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The Prevalence of Metabolic Syndrome and Related Factors in Patients With Schizophrenia

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Abstract

Objective: *The aim of this study was to examine the prevalence of metabolic syndrome (MS) and related factors in patients with schizophrenia at an outpatient clinic.*

Method: *All 108 patients with schizophrenia or schizoaffective disorder that presented to the outpatient clinic between 12 May and 12 June 2006 were included in the study. Of the 108 patients, 100 whose biochemical analyses were completed were assessed.*

Results: *The prevalence of MS was 21%, 34%, and 41% according to ATP III, ATP III-A, and IDF criteria, respectively. Increased waist circumference and low HDL level were frequent among the patients. The prevalence of MS increased with age. Mean age, duration of illness and duration of treatment were higher and family history of obesity was common in the patients with MS.*

Discussion: *The prevalence of ATP III-defined MS in patients with schizophrenia was lower compared to that reported in other studies; however, the prevalence of MS was high based on ATP III-A and IDF criteria. Patients with schizophrenia are at increased risk for MS or related metabolic problems. In particular, when risk factors such as older age, female gender, long duration of illness and treatment, and family history of obesity exist, clinicians should examine the metabolic condition of the patient. Increased waist circumference and low HDL level are probably the best predictors of MS.*

Key Words: *Schizophrenia, metabolic syndrome, ATP III*

INTRODUCTION

In recent years, especially after the introduction of new generation antipsychotics, researchers have frequently discussed on metabolic problems seen in patients with schizophrenia (Allison and Casey, 2001). These metabolic problems involve anomalies in glucose metabolism, the cardio-vascular system, lipid metabolism, and weight gain. As a result these problems cause not only increased cardiovascular mortality (Brown et al., 2000), but also decreased functionality (Lyketsos et al., 2002), exacerbation of psychotic and depressive symptoms (Dixon et al., 1999), and decreased treatment compliance in schizophrenic patients (Robinson et al., 2002).

Metabolic syndrome (MS) (in other words, syndrome X, dysmetabolic syndrome) has been investigated for the past 20 years within the cardiology and endocrinology specialties. In particular, within the past 5 years the number of studies that examine this issue has been increasing (McEvoy et al., 2005). MS is marked by disorder of some metabolic parameters, such as increased central obesity, disorder in lipid profiles (causing atherosclerosis), increased blood pressure, and high fasting blood glucose. Definitions of MS are presented in Table I. The Third Adult Treatment Panel of The National Cholesterol Education Program (NCEP ATP III) (Adult Treatment Panel III, 2001) provided the most frequently used definition of MS. In addition, the American Heart Association (AHA) provided another definition of MS (ATP III-A) (Grundy et al., 2004). According to both definitions (ATP III and ATP III-A), 3 of the 5 criteria should be positive to meet the MS diagnosis, ATP III requires 110 mg/dl for a fasting blood glucose level while ATP III-A requires 100 mg/dl for MS diagnosis. The

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International Diabetes Federation (IDF, 2005)) provided a recent definition of MS, in which there are 5 criteria, one of which includes smaller waist circumference. This criterion and 2 others should be satisfied to diagnosis MS. In summary, according to ATP III and ATP III-A, any positive 3 criteria of 5 should be present to diagnose MS, but according to IDF, the waist circumference criterion and 2 additional criteria should be present to diagnose MS. Nonetheless, according to all definitions, if a patient receives anti-hypertensive treatment the blood pressure criteria accepted as positive while receiving insulin/hypoglycemic treatment provides the fasting blood glucose criterion positive.

MS is related to increased risk of diabetes (Haffner et al., 1992), cardiovascular disease (Isomaa et al., 2001), and mortality (Trevisan et al., 1998). Individuals with MS are 3 times more likely to be at risk of coronary artery diseases and stroke, and 6 times more likely to be at risk of cardiovascular-related mortality (Isomaa et al., 2001).

According to ATP III, the MS prevalence among adults in the USA is 21.8% (Ford et al., 2002). Kozan et al. (2003) who conducted MS research (MSR) in Turkey found that the MS prevalence among adults aged 20 years and older was 33.9% in Turkey according to ATP III.

There has been growing interest in metabolic anomalies in patients with schizophrenia since the widespread prescription of new generation antipsychotics. In particular, during the last 2-3 years, the MS prevalence in schizophrenia has been a major topic of concern. We present some related studies conducted during this period in Table II.

