

Prevalence and Determinants of Metabolic Syndrome in Schizophrenia Patients Treated with Antipsychotics Medications

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Abstract

Objectives

This study was designed to assess the demographic characteristics, prevalence of metabolic syndrome (MetSy) among patients with schizophrenia in Saudi Arabia.

Methods

This is a disease-oriented and observational study. Schizophrenia was defined by DSM-IV criteria. MetSy were assessed based on the international criteria (NCEP-ATP III and AHA/NHLB).

Results

90% of the participants are without a university degree and 56.4% are single. Chronic and acute cases of schizophrenia were 95% and 5%, respectively. The treatment of schizophrenia was combination therapy and monotherapy with percentages of 56% and 44%, respectively. Systolic and diastolic blood pressures were 121.92 ± 11.07 mmHg and 77.29 ± 0.45 mmHg, respectively. Surprisingly, all patients have abnormal HDL. A mean waist circumference of 90.23 ± 14.88 cm for men, and 93.38 ± 15.28 cm for women. The analysis of 101 patients showed a prevalence of the MetSy is 15.8%. Chi-square test of independence showed lack of independency of MetSy on type of therapy. Modeling of MetSy and risk factors was also conducted.

Conclusion

The metabolic syndrome is greatly established among schizophrenic patients. It signifies a vital hazard for metabolic and cardiovascular ailments. Evaluation of the incidence and examining of the related threats of the metabolic syndrome should be an element of the clinical managing of patients cured with antipsychotics.

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Introduction

Schizophrenia is a mental illness that influences about one percent worldwide. Schizophrenic patients have shorter life span as balanced to their healthy associates [1,2]. Mortality and morbidity among patients with schizophrenia has been related to high occurrence of cardiovascular diseases and metabolic syndrome (MetSy) [3,4]. Olanzapine, amisulpride, quetiapine, risperidone, clozapine are the most frequently used anti-schizophrenic drugs in Saudi Arabia (KSA) with no previous research reported to evaluate their side effects [5]. Weight gain, obesity, increased risk for dyslipidemia, accelerated cardiovascular ailment, diabetes, and premature fatality have been connected to drugs in this group as well. Previous research showed that Saudi patients on antipsychotic medications acquire numerous risk factors. The need for detailed studies on these issues is supported by a metabolically unwanted postnatal and gestational environment, which is common in the KSA, adjoins to the receptivity of the previously genetically predisposed people to a lifetime of insulin resistance. Moreover, the prevalence of ordinary risk factors for diabetes mellitus type 2, such as the full MetSy and its individual indicators and criteria, has been documented in Saudi adults, 37% of whom have the full MetSy [6-8]. Literature survey is indicative of an urgent demographical study and epidemiological assessment to determine individuals affected with schizophrenia, this will appendage the ways to create strategy to address different issues pertaining to structural alterations in health care services provided to the mentally ill patients in KSA. 22.4% of Saudi patients reporting to services for mental disorders are suffering from schizophrenia [9-11].

Earlier studies were only highlighted on the incidence of mental sickness without attempt to examine the characteristics of schizophrenia [12,13]. Nevertheless, a few studies have revealed that amongst all the psychoactive drugs, antipsychotics were intensely used and the promptness was noticed to be considerably increased in the case of inpatients balanced with out-patients [14,15]. Side effects of antipsychotic medications in KSA have been reported [16] with, no specific research conducted on the prevalence of MetSy on schizophrenic patients using antipsychotic medications. Therefore, the current study was designed

to assess the demographic characteristics, prevalence of MetSy and metabolic abnormalities among Saudi schizophrenic patients. Correlation between MetSy and risk factors among schizophrenic patients was examined as well.

