Metabolically healthy obesity and metabolic syndrome in Nigerian adults with major mental illness

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Background
An understanding of the interplay between mental illnesses and metabolic disorders is crucial. At present, in Nigeria, studies on coexistence of these conditions are scarce. Therefore, this study was carried out to determine the prevalence of obesity, metabolically healthy obesity (MHO) and metabolic syndrome (MS) in adults with major mental illnesses.

Materials and methods
One hundred and twenty four patients with schizophrenia, depression and bipolar disorder were recruited into this cross-sectional study. Blood pressure and anthropometric indices were obtained using standard methods. After an overnight fast, plasma glucose levels and lipid profile were determined. MS was diagnosed using the Joint Interim Statement. MHO was defined as overweight/obesity with less than or equal to one MS risk factor, whereas metabolically unhealthy obesity (MUO) was defined as overweight/obesity with greater than or equal to two MS risk factors.

Results
More than half (55.6%) of the patients had normal body weight. The prevalence of overweight, obesity and MS was 25.8, 18.5 and 20.2%, respectively. Similarly, the prevalence of MHO and MUO among the overweight/obese patients was 21.8 and 78.2%, respectively. MUO was more prevalent in patients with schizophrenia compared with patients with depression and bipolar disorder. Low HDL and central obesity were the most common components of MS in the study participants.

Conclusion
It could be concluded from this study that metabolic disorders are not uncommon in Nigerians with major mental illness. Therefore, early identification of patients with metabolic alteration and introduction of preventive measures might forestall further cardiometabolic deterioration, especially in patients with schizophrenia.

Keywords:
mental illness, metabolic syndrome, metabolically healthy obesity, schizophrenia

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Introduction

Mental illnesses continue to be the leading causes of disability worldwide. It is reported that about 340 million people worldwide suffer from mental illnesses, with the majority living in the developing world (Ali *et al*., 2006). Gureje *et al*. (2007) reported that one out of every five Nigerian has a mental illness.

Recent evidences showed that there is a significant association between mental illnesses and metabolic disorders (Belslnier et al., 2003; Dixon and Wohlheiter, 2003). Increasingly, obesity, dyslipidaemia, hypertension and type 2 diabetes mellitus (T2DM) are becoming recognized as common comorbidities in individuals with major mental illnesses such as schizophrenia, bipolar disorder and schizoaffective disorders (Toalson *et al*., 2004).

The mechanism underlying metabolic alteration in mental illnesses is poorly understood. However, factors such as sedentary lifestyle, poor nutritional habits, lack of access to healthy foods, the effect of the mental illness itself, poor health maintenance, carbohydrate craving, smoking (Toalson *et al*., 2004; Mendelson, 2008) and disequilibrium in the hypothalamus–pituitary–adrenal axis (Bradley and Dinan, 2010) can be attributed to these metabolic alterations. Linkage analyses have identified several loci that are associated with schizophrenia, and some

of these have also been observed in T2DM (Alkelai *et al.*, 2012).

Furthermore, antipsychotic medications, especially the second-generation antipsychotic medications, could negatively affect normal metabolism, causing a marked increase in body weight and alteration in plasma lipid profiles, among others. This medication-associated metabolic alteration is a clinical challenge, especially in patients who require long-term treatment with such medications (American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists, North American Association for the Study of Obesity, 2004; Nemeroff, 2007).

An understanding of the interplay between mental illnesses and metabolic disorders is crucial, because even in the general medical unit an estimated 21–46% of patients on admission have a mental disorder (Vincze *et al.*, 2004). Yet clinicians have the tendency to always erroneously ignore the presence of somatic symptoms in the mentally ill or are less likely to thoroughly physically examine them (Folsom *et al.*, 2002). This constitutes a high economic burden because of the cost of hospitalization, with an associated increased utilization of general medical services (Schrader *et al.*, 2005), long hospitalization (Strain *et al.*, 1991) and management difficulty (Mendelson, 2008).

