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Research / Araştırma

The Correlation Between Incidence of Metabolic Syndrome and Sociodemographic and Clinical Characteristics in Schizophrenia Patients

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ABSTRACT

The correlation between incidence of metabolic syndrome and sociodemographic and clinical characteristics in schizophrenia patients

Objective: The purpose of this study was to determine the frequency of metabolic syndrome (MetS) in schizophrenia patients who are receiving treatment with antipsychotic drugs and also the sociodemographic and clinical characteristics of schizophrenia patients with MetS.

Methods: 111 schizophrenia patients diagnosed on the basis of DSM-IV diagnostic criteria and receiving antipsychotic therapy for at least 3 months were included in the study. MetS was diagnosed on the basis of International Diabetes Fedaration (IDF) diagnostic criteria. Schizophrenia patient groups with and without diagnosed MetS were compared in terms of sociodemographic and clinical characteristics.

Results: MetS was determined in 27% of the patients. The most commonly determined parameter was elevated waist circumference (65.8%). The least common parameter was elevated blood pressure (10.8%). The waist circumference parameter in women and the blood pressure parameter in men were more frequently determined. No difference was determined between schizophrenia patients with or without MetS in terms of sociodemographic characteristics, schizophrenia subtypes and symptoms or other clinical characteristics.

Conclusion: MetS is a significant problem in schizophrenia patients receiving antipsychotic therapy. Elevated waist circumference is an important parameter in monitoring. The findings in the literature regarding the relationship between MetS and sociodemographic and clinical characteristics are contradictory. No correlation was determined in our study. Further studies are now needed to shed light on this subject. There would seem to be no correlation between MetS and schizophrenia subtypes and symptoms.

Key words: Clinical characteristics, metabolic syndrome, schizophrenia, sociodemographic characteristics

ÖZET

Şizofreni hastalarında metabolik sendrom sıklığının sosyodemografik ve klinik özelliklerle ilişkisi

Amaç: Bu çalışmada, antipsikotik ilaçlarla tedavi altında olan şizofreni hastalarında metabolik sendrom (MetS) sıklığı ve metabolik sendromlu hastaların sosyodemografik ve klinik özelliklerinin saptanması amaçlanmıştır.

Yöntem: DSM-IV tanı kriterlerine göre tanısı konan ve en az 3 aydır antipsikotik tedavi almakta olan 111 şizofreni hastası çalışmaya alındı. MetS tanısı Uluslararası Diyabet Fedarasyonu (IDF) tanı kriterlerine göre kondu. MetS tanısı konan ve konmayan hasta grupları arasında sosyodemografik ve klinik özellikler açısından karşılaştırma yapıldı.

Bulgular: Hastaların %27'sinde MetS saptandı. En sık saptanan kriter, bel çevresi genişliğiydi (%65.8). Sıklığı en az olan kriter ise kan basıncı yüksekliğiydi (%10.8). Bel çevresi genişliği kriteri kadınlarda, kan basıncı yüksekliği kriteri ise erkeklerde daha sık karşılandı. MetS'i olan ve olmayan şizofreni hastaları arasında sosyodemografik özellikler, şizofreni tipi, semptomları ve diğer klinik özellikler açısından fark saptanmadı.

Sonuç: Antipsikotik tedavi altında olan şizofreni hastalarında MetS önemli bir sorundur. Bel çevresi genişliği takipte önemli bir kriterdir. Literatürde MetS ile sosyodemografik ve klinik özelliklerin ilişkisine dair bulgular çelişkilidir. Bizim çalışmamızda ilişki saptanmamıştır. Bu konuyu aydınlatmak için daha fazla sayıda çalışmaya ihtiyaç vardır. MetS ile şizofreni alt tipleri ve şizofreni semptomları ilişkisiz gibi görünmektedir.