We can summarize some important findings of the studies on the prevalence of MS in schizophrenia as follows: Firstly, the prevalence of MS is higher in schizophrenic patients than in the general population (Heiskanen et al. 2003; Kato et al. 2004; DeHert et al., 2006). Heiskanen et al. (2003) found that the MS prevalence in schizophrenic patients was 2-4 times higher than in the general population from the same region. Secondly, the prevalence of MS is higher in men than in women (McEvoy et al., 2005; De Hert et al., 2006). McEvoy et al. (2005) reported that the frequency of MS was 36% in men and 51.6% in women. Lastly, the frequency of MS varies with race. For example, in some studies researchers found that the frequency of MS among black males was lower than among white men (Ford et al., 2002; McEvoy et al., 2005).

Having a schizophrenia diagnosis causes 85% more risk for males and 140% more risk for females to have MS in comparison to the general population (McEvoy et al., 2005). There are several MS risk factors in patients with schizophrenia, including lack of physical activity, malnutrition, use of antipsychotic drugs, smoking, obesity, inadequate maintenance of physical health, and lack of treatment for physical health issues. The present study aimed to determine the prevalence of MS and related factors in patients with schizophrenia followed-up at the Kocaeli University Medicine Faculty, Department of Psychiatry, Psychotic Disorders Outpatient Clinic.

METHOD

All 108 patients with schizophrenia or schizoaffective disorder that presented to the psychotic disorders out-

Table I. Definitions of MS.

	ATP III	ATP III-A	IDF
Waist circumference (cm)	Male > 102 Female > 88	Male > 102 Female > 88	Male ≥ 94 Female ≥ 80
Blood pressure (mm/hg)	≥ 130/85	≥ 130/85	≥ 130/85
HDL (mg/dl)	Male < 40 Female < 50	Male < 40 Female < 50	Male < 40 Female < 50
Triglyceride (mg/dl)	≥ 150	≥ 150	≥ 150
Glucose (mg/dl)	≥ 110	≥ 100	≥ 100

ATP III: Third Adult Treatment Panel; ATP III-A: Third Adult Treatment Panel criteria revised by the American Heart Association; IDF: International Diabetes Federation; HDL: high-density lipoprotein.

Table II. Some studies that investigated the prevalence of MS in patients with schizophrenia.

	Country	n	Diagnostic criteria	Prevalence (%)
Heiskanen et al. (2003)	Finland	35	ATP III	37.1
Cohn et al. (2004)	Canada	240	ATP III	44.7
Basu et al. (2004)	USA	33	ATP III	42.4
Mc Evoy et al. (2005)	USA	1460	ATP III ATP III-A	40.9 42.7
DeHert et al. (2006)	Belgium	430	ATP III ATP III-A IDF	28.4 32.3 36.0
Yazıcı et al. (2005)	Turkey	161	ATP III	33.5

ATP III: Third Adult Treatment Panel; ATP III-A: Third Adult Treatment Panel criteria revised by the American Heart Association; IDF: International Diabetes Federation.

patient clinic of Kocaeli University Medicine Faculty Psychiatry Department between 10 May and 12 June 2006 were included in the study. We recorded the demographic information and clinical data of these patients. We measured their waist circumference and blood pressure, and requested them to complete biochemical tests (i.e. lipid profiles and fasting blood glucose level). Biochemical test results of 8 patients were not completed and, therefore, we evaluated the data of 100 patients. Statistical analyses were conducted with the Statistical Package For Social Sciences v.11.0 (SPSS Inc., Chicago). Descriptive analyses are presented as percents and means. T-tests were used for continuous variables. The statistical significance level was accepted as $P< 0.05$.

Table III. Demographic and clinical characteristics of the patients.

Age (years, mean ± SS)	34.65 ± 11.92
Sex (n, %)	
Female	41 (41%)
Male	59 (59%)
Illness duration (months, mean ± SD)	121.47 ± 94.22
Treatment duration (months, mean ± SD)	98.65 ± 90.19
Drug type (n, %)	
Atypical	67 (67%)
Typical	33 (33%)
Diagnosis (n, %)	
Paranoid	54 (54%)
Undifferentiated	22 (22%)
Residual	10 (10%)
Schizoaffective Disorder	14 (14%)
Smoking (n)	
Present	51 (51%)
Not Present	49 (49%)
Diabetes in Family (n)	
Present	41 (41%)
Not Present	59 (59%)
Hypertension in Family (n)	
Present	54 (54%)
Not Present	46 (46%)
Obesity in Family (n)	
Present	61 (61%)
Not Present	39 (39%)

Treatment duration: period from initiation of drug treatment until present time.