There is a dearth of relevant data in Nigeria, the most populous black Nation in the world (National Population Commission of Nigeria, 2013), despite the WHO report that the country has a poor general health profile (World Health Organization, 2004). Therefore, this study was designed to determine the prevalence of obesity, metabolically healthy obesity (MHO) and metabolic syndrome (MS) in adults with major mental illnesses.

Materials and methods

Study area

The study was carried out at New World Psychiatric Hospital Ibadan between January and April, 2015. The hospital is a 60-bedded facility that has both inpatient and outpatient services. It receives consults from various parts of the country and from the West African Coast.

Sampling technique

Consecutive patients who used the study site during the study period were interviewed. The first participant was randomly selected, and subsequent ones were selected consecutively until they were all interviewed. A total of 135 adults were recruited into this cross-sectional study; however, only 124 of them had the major mental illnesses, schizophrenia, depression or bipolar disorder, and were thus considered for this study.

Exclusion criteria

Patients with serious and unstable medical conditions were excluded from this study. In addition, patients who are less than 18 years were excluded.

Informed consent and ethical approval

Participants were enrolled into this study after obtaining an ethics approval from the University of Ibadan/University College Hospital Joint Ethics Review Committee (UI/UCH IRC/14/0239). In addition, written informed consent was obtained from each participant; otherwise, assent was obtained from their appropriate relatives or caregivers.

Sociodemographic measures

Information on sociodemographic characteristics of respondents including age of respondents, sex, educational background, age at onset of illness and duration of illness was obtained using a short-structured questionnaire.

Diagnosis of mental health illnesses

Diagnosis of a mental disorder was carried out by one of us (V.O.L.) using Structural Clinical Interview for Diagnostic and Statistical Manual (DSM) IV Axis 1 Disorder, Version 2.0. The SCID can be used by the clinician as part of a normal assessment procedure to confirm a particular diagnosis or in research or screening as systematic evaluation of a whole range of medical states. The SCID is available in a patient edition for use with subjects who have been identified as psychiatric patients and in a nonpatient edition, which is suitable for use in epidemiological studies.

Diagnosis of metabolic syndrome, overweight, obesity and metabolically healthy obesity

MS was diagnosed using the Joint Interim Statement (Alberti *et al.*, 2009). The diagnosis was made when three or more of the following risk factors are present: blood pressure greater than or equal to 130/85 mmHg or on treatment for hypertension, waist circumference (WC) up to 94 cm in men or up to 80 cm in women, fasting plasma glucose level up to 100 mg/dl or on treatment for diabetes, triglyceride (TG) level up to 150 mg/dl or on treatment for hypertriglyceridaemia and HDL-cholesterol level less than 40 mg/dl in men

or less than 50 mg/dl in women or on treatment for dyslipidaemia. Overweight and obesity were defined as BMI greater than or equal to 25 kg/m^2 and greater than or equal to 30 kg/m^2, respectively. MHO was defined as a BMI of greater than or equal to 25 kg/m^2 with none or one of the risk factors for MS listed above, whereas metabolically unhealthy obesity (MUO) was defined as BMI greater than or equal to 25 kg/m^2 with two or more of the aforementioned risk factors (Velho *et al.*, 2010; Stefan *et al.*, 2013; Heianza *et al.*, 2014). WC was not included among the risk factors used in defining MHO and MUO, as it has been shown to correlate well with BMI (Klein *et al.*, 2007).

Measurement of blood pressure and anthropometric indices

Blood pressure was obtained using a mercury sphygmomanometer after at least 10 min of rest. WC (cm) was measured using a measuring tape placed at the umbilical level, whereas the hip circumference (cm) was measured at the widest circumference of the hip over light clothing, using a nonstretchable measuring tape, without any pressure to the body surface and were recorded to the nearest 0.1 cm. Height (m) was taken using a Stadiometer, whereas body weight (kg) was taken using a body-weight weighing scale with the participant wearing light clothing and without shoes. BMI was calculated as the ratio of weight (kg) to the square of height (m^2).

