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Metabolic Syndrome and Related Factors in Patients with Schizophrenia

Necla Keskin[1], **Yağmur Güzel**[2]

1 University of Health Science Diyarbakır Gazi Yaşargil Training and Research Hospital*, Department of Psychiatry, Diyarbakır, Türkiye*

2 University of Health Science Diyarbakır Gazi Yaşargil Training and Research Hospital*, Department of Child and Adolescent Psychiatry, Diyarbakır, Türkiye*

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Abstract

Aim: To assess the prevalence rate of metabolic syndrome (MetS) in patients with schizophrenia and to determine related socio-demographic features and clinical characteristics.

Methods: Fifty-five inpatients diagnosed with schizophrenia were included. A demographic and clinical data form was completed. The laboratory results were retrieved from the hospital information system. Patients' weight, height, waist circumference, and blood pressure were measured. The diagnosis of MetS was made based on the NCEP ATP III (Adult Treatment Protocol of the National Cholesterol Education Program), ATP III-A (Adapted) and IDF (International Diabetes Federation) criteria.

Results: The prevalence rate of MetS was 38.2% according to the IDF and 25.5% based on ATP III and ATP III-A criteria. The mean age, duration of illness, length of medication use, and time between symptom onset and diagnosis were significantly higher in patients with schizophrenia with MetS ($p<0.05$). The groups differed significantly in height, weight, and body mass index (BMI) ($p<0.05$). Regarding the MetS criteria, there was a significant difference between groups in waist circumference, fasting triglycerides, and fasting HDL levels ($p<0.05$). Patients with MetS were more frequently treated with depot antipsychotics ($p<0.05$).

Conclusion: Patients with schizophrenia are at a high risk of MetS. This risk increases with age, a longer duration of illness, extended medication use, and the use of depot antipsychotics. BMI, waist circumference, and lipid profile are the most significant variables in predicting MetS. Since MetS is often asymptomatic, regular monitoring of these parameters and early recognition of MetS are essential.

Keywords: Schizophrenia, metabolic syndrome, body mass index

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Correspondence / Yazışma Adresi: *Necla Keskin Ozdemir, University of Health Science Diyarbakır Gazi Yaşargil* Training and Research Hospital*, Department of Psychiatry, 21070 Diyarbakır, Türkiye e-mail: neclakeskin@yahoo.com.tr*

Şizofreni Tanılı Hastalarda Metabolik Sendrom ve İlişkili Faktörler

Öz

Amaç: Bu çalışma, şizofreni tanısı almış hastalarda metabolik sendrom (MetS) yaygınlığı ile ilişkili sosyodemografik ve klinik özellikleri belirlemeyi amaçlamıştır.

Yöntemler: Çalışmaya 55 şizofreni tanılı yatan hasta dahil edildi. Demografik ve klinik veri formu dolduruldu. Laboratuvar sonuçları hastane bilgi sisteminden tarandı. Hastaların boy, kilo, bel çevresi ve kan basıncı ölçümleri yapıldı. MetS tanısı, NCEP ATP III, ATP III-A (uyarlanmış) ve Uluslararası Diyabet Federasyonu (IDF) ölçütlerine göre koyuldu.

Bulgular: MetS yaygınlığı, IDF kriterlerine göre %38,2, ATP III ve ATP III-A kriterlerine göre ise %25,5 olarak bulundu. MetS tanısı alan şizofreni hastalarında ortalama yaş, hastalık süresi, ilaç kullanım süresi ve belirtilerin başlangıcı ile tanı alma arasındaki süre anlamlı olarak daha yüksekti ($p<0.05$). Gruplar boy, kilo ve vücut kitle indeksi (VKİ) açısından anlamlı düzeyde farklılaştı ($p<0.05$). MetS ölçütlerinden bel çevresi, açlık trigliserit ve açlık HDL düzeylerinde gruplar arasında anlamlı fark bulundu ($p<0.05$). MetS tanısı alan hastaların depo antipsikotik kullanım oranları daha yüksekti ($p<0.05$).