Methods

Research Design, Selection Criteria and Sample Size Determination

This is disease-oriented and observational study was conducted in Saudi Arabia from August 2016 until December 2016. All patients attending Jazan Psychiatric Hospital Center during the course of the study with the next criteria were requested to contribute: 1) their age should be above 16 years old, and 2) they were recognized with schizophrenia as stated by DSM-IV criteria [17]. In order to evaluate with sufficient accuracy the prevalence of MetSy, we used 22.4% as a previous prevalence of MetSy for sample size calculation (99% confidence interval $\pm 10\%$). A sample size of at least 100 patients was recruited. On the measurement day, demography and clinical data were collected. The following types of information were collected: age, gender, marital status, occupation, admissions history, length of psychiatric illness, antipsychotic medications; waist circumference (WC), weight and height, fasting plasma glucose (FPG) measured in mg/dL, and lipid profile.

Quality Control

Focus group discussions were conducted to preserve consistency and rationality of the research data acquiring process. Evaluations were done regularly during the study to recognize any troubles in data collection, the elucidation of variables, and the application of study guidelines. Before starting data analysis, a wide sequence of checks was done for data uniformity, suitable sequences of data, and an assessment of incomplete or missing data. The questionnaire was modified by the principal researchers and the customized version was checked by experts to guarantee construct and content validity. Data from the pre-test assessment was not incorporated in the final analysis.

Ethical Approval

Approval to conduct the study was obtained from Standing Committee for Biomedical Research Ethics

(SCBRE) at Jazan University (Approval No. 37/60/37532). A written consent was obtained to use the medical records according to the local regulations. Metabolic screening and blood tests for schizophrenia patients were considered standard of care in schizophrenia treatment in Psychiatry and Mental Health Centers according to European and American Standards [18,19]. Therefore, the ethical committee approved that obtaining blood samples did not hinder as this observational study. Medical cases such as schizophrenia in themselves were no longer referred to be an obstacle to individual permission or research contribution. If the consent is going to be obtain from a proxy, the consent of the participant is still always necessary [18].

The Antipsychotic Use Patterns

The types and dosages of antipsychotic medications were obtained. The number of antipsychotics used was classified as monotherapy, presently using only one type of antipsychotic medication, and combination, presently taking more than one type of antipsychotic. Medical data concerning the period of current antipsychotic treatment or preceding antipsychotic treatment was not attained due to restrictions related to information in their documents.

Waist Circumference, Weight and Height

Waist circumference (WC) was obtained by a stretched tape-meter, without any force to the body exterior, and was recorded to the closest 0.1 cm. The waist measurement was obtained with the tape-meter in a horizontal plane, midway between the inferior margin of the ribs and the superior border of the iliac crest [20]. To avoid inter-researcher inaccuracy, all measurements were obtained by the same person. We utilized a portable spring balance to measure weight. The scale was obtained to zero before weighing. The weight is recorded to nearest 0.1Kg. Height is the distance from the crown of the head to the soles of the feet. The subject stood erect and bare foot on stadiometer with movable head piece was leveled with skull vault and height was recorded to nearest 0.1cm.

Blood Pressure

Blood pressure (BP) was measured in a sitting position. Two measurements were taken made by two independent medical officers in the right arm after the participant sat and rested for at least 5 min. In case of

difference in BP reading, a third one was obtained out and the arithmetic mean was calculated.

Fasting Blood Pressure

For fasting plasma glucose (FPG), blood samples were obtained from all fasted participants in the morning while they were in a sitting position according to the standard protocol. Blood was obtained from an antecubital vessel punctures. Blood samples were centrifuged within 30 to 45 minutes of collection. Glucose in plasma was measured using Chemistry Auto-analyzer.

Biochemical Analysis

Fasting plasma samples were used to conduct biochemical analysis. Lipid profile was performed at Jazan Psychiatric Hospital laboratory on the day of blood collection. For lipid measurement, LDL-C, HDL-C, TC, and TG were measured using commercially available kit. The MS was defined according to ATP III and NCEP definitions as shown in Table 1[21].