Sample collection

After an overnight fast of about 8–10 h, 10 ml of venous blood was obtained from each participant. The blood samples obtained were appropriately dispensed into fluoride oxalate and lithium heparin bottles. Plasma samples were appropriately obtained and stored at −20°C until analysis.

Laboratory analyses

Plasma levels of glucose were determined using the glucose oxidase method. Total cholesterol, TG and HDL-cholesterol levels were determined using enzymatic colorimetric assay. Thereafter, plasma LDL level was calculated using the Friedewald formula (Friedewald *et al.*, 1972).

Statistical analysis

Statistical analysis was carried out using analysis of variance, χ^2-test and Fisher's exact test. *P*-values less than 0.05 were considered to be statistically significant.

Results

The characteristics of the study participants are shown in Table 1. The mean BMI was in the overweight category, whereas the mean levels of fasting plasma glucose and TG were within the acceptable range. In addition, there were no significant differences in the mean levels of these biochemical parameters in patients with schizophrenia, major depression and bipolar disorder (Table 2).

Table 1 Demographic, anthropometric and biochemical parameters in the study participants

Parameters	
Demographic and anthropometric indices	
Number	124
Male [*n* (%)]	62 (50)
Female [*n* (%)]	62 (50)
Age (years)	37.8±11.1
Height (m)	1.68±0.1
Body weight (kg)	71.7±17.1
BMI (kg/m^2)	25.3±5.4
WC (cm)	86.9±14.0
SBP (mmHg)	113.0±14.6
DBP (mmHg)	74.9±10.7
Biochemical parameters (mg/dl)	
FPG	91.4±15.7
TC	184.7±58.3
TG	80.2±24.1
HDL	44.6±15.4
LDL	124.0±52.4

DBP, diastolic blood pressure; FPG, fasting plasma glucose; PG, plasma glucose; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride; WC, waist circumference.

Table 3 shows the metabolic profile of all the study participants. A total of 62 (55.6%) patients had normal body weight, whereas 25.8 and 18.5% were overweight and obese, respectively. In addition, seven (six schizophrenia and one bipolar disorder) patients were underweight. Not all the patients with normal body weight were metabolically healthy, as 18 of them had MUNW. Overweight and obesity were more prevalent in patients with bipolar disorder and schizophrenia than in patients with depression (Table 4).

Fifty-five patients (44.4%) had BMI greater than or equal to 25 kg/m^2. Of this number, 12 (21.8%) had MHO, whereas 43 (78.2%) had MUO. The prevalence of MUO was highest in patients with schizophrenia followed by depression and bipolar disorder (Table 4).

In addition, in Table 4, it was observed that 25 (20.2%) patients had MS, with higher prevalence rates in patients with depression and schizophrenia than in patients with bipolar disorder. Of the 25 patients with MS, eight (five schizophrenia, one bipolar and two depression) of them had normal body weight.

Table 2 Demographic, anthropometric and biochemical parameters in patients with schizophrenia, depression and bipolar disorder

	Schizophrenia (*n*=82)	Depression (*n*=14)	Bipolar (*n*=28)	*F*-value	*P*-value
Age (years)	38.0±10.6	40.0±13.1	36.1±11.4	0.596	0.552
Weight (kg)	72.2±16.9	70.6±15.8	70.5±18.8	0.138	0.871
BMI (kg/m^2)	24.8±5.0	25.1±4.5	26.8±6.6	1.534	0.220
WC (cm)	86.6±13.8	87.0±12.1	88.0±15.4	0.107	0.899
SBP (mmHg)	114.5±15.9	110.5±12.7	109.8±10.6	1.325	0.270
DBP (mmHg)	75.3±11.0	74.3±9.5	74.0±10.5	0.186	0.831
FPG (mg/dl)	92.8±16.3	87.4±12.2	89.2±15.1	1.063	0.349
TC (mg/dl)	182.7±59.6	190.8±56.8	187.4±56.8	0.153	0.859
TG (mg/dl)	78.8±24.8	84.2±31.2	82.5±18.0	0.460	0.633
HDL (mg/dl)	43.8±14.6	47.1±18.3	45.9±16.3	0.395	0.674
LDL (mg/dl)	123.2±54.8	126.9±47.2	125.0±49.1	0.036	0.965

DBP, diastolic blood pressure; FPG, fasting plasma glucose; PG, plasma glucose; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride; WC, waist circumference.