Anahtar kelimeler: Klinik özellikler, metabolik sendrom, şizofreni, sosyodemografik özellikler

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INTRODUCTION

The most common cause of natural death in patients with schizophrenia is cardiovascular disorders (1,2). Metabolic syndrome (MetS), sets the ground for diabetes and cardiovascular disorders (CVD) by causing some clinical and metabolic problems (3-7). MetS (Syndrome X=insulin resistance syndrome=dysmetabolic syndrome), was defined first by Reaven (8). Dyslipidemia, hypertension (HT), obesity, and type 2 diabetes, which are associated with MetS and CVD, are 1.5-2 times more common in schiozphrenia patients when compared with general population (2,9). Sedantary and unhealthy life styles, decreased physical activity, poor diet, smoking, alcohol and susbtance abuse and weight gain due to antipsychotics make schizophrenia patients more liable to MetS by having a negative effect on lipid and glucose metabolisms (1,2,6,10).

There are three definitions of MetS in the literature. Criteria used in these definitions include waist circumference, reduced high density lipoprotein (HDL) level and raised triglycerides (TG), fasting plasma glucose (FPG) and blood pressure (BP). First definition belongs to The US National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III). This has been revised by American Heart Association (ATP III A). The two definitions are similar in terms of waist circumference, blood pressure, HDL and TG. The only difference is in FPG measurement. FPG criteria in ATP III is 110 mg/dL or more while in the ATP III A it is 100 mg/dL or higher. The third and most current definition was done by International Diabetes Federation (IDF). Waist circumference is smaller than ATP III and III A; for MetS diagnosis, raised waist circumference is absolutely necessary along with two other positive criteria. Therefore, IDF criteria leads to more MetS diagnosis when compared with ATP III and ATP III A criteria (2).

MetS prevalence is between 13.4% and 69.3% per IDF criteria among patients with schizophrenia (1,11-31). Several studies did not find gender differences between schizophrenia patients with or without MetS (1,14,16,19,27,28,32,33). However, there are other studies which reported increased MetS prevalence in women (17,24,25,28-30,35) or men (26). While several studies found MetS to be more common in older patients (1,17,23,27,29-31,35), fewer studies reported no age differences (26,32,36). There have been conflicting results regarding age of onset of the disorder (19,26,27), duration of the disorder (1,24,26,27,29,31,32,34), education (28,31,32) and number of hospitalizations (15,19,32). Other studies reported higher body mass index (BMI) in schizophrenia patients with MetS (30,33,35). There were no differences in terms of smoking (24,26,27,32,36).

There were no differences between schizophrenia patients with or without MetS in terms of family history of schizophrenic disorders (27), HT (19,24,27,29,32), dyslipidemia (19) and cerebrovascular disorders (29). While two studies suggested that diabetes and obesity are more common (24,31), results of several studies argued against it (19,24,27,29,32,36). Hägg and colleagues (33), found higher prevalence of CVDs among families of patients with MetS, however, this was not replicated in two other studies (27,36).

The most common criteria fulfilled among schizophrenia patients with MetS is raised waist circumference (1,19,24,27-29,35-40), while the least common was raised FPG level (28,35,38). De Hert and associates (40) suggested that adding FPG measurement to waist circumference was the most sensitive (100%) method to follow MetS in patients with schizophrenia.

Antipsychotic treatment is one of the most important causes of MetS in patients with schizophrenia. Clozapine, olanzapine and risperidone are the antipsychotics that most commonly cause metabolic syndrome (1,12,22,30,34,41). Risk is lower for amisulpride, aripiprazole, sertindole, ziprasidone, haloperidol and chlorpromazine (7,12,22,41). MetS is more common during multiple antipsychotic use (35,42). Cerit and colleagues (24) reported longer duration of treatment with antipsychotics in schizophrenia patients with MetS, however, other studies did not find any difference (19,32,36).

The aim of this study was to detect prevalence of MetS per IDF criteria among schizophrenia patients who were on a fixed dose of antipsychotic for at least 3 months and to investigate the association of MetS with sociodemographical and clinical features.