Statistical Analysis

Descriptive statistics included frequencies and percentages were calculated for all categorical variables. Means and standard deviations were obtained for all continuous variables. Inferential statistics including t-test and Chi-square test were performed for mean differences and association, respectively. Risk factors for MetSy were analyzed using logistic regression. The presence of MetSy was used as the dependent categorical variable. SPSS for Windows was used to analyze the data. The conventional 5 percent significance level was used throughout the study.

Results

The current study includes 101 schizophrenic patients recruited according to meet the diagnostic criteria defined by DSM-IV. 90% of the participants are without a university degree and 56.4% are single. The age ranged between 18 and 69 years, with upper and lower quartiles of 38 and 42 years, respectively. Women had a mean age of 38.69±14.89 years, for men it was 40.98±11.13 years. For details on demographics, see Table 2. Chronic and acute cases of schizophrenia were 95% and 5%, respectively (Table 3). The mean time since first diagnosis was 12.70±8.77 years, ranging from 2 to 38 years. 59.4% of the patients were admitted to

Table 1. Definitions and reference ranges for metabolic syndrome according to NCEP-ATP III and AHA/NHLB

Risk factor	Defining measure NCEP	ATP III Defining measure AHA/NHLB
Abdominal obesity (waist circumference)		
Men	> 102 cm	≥102 cm
Women	> 88 cm	≥88 cm
Triglycerides	≥ 150 mg/dL	≥ 150 mg/dL or on drug treatment for elevated triglycerides
High density lipoprotein (HDL)		
Men	< 40 mg/dL	< 40 mg/dL or on drug treatment for reduced HDL-cholesterol
Women	< 50 mg/dL	< 50 mg/dL or on drug treatment for reduced HDL-cholesterol
Blood pressure	Systolic ≥ 130 or diastolic ≥ 85 mmHg	Systolic ≥ 130 or diastolic ≥ 85 mmHg or on anti-hypertensive medication
Fasting glucose	≥ 110 mg/dL	≥ 100 mg/dL or on antidiabetic medication

Abbreviations: AHA/NHLB = American Heart Association/National Heart, Lung and Blood Institute; NCEP-ATP III = National Cholesterol Education Program, Adult Treatment Panel 3rd report. According to both definitions, a diagnosis of metabolic syndrome is established if at least three of the above risk factors are present.

the hospital at least a once during the last 12 months with average of 12 days per admission. Adherence to the treatment of schizophrenia is shown in Table 3, whereby, 72.4% of the studied sample was partially adhered to the treatment. And the treatment of schizophrenia was combination therapy and monotherapy with percentages of 56% and 44%, respectively. As shown in Table 4, 25% of the sample uses valporate as a concurrent non-antipsychotic medication. It is also observed that 50.5% of patients are using combined medications, while resperidone, haloperidol and olanzapine were used by 17.8%, 9.9% and 8.9%, respectively, of sample.

Measurements of metabolic syndrome indicators according to the guidelines (Table 1) are depicted in Table 5. Systolic and diastolic blood pressures were 121.92±11.07 mmHg and 77.29±.45 mmHg, respectively. Surprisingly, all patients have abnormal HDL with an average of 18.63±5.23. A mean waist circumference of 90.23 ± 14.88 cm for men, and 93.38 ± 15.28 cm for women indicated overweight in a considerable proportion of the patients. Anthropometric

parameters of weight and height are shown in Table 5. As shown in Figure 1, the prevalence of metabolic syndrome among schizophrenic patients as defined by the Adult Treatment Panel (ATP) III in 2001 is 15.8%.

