Metabolic syndrome in psychiatric patients (comparative study)

Fatma A. Mousa[a], Hani H. Dessoki[c], Sarah M. El Kateb[b], Ahmed A. Ezzat[c,b], Mohamed R. Soltan[d]

Departments of [a]Psychiatry, [b]Chemical Pathology, Faculty of Medicine, Cairo University, Cairo, [c]Department of Psychiatry, Faculty of Medicine, Beni Suef University, Beni Suef, [d]Department of Psychiatry, Faculty of Medicine, Fayoum University, Fayoum, Egypt

Correspondence to Mohamed R. Soltan, MD, Department of Psychiatry, Faculty of Medicine, Fayoum University, El-Fayoum 63514, Egypt
Tel: +20 480 101 072 3636/20 482 999 084/ 20 122 156 2006; e-mails: dr.mohamedsoltan1979@gmail.com, Mrs04@fayoum.edu.eg

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Background
It is generally estimated that metabolic syndrome (MetS) is especially common in patients with severe mental illness, with a high prevalence ranging from 30 to 60% for schizophrenic and bipolar disorders, which predispose them to further medical complications up to premature death.
Objective
The aim of this study was to compare the prevalence of MetS in patients with major depressive disorder (MDD), schizophrenic patients, and healthy general individuals, and to assess the relation between cortisol levels and presence of MetS.
Patients and methods
The study included 120 participants (40 patients with drug-naive MDD, 40 patients with drug-naive schizophrenia, and 40 healthy individuals who served as the control group). Full history was taken. Blood pressure and waist circumference (WC) were measured and BMI was calculated. Laboratory investigations were carried out, including fasting blood glucose (FBG), serum triglycerides, serum high-density lipoprotein, and a morning level of serum cortisol.
Results
The study revealed a similar prevalence of MetS in the MDD and the schizophrenic group (27.5%) compared with a prevalence of 22.5% in the control group. The WC and the BMI were significantly higher in the MetS patients of the MDD and the schizophrenic group compared with those of the control group. FBG was significantly higher among MetS patients in the MDD group as compared with those in the schizophrenic and the control group. Cortisol level was significantly higher in MetS patients in the MDD and the schizophrenic group as compared with those in the control group.
Conclusion
The prevalence of MetS is higher in MDD and schizophrenic patients than in the general population, and is related to high WC, BMI, FBG, and serum cortisol. Hence, screening of such patients for metabolic disturbances is recommended.

Keywords:
major depressive disorder, metabolic syndrome, schizophrenia

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Introduction

Metabolic syndrome (MetS) is receiving paramount importance in clinical medicine. Its relevance to cardiovascular diseases and many other illnesses are getting a lot of attention in current medical literature (Citrome, 2005).

Although the prevalence of obesity and other risk factors such as hyperglycemia are increasing in the general population, patients with major mental illnesses have an increased prevalence of overweight and obesity, hyperglycemia, dyslipidemia, hypertension, and smoking, and substantially greater mortality, compared with the general population (Zaki *et al.*, 2014).

MetS was reported in 19–63% of schizophrenic patients, in 42.4% of patients with schizoaffective disorder, in 24.6–50% of bipolar patients, and in 12–36% of the patients with recurrent depression (Jakovljević *et al.*, 2007).

The aim of this work was to study the prevalence of MetS and its components in drug-naive psychiatric patients, and to examine the link between psychiatric disorders and development of MetS and its components.

Patients and methods

This study consisted of two groups: group A (the case group) and group B (the control group). Group A

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(cases) consisted of 80 patients who attended the psychiatric outpatient clinic, who were subdivided into two subgroups: group A1 (n=40), which included patients with major depressive disorder (MDD) and group A2 (n=40), which included patients with schizophrenia. Cases were diagnosed according to *Diagnostic and statistical manual of mental disorders*, 5th ed. (DSM-5). Both sexes were included, and their ages ranged from 15 to 55 years. They fulfilled DSM-5 criteria for current MDD and schizophrenia. Drug-naive patients had not received antipsychotic medications, depot or oral forms, for at least 6 months before the study. Suicidal, excited, and catatonic patients were excluded.

Group B (the control group) included 40 normal individuals who were selected from the employees of Kasr El Aini Psychiatric Hospital and matched with the patients group in age, sex, education, sociodemographic, and economic status with no current or lifetime history of psychiatric disorders, and informed consent was taken from them. Individuals with diabetes mellitus (DM) or cardiovascular disorders and mental retardation were excluded.

Informed written consent was obtained from both groups. Diabetic, cardiac, and mentally retarded patients were excluded from both groups.

All participants of the study were subjected to the following:

(1) Clinical assessment using clinical psychiatric sheet for clinical assessment of personal data, including age, sex, marital status, education, occupation, residency, psychiatric diagnosis of the cases and control groups, family history of medical or psychiatric disorders, past history of medical or psychiatric disorders, psychiatric and medical investigations, and general medical examination. A short Arabic–English version of a Semi-structured Psychiatric Interview (PSE-10) (World Health Organization, 1992) was used for clinical assessement of symptoms and to ensure diagnosis of cases.
(2) MetS assessment: The MetS and metabolic risk factors were defined according to the Modified National Cholesterol Education Program ATP III Guidelines (2005) (National Cholesterol Education Program (NCEP), 2005). Participants having three or more of the following criteria were defined as having MetS:
    (a) Elevated waist circumference (WC) greater than or equal to 102 cm in men and 88 cm in women.
    (b) Elevated triglycerides (TG) greater than or equal to 150 mg/dl (1.7 mmol/l) or drug treatment for elevated TG.
    (c) Reduced high-density lipoprotein-cholesterol (HDL-C) less than 40 mg/dl (0.9 mmol/l) in men and 50 mg/dl (1.1 mmol/l) in women or drug treatment for low HDL-C.
    (d) Elevated blood pressure greater than or equal to 130 mmHg systolic blood pressure (SBP) or 85 mmHg diastolic blood pressure (DBP) or drug treatment for hypertension.
    (e) Elevated fasting blood glucose (FBG) greater than 100 mg/dl or drug treatment for elevated glucose.