Sonuç: Şizofreni tanılı hastalar MetS açısından yüksek risk taşımaktadır. Bu riski; artan yaş, uzayan hastalık ve ilaç kullanım süresi ile depo antipsikotik kullanımı artırmaktadır. VKİ, bel çevresi ve lipid profili MetS'nin en belirleyici parametreleri olarak öne çıkmaktadır. Bu parametrelerin düzenli olarak izlenmesi ve erken dönemde tanı koyulması, MetS genellikle asemptomatik seyrettiğinden büyük önem taşımaktadır.

Anahtar kelimeler: Şizofreni, metabolik sendrom, vücut kitle indeksi.

INTRODUCTION

Schizophrenia is a severe, chronic, and disabling brain disease characterized by the presence of positive symptoms such as hallucinations, delusions, disorganization, and negative signs, including amotivation, diminished emotional expression, avolition, and cognitive impairment[1]. According to the DSM-5-TR, significant functional impairment must be observed since symptom onset and continuous signs of schizophrenia must persist for at least 6 months, including at least 1 month of symptoms, which might be less if successfully treated[2].

Schizophrenia affects 1% of people around the world and is estimated to be more prevalent in males[3]. Schizophrenia is considered to be a life-shortening disease, and compared to the general population, life expectancy in patients with schizophrenia is reduced by 15-20 years[3,4]. Patients with schizophrenia are at increased risk of suicidal thoughts and behaviors, and suicide is a major cause of premature death in schizophrenia[4]. Schizophrenia can also lead to physical complications and premature mortality due to preventable natural causes, such as cardiovascular disease, infections, respiratory tract diseases, and cancer, alongside unnatural causes like suicide, homicide, and accidents[1,4]. An unhealthy and sedentary lifestyle, including reduced physical activity and poor diet, smoking, alcohol/substance abuse, disease-related factors, such as metabolic abnormalities, and difficulty in accessing treatment due to psycho-social reasons, such as stigmatization, may contribute to physical morbidity[4,5].

Metabolic Syndrome (MetS) is an accumulation of risk factors for the development of cardiovascular disease that includes central obesity, insulin resistance, hypertension, and dyslipidemia[6-8]. The most widely used definitions of the MetS are NCEP ATP III (Adult Treatment Protocol of the National Cholesterol Education Program) (2001), ATP III-A (AHA/NHLB1: American Heart Association / National Heart, Lung, and Blood Institute,

adapted by Grundy et al. 2005) and IDF (International Diabetes Federation) (2005) criteria[6-8]. According to these definitions, the same threshold values were determined for blood pressure, fasting triglyceride, and HDL cholesterol levels[10-12]. Different threshold values were determined for fasting blood glucose and abdominal circumference[10-12]. ATP III and ATP III-A criteria are defined as meeting at least three of five clinical criteria, and the IDF criterion is defined as the presence of at least two more criteria, along with the abdominal circumference criteria[6-8].

MetS is highly prevalent and is associated with increased cardiovascular morbidity and mortality in patients with schizophrenia[4,9]. In a meta-analysis, the overall rate of MetS in patients with schizophrenia was reported to be 32.5%, and this rate was especially influenced by the duration of illness[10]. It was also noted that there were only minor differences in the rates of MetS reported across countries and treatment settings (inpatient vs outpatient), with no appreciable difference found between genders[10]. On the other hand, in a recent meta-analysis conducted by Salari et al., the pooled prevalence of MetS in schizophrenia patients was found to be 41.3%, with significant heterogeneity among studies, and the highest prevalence was reported in France (79.1%) while the lowest was in China (18.03%)[11]. In our country, the prevalence rate of MetS in patients with schizophrenia was reported to vary between 18.9% and 47.1% in different studies that used varying diagnostic criteria for MetS[12,13].