This study included metabolic syndrome (16 metabolic syndrome and 84 non-metabolic syndrome) and type of therapy (44 monotherapy and 56 combination the). A 2X2 chi-square test of independence was used to determine if metabolic syndrome is dependent on type of therapy. Given $\alpha = 0.05$, the results suggest lack of dependency, $\chi^2(1, N = 101) = 0.278, p = 0.598$. The results also show that metabolic syndrome is independent of the participants gender ($P > 0.05$). The mean age for metabolic syndrome ($n = 16$) and no metabolic syndrome ($n = 85$) was statistically compared using a two-tailed independent sample t -test at $\alpha = 0.05$. The results suggest that average metabolic syndrome scores ($M = 48.63, SD = 11.212$) are significantly greater than average no metabolic syndrome scores ($M = 39.19, SD = 11.135$), $t(99) = 3.107, p = 0.002$. Logistic regression model findings are shown in Table 6. Variables included in the

Table 2. Demography of the study sample

Variable	Frequency	Percentage
Nationality		
Saudi	98	97.0
Non-Saudi	3	3.0
Gender		
Male	88	87.1
Female	13	12.9
Marital status		
Single	57	56.4
Married	30	29.7
Divorced	14	13.9
Educational level		
Illiterate	28	27.7
Primary	20	19.8
Intermediate	21	20.8
Secondary	26	25.7
University degree	6	5.9
Financial situation		
High	1	1.0
Normal	34	33.7
Poor	64	63.4
None	2	2.0
Occupation		
Government employee	4	4.0
Free businesses	1	1.0
House wife	2	2.0
Retired	22	21.8
Unemployed able to work	29	28.7
Unemployed unable to work	43	42.6
Classification of housing type		
Rural	64	63.4
Urban	37	36.6
Accommodation type		
Residence	60	60.0
Rent	28	28.0
Private House	12	12.0
Age (years)		
(Mean±SD)	40.68±11.62	
Upper and lower quartiles	38 and 42	
Number of family members(Mean±SD)	7.83±3.39	

Table 3: Patients and schizophrenia characteristics

	Frequency	Percentage
Status		
Chronic disease	96	95.0
Acute disease	5	5.0
Treatment adherence		
Consistently adhered	25	25.5
No adherence treatment	2	2.0
Partially adhered	71	72.4
Hospital admission (Last 12 months), days		
1	60	59.4
2	29	28.7
3	10	9.9
4	1	1.0
5	1	1.0
Days admitted (Last 12 months)	12.70±8.77	
Duration since initial diagnosis	106.51±119.41	
Type of therapy		
Monotherapy	44	44.0
Combination therapy	56	56.0

Table 4. Pattern of use of non-antipsychotic and antipsychotic drugs

	Frequency	Percentage
Non-antipsychotic drugs		
Valporate	25	25.0
Benzotropine	13	13.0
Benzhexol	1	1.0
Valporate+Benzhexol	1	1.0
None	60	60
Antipsychotic		
Olanzapine	9	8.9
Risperidone	18	17.8
Quetiapine	2	2.0
Amisulpiride	5	5.0
Haloperidol	10	9.9
Aripirazole	3	3.0
Trifluoperazine	2	2.0
Paliperidone	1	1.0
Combined medications	51	50.5

Table 5. Measurements of metabolic syndrome indicators according to the guidelines

	Mean	SD	Normal (n,%)	Abnormal (n,%)
Systolic Blood Pressure	121.92	11.07	87(86.1)	14(13.9)
Diastolic Blood Pressure	77.29	6.45	92(91.1)	9(8.9)
Triglycerides (mg/dl)	26.56	16.44	74 (73.3)	27(26.7)
HDL-C (mg/dl)	18.63	5.23	100 (100)	0(0)
LDL (mg/dl)	45.14	17.30		
Waist Circumference	90.61	14.89	74(73.3)	27(26.7)
Fasting Blood Glucose FBG (mg/dl)	91.53	29.95	81(80.2)	20(19.8)
BMI (kg/m ²)	61.02	3.04		
Height (cm)	164.25	7.94		
Weight (kg)	69.31	17.09		