    WC was measured in the clinical examination in centimeters at the level midway between the lowest rib margin and the iliac crest. BP was measured during the clinical examination. Two BP readings were obtained, and the average of the SBP and DBP readings were used in the analysis. Venous blood samples were drawn after overnight fasting or at least 12 h fasting for determination of serum TGs, serum cholesterol, HDL-C, and low-density lipoprotein-cholesterol. Serum fasting glucose was measured using the blood sample.
(3) Serum cortisol was assessed by collecting venous blood samples from all patients to determine cortisol level using the competitive enzyme immunoassay technique.

Statistical analysis

All data were recorded and entered in a statistical package on a compatible computer and varied. Analysis was performed using statistical program for the social science (SPSS, 17th version, 2009). The results were tabulated, grouped, and statistically analyzed using the following tests:

(1) Descriptive statistics was performed for comparison between percentages of the different variables of MetS among groups of patients and controls using mean and SD.
(2) Analytic statistics was performed using the Pearson χ^2 and t-test to detect whether there is a significant difference between categorical variables.

P-value is used to indicate the level of significance:

P-value greater than 0.05: nonsignificant.
P-valueless than 0.05: significant.

P-value less than 0.01: highly significant.
P-value less than 0.001: very highly significant.

Results

On comparing between cases (schizophrenic and major depressive patients) and controls as regards socio-demographic data (Table 1), there was no statistically significant difference among the three groups as regards age, sex, marital status, educational level, residence, socioeconomic level, cigarette smoking, history of substance abuse, and family history of psychiatric disorders, substance abuse, and cardiac diseases. However, there was significantly higher family history of DM and cerebrovascular stroke in major depression and schizophrenic patients compared with controls.

As regards the number of MDD patients in the sample, there were seven (6%) patients with mild episode, 16 (13%) patients with moderate episode, and eight (7%) patients with severe episode without psychotic features and nine (8%) patients with severe episode with psychotic features, whereas as regards the number of schizophrenic patients 16 (13%) patients were paranoid type and 24 (20%) patients were diagnosed as schizophrenic undifferentiated type according to DSM-5 (Fig. 1).

As regards clinical and laboratory investigation (Table 2), there was no statistically significant difference among the three groups as regards BP values greater than or equal to 130/85, the presence of increased SBP (≥130 mmHg), the presence of increased DBP values (≥85 mmHg), values of WC, values of FBG, values of serum TGs, and values of serum HDL-C. However, the MDD group showed the highest proportion of patients with increased

Table 1 Comparison between cases (schizophrenia and major depressive patients) and the control group as regards sociodemographic data, history, and clinical data

	Major depression cases (*n*=40) [*N* (%)]	Schizophrenic cases (*n*=40) [*N* (%)]	Control group (*n*=40) [*N* (%)]	Total [*N* (%)]	Test	*P*-value
Age (mean±SD)	32.32±8.82	34.40±11.01	32.90±10.36	–	*t*-Test=1.764	0.073
Sex						
Female	19 (47.5)	11 (27.5)	17 (42.5)	47 (39.2)	χ^2=3.637	0.162
Male	21 (52.5)	29 (72.5)	23 (57.5)	73 (60.8)		
Marital status					χ^2=9.239	0.161
Single	14 (35)	24 (60)	19 (47.5)	57 (47.5)		
Married	21 (52.5)	15 (37.5)	20 (50)	56 (46.7)		
Divorced	3 (7.5)	1 (2.5)	0 (0.0)	4 (3.3)		
Widow	2 (5)	0 (0.0)	1 (2.5)	3 (2.5)		
Education						
Illiterate	16 (40)	15 (37.5)	9 (22.5)	40 (33.3)	χ^2=20.20	0.063
Read and write	4 (10)	5 (12.5)	4 (10)	13 (10.8)		
Primary	5 (12.5)	2 (5)	1 (2.5)	8 (6.7)		
Preparatory	1 (2.5)	3 (7.5)	0 (0.00)	4 (3.3)		
Secondary	1 (2.5)	5 (12.5)	0 (0.00)	6 (5.0)		
Technical	10 (25)	10 (25)	17 (42.5)	37 (30.8)		
University	3 (7.5)	0 (0.00)	9 (22.5)	12 (10)		
Residence						
Rural	20 (50)	22 (55)	22 (55)	64 (53.3)	χ^2=0.268	0.875
Urban	20 (50)	18 (45)	18 (45)	56 (46.7)		
Socioeconomic level						
Low	21 (52.5)	30 (75)	25 (62.5)	76 (63.3)	χ^2=8.447	0.076
Moderate	16 (40)	7 (17.5)	15 (37.5)	38 (31.7)		
High	3 (7.5)	3 (7.5)	0 (0.0)	6 (5)		
Cigarette smoking	17 (42.5)	30 (75)	11 (27.5)	58 (48.4)	χ^2=29.26	**<0.001**
Substance abuse	9 (22.5)	15 (37.5)	2 (5)	26 (78.3)	χ^2=12.471	0.002
Family history of psychiatric disorders	12 (30)	10 (25)	9 (22.5)	26 (25.8)	χ^2=14.451	0.072
Family history of substance abuse	15 (37.5)	12 (30)	6 (5)	26 (27.5)	χ^2=0.084	18.451
Family history of DM	20 (50)	16 (40)	7 (17.5)	43 (35.8)	χ^2=9.641	0.008
Family history of cardiac diseases	16 (40)	10 (25)	5 (12.5)	26 (24.2)	χ^2=5.584	0.063
Family history of cerebrovascular stroke	12 (30)	8 (20)	1 (2.5)	21 (17.5)	χ^2=10.736	0.005