RESULTS

Demographic and clinical characteristics of the patients are given in Table III. Mean age of the patients was 34.65 ± 11.92 years; 41 patients (41%) were female and 59 were male (59%). Mean duration of illness was 121.47 ± 94.22 months and mean duration of treatment (from the initiation of drug treatment until present time) was 98.65 ± 90.19 months. In all, 67 patients (67%) used atypical antipsychotics and 33 (33%) used typical antipsychotics. Drugs taken and their mean doses are provided in Table IV. More than half of the patients (54%) were diagnosed with paranoid schizophrenia. In all, 51 patients (51%) were smokers, 41 patients (41%) had family members with diabetes, 54 patients (54%) had family members with hypertension, and 61 (61%) had a family history of obesity.

MS diagnoses based on different definitions and MS criteria frequency are presented in Table V. MS frequency was 21% according to ATP III, 34% according to ATP III-A and 41% based on IDF (Figure I). For each definition, the frequency of MS was higher among female patients than males. Waist circumference and HDL

Table IV. Antipsychotic drugs and their average dose taken by the patients.

Drug type	Average dosage (mg/g)
Quetiapine (n = 2)	1050 ± 212.13
Olanzapine (n = 24)	12.08 ± 5.29
Ziprasidone (n = 14)	181.42 ± 42.58
Amisulpride (n = 2)	300 ± 141.42
Zuclopenthixol (n = 18)	18.00 ± 7.63
Fluphenazine (n = 14)	2.50 ± 1.00
Risperidone (n = 17)	4.05 ± 2.21
Clozapine (n = 7)	342.85 ± 117.00
Pimozide (n = 1)	8.00 ± 0.0
Aripiprazole (n = 1)	15.00 ± 0.0

parameters were striking among positive MS criteria (Figure II). The high frequency of positive waist circumference and HDL criteria in females and waist circumference, HDL and triglyceride (TG) criteria in males was particularly noteworthy. Based on ATP III-A and IDF definitions, the fasting blood glucose level criterion was satisfied twice as often as ATP III criteria (Table V). When we looked at the positive criteria rate, we found that for all MS definitions nearly 1 of 3 patients satisfied 2 criteria and were not diagnosed with MS. None of the patients in the present study satisfied the all 5 diagnostic criterias for MS.

The mean values for MS diagnostic criteria are shown in Table 6. Mean waist circumference of the female patients (94.26 ± 14.04 cm) was high according to all MS definitions, whereas then mean value for males was high only according to IDF criteria. Mean HDL level was low for females (44.90 ± 14.11 mg/dl) and avarage for males (40.11 ± 8.10 mg/dl). Mean TG level was high for males (159.20 ± 125.18 mg/dl) and was normal for females (106.60 ± 55.68 mg/dl). Mean fasting blood glucose level in males (109.81 ± 76.37 mg/dl) was high accord-

Table IV. The prevalence of MS and MS criteria according to different definitions.

	ATP III			ATP III-A			IDF		
	All patients (n = 100)	Female (n = 41)	Male (n = 59)	All patients (n = 100)	Female (n = 41)	Male (n = 59)	All patients (n = 100)	Female (n = 41)	Male (n = 59)
MS Frequency (%)	21.0	26.8	16.9	34.0	41.5	28.8	41.0	53.7	32.2
Positve Criteria Frequency (%)									
Waist circumference	47.0	61.0	37.3	47.0	61.0	37.3	70.0	82.9	61.0
Blood pressure	8.0	14.6	3.4	8.0	14.6	3.4	8.0	14.6	3.4
HDL	61.0	68.3	55.9	61.0	68.3	55.9	61.0	68.3	55.9
TG	29.0	12.1	40.6	29.0	12.1	40.6	29.0	12.1	40.6
HBGL	22.0	29.3	16.9	50.0	53.7	47.5	50.0	53.7	47.5
Positive Criteria Frequency Rate (%)									
0	18.0	14.6	20.3	12.0	14.6	10.2	8.0	9.8	6.8
1	22.0	19.5	23.7	23.0	14.6	28.8	20.0	12.2	25.4
2	39.0	30.0	39.0	31.0	29.3	32.2	28.0	24.4	30.5
3	17.0	19.5	15.3	27.0	31.7	23.7	34.0	43.9	27.1
4	4.0	7.3	1.7	7.0	9.8	5.1	10.0	9.8	10.2
5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Average Positive Criteria Frequency (%)	1.67 ± 1.08	1.85 ± 1.13	1.54 ± 1.03	1.94 ± 1.12	2.07 ± 1.21	1.84 ± 1.06	2.18 ± 1.11	2.31 ± 1.12	2.08 ± 1.10