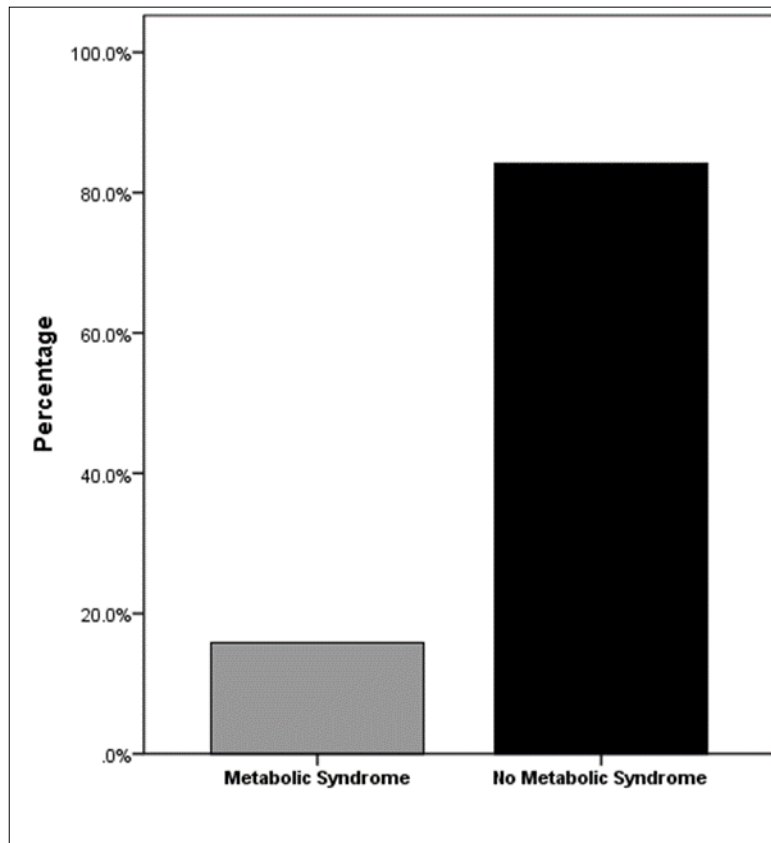


Figure 1. Prevalence of metabolic syndrome among schizophrenic patients as defined by the Adult Treatment Panel (ATP) III in 2001 [21].

model were gender, age, residence, accommodation type, number of family members and duration. Odd ratios for all variables are shown in Table 6 with their upper and lower confidence intervals. OR considered statistically significant if the intervals don't enclose the value of 1. In the current study, only age and duration are the significant factors with the values of 0.855 and 1.121, respectively. At 0.05 level of significance, only age and duration of the disease have contributed significantly in the development of MetSy.

Discussion

The current study was designed to assess the demographic characteristics, prevalence of MetSy and metabolic abnormalities among Saudi schizophrenic patients. Correlation between MetSy and risk factors among schizophrenic patients was examined as well. Side effects of antipsychotic medications in KSA have been reported and were found to be associated with numerous risk factors, such as overweight, dyslipidemia, obesity and smoking [16, 21-23]. However, no specific research was conducted on the prevalence of MetSy on schizophrenic patients undergoing antipsychotic

medications. A recent study noticed that patients on antipsychotic drugs in Saudi Arabia possess numerous risk factors [14]. Prevalence of MetSy among patients with various psychiatric diagnoses and treatments were also reported with no an in-depth emphasis on schizophrenic patients and that study also did not consider Jazan region [24]. Whereby, our study only focuses in Jazan region.