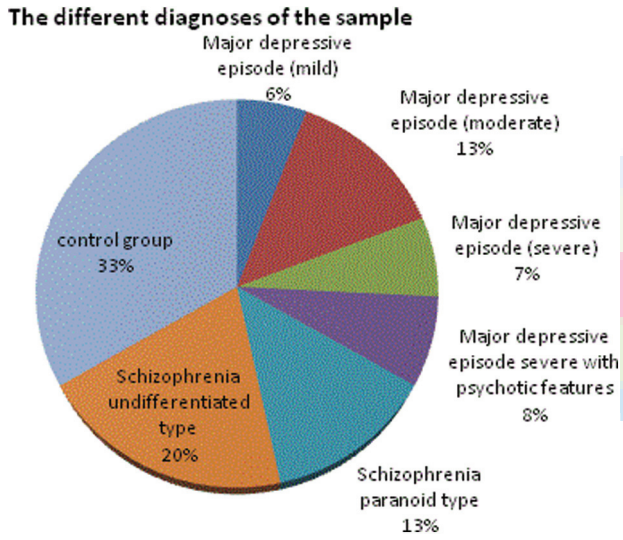
DM, diabetes mellitus. $P<0.05$, significant.

SBP and DBP. However, there was a highly statistically significant difference as regards increased serum cortisol levels in the major depression and schizophrenic groups compared with the control group.

The distribution of MetS in the studied groups is shown in Fig. 2. There was no statistically significant difference between the major depression, schizophrenic, and control groups as regards prevalence of MetS (P=0.084); however, the patient group (major depression and schizophrenia cases) showed higher prevalence of MetS [11(27.5%)] in each group compared with nine (22.5%) in the control group (Fig. 3).

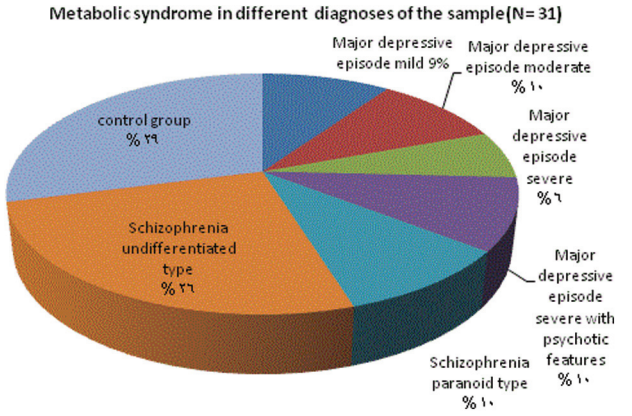
On comparing between MetS patients in the three study groups as regards sociodemographic data (Table 3), there was no statistically significant difference among the MetS patients with schizophrenia, MetS patients with depression, and MetS patients in the control group as regards the

Figure 1



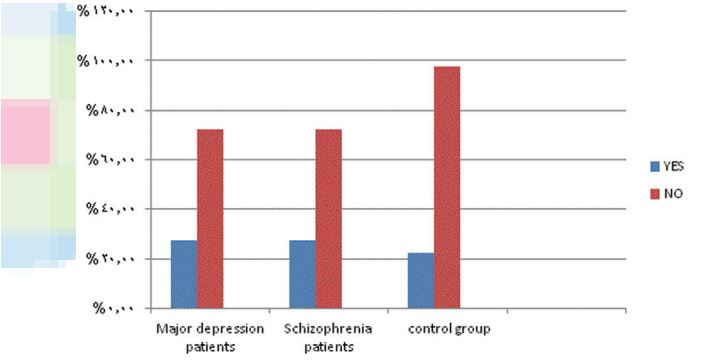
Percentage of different diagnoses of the sample (N=120).

Figure 2



The prevalence of metabolic syndrome among the different diagnoses of the sample.

Figure 3



Percentage of prevalence of metabolic syndrome in major depressive disorder, schizophrenic patients, and the control group.

Table 2 Comparison between major depression, schizophrenic cases, and control as regards laboratory investigation

	MDD cases (n=40)	Schizophrenic cases (n=40)	Control group (n=40)	Total	Test	P-value
Blood pressure values≥130/85	11 (27.5)	5 (12.5)	4 (10)	20 (16.6)	χ^2=0.348	0.076
Systolic BP≥130 mmHg	11 (27.5)	5 (12.5)	4 (10)	20 (16.6)	χ^2=0.348	0.076
Diastolic BP≥85 mmHg	16 (40)	14 (35)	12 (30)	42 (35)	χ^2=0.879	0.644
Waist circumference≥102 and 88 cm in male and female patients	18 (45)	15 (37.5)	23 (57.5)	64 (53.3)	χ^2=3.281	0.194
Fasting blood glucose>100 mg/dl	10 (25)	8 (20)	13 (32.5)	31 (25.8)	χ^2=1.653	0.438
Serum triglycerides≥150 mg/dl	17 (42.5)	12 (30)	10 (25)	39 (32.5)	χ^2=2.963	0.227
Serum HDL-cholesterol<40 and 50 mg/dl in male and female patients, respectively	17 (42.5)	21 (52.5)	22 (55)	60 (50)	χ^2=1.4	0.497
Serum cortisol>22 and 21.7 μg/dl in male and female patients, respectively	19 (47.5)	13 (32.5)	1 (2.5)	33 (27.5)	χ^2=21.066	<**0.001**
Serum cortisol (μg/dl) (normal: 5.0–22.0 μg/dl in males and 5.2–21.7 μg/dl in females)						
Range	7.6–53.2	7.9–38.5	5–26.1		t-Test=2.974	0.055
Mean±SD	20.57±9.27	18.44±7.41	12.21±4.76			

BP, blood pressure; HDL, high-density lipoprotein; MDD, major depressive disorder. P<0.05, significant.