METHOD

Sample

The study included 111 consecutive schizophrenia patients who were being followed and treated at Ondokuz Mayis University, Faculty of Medicine, Department of Psychiatry, Psychotic Disorders Unit during September 2006-December 2007 and who were between 18-70 years of age and were on the same antipsychotic at least for the last three months. Schizophrenia diagnosis were made per DSM-IV-TR diagnostic criteria (43). Exclusion criteria were having a comorbid psychiatric disorder, chronic medical disorders (except hypertension and diabetes), pregnancy, alcohol and substance abuse other than nicotine.

Measurement

Sociodemographical and Clinical Information Form: Sociodemographical information of the patients were in our Psychotic Disorders Unit, sociodemographical, premorbid and familial features are registered in files along with clinical information obtained by detailed interviews conducted with patients and their relatives. Sociodemographical features of the patients were obtained via these files.

Positive and Negative Symptom Scale (PANSS): This is a 30-item semi-structured interview including a 7-point severity assessment which was developed by Kay and colleagues (44). Positive symptoms and negative symptoms subscales include seven items each, the remaining sixteen items form general psychopathology subscale. Kostakoglu and associates conducted Turkish validity and reliability studies (45). Symptoms of the patients with schizophrenia during first admission, follow-up and hospitalization were evaluated with PANSS and semi-structured psychosis follow-up form (a form to assess whether schizophrenia symptoms are present) which has been used in our psychosis department. When any symptom (e.g. auditory hallucinations) was detected during follow-up period, that symptom was recognized as positive.

Laboratory Method

Fasting plasma samples were obtained for FPG, TG, HDL measurements. The measurement was conducted in the biochemistry laboratory of our university. Plasma glucose (kit: Roche/Hitachi Kat. No. 05168791 Lot No: 658833, %CV:1.7), TG (kit: Roche/Hitachi Kat. No. 05171407 Lot No: 636318, %CV:0.9) and HDL (kit: Roche/Hitachi Kat. No. 05168805 Lot No: 639540, %CV:0.6) levels were measured with Roche Hitachi Cobas 8000 autoanalyzer.

Waist circumference and blood pressure measurement: Waist circumference was measured with measuring tape, naked, from the first border of iliac crest. Blood pressure was measured after at least 5 minutes rest and when sitting.

Metabolic Syndrome (MetS) Diagnosis

MetS diagnosis were made per International Diabetes Federation (IDF) diagnostic criteria (46). The criteria were: waist circumference (cm) men≥94, women≥80; blood pressure (mm/Hg)≥130/85; HDL (mg/dl) men<40, women<50; TG (mg/dL)≥150; FPG (mg/dL)≥100. Increased waist circumference is absolutely necessary along with two other criteria to make MetS diagnosis per IDF criteria. In our study, we accepted blood pressure criteria positive in patients who were on antihypertensive drugs, and plasma glucose criteria positive in patients who were on hyperglycemic treament.

Patients were divided into two groups on the basis of presence of MetS. Two groups were compared for sociodemographical, familial and clinical features.

This study was conducted in accordance with Helsinki decleration of ethical standards. After detailed explanation of aims of the study, those who volunteered and gave written informed consent (the patient or one of the relatives) were included in the study.

Statistical Analysis

Statistical analyses were computed with SPSS (Statistics Package for Social Science) software version 16.0. Chi-square test was used to compare categorical

variables. Since blood pressure criteria, one of the MetS criteria, was not fulfilled in any female patient, Fisher chi-square analysis were used to compare variable in terms of gender. Student-t test was used to compare continuous variables. Categorical varaibles were summarized as percentage, and continuous variables were summarized as mean±standard deviation. $p<0.05$ was reported as significant.

RESULTS

Study group consisted of 111 patients with schizophrenia. Mean age was 34.94±9.71 years. 54.9% of the patients were male, 71% were single, 62.2% were from lower socioeconomic level, 56.7% were living in towns and villages. Mean years of education was 10.42±4.1.