Antipsychotics are the primary medications used in the treatment of schizophrenia and are particularly effective in managing positive symptomatology[4,14]. The frequency of extrapyramidal side effects has decreased with the use of second-generation antipsychotics; however, the risk of cardiometabolic dysfunction has notably increased[14]. Second-generation antipsychotic medications can lead to rapid weight gain, dyslipidemia, hypertension, and type 2 diabetes mellitus. These adverse effects elevate the risk of cardiovascular disease and contribute to negative health outcomes, particularly due to factors such as the sedentary lifestyle of patients and negative symptoms[15]. Despite the well-documented cardiometabolic adverse effects of second-generation agents, long-term antipsychotic use significantly decreases long-term all-cause mortality, including rates of suicide and cardiovascular mortality, in patients with schizophrenia[4]. However, poor adherence to and disengagement from mental health treatment may hinder the effective management of schizophrenia[16].

We hypothesized that the prevalence of MetS is higher in patients with schizophrenia and that the risk is influenced by age, illness duration, and the duration and type of antipsychotic medication used. This study aimed to provide prevalence data from an eastern region of our country, identify sociodemographic and clinical factors associated with MetS, and evaluate the impact of antipsychotic treatment patterns on metabolic risk. By identifying these risk factors at an early stage, we aimed to emphasize the importance of routine screening and integrated care, thereby contributing to the prevention of metabolic complications and enhancing overall health outcomes in this vulnerable population.

METHODS

Study setting and subjects

This is a cross-sectional study aimed to assess MetS and related factors in patients with schizophrenia hospitalized in the psychiatry inpatient unit of a tertiary care hospital in the eastern region of Turkey between April 2018 and April 2019. Patients with mental retardation, those who were pregnant or lactating, and those who were clinically unstable and unable to participate in the assessments were excluded. The inclusion criteria were as follows: (1) age ≥ 18 years, (2) a confirmed diagnosis of schizophrenia according to the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I)[17], and (3) ability to provide informed consent. Of the 62 patients who initially consented to participate, 7 were

excluded due to missing laboratory test results. The final study sample consisted of 55 patients.

Procedures and assessment instruments

A demographic data form for socio-demographic features and another for clinical characteristics of schizophrenia were completed by the staff psychiatrist. The laboratory results were retrieved from the hospital information system. Patients' weight, height, waist circumference, and blood pressure were measured by a clinic nurse at hospital admission. For statistical purposes, patients with primary education or lower, those who have been divorced, and those who have never been married were grouped; housewives, students, and retired patients were categorized with the unemployed group. Patients who consume caffeinated drinks several times a day (at least two) or consume caffeine after 5:00 p.m. were classified as "caffeine users". The diagnosis of MetS was made based on the ATP III, AHA/NHLB1 (ATP III-A), and IDF criteria. Three of the five criteria are necessary for the diagnosis of MetS based on ATP and ATP III-A, and IDF requires the presence of abdominal obesity along with at least two of the following four criteria. The MetS criteria are shown in Table 1.

Table I: Metabolic Syndrome Criteria

	ATP III	***ATP III-A***	***IDF***
Waist circumference	≥ 102 cm for males ≥ 88 cm for females	≥ 102 cm for males ≥ 88 cm for females	≥ 94 cm for males ≥ 80 cm for females
Hypertension or anti-HT use Systolic blood pressure Diastolic blood pressure	≥ 130 mm Hg and/or ≥ 85 mm Hg	≥ 130 mm Hg and/or ≥ 85 mm Hg	≥ 130 mm Hg and/or ≥ 85 mm Hg
Hypertriglyceridemia or treatment for this disorder	Triglyceride≥150 mg/dl	Triglyceride≥150 mg/dl	Triglyceride≥150 mg/dl
Low HDL-C	< 40 mg/dl in males < 50 mg/dl in females	< 40 mg/dl in males < 50 mg/dl in females	< 40 mg/dl in males < 50 mg/dl in females
High fasting plasma glucose or a diagnosis of T2DM	≥ 110 mg/dl	≥ 100 mg/dl	≥ 100 mg/dl