Table 5 shows the prevalence of components of MS in the study participants. The most common component of MS was low HDL, which was present in more than 50% of the study participants. In addition, central obesity was present in almost half (47.6%) of the study participants. In contrast, hypertriglyceridaemia and hypertension were the least common components of MS in the study participants. Considering each mental illness, low HDL was most common, whereas hypertriglyceridaemia was least common in patients with schizophrenia. In bipolar patients, low HDL and central obesity were most common, whereas hypertriglyceridaemia was not observed at all in the patients. In patients with depression, low HDL was most common, whereas hypertension and hypertriglyceridaemia were least common in the patients.

In Table 5, about one-third (32.3%) of the study participants had one component of MS. Similarly, 30.5 and 42.9% of patients with schizophrenia and depression, respectively, had one component of MS. In bipolar disorder patients, however, 32.1 and 35.7% of the patients had one and two components of MS, respectively.

Discussion

The inter-relationship between major mental disorders and metabolic disorders are well documented (Toalson *et al.*, 2004). Although each disorder can occur independently, the presence of one is seen as a potential risk factor for the other (Akinlade *et al.*, 1996).

Table 3 Metabolic profile of the study participants

Metabolic disorders	*n* (%)
Overweight	32 (25.8)
Obesity	23 (18.5)
MHO	12 (9.7)
MUO	43 (34.7)
MHNW	44 (35.5)
MUNW	18 (14.5)
MS	25 (20.2)

MHO, metabolically healthy obesity; MS, metabolic syndrome; MUO, metabolically unhealthy obesity.

The observed insignificant differences in the metabolic factors in the three groups of mental illness confirm that metabolic alteration is a common feature among the three groups and may signify a commonality between them. For example, it had been argued that psychoses are phenotypic expressions of a 'single underlying entity' (Crow, 1994), and that schizophrenia and bipolar disorder have commonalities in the areas of symptom profile and dopamine blockade (Murray *et al.*, 2004). Over two decades ago, it had been suggested that both schizophrenia and depression have the same 'familial relationship' (Maier *et al.*, 1993). However, the phenotypic expression of the metabolic expression might differ depending on the type of mental illness.

Obesity is a complex and multifactorial chronic disorder that requires continuous care, support and follow-up. It is a known risk factor for many other diseases (American Association of Clinical Endocrinologists/American College of Endocrinology Obesity Task Force, 1998). In this study, the observed prevalence of overweight and obesity was slightly different, but it falls in between the reported prevalence rates in adult Nigerians. Puepet *et al.* (2009) reported prevalence rates of 17.5 and 4.2% for overweight and obesity, respectively, in adults living in Jos. Similarly, Charles-Davies *et al.* (2012) reported prevalence rates of 32.96 and 23.41% among traders in Ibadan. The prevalence rates of overweight and obesity observed in patients with bipolar disorder was similar to that reported by Charles-Davies *et al.* (2012). This observation could be attributed to sedentary lifestyle, poor nutritional choices or lack of access to healthy foods, the effects of both the mental disorder itself, the medications used to treat it and lack of access to adequate preventative medical care (Toalson *et al.*, 2004; Mendelson, 2008). As these factors are common in major mental disorders, our observed higher prevalence rates of overweight and obesity in patients with bipolar disorder and schizophrenia compared with

Table 4 Prevalence rates of obesity, metabolically healthy obesity, metabolically unhealthy obesity and metabolic syndrome in patients with schizophrenia, depression and bipolar disorder