Table 3 Comparison between metabolic syndrome patients in the three study groups as regards sociodemographic data

	Major depression cases (*n*=11) [*N* (%)]	Schizophrenic cases (*n*=11) [*N* (%)]	Control group (*n*=9) [*N* (%)]	Total [*N* (%)]	Test	*P*-value
Age (mean ±SD)	39.82±10.28	31.91±11.44	40±10.17	–	*t*-Test=1.987	0.156
Sex						
Female	8 (72.7)	6 (54.5)	4 (44.4)	18 (58.1)	χ^2=1.7	0.42
Male	3 (27.3)	5 (45.5)	5 (55.6)	13 (41.9)		
Marital status						
Single	2 (18.2)	7 (63.6)	1 (11.1)	10 (32.3)	χ^2=10.55	0.103
Married	6 (54.5)	4 (36.4)	7 (77.8)	17 (54.8)		
Divorced	1 (9.1)	0 (0)	0 (0.0)	1 (3.2)		
Widow	2 (18.2)	0 (0.0)	1 (11.1)	3 (9.7)		
Education						
Illiterate	7 (63.6)	3 (27.3)	3 (33.3)	13 (41.9)	χ^2=11.889	0.293
Read and write	1 (9.1)	0 (0.00)	1 (11.1)	2 (6.5)		
Primary	1 (9.1)	0 (0.00)	1 (11.1)	2 (6.5)		
Preparatory	1 (9.1)	2 (18.2)	0 (0.00)	3 (9.7)		
Secondary	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)		
Technical	1 (9.1)	6 (54.5)	3 (33.3)	10 (32.3)		
University	0 (0.00)	0 (0.00)	1 (11.1)	1 (3.2)		
Residence						
Rural	6 (54.5)	6 (54.5)	3 (33.3)	15 (48.4)	χ^2=1.151	0.562
Urban	5 (45.5)	5 (45.5)	6 (66.7)	16 (51.6)		
Socioeconomic level						
Low	5 (45.5)	11 (100)	5 (55.6)	21 (67.7)	χ^2=8.35	0.015
Moderate	6 (54.5)	0 (0.00)	4 (44.4)	10 (32.3)		
High	0 (0.00	0 (0.00)	0 (0.00)	0 (0.00)		
Cigarette smoking	3 (27.3)	9 (81.8)	1 (11.1)	13 (41.9)	χ^2=11.669	0.003
History of substance abuse	2 (18.2)	5 (45.5)	0 (0.00)	7 (22.6)	χ^2=6.039	0.049
Family history of psychiatric disorders	4 (36.4)	7 (63.6)	2 (77.8)	13 (41.9)	χ^2=9.414	0.052
Family history of substance abuse	3 (27.3)	2 (18.2)	1 (11.1)	6 (19.4)	χ^2=0.843	0.656
Family history of DM	7 (63.6)	5 (45.5)	2 (22.2)	14 (45.2)	χ^2=3.429	0.18
Family history of cardiac diseases (yes)	5 (45.5)	5 (45.5)	1 (11.1)	11 (35.5)	χ^2=3.291	0.193
Family history of cerebrovascular strokes					χ^2=1.668	0.434
Yes	3 (27.3)	4 (36.4)	1 (11.1)	8 (25.8)		
Total	11 (100)	11 (100)	9 (100)	31 (100)		

DM, diabetes mellitus. $P<0.05$, significant.

mean age, sex representation, marital status, the educational level, and residence.

However, as regards socioeconomic level, the difference was statistically significant (P=0.015). All MetS patients in the schizophrenic group had low socioeconomic level. Low socioeconomic level was also more prevailing in patients having MetS in the three groups compared with moderate socioeconomic level.

The history of cigarette smoking was also a significant risk factor for developing MetS in the schizophrenic group compared with the MDD group and the control group. This difference was statistically significant (P=0.003).

The presence of history of substance abuse, a family history of psychiatric disorders, substance abuse, DM, cardiac disease, and or cerebrovascular strokes did not affect the development of MetS in the MDD, schizophrenic, or control groups ($P>0.05$).

On comparing between MetS patients in the three groups as regards MetS components (Table 4), the MetS patients in the MDD group showed the highest proportion of having increased SBP values (≥130 mmHg); however, the difference was not significant (P=0.198). The occurrence of increased DBP values (≥85 mmHg) was highest among MetS patients in the control group; however, the difference was not statistically significant (P=0.987).

Table 4 Comparison between metabolic syndrome patients in the three groups as regards metabolic syndrome components