** anti-HT: antihypertensive T2DM: Type 2 diabetes mellitus ATP III/ATP III-A: Three of the five criteria are necessary for the diagnosis of metabolic syndrome. IDF requires the presence of abdominal obesity along with at least two of the following four criteria.*

Psychometric Tests

Global Assessment of Functioning (GAF) Scale: The functionality of patients was evaluated using the GAF Scale (DSM-IV-TR). GAF scale is a quick and simple test used to measure psychological, social, and occupational functioning and the severity of illness in psychiatry. GAF is Axis V of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition Text Revision (DSM-IV-TR). Although GAF was excluded in DSM-5 and replaced by the WHO Disability Assessment Schedule (WHODAS 2.0) to increase the reliability of scores, within the limits of the indicators used, GAF is proven to be a reliable and valid measure[18]. Scores range from 1 to 100, indicating severely impaired to extremely high functioning.

Compliance with Ethical Standards

Ethics approval for the study protocol was obtained from the institutional review board. The study was conducted per the Declaration of Helsinki.

Statistical Analysis

Statistical analysis was performed using the SPSS for Windows version 24.0 software. Descriptive statistical analyses were conducted to evaluate the sample group. Frequencies and rates of categorical variables were identified. The patients were divided into two groups based on whether they were diagnosed with or without MetS. The groups were compared regarding socio-demographic and clinical features. The assumption of normality was assessed using the Shapiro-Wilk test. The t-test was applied to compare parametric continuous variables if the sample was normally distributed. The Mann-Whitney U test was used to compare differences between two independent groups when the dependent variable was either ordinal or continuous. The chi-squared test was employed to compare categorical variables. All p-values were two-tailed and $p < 0.05$ set as the cut-off for statistical significance.

RESULTS

The socio-demographic features of the sample group and the comparison of the socio-demographics of schizophrenia patients with and without MetS are shown in Table 2. The mean age of the sample group was 36.9±10.8 years (ranging from 19 to 68 years). The majority of patients were male (72.7%), single (65.5%), unemployed, had an education level of primary school or below (63.6%), were of low socioeconomic status (65.5%), lived in a county (69.1%), and resided in a nuclear family setting (70.9%). Half of the patients reported having sufficient social support. The rates of patients who had comorbid physical illness and those who used at least one medication regularly were 21.8% and 90.9%, respectively. The rate of current cigarette smokers was 49.1%. All patients reported using caffeinated drinks every day. Among them, 3.5% used alcohol, and 10.9% used illicit drugs at some point in their lifetime. None of them were defined as alcohol and/or substance use disorder.

Table II: Socio-demographic characteristics of schizophrenia patients and comparison of sociodemographic features according to the comorbidity of Metabolic Syndrome