	Schizophrenia (*n*=82) [*n* (%)]	Depression (*n*=14) [*n* (%)]	Bipolar (*n*=28) [*n* (%)]	*N* (%)	χ^2	*P*-value
BMI						
Underweight	6 (7.3)	–	1 (3.6)	7 (5.6)	6.994	0.321
Normal body weight	42 (51.2)	10 (71.4)	10 (35.7)	62 (50.0)		
Overweight	21 (25.6)	2 (14.3)	9 (32.1)	32 (25.8)		
Obesity	13 (15.9)	2 (14.3)	8 (28.6)	23 (18.5)		
Metabolic health status[a]						
MHO	6 (17.6)	1 (25.0)	5 (29.4)	12 (21.8)	0.945	0.623
MUO	28 (82.4)	3 (75.0)	12 (70.6)	43 (78.2)		
Metabolic syndrome						
Yes	17 (20.7)	3 (21.4)	5 (17.9)	25 (20.2)	0.123	0.940
No	65 (79.3)	11 (78.6)	23 (81.5)	99 (79.8)		

MHO, metabolically healthy obesity; MUO, metabolically unhealthy obesity. [a]Percentage obtained from 55 patients with BMI ≥25 kg/m^2.

Table 5 Prevalence of components of metabolic syndrome in the study participants

	Schizophrenia [*n* (%)]	Bipolar [*n* (%)]	Depression [*n* (%)]	*N* (%)	χ^2	*P*-value
Central obesity						
No	46 (56.1)	11 (39.3)	8 (57.1)	65 (52.4)	2.506	0.286
Yes	36 (43.9)	17 (60.7)	6 (42.9)	59 (47.6)		
Hypertension						
No	64 (78.0)	24 (85.7)	13 (92.9)	101 (81.5)	2.171	0.338
Yes	18 (22.0)	4 (14.3)	1 (7.1)	23 (18.5)		
Hyperglycemia						
No	62 (75.6)	22 (78.6)	12 (85.7)	96 (77.4)	0.726	0.696
Yes	20 (24.4)	6 (21.4)	2 (14.3)	28 (22.6)		
Hypertriglyceridaemia						
No	80 (97.6)	28 (100.0)	13 (92.9)	121 (97.6)	2.017	0.365
Yes	2 (2.4)	0 (0.0)	1 (7.1)	3 (2.4)		
Low HDL						
No	38 (46.3)	11 (39.3)	7 (50.0)	56 (45.2)	0.569	0.752
Yes	44 (53.7)	17 (60.7)	7 (50.0)	68 (54.8)		
Number of components						
None	16 (19.5)	4 (14.3)	3 (21.4)	23 (18.5)	2.524	0.866
1 component	25 (30.5)	9 (32.1)	6 (42.9)	40 (32.3)		
2 components	24 (29.3)	10 (35.7)	2 (14.3)	36 (29.0)		
≥3 components (MS)	17 (20.7)	5 (17.9)	3 (21.4)	25 (20.2)		

MS, metabolic syndrome.

depression could indicate that medications used in schizophrenia and bipolar disorder management might have more weight-gaining effect than those used in depression management.

It is well known that not all individuals with obesity have an adverse metabolic profile predisposing them to the development of T2DM and cardiovascular diseases (CVDs) (van Vliet-Ostaptchouk *et al.*, 2014). This serves as the basis for the stratification of obesity into metabolically healthy and MUO phenotypes, as it makes it easy in ascertaining the appropriate therapeutic or intervention strategy (Phillips *et al.*, 2013). The MHO phenotype was first described in 1982 by Sims (Samocha-Bonet *et al.*, 2014; Rey-López *et al.*, 2015). It is a benign obesity with no association with obesity-related metabolic abnormalities (Heianza *et al.*, 2014). According to Bell *et al.* (2014, 2015), the long-term prognosis of healthy obesity is metabolic deterioration, as adults with MHO have a substantial increased risk of developing T2DM and other cardiometabolic complications compared with metabolically healthy normal-weight adults. Eshtiaghi *et al.* (2015) looked at the natural course of MHO in Tehran adults and observed that it is a relatively unstable condition, as 42.1% of the study participants lost their metabolic health after 10 years of follow-up. Thus, MHO continues to be an important condition through which the continuum of metabolic deterioration associated with obesity is explored. The observed prevalence of MHO in the study participants indicates that about three in four overweight and obese patients with major mental