	MDD cases (*n*=11) [*N* (%)]	Schizophrenic cases (*n*=11) [*N* (%)]	Control group (*n*=9) [*N* (%)]	Total [*N* (%)]	Test	*P*-value
Systolic BP≥130/mmHg	6 (54.5)	2 (18.2)	4 (44.4)	12 (38.7)	χ^2=3.241	0.198
Diastolic BP≥85 mmHg	7 (63.6)	7 (63.6)	6 (66.7)	20 (64.5)	χ^2=0.026	0.987
Waist circumference normal up to 88 cm, and 102 cm in female and male patients, respectively (mean±SD)	122.11±11.94	108.82±13.67	6.13±103.27		*t*-Test=7.518	0.002
Waist circumference≥102 and 88 cm in male and female patients, respectively	9 (81.8)	9 (81.8)	9 (100)	27 (87.1)	*t*-Test=1.879	0.391
BMI (mean±SD)	33.07±5.78	31.67±2. 66	26.82±1.5		*t*-Test=7.518	0.002
BMI groups (kg/m^2)					*t*-Test=8.09	0.088
Normal (18.5–24.9)	1 (9.1)	2 (18.2)	2 (22.2)	5 (16.1)		
Overweight (25–30)	2 (18.2)	3 (27.3)	3 (33.3)	8 (25.8)		
Obese (>30)	8 (72.7)	6 (54.5)	4 (44.5)	18 (58.1)		
Fasting blood glucose (mg/dl) (normal: 70–110 mg/dl) (mean±SD)	109.67±9.43	96±12. 31	103.82±10.63		*t*-Test=3.937	0.031
Fasting blood glucose>100 mg/dl	6 (54.5)	7 (63.6)	8 (88.9)	21 (67.7)	*t*-Test=2.803	0.246
Serum triglycerides≥150 mg/dl	10 (90.9)	6 (54.5)	7 (77.8)	23 (74.2)	*t*-Test=3.884	0.143
Serum HDL-cholesterol(<40, 50 mg/dl in male and female patients, respectively	9 (81.8)	11 (100)	8 (88.9)	28 (90.3)	*t*-Test=2.11	0.348
Serum cortisol>22, 21.7 µg/dl in males and females, respectively	6 (54.5)	8 (72.7)	0 (0.00)	14 (45.2)	*t*-Test=11.178	0.004
Serum cortisol (normal: 5.0–22.0 µg/dl in male and 5.2–21.7 µg/dl in female patients)(mean±SD)	24.52±11.56	23.17±7.25	15.51±3.4		*t*-Test=2.634	0.049

BP, blood pressure; HDL, high-density lipoprotein; MDD, major depressive disorder. *P*<0.05, significant.

There was a significant difference in the WC of the MetS patients in the three groups, with MetS patients of the MDD group having the highest WC (122.11± 11.94 cm) compared with 108.82±13.67 cm in the schizophrenic group and 103.27±6.13 cm for MetS patients in the control group (*P*=0.002). Increased WC (≥102 and 88 cm in male and female patients, respectively) was higher in MDD patients with MetS as compared with those without MDD (*P*=0.391). Of note, 87% (27/31) of the MetS patients had increased WC.

The BMI of the MetS patients in the MDD and schizophrenic groups was significantly higher than that in the control group (*P*=0.011). The BMI groups (normal, overweight, and obese) were not significantly different between MetS patients in the three groups (*P*=0.088). Of note, more than half (58.1%) of the MetS patients were encountered in the obese group.

There was a statistically significant difference between the values of FBG of the MetS patients in the three groups. The highest values were in the MetS patients of the MDD group (109.67± 9.43 mg/dl) compared with 103.82±10.63 and 96± 12.31 mg/dl for the MetS patients in the control and the schizophrenic groups, respectively (*P*=0.031). Increased FBG was not significantly different between MetS patients in the three groups (*P*=0.246). Of note, about two-thirds (67.7%) of MetS patients had FBG greater than 100 mg/dl.

The occurrence of increased serum TG levels was not significantly different between MetS patients in the three groups (*P*=0.143). Of note, about three-fourths (74.2%) of the MetS patients had serum TGs greater than or equal to 150 mg/dl.

The presence of decreased serum HDL was not significantly different between MetS patients in the three groups (*P*=0.348). Of note, 90.3% of MetS patients had decreased HDL, and all MetS patients in the schizophrenic group had decreased HDL.

There was a statistically significant difference in the serum cortisol level between MetS patients in the three groups (*P*=0.049) with the highest cortisol level seen in the MDD group (24.52±11.56 mg/dl) followed by serum cortisol level in the schizophrenic group (23.17±7.25 mg/dl), whereas the lowest level of serum cortisol was found in the control group (15.51± 3.4 mg/dl).

The presence of increased serum cortisol levels was significantly higher in MetS patients of the

MDD and schizophrenic groups [six (54.5%) and eight (72.7%), respectively] than in MetS patients of the control group (P=0.004). None of the MetS patients of the control group had elevated serum cortisol.

On comparing between patients with MetS and those without MetS in the three groups as regards age, sex, and the serum cortisol level (Table 5), MetS patients were significantly older compared with the non-MetS patients in the control group (40±10.17 vs. 30.87±10 years, P=0.021). However, the age was not significantly different between MetS patients and non-MetS patients in the MDD and the schizophrenic group (P=0.054 and 0.88, respectively).

Moreover, there was a statistically significant difference between MetS patients and non-MetS patients as regards sex in the MDD and the schizophrenic group (P=0.049 and 0.018, respectively). However, the difference in sex representation between MetS patients and non-MetS patients was not statistically significant in the control group (P=0.893).

Moreover, there was a statistically significant difference between MetS patients and non-MetS patients in the schizophrenic group as regards the serum cortisol level (P=0.001). However, the difference in the serum cortisol level between MetS patients and non-MetS patients in the MDD and the control groups was not statistically significant (P=0.583 and 0.585, respectively).

Discussion

The results have shown that the study groups (the major depression, schizophrenic, and control groups) were homogenous with no statistically significant difference as regards the age, sex distribution, marital status, educational level, residence, socioeconomic level, family history of psychiatric disorders, substance abuse, or family cardiac diseases (Table 1).