		MetS (+)	MetS (-)	p
Mean age (years) (mean ±SD) Age (min-max)	36.9 ± 10.8 (19-68)	40.9±11.8	34.4±9.5	**0.029**
Gender N (%)				
Male	40 (72.7)	13 (61.9)	27 (79.4)	0.157
Female	15 (27.3)	8 (38.1)	7 (20.6)	
Marital status				
Married	13 (23.6)	8 (38.1)	5 (14.7)	0.139
Single	36 (65.5)	11 (52.4)	25 (73.5)	
Divorced	6 (10.9)	2 (9.5)	4 (11.8)	
Education				
Elementary school and below	35 (63.6)	16 (76.2)	19 (55.9)	0.314
Middle school	12 (21.8)	3 (14.3)	9 (26.5)	
Higher education	8 (14.5)	2 (9.5)	6 (17.6)	
Economic status				
Low	36 (65.5)	14 (66.7)	22 (64.7)	0.980
Mid	16 (29.1)	6 (28.6)	10 (29.4)	
High	3 (5.5)	1 (4.8)	2 (5.9)	
Place of residence				
County	38 (69.1)	15 (71.4)	23 (67.6)	0.768
Rural	17 (30.9)	6 (28.6)	11 (32.4)	
Employment				
Employed	4 (7.3)	1 (4.8)	3 (8.8)	0.573
Unemployed	51 (92.7)	20 (95.2)	31 (91.2)	
Family unit				
Nuclear	39 (70.9)	14 (66.7)	25 (73.5)	0.586
Extended/single	16 (29.1)	7 (33.3)	9 (26.5)	
Perceived social support				
Sufficient	30 (54.5)	12 (57.1)	18 (52.9)	0.658
Unsufficient	14 (25.5)	4 (19)	10 (29.4)	
None	11 (20)	5 (23.8)	6 (17.6)	
Cigarette	27 (49.1)	9 (42.9)	18 (52.9)	0.467
Alcohol	2 (3.5)	1 (4.8)	1 (2.9)	0.726
Substance	6 (10.9)	1 (4.8)	5 (14.7)	0.250
History of physical disorders	12 (21.8)	7 (33.3)	5 (14.7)	0.104
Comorbid Physical Disorder				
DM	3 (5.5)	2 (9.5)	1 (2.9)	0.296
HT	1 (1.8)	1(4.8)	0 (0)	
Other	8 (14.5)	4 (19)	4 (11.8)	
Using any medication regularly	50 (90.9)	21 (100)	29 (85.3)	0.065
Family history of psychiatric disorders	22 (40)	10 (47.6)	12 (35.3)	0.365

Bold values indicate significance of p<0.05. SD: Standard Deviation

The median age of onset of illness was 22 years, and the duration was 10 years. The majority of patients had recurrent psychotic episodes (92.7%), attempted suicide at least once in their lifetime (72.7%), and had regular control visits (76.4%). 63.6% of the patient group were

treated intermittently, and the median duration of medication use was 5 years. ECT was administered to 23.6% of the patient group, and 36.4% were followed up in a community mental health center (CMCH). All patients used atypical antipsychotics and combined therapy. More than half of the patient group was treated with depot antipsychotics (54.5%) and required additional treatment with mood stabilizers and/or antidepressants (58.2%).

The prevalence rate of MetS was 38.2% according to IDF and 25.5% based on ATP III and ATP IIIA criteria (Table 3). There was no statistically significant difference between the socio-demographic features of the groups regarding gender, years of education, employment, marital status, place of residence, family setting, economic status, history of physical illness, including DM and hypertension, and family history of psychiatric disorders. The mean age was significantly higher in schizophrenia patients with MetS compared to those without, indicating a statistically significant difference between groups. Although not statistically significant, the regular use of any medication was more frequent among patients with MetS. Statistical analysis revealed no significant differences between groups concerning perceived social support, smoking, alcohol consumption, and illicit substance use. Since all patients were caffeine consumers, intergroup comparisons were not feasible.

Table III: The prevalence rate of Metabolic Syndrome in the sample group

Sample group (N): 55	ATP III	ATP III-A	IDF
MetS (+)/ N (%)	14 (25.5)	14 (25.5)	21 (38.2)

The effects of clinical features of schizophrenia on MetS have been investigated. The groups differed significantly in terms of the duration of illness, length of medication use, and the time between symptom onset and diagnosis ($p<0.05$). Significant differences were found between groups in height, weight, and body mass index (BMI) ($p<0.05$). Patients with MetS had shorter stature, higher weight, and consequently elevated BMI values. Concerning MetS criteria, the groups differed significantly in terms of waist circumference, fasting triglyceride, and fasting HDL levels ($p<0.05$), whereas the differences in fasting blood glucose and blood pressure (systolic and diastolic) were not statistically significant. Patients with MetS were found to be treated with depot antipsychotics more frequently, and the difference between groups reached a statistically significant level ($p<0.05$). However, no statistically significant difference was noted between groups in other clinical features such as age of onset, single or recurrent psychotic episodes, intermmittent or regular therapy after diagnosis, last regular medication use, the number of hospital admissions, history of suicide attempts, administration of ECT, and medications used (antipsychotics, other psychotropic medications, antihypertansives, antihyperlipidemic, and antidiabetics). Since all participants were using atypical and multiple antipsychotics, comparisons involving atypical antipsychotics and antipsychotic monotherapy could not be conducted. No statistically significant differences were found between the groups in terms of follow-up in CMCH, GAF score, and treatment compliance. Clinical characteristics of schizophrenia and comparison of groups are presented in Table 4.