Table 1: MetS prevalence per IDF criteria and frequency and percentage of (+) criteria

	All patients (n=111)	%	Men (n=61)	%	Women (n=50)	%	χ^2	p
MetS prevalence (%)	**30**	**27.0**	**18**	**29.5**	**12**	**24.0**	0.19	0.66
Frequency of (+) criteria								
Waist circumference	73	65.8	34	55.7	40	80.0	6.23	<0.01
Reduced HDL	43	38.7	21	34.4	22	44.0	0.70	0.40
Raised TG	32	28.8	21	34.4	11	22.0	1.51	0.22
Raised FPG	27	24.3	16	26.2	11	22.0	0.09	0.77
Raised BP	12	10.8	12	19.7	0	0.0	-----	<0.001*

MetS: Metabolic syndrome, high density lipoprotein (HDL) level and raised triglycerides (TG), fasting plasma glucose (FPG) and blood pressure (BP), χ^2: Chi-square test, *p<0.001 (Fisher chi-square test)

Table 2: Sociodemographical, familial and clinical features of the groups

	MetS (+) (n=30)		MetS (-) (n=81)			
	n	%	n	%	χ^2	p
Gender						
Male/Female	18/12	60.0-40.0	43/38	53.1-46.9	0.19	0.66
Marital status						
Single/Married	23/7	76.7-23.3	57/24	70.4-29.6	0.17	0.68
Place of residence						
City/Town-Village	12/18	40.0-60.0	36/45	44.4-55.6	0.04	0.84
Economical status						
Poor/Medium-Well	22/ 8	73.3-26.7	47/34	58.0-42.0	1.58	0.21
Premorbid history	18	60.0	55	67.9	0.31	0.58
Antipsychotic						
Atypical	21	70.0	56	69.2	0.02	0.99
Classical	2	6.7	6	7.4		
Atypical+Classical	7	23.3	19	23.5		
Smoking	13	43.3	43	53.1	0.49	0.48
Psychiatric history (first degree relative)	10	33.3	23	28.4	0.07	0.79
Psychiatric history (second degree relative)	11	36.7	33	40.7	0.03	0.86
Diabetes history (first degree relative)	11	36.7	22	27.2	0.55	0.46
CVD history (first degree relative)	12	40.0	33	40.7	0.00	1.00
Cerebrovascular disorder history (first degree relative)	3	10.0	18	22.2	1.41	0.23
	Mean±SD		**Mean±SD**		**t**	**p**
Age	35.93±9.23		34.74±9.95		0.57	0.57
Total years of education	11.13±3.56		10.02±4.24		1.27	0.21
Age of onset of illness	22.63±7.02		22.79±7.26		-0.10	0.92
Duration of illness	12.87+7.98		11.72+8.33		0.65	0.52
Number of hospitalizations	3.10±3.32		2.97±3.15		0.18	0.86
Duration of last treatment (months)	28.13±33.64		15.84±20.57		1.88	0.07

CVD: Cardiovascular disorder, SD: Standard Deviation, χ^2: Chi-square test, t: Student T test,

Table 3: Comparison of the groups in terms of schizophrenia subtypes and symptoms