illness are at the risk of being metabolically unhealthy. This observed prevalence of MHO is higher than that reported by van Vliet-Ostaptchouk *et al.* (2014) in healthy cohorts from seven countries but lower than that reported by Ijeh *et al.* (2010) in Nigerians. Differences in observations could be due to variations in the diagnostic criteria of MHO, as at present there is no uniform diagnostic criteria. In addition, differences in physical activity level, diet, smoking, alcohol use and even genetic factors could account for the differences (Cornier *et al.*, 2008; Pataky *et al.*, 2010; Velho *et al.*, 2010). Eshtiaghi *et al.* (2015) showed that low HDL and elevated TG are significant predictors of metabolic health condition. A similar pattern was observed in this study, as more than half of the study participants had low HDL.

Wildman *et al.* (2008), Pataky *et al.* (2010) and Velho *et al.* (2010) reported that behavioral factors and psychosocial profile affect the metabolic profile. Our observed high prevalence of MUO in schizophrenia compared with the other two groups might indicate that overweight and obese patients with schizophrenia have a higher risk of metabolic deterioration. This observation could be attributed to the differences in psychosocial profile and even medications.

MS is a constellation of factors that increase the risk of developing T2DM and CVDs (Roberts and Sindhu, 2009). It continues to be a major public health challenge worldwide, as it is strongly associated with CVD risk (Alberti *et al.*, 2005; Charles-Davies *et al.*, 2012). The mechanisms that link the metabolic abnormalities of MS with the pathophysiology of clinical diseases associated with MS are numerous and poorly understood (Rahamon *et al.*, 2014). The observed prevalence of MS in the study was slightly higher than the prevalence of 14.9 and 16.3% reported in urban dwellers by Adediran *et al.* (2012) and Charles-Davies *et al.* (2012), respectively. This observation probably indicates that MS is more prevalent in individuals with major mental illness than in the general population. Furthermore, our observation that eight of the patients with MS had normal body weight indicates that MS can occur in all BMI categories. Dhana *et al.* (2016) reported that MS is strongly associated with CVD risk, and the increased risk is in all BMI categories.

Previous report has shown that the prevalence of MS is higher in patients with schizophrenia than in patients with bipolar disorder (Bly *et al.*, 2014). A similar pattern was observed in this study, as the prevalence of MS was slightly higher in patients with depression and schizophrenia than in patients with bipolar disorder. This observation suggests that metabolic alteration could be more associated with schizophrenia and depression than bipolar disorder, as we also observed higher prevalence rates of MUO in patients with schizophrenia and depression than in patients with bipolar disorder.

A combination of sedentary lifestyle, low consumption of fruits and vegetables, and drugs used in the management of mental illnesses might be responsible for the observed prevalence rates in this study.

The study has a number of limitations. The first limitation is that the participants were not matched by age and sex and other clinical factors that are potential confounders of MS. We found this difficult given the general demographic differences in patients with schizophrenia and mood disorders seeking treatment in clinical setting. The small sample size and the noninclusion of apparently healthy population as a control group were additional limitations of this study. However, our findings act as a template for a larger sample case–control study on this important subject.

It could be concluded from this study that metabolic disorders are not uncommon in Nigerians with major mental illnesses. This study provides further evidence that there is an association between mental health disorders and metabolic alterations. Therefore, identification of patients with MUO and MS is important, as preventive measures could be initiated to forestall further deterioration to T2DM and other cardiometabolic complications, especially in patients with schizophrenia.

Authors' contribution: K.S.A. designed the study; V. O.L. made the diagnosis; all authors recruited the patients and wrote the manuscript and K.S.A. supervised the entire research.

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Conflicts of interest

There are no conflicts of interest.

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