Table IV: The clinical features of patients with schizophrenia and comparison of clinical features according to the comorbidity of Metabolic Syndrome

		MetS (+)	MetS (-)	p
Age of onset (years)* (median) (25 percentiles-75 percentiles)	22**(18-29)***	18(16.5-30.5)	23(19-28.2)	0.650
Duration of illness (months) (median)	120(60-216)	180(96-252)	90(54-168)	**0.029**
Time to diagnosis (months) (median)	1(1-24	11(1-36)	1(1-21)	**0.035**
Duration of medication use (months) (median)	96(36-168)	120(81-240)	84(24-132)	**0.010**
Last regular medication use period (months) (median)	19.5(2.75-75)	24(3-96)	12(2-60)	0.730
Number of hospital admissions (median)	3(2-6)	3(2-6)	2.5(1.75-4.25)	0.286
GAF score (median)	55(45-65)	55(45-65)	55(45-65)	0.311
Fasting triglyceride level (median)	140(97-203)	207(181-297)	111(78.5-139)	**<0.001**
Fasting Blood Sugar (median) (25 percentiles-75 percentiles)	82(76-91)	82(77-94)	82(73.5-91)	0.633
Systolic blood pressure(median) (25 percentiles-75 percentiles)	110(100-120)	110(100-120)	110(100-112)	0.189
Diastolic blood pressure(median) (25 percentiles-75 percentiles)	70(70-80)	70(70-80)	70(67.5-72.5)	0.406
Fasting HDL (mean ±SD)	41.9±10.6	36.3±7.3	45.3±10.9	**0.002**
Waist circumference(mean±SD)	97.8±12.7	102.4±11.8	94.9±12.6	**0.032**
Height (mean ±SD)	165.2±10.1	160.9±10.1	167.8±9.2	**0.012**
Weight (mean ±SD)	78.7±13.6	83.2±15.3	75.8±11.7	**0.049**
BMI (mean ±SD)	28.8±5.5	31.5±4.9	27.1±5.2	**0.004**
Single psychotic episode (N/%)	4 (7.3)	1(4.8)	3 (8.8)	0.573
Recurrent psychotic episodes	51 (92.7)	20 (95.2)	31 (91.2)	
Treatment after diagnosis				
Intermittent therapy	35 (63.6)	15 (71.4)	20 (58.8)	0.345
Regular treatment	20 (36.4)	6 (28.6)	14 (41.2)	
Administration of ECT	13 (23.6)	6 (28.6)	7 (20.6)	0.498
History of a suicide attempt	40 (72.7)	16 (76.2)	24 (70.6)	0.650
Follow-up at CMCH	20 (36.4)	10 (47.6)	10 (29.4)	0.173
Treatment				
Atypical antipsychotic	55 (100)	21 (100)	34 (100)	[a]
Typical antipsychotic	20 (36.4)	8 (38.1)	12 (35.3)	0.834
Additional Treatment	32 (58.2)	15 (71.4)	17 (50)	0.118
Mood-stabilizers	20 (36.4)	9 (42.9)	11 (32.4)	0.298
Antidepressant	11 (20)	5 (23.8)	6 (17.6)	
Others	1 (1.8)	1 (4.8)	0 (0)	
Clozapine	9 (16.4)	3 (14.3)	6 (17.6)	0.743
Olanzapine	36 (65.5)	12 (57.1)	24 (70.6)	0.308
Ketiapine	31 (56.4)	9 (42.9)	22 (64.7)	0.112
Depot antipsychotic	30 (54.5)	15 (71.4)	15 (44.1)	**0.048**
Treatment compliance				
No control visits	5 (9.1)	3(14.3)	2 (5.9)	0.188
Partial compliance (2-6controls/year)	8 (14.5)	1 (4.8)	17 (81)	
Regular controls (>6 controls/year)	42 (76.4)	17 (81)	25 (73.5)	
Medication use				
Regular	39 (70.9)	16 (76.2)	23 (67.6)	0.498
Irregular	16 (29.1)	5 (23.8)	11 (32.4)	
Antihypertensive treatment	2 (3.6)	2 (9.5)	0 (0)	0.067
Antihyperlipidemic treatment	0 (0)	0 (0)	(0)	[a]
Antidiabetic treatment	3 (5.5)	2 (9.5)	1 (2.9)	0.296