	MetS (+) (n=30)		MetS (-) (n=81)			
	n	%	n	%	χ^2	p
Schizophrenia subtype						
Paranoid	10	33.3	30	37.0	0.55	0.91
Undifferentiated	16	53.3	38	46.9		
Dysorganized	3	10.0	11	13.6		
Residual	1	3.3	2	2.5		
Schizophrenia symptoms						
Hallucination (auditory)	27	90.0	71	87.7	0.00	0.99
Hallucination (other)	14	46.7	46	56.8	0.54	0.46
Delusion (grandiosity)	10	33.3	16	19.8	1.56	0.21
Delusion (persecution)	26	86.7	73	90.1	0.03	0.86
Delusion (control)	10	33.3	37	45.7	0.91	0.34
Delusion (thought insertion, broadcast)	11	36.7	31	38.3	0.00	1.00
Delusion (other)	16	53.3	36	44.4	0.35	0.54
Incoherence	17	56.7	39	48.1	0.34	0.56
Agitation	19	63.3	46	56.8	0.16	0.69
Depression	16	53.3	41	50.6	0.00	0.97
Violence (to people)	12	40.0	39	48.1	0.30	0.58
Suicide attempt	10	33.3	24	29.6	0.02	0.88
Bizzare behavior	17	56.7	46	56.8	0.00	1.00
Hyperactivity	17	56.7	43	53.1	0.01	0.90
Violence (property)	13	43.3	40	49.4	0.12	0.74
Social withdrawal	18	60.0	53	65.5	0.09	0.76
Formal thought disorder	8	26.7	22	27.2	0.00	1.00
Unusual thought content	12	40.0	41	50.6	0.61	0.43
Impaired role functions	7	23.3	33	40.7	2.17	0.14
Blunted affect	12	40.0	40	49.4	0.44	0.51
Poor hygiene	11	36.7	35	43.2	0.39	0.53
Unusual perception	10	33.3	29	35.8	0.00	0.99

χ^2: Chi-square test

27% of our patients (men=29.5%, women=24%) were diagnosed with MetS per International Diabetes Federation (IDF) criteria. There were no gender differences regarding MetS (p>0.05). The most common criteria was waist circumference (65.8% of the patients), while the least common criteria was high blood pressure (10.8% of the patients). Increased waist circumference was more common in women (p<0.05). All patients with raised blood pressure were men (p<0.05) (Table 1).

There were no differences between the groups in terms of gender, mean age, marital status, economic level, place of residence, education, psychiatric disorders in the first and second degree relatives, diabetes in the first degree relatives, cardiovascular and cerebrovascular disorders, age of onset of schizophrenia, duration of disorder, number of hospitalizations, premorbid history, antipsychotic treatment group (atypical, classical, atypical+classical), duration of last treatment and smoking (p>0.05) (Table 2). We detected MetS in 19.4%, 31.8%, 28.6%, and 37.5% of the subjects in 19-29, 30-39, 40-49, 50-59 years age groups, respectively.

There were no differences between the groups regarding schizophrenia subtype and symptoms (p>0.05) (Table 3).

DISCUSSION

MetS prevalence in patients with schizophrenia per IDF criteria varies between 13.4%-69.3% (1,11-31).

One of the most important causes for MetS in patients with schizophrenia is antipsychotic treatment. MetS is not common in patients who are not on antipsychotics. Padmavati and associates (47), reported MetS prevalence as 3.9%, and Patel and associates as 4.3% (11) in antipsychotic naive patients with schizophrenia. In our study, consistent with previous studies, we found MetS in 27% of the subjects who were using antipsychotic drugs for at least three months.

In a large adult population sample representing all geographical regions of Turkey, Sanisoglu and associates (48), reported MetS prevalence in all country as 17.9% and 14.2% in Black Sea region. In our study, which was conducted in Black Sea region, the prevalence of MetS we found in patients with schizophrenia (27%) was almost two times higher than the figure reported by Sanisoglu and colleagues (48) in the general population sample (14.2%). In another study, we found that MetS prevalence per IDF criteria was 32% among chronic inpatients hospitalized in the regional mental health hospital (25). These results indicate that MetS is an important health problem in patients with schizophrenia in our region.

In a study conducted in our country (METSAR), it was reported that MetS incidence increased with age in the adult population 20 years and over (age 20-29 10.2%, age 30-39 26.8%, age 40-49 44.4%, age 50-59 54.7%) (49). In our study, we detected MetS in 19.4%, 31.8%, 28.6%, and 37.5% of the subjects in 19-29, 30-39, 40-49, 50-59 years age groups, respectively. MetS prevalence in our patients in 19-29 age group was higher than reported in the METSAR study (10.2% vs 19.4%), on the other hand, our rates were lower in the 40-49 and 50-59 years age groups (44.4% vs 28.6% and 54.7% vs 37.5%). Similarly, in another study, MetS rate in the 20-29 years age group was found to be higher than METSAR rates (10.2% vs 22.4%) (27). When increased prevalence of MetS with age in the population sample was taken into account, it was interesting to observe that MetS was more common than the population in our young patients with schizophrenia while it was less common than the general population in older patients. MetS in young patients with schizophrenia may lead to CVD in young ages. Therefore, it is important to follow MetS in the young age group.