Amisulpride, olanzapine, risperidone, clozapine, quetiapine are the most commonly used anti-schizophrenic medications in KSA with no previous studies reported to assess their unwanted side effects specially on schizophrenic patients [5, 24]. The need for detailed research on this matter is compounded by a metabolically undesirable postnatal and gestational environment, which is widespread in the KSA, adjoins to the receptiveness of the already genetically predisposed person to a lifetime of insulin resistance and associated morbidities [25]. More, the prevalence of conventional risk factors for diabetes mellitus type 2, such as the full metabolic syndrome (MetSy) and its individual symptoms and criteria, have been reported in adult

Table 6. logistic regression model

Variables	B-coefficient	P-value	OR	95% C.I. for OR	
				Lower	Upper
Gender					
Male	1.468	0.106	4.340	0.734	25.681
Female (reference)					
Age*	-0.157	0.001*	0.855	0.782	0.935
Marital status		0.999			
Divorced(reference)					
Single	-0.035	0.975	0.966	0.114	8.160
Married	-0.003	0.998	0.997	0.112	8.886
Residence		0.945			
Urban (reference)					
Rural	0.049	0.954	1.051	0.197	5.615
Accommodation type		0.249			
Private House (reference)					
Residence	-2.203	0.131	0.110	0.006	1.922
Rent	-3.123	0.098	0.044	0.001	1.784
Number of Family members	0.029	0.805	1.030	0.815	1.301
Duration*	0.114	0.017*	1.121	1.021	1.231
Constant	29.067	0.999	420		

Saudis, 37% of whom have the full MetSy, while just recently partial MetSy [21, 26]. The published literature survey is suggestive of an urgent demographical analysis and epidemiological survey to ascertain number of individuals affected with schizophrenia, this will pave the ways to formulate strategy to address various issues pertaining to structural adjustments in health care services provided to the mentally ill patients in KSA.

The prevalence (15.8%) of MetSy among schizophrenic patients in our study is lower than that reported in other studies with Asians including reports from Thailand (22.8%), Taiwan (34.9% and 23.8%), Japan (27.5%), and Korea (31.7%) and was more comparable to the rates reported from western countries. The current study used NCEP and ATP III criteria which considered abdominal obesity (waist circumference) to be more than 88cm, whereby these countries used a lower criterion (≥ 80 cm) of abdominal obesity than we did (≥ 88 cm). Previous studies on MetSy obtained in the Arabian world are not many. A study carried in 63 Egyptian schizophrenic patients to investigate the risk factors of MetSy using the IDF criteria found that twenty four schizophrenic patients (38.09%) met the criteria for MetSy [27]. Another research conducted using 220 UAE psychiatric inpatients found that the prevalence of MetSy was about 48.1% [28]. To get also more comparable results; we can consider a Palestine study which recruited 250 patients with schizophrenia. The MetSy prevalence was assessed based on Adult Treatment Panel III Adapted criteria. The overall MetSy prevalence among patients with schizophrenia in Palestine was 43.6% [29]. Current studies on MetSy in the general population have certainly supplied substantiation for the expansion of ethnic-/race-specific criteria. Even though there is a substantial discrepancy in criteria and methodology among published studies, the MetSy prevalence in our study was within the range of prior reports published regionally and worldwide. It is difficult to identify the reasons for this discrepancy because many factors affect the development of MetSy, including medication, age, gender, definition of MetSy, and lifestyle. However, one of the important causes may be the trend for an increase in obesity and MetSy during the past two decades in the Saudi healthy population. A community-based study (n=17,293) has reported that

the overall age-adjusted prevalence of MetSy in Saudi subjects is 39.3%.25. Another study conducted using total of 4578 Saudis aged 15-64 selected from 20 regions in Saudi Arabia showed the prevalence of 28.3% [21].

Predisposing and risk factors for MetSy of the Saudi population are a warranting feature of schizophrenic patients [21, 22, 30]. Our current study revealed new findings on the prevalence of MetSy and its associated risk factors among schizophrenic patients. The present findings may highlight the serious need for metabolic screening and supervision particularly among older patients with chronic schizophrenia. Further future studies are required to corroborate the current results and assess different preventive initiatives to address metabolic disturbances in the population with schizophrenia.

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Competing Interests

The authors declare that they have no competing of interests.

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