*a: No statistics are computed because the variable is constant Bold values indicate significance of p<0.05. SD: Standard Deviation *Mann Whitney U test is used for comparing continuous variables. Median**. (25 percentiles-75 percentiles) ****

DISCUSSION

The findings of the present study indicate an increased prevalence of MetS among patients with schizophrenia, with rates of 25.5% and 38.2% based on the ATP and IDF criteria, respectively. The prevalence of MetS varies widely across different studies, ranging from 18.03% to 79.1%. Variations between studies seem to be related to sample size, heterogeneity of sample groups, different study designs, and the definition of MetS[9-13]. In a recent meta-analysis, it is estimated that more than one-third of schizophrenia patients suffer from MetS[11], and our findings align with prior research on the prevalence of MetS in schizophrenia patients.

Findings on gender differences in the prevalence of MetS among patients with schizophrenia are inconsistent. Although several studies have demonstrated that MetS is more prevalent in women than men[11,12], other studies indicate no significant gender differences[10]. Specific risk factors for women, such as pregnancy, oral contraceptive therapy, and menopause, as well as factors like more common subclinical positive symptoms and seeking treatment more for psychiatric and medical issues, show that being female is an independent risk factor for affective psychosis, which is associated with increased prevalence of MetS in females[11,19]. In our study, the prevalence of MetS was proportionally higher among women; however, the difference between genders did not reach statistical significance, possibly related to the small sample size and male-dominated sample group.

MetS has been reported to become more prevalent as patients age and the duration of illness increases in several studies[10-13,20]. All metabolic risk factors were found to be significantly less common in early schizophrenia, with waist circumference, blood pressure, and smoking rates being substantially lower in unmedicated patients compared to those classified as first-episode psychosis[21]. Cardiometabolic risk is higher in chronic schizophrenia than in early schizophrenia[21]. Our sample group consisted of chronic schizophrenic patients, with an average illness duration of 10 years. Consistent with the existing literature, our study found that the prevalence of MetS increases with age and illness duration. Additionally, the time until diagnosis was significantly longer in patients with MetS, which may be related to a longer disease duration.

The metabolic abnormalities and weight gain are associated with antipsychotic drugs in the literature[5]. Studies have shown that second-generation (atypical) antipsychotics double the rate of new incident cases of MetS compared to those treated with first-generation (typical) antipsychotic agents, and that starting atypical antipsychotics is linked to a higher risk of developing metabolic abnormalities in patients without MetS at baseline[22]. Among antipsychotic agents, clozapine and olanzapine are most strongly associated with metabolic disturbances, while quetiapine, risperidone, and amisulpride present a moderate risk of developing MetS[23]. We found no difference between groups regarding the use of antipsychotic agents or the need for additional treatment with antidepressants or mood stabilizers, and these findings may be the result of the small sample size and the exclusive use of atypical and multiple antipsychotic drugs in the sample group.