Raised waist circumference was the most common MetS criteria (65.8%). This finding was consistent with the literature (1,17,24,27-29,35-40). In consistent with previous studies, waist circumference was larger in women (17,32). De Hert and associates (50) reported that the most common MetS criteria among first episode, (<1.5 years), new onset (1.5-10 years), sub-chronic (10-20 years) and chronic (>20 years) schizophrenia patients was waist circumference. These findings suggest that waist circumference is an important criteria to follow the patients. The least common criteria was increased blood pressure (10.8%). All 12 patients with increased blood pressure were men.

Several studies did not find gender differences between schizophrenia patients with or without MetS (1,14,16,19,27,28,32,33). However, there are other studies which reported increased MetS prevalence in women (17,24,25,28-30,35) or men (26). Our results supported those studies which did not find gender differences. There was no difference in marital status in our study. This was contrary to Pallawa and colleagues (31) results indicating that MetS was more common in married patients with schizophrenia. While several studies found MetS to be more common in older patients (1,17,23,27,29-31,35), fewer studies reported no age differences (26,32,36). We did not find any age difference. Pallawa and associates (31) reported higher education in schizophrenia patients with MetS. Grover and colleagues (28) and Oyeckin and associates (32) argued that there was no difference regarding education. Our study was consistent with the two latter studies. Besides, we did not find any difference in terms of economical level and place of residence. Studies with bigger samples are necessary to detect sociodemographical features of patients with MetS.

Previous studies reported no differences in family history of schizophrenic disorder (27) and cerebrovascular disorders (29) in patients with MetS. In our study, we did not find any difference in family history of psychiatric disorders in the first and second

degree relatives and cerebrovascular disorders in the first degree relatives. While there is one study suggesting that family history of diabetes is more common (31), several studies have not supported this finding (19,24,27,29,32,36). Our findings support the latter studies. Hägg and associates (33) reported increased CVDs in families of patients with MetS, however, two other studies did not find that association (27,36). We did not detect any difference regarding CVD.

We did not find any association between schizophrenia subtypes and MetS. This was consistent with the literature (29,32). Besides, we did not find any difference regarding schizophrenia symptoms in patients with or without MetS. To the best of our knowledge, this is the first study to evaluate the association of MetS with schizophrenia symptoms. It can be argued that there is no association between MetS and schizophrenia symptoms or subtypes.

While Srisurapanont and colleagues (19) and Kaya and associates (26) did not find any difference regarding age of onset; Yazici and colleagues (27), reported older age of onset in schizophrenia patients with MetS. Our study was consistent with the first two studies. While several studies reported longer duration of illness in schizophrenia patients with MetS (1,24,29,31,34), other studies did not (26,27,32). We did not find any difference in terms of duration of illness. Sugawara and colleagues (15) reported higher number of hospitalizations in schizophrenia patients with MetS. However, similar to our study, two other studies did not find such an association (19,32). Smoking was not different between schizophrenia patients with or without MetS (24,26,27,32,36). This was consistent with our results. Besides, we did find any difference regarding premorbid history. Antipsychotic use is one of the most important causes of MetS in patients with schizophrenia. In our study, there were no differences in terms of antipsychotic group (typical, atypical, typical+atypical combination).

In conclusion, MetS is an important problem in schizophrenia patients using antipsychotics. Waist circumference may be an important criteria in clinical follow-up. There are conflicting results in the literature on the association of MetS and sociodemographical and clinical variables. More studies are necessary to enlight this issue. It seems like MetS is not associated with schizophrenia symptoms or subtypes.

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