Moreover, the results have revealed significantly higher incidence of family history of DM in the schizophrenic (40%) and MDD groups (50%) as compared with the control group (17.5%) (Table 1). This is in agreement with the results of two family studies that have also found that the relatives of people with schizophrenia have an increased risk for type 2 diabetes (Mukherjee *et al.*, 1989; Spelman *et al.*, 2007). Our results have also shown that the presence of a family history of cerebrovascular strokes was significantly higher in the schizophrenic (20%) and MDD groups (30%)

Table 5 Comparison between patients with metabolic syndrome and those without metabolic syndrome in the three groups

Age	Metabolic syndrome		Total	Test	*P*-value
	Yes	No			
The major depression group	39.82±10.28	32.34±10.74		*t*-Test=−1.987	0.054
The schizophrenic group	31.91±11.44	32.48±7.84		*t*-Test=0.153	0.88
The control group	40±10.17	30.87±10		*t*-Test=−2.402	0.021
Sex					
The major depression group					
Female	8 (72.7)	11 (37.9)	19 (47.5)	χ^2=3.872	0.049
Male	3 (27.3)	18 (62.1)	21 (52.5)		
The schizophrenic group					
Female	6 (54.5)	5 (17.2)	11 (27.5)	χ^2=5.566	0.018
Male	5 (45.5)	24 (82.8)	29 (72.5)		
The control group					
Female	4 (44.4)	13 (41.9)	17 (42.5)	χ^2=0.018	0.893
Male	5 (55.6)	18 (58.1)	23 (57.5)		
Serum cortisol level					
The major depression group					
Normal	5 (45.5)	16 (55.2)	21 (52.5)	χ^2=0.302	0.583
High	6 (54.5)	13 (44.8)	19 (47.5)		
The schizophrenic group					
Normal	3 (27.3)	24 (82.8)	27 (67.5)	χ^2=11.192	**0.001**
High	8 (72.7)	5 (17.2)	13 (32.5)		
The control group					
Normal	9 (100)	30 (96.8)	39 (97.5)	χ^2=0.298	0.585
High	0 (0.00)	1 (3.2)	1 (2.5)		

P<0.05, significant.

as compared with the control group (2.5%) (Table 1).

This can be attributed to the underlying genetic risk for the development of metabolic abnormalities (Ellingrod *et al.*, 2012). Again, they may share unhealthy nutritional habits and sedentary lifestyle.

In this study, the three study groups (the MDD, schizophrenic, and control groups) were comparable as regards the presence of hypertension, the WC, and the levels of the laboratory investigations (FBG, serum TGs, serum HDL, and serum cortisol) (Table 2).

This is in agreement with other studies, which concluded that never-medicated newly diagnosed schizophrenic patients showed nonsignificant differences from normal controls as regards serum glucose, cholesterol, and cortisol levels. They also show nonsignificant differences as regards their anthropometric measures (Mohamed *et al.*, 2006).

However, increased serum cortisol levels (>22 and 21.7 μg/dl in male and female patients, respectively) was significantly higher in the MDD group (47.5%) as compared with the schizophrenic (32.5%) and the control group (2.5%) (Table 2).

Stressful life events play an important role in the pathogenesis of depressive disorders and are well established as acute triggers of psychiatric illness (Kendler *et al.*, 2002).

In this study, MetS was found in 25.83% of all study participants. On further analysis, MetS was found in 27.5% patients of the MDD group, 27.5% patients of the schizophrenic group, and 22.5% of the control group (Fig. 2).

The prevalence of MetS in our study groups was near to those reported by previous studies. A meta-analysis performed by Vancampfort *et al.* (2013) has revealed a mean prevalence of 30.5% for MetS in MDD. Moreover, the prevalence of MetS in MDD has been reported in previous studies [27.3% (Ljubicic *et al.*, 2013), 24.5% (Vogelzangs *et al.*, 2007), and 31% (Vancampfort *et al.*, 2013)].

Malhotra *et al.* (2013) performed a systematic review of studies that examined the prevalence of MetS in schizophrenic patients. They stated that the sample size in the drug-naive patients has been less than 100 and that the prevalence of MetS in schizophrenic patients has ranged from 4 to 26% (Malhotra *et al.*, 2013).

Similarly, a meta-analysis has been performed by Reddy *et al.* (2013) about the association of untreated schizophrenia with MetS. The authors stated that 12 studies were identified, in which 893 patients were evaluated. The mean prevalence of MetS was 10.8% (Reddy *et al.*, 2013).

Other studies have also examined the prevalence of MetS in schizophrenic patients; the prevalence rates were also near to ours [19% (Grover *et al.*, 2014), 28% (Bajaj *et al.*, 2013), and 32% (Boke *et al.*, 2008)].

Very few studies have used proper control groups and studies; the studies that have done so suggest that the prevalence of MetS appears to be higher in schizophrenic than in healthy controls (Guveli *et al.*, 2011; Subashini *et al.*, 2011) and comparable to other disorders such as bipolar affective disorder (Correll *et al.*, 2010; Baptista *et al.*, 2011; Ellingrod *et al.*, 2012).

Although antipsychotic medications are considered a cornerstone in MetS development in severe mental illness, the high prevalence of stress and its effect on hypothalamic–pituitary–adrenal (HPA) axis, obesity, insulin resistance, sedentary lifestyle, physical inactivity, smoking, and poor diet is considered a contributing factor in physical morbidity and MetS occurrence in this group of patients (Ohlsen *et al.*, 2005).

In this study, a comparison was made between the MetS patients in the three study groups. This comparison revealed no significant difference as regards the age among MetS patients of the three study groups (Table 3). However, comparison of patients with MetS with those without MetS in each group revealed that, in the control group only, patients with MetS were significantly older (40± 10.17 years) than those without MetS (30.87± 10 years). This difference was not significant in the MDD or the schizophrenic groups (Table 5).

The presence of MetS is significantly higher age in the healthy control group in this study meets the previous reports in the literature. In a secondary data analysis of data from NHANES (2003–2006) survey, Ervin in 2009 reported that the prevalence of MetS increased with each age grouping in both male and female patients

among adults over 20 years of age living in the USA. Under 40 years of age 20% of male and 17% of female patients met the criteria for MetS compared with 52% of male and 54% of female patients over 60 years of age who met the criteria (Ervin, 2009). Similar to the finding in the US population, other researchers across the world, including Canada, Korea, Sweden, France, Brazil, and Portugal reported a direct relationship between age and prevalence of MetS (Lidfeldt *et al.*, 2003; Dallongeville *et al.*, 2005; Marquezine *et al.*, 2008; Cho *et al.*, 2009).