Although several studies reported no significant differences in the rates of metabolic abnormalities between long-acting injectable antipsychotics and oral formulations, olanzapine and, particularly, clozapine, were exceptions[24,25]. In the present study, using long-acting antipsychotic medications was significantly more common among patients with MetS. Although the majority of our sample reported consistently attending outpatient

follow-ups and adhering to medication regimens, the increased frequency of MetS observed in patients receiving depot antipsychotics may be due to improved treatment adherence. Depot antipsychotics are linked to high rates of MetS but low rates of regular monitoring[25]. Therefore, it is recommended that patients treated with depot antipsychotics be screened for MetS, including the measurement of individual metabolic parameters[25].

The literature presents diverse findings regarding the association between the duration of antipsychotic treatment and the risk of developing MetS in patients with schizophrenia. While several studies found a positive correlation, others found no significant association[26]. In our study, a longer duration of antipsychotic treatment was linked to a higher frequency of MetS in patients with schizophrenia.

Patients receiving antipsychotic polytherapy exhibit higher rates of MetS compared to those who use antipsychotic monotherapy[27]. In our study, the majority of the sample group comprised chronic schizophrenic patients who had experienced recurrent psychotic episodes and required treatment with polytherapy. Therefore, a comparison between patients receiving monotherapy and those using polypharmacy could not be performed.

Although the Body Mass Index (BMI) is not a diagnostic criterion, it has been suggested that it can serve as a screening tool for MetS[28]. We found that BMI was significantly higher in schizophrenia patients with MetS compared to those without MetS. This result aligns with the literature, indicating that the prevalence of obesity is greater in schizophrenia due to the effects of antipsychotic medications and that MetS is more prevalent among schizophrenia patients who are overweight or obese[11].

In our study, waist circumference, one of the MetS criteria and an indicator of central obesity, significantly differed between groups with and without MetS. Also, low HDL and high triglyceride levels were more frequently observed in patients with MetS. In similar studies, waist circumference and lipid profile appear to be the most crucial variables predicting the risk of MetS, and waist circumference may serve as an early warning sign of MetS[12,29]. There was no difference between the groups regarding other MetS criteria, including blood pressure, fasting blood sugar, and the use of antihypertensive and antidiabetic medications in the present study. ATP III and ATP III-A criteria differ in fasting blood sugar levels[14,15]. In our study, no difference was observed concerning blood sugar, and within the sample group, the rate of patients diagnosed with MetS based on ATP III and ATP III-A criteria was found to be equal.

We evaluated the functionality levels of the patients using the GAF score, which was found to be an average of 55, indicating moderate difficulty in social or occupational functioning. MetS in schizophrenia impacts functional mobility, cognition, and quality of life[30]. There was no significant difference in functionality as measured by the GAF scale, which may result from the small sample size.

This study has several limitations. The primary limitation is the small sample size, lack of advanced statistics and power analysis, and the predominance of male participants, which may restrict the generalizability of the findings. Another limitation is that all patients were treated with polydrugs and atypical antipsychotics, which precludes comparison between different drugs. Additionally, the absence of a drug-free patient group and healthy control subjects limits the generalizability of the results.

Finally, this study identifies patients with schizophrenia as a vulnerable group for MetS,

emphasizing not only well-known risk factors such as age, illness duration, and the length of medication used but also drawing attention to the less recognized role of long-acting injectable antipsychotics. Because individuals with MetS are often asymptomatic, early detection is vital and enables prompt intervention, which can lower the risk of cardiovascular problems and enhance long-term clinical outcomes. BMI, waist circumference, and lipid profile are likely to be the key variables for predicting MetS, and regular monitoring of these should be integrated into the clinical management of patients with schizophrenia. Future longitudinal studies with larger sample sizes are needed to confirm these results and help develop strategies to reduce metabolic risk in schizophrenia.

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