation of psychiatric disorders. *Pak J Biol Sci* 12, 252-257.
- Ryan M.C., Collins P. and Thakore J.H. (2003) Impaired fasting glucose tolerance in firstepisode, drug-naive patients with schizo-

phrenia. Am J Psychiatry 160, 284-289.

- Saari K., Koponen H., Laitinen J., Jokelainen J., Lauren L., Isohanni M. and Lindeman S. (2004) Hyperlipidemia in persons using antipsychotic medication: a general population-based birth cohort study. J Clin Psychiatry 65, 547-550.
- Saha S., Chant D. and McGrath J. (2007) A systematic review of mortality in schizophrenia: is the differential mortality gap worsening over time? *Arch Gen Psychiatry* 64, 1123-1131.
- Sernyak M.J., Leslie D.L., Alarcon R.D., Losonczy M.F. and Rosenheck R. (2002) Association of diabetes mellitus with use of atypical neuroleptics in the treatment of schizophrenia. *Am J Psychiatry* 159, 561-566.
- Suvisaari J.M., Saarni S.I., Perala J., Suvisaari J.V., Harkanen T., Lonnqvist J. and Reunanen A. (2007) Metabolic syndrome among persons with schizophrenia and other psychotic disorders in a general population survey. *J Clin Psychiatry* 68, 1045-1055.
- Taylor D., Young C., Mohamed R., Paton C. and Walwyn R. (2005) Undiagnosed impaired fasting glucose and diabetes mellitus amongst inpatients receiving antipsychotic drugs. *J Psychopharmacol* 19, 182-186.
- Taylor D.M. and McAskill R. (2000) Atypical antipsychotics and weight gain--a systematic review. *Acta Psychiatr Scand* 101, 416-432.
- Taylor V. and MacQueen G. (2006) Associations between bipolar disorder and metabolic syndrome: A review. J Clin Psychiatry 67, 1034-1041.
- Turkson S.N. (1998) Psychiatric diagnosis among referred patients in Ghana. *East Afr Med J* 75, 336-338.
- World Health Organization (1999) Definition, diagnosis and classification of diabetes mellitus and its complications: report of a WHO Consultation. Part 1: diagnosis and classification of diabetes mellitus. Geneva, Switzerland: World Health Organization.
- Zhang Z.J., Yao Z.J., Liu W., Fang Q. and Reynolds G.P. (2004) Effects of antipsychotics on fat

MetS in psychiatric patients Owiredu et al.,

deposition and changes in leptin and insulin levels. Magnetic resonance imaging study of previously untreated people with schizophrenia. Br J Psychiatry 184, 58-62.