In accordance with our findings, Heiskanen *et al.* (2003) conducted a cross-sectional study at Kuopio University Hospital in Finland with a 6-year follow-up to examine the prevalence of MetS (NCEP ATP III) and depression. No significant difference was found between age and MetS.

Although many attempts have been made to study the sociodemographic predictors of MetS in patients with schizophrenia, none of the sociodemographic variable has emerged as a consistent predictor of MetS (Malhotra *et al.*, 2013). Among the various sociodemographic variables, many studies have shown higher prevalence of MetS in those who are older (Roshdy, 2011; Grover *et al.*, 2012; Sweileh *et al.*, 2012; Medeiros-Ferreira *et al.*, 2013). Kang *et al.* (2011) showed that the relationship of older age with MetS was limited only to male population; however, their study was performed on schizophrenic patients taking clozapine.

The difference between this result and that of the previous studies as regards age difference may be attributed to the smaller sample size in this study. Larger sample size may clarify an age difference in the MetS between the study groups. Moreover, this could be attributed to the fact that, with increasing age in healthy people, there is a decrease in physical activity and an increase in both sedentary lifestyle and medical disorders (e.g. hypertension, atherosclerotic diseases, and DM). In contrast, increasing age in patients with MDD may be associated with frequent episodes of depression, which manifest by poor appetite, poor health, weight reduction, and early mortality, which is also seen in schizophrenia.

In this study, there was no significant difference as regards the sex distribution between MetS patients of the three study groups (Table 3). However, examination of the sex difference between patients with MetS and those without MetS within each group revealed that MetS was significantly more prevalent in female than in male patients in the MDD (72.2 vs. 37.9% and 27.3 vs. 62.1%, respectively) and the schizophrenic group (54.5 vs. 17.2% and 45.5 vs. 82.8%, respectively), but no sex difference was detected between patients with MetS and those without MetS in the control group (44.4 vs. 41.9% and 55.6 vs. 58.1%, respectively) (Table 3).

This could be attributed to the greater prevalence of obesity in female than in male patients, and to the fact that, as body fat increases, so does the number of abnormal metabolic indicators individuals are likely to possess.

Researchers have found no sex differences in the prevalence of MetS in general population (Remsberg *et al.*, 2007; Dunbar *et al.*, 2008).

A cross-sectional study conducted in Australia found no sex-based differences among those with MetS (Dunbar *et al.*, 2008). However, there are sex differences in depression. These results are supported by many studies that showed a significantly greater prevalence of depression in female than in male patients (Kinder *et al.*, 2004; Skilton *et al.*, 2007; Toker *et al.*, 2008; Akbaraly *et al.*, 2009).

However, many previous studies reported no sex differences in the prevalence rates of MetS in patients with schizophrenia (Brunero *et al.*, 2009; Fan *et al.*, 2010; Malhotra *et al.*, 2013).

These results are not supported by the results of previous studies that have reported that MetS is more common in schizophrenic female patients (Huang 2009; Rezaei *et al.*, 2009; Sweileh *et al.*, 2012). Only a few studies have reported a higher prevalence in male patients (Yoon *et al.*, 2008; Kramer *et al.*, 2013). This may be due to ethnic and cultural, and socioeconomic differences among different populations.

Our results have shown no significant difference between MetS patients in the three study groups as regards the marital status, the educational level, the residence, or the presence of a family history of psychiatric disorders, substance abuse, DM, cardiac diseases, or cerebrovascular strokes (Table 3).

On reviewing the literature, occasional studies have reported association of MetS with higher education

level (Grover *et al.*, 2011; Pallava *et al.*, 2012) and marital status (Grover *et al.*, 2013).

In this study, all MetS patients in the schizophrenic group had low socioeconomic level, whereas MetS patients with moderate socioeconomic level were significantly higher in the MDD group (54.5%) than in the control group (44.4%) (Table 3).

This is in agreement with what has been mentioned in a previous study that poor lifestyle habits are associated with MetS in schizophrenic patients (James *et al.*, 2010). Patients characterized by low standards of life were recruited for the study from Kasr Al Aini Hospital. High prevalence of schizophrenic patients in low socioeconomic status had previously been attributed to the social drift phenomenon, in which afflicted or vulnerable individuals tend to lose their occupation and social niche and drift toward pockets of poverty and inner city areas.

In this study, smoking and substance abuse were significantly more prevalent in MetS patients of the schizophrenic group (81.8 and 45.5%, respectively) as compared with MetS patients of the MDD (27.3 and 18.2%, respectively) and the control group (11.1 and 0%, respectively) (Table 4).

There are some studies reporting a higher prevalence of MetS in patients who smoke (Boke *et al.*, 2008; Heiskanen *et al.*, 2003), whereas others have reported no association between MetS and smoking (Brunero *et al.*, 2009). This contradiction could be attributed to the different selection of sample study or the study design. The higher prevalence of smoking and substance abuse in MetS patients with schizophrenia may be attributed to the presence of schizophrenia rather than the presence of MetS.

In this study, the WC and the BMI were significantly higher in MetS patients of the MDD and the schizophrenic groups as compared with those of the control group. These results have shown that more than half (58.1%) of the MetS patients were in the obese category (BMI $>30\,kg/m^2$).

This can be attributed to bad lifestyle factors commonly seen in mentally ill patients, such as physical inactivity, poor dietary habits, smoking, and drinking. McLaren and Marangell (2004) explained that the disease-specific symptoms and behaviors, particularly those that occur during depressive episodes, such as increased appetite, decreased physical activity, and reduced energy expenditure, increase the risk for obesity.

Hatata *et al.* (2009) examined the risk factors of MetS among Egyptian patients with schizophrenia. They found that increased WC and higher BMI emerged as significant predictors of MetS in the sample (Hatata *et al.*, 2009).

Evidence suggests that prior depression may increase the risk for the subsequent development of adiposity (Shelton and Miller, 2010).

A study that aimed to examine in a sample representative of the general population whether depression, anxiety, and psychological distress are associated with MetS (according to the NCEP ATP III and International Diabetes Federation criteria) and its components showed that MetS was associated with depression but not psychological distress or anxiety. Large WC and low HDL-C showed significant and independent associations with depression (Dunbar *et al.*, 2008).

Both MetS and obesity are comorbid with mental health disorders in 45% of cases (Carpiniello, 2012). Obesity and mental health issues are often comorbid in compulsive eating disorders such as night-time eating syndrome and binge eating. Binge eating disorder (De Zwaan, 2001) and night eating syndrome (Cleator, 2012) are widespread in the obese population, and night eating syndrome is associated with obesity (Milano, 2012), anxiety (Vander Wal, 2012), and depression (Grilo, 2012; Milano, 2012; Vander Wal, 2012). Childhood (Halfon *et al.*, 2013) and adult obesity is associated with an increased risk for depression (Scott, 2008; Zhong, 2010; Zhao, 2011).

In this study, the levels of TGs, HDL, SBP, and DBP were not significantly different among MetS patients in the three study groups (Table 4).

This is in agreement with the results of a study conducted in 2010 in which the authors reported a weak association between depression and low HDL-C (Foley *et al.*, 2010). Moreover, another study had shown that there was no significant difference between schizophrenic patients and healthy controls as regards TG, low-density lipoprotein-cholesterol, and HDL-C (Grover *et al.*, 2013).

In this study, the FBG levels were significantly higher in the MetS patients of the MDD group (109.67 ±9.43 mg/dl) as compared with the MetS patients of

the schizophrenic (96±12.31 mg/dl) and the control group (103.82±10.63 mg/dl) (Table 4).

Although body weight is a stronger predictor of depression compared with diabetes (Nichols and Brown, 2003), evidence shows that diabetes, independent of weight status, is linked with higher rates of depression (Bajaj, 2012; Mezuk, 2013).

Diabetes may contribute to depression through the fear and lifestyle restriction potentially associated with receiving this diagnosis (Nouwen, 2010), as well as symptoms such as hyperglycemia-induced fatigue (Nouwen, 2010). Indeed, there are peaks in antidepressant use after a diagnosis of diabetes (Kivimaki, 2010) and when treatment begins (Knol, 2009).

The mechanisms that underlie the associations between depression and onset of type 2 diabetes are unclear (Engum, 2007). Symptoms of depression may predict diabetes independently or through established risk factors for diabetes.

Lifestyle factors, metabolic factors, and neuro-endocrinological factors have been linked to increased risks of developing diabetes in individuals with depressive symptoms. Possible mechanisms include the influence of depressive symptoms on behavioral factors, such as sedentary lifestyles, smoking, and overeating, resulting in metabolic disturbances, which may explain the onset of diabetes. Altered activities in the HPA axis with cortisol elevations during depressive episodes, which affect approximately half of all patients, may also increase the risk for type 2 diabetes (Brown *et al.*, 2004).

Depression is at least twice as common among those with diabetes and is associated with a more unfavorable prognosis (Anderson *et al.*, 2001).

A recent systematic review and meta-analysis found a small but significant cross-sectional association between depression and insulin resistance (Kan *et al.*, 2013). Individuals with insulin resistance who are overweight or obese, with MetS (Akbaraly *et al.*, 2009; Almeida *et al.*, 2009) or with abdominal obesity and MetS (Hamer *et al.*, 2012) are more likely to develop depression.

However, some literature point toward little or no association between MetS/insulin resistance and depression (Adriaanse *et al.*, 2006; Shen and Bergquist-Beringer, 2013).

This difference may be attributed to the difference in the study sample, such as selection of the sample in early stages of illness or the proper medical care for psychiatric patients for early detection and management of metabolic abnormality.

Patients with schizophrenia appear to have higher rates of impaired glucose tolerance, insulin resistance, and type II DM compared with the general population (Ryan and Thakore, 2002).

In a study by Ryan *et al.*, 2004, 15.4% of the drug-naive, first-episode patients with schizophrenia had impaired fasting glucose tolerance, compared with none of the matched healthy individuals. The patients also had higher levels of plasma glucose, insulin, and cortisol and were less insulin sensitive compared with controls. The authors stated that the findings of this and other studies suggest that the illness of schizophrenia is associated with various aspects of the MetS, which in turn may explain why patients with this illness die prematurely.

In the present study, serum cortisol levels were significantly higher in the MetS patients of the MDD (24.52±11.56 μg/dl) and the schizophrenic group (23.17±7.25 μg/dl) as compared with the MetS patients of the control group (15.51±3.4 μg/dl). Moreover, the presence of an increased level of serum cortisol (>22 and 21.7 μg/dl in male and female patients, respectively) was significantly more in the MetS patients of the MDD (54.5%) and the schizophrenic groups (72.7%) as compared with the MetS patients of the control group (0%) (Table 5).

This is in agreement with Vogelzangs *et al.* (2007), who conducted a study to investigate the cross-sectional relationship between depression, urinary cortisol, and MetS in an older population. Their results suggested a synergistic relationship between depression, cortisol, and the MetS in an elderly population. They concluded that individuals with hypercortisolemic depression in particular may be at risk of having the MetS, and therefore have an increased risk of developing cardiovascular disease or diabetes (Vogelzangs *et al.*, 2007).

Moreover, schizophrenia is also associated with abnormalities of the HPA axis. In the study by Chan *et al.* (2011), a meta-analysis was performed for examining blood-based biomarkers of schizophrenia. They stated that the process was accompanied by altered cortisol levels, which suggested activated stress

response and altered HPA axis function in patients with schizophrenia (Chan *et al.*, 2011).

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Conflicts of interest
There are no conflicts of interest.

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