ATP III: Third Adult Treatment Panel; ATP III-A: Third Adult Treatment Panel criteria revised by the American Heart Association; IDF: International Diabetes Federation; MS: metabolic syndrome; HDL: high-density lipoprotein; triglyceride, FBSL: fasting blood glucose level.

Table VI. Mean values of MS criterias.

	All patients (n = 100)	Male (n = 59)	Female (n = 41)
Waist circumference (cm)	96.29 ± 13.49	97.69 ± 13.03	94.26 ± 14.04
Systolic blood pressure (mm/Hg)	114.00 ± 14.63	114.06 ± 10.19	113.90 ± 19.47
Diastolic blood pressure (mm/Hg)	74.25 ± 9.80	74.74 ± 7.03	73.53 ± 12.85
HDL (mg/dl)	42.08 ± 11.16	40.11 ± 8.10	44.90 ± 14.11
TG (mg/dl)	137.64 ± 105.40	159.20 ± 125.18	106.60 ± 55.68
Glucose (mg/dl)	106.04 ± 59.30	109.81 ± 76.37	100.60 ± 14.00

HDL: High-density lipoprotein; TG: triglyceride.

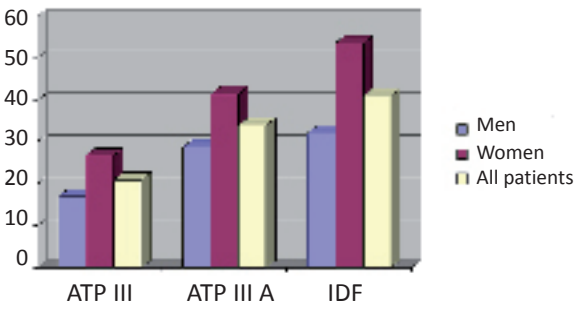

Figure I. MS prevalence for Different Definitions (%).

ing to ATP III-A and IDF criteria, whereas for females (100.60 ± 14.00 mg/dl) it was considered normal.

The frequency of MS according to patient age is given in Table VII. As patient age increased so did the frequency of MS diagnoses. For instance, 7% of 43 patients between 18 and 29 years of age had MS, while 50% of 12 patients that were older than 50 years of age had MS. Figure 3 illustrates that as age increased the prevalence of MS also increased.

We presented the comparison of demographic and clinical characteristics of the patients with or without a diagnosis of MS according to ATP III in Table VIII. Mean age of the patients with MS was 41.90 ± 11.15 years, which was higher than the mean age of the patients without MS diagnosis (32.72 ± 11.43 years). The frequency of MS was higher among women, but differences in the frequency of MS based on gender did not reach the level of statistical significance. Illness duration and treatment duration of patients with MS (183.90 ± 110.40 months and 104.87 ± 82.55 months, respectively) were higher than in patients without MS (154.19 ± 120.92 and 83.88 ± 74.33 months, respectively). There were no differences in the type of antipsychotic drugs used between the patients with and without MS. Similarly, there were no differences between these 2 groups in smoking, and family history of hypertension or diabetes. Obesity was more common in the family members of patients with MS compared to those of the patients without MS.

DISCUSSION

In the present study the MS prevalence in schizo-

Table VII. MS prevalence according to age.

	All patients			Female			Male		
Age (years)	ATP III	ATP III-A	IDF	ATP III	ATP III-A	IDF	ATP III	ATP III-A	IDF
18-29 (n = 43) (f = 12, m = 31)	7.0%	20.9%	18.6%	16.7%	25.0%	33.3%	3.2%	19.4%	12.9%
30-39 (n = 25) (f = 10, m = 15)	20.0%	32.0%	48.0%	10.0%	30.0%	50.0%	26.7%	33.3%	46.7%
40-49 (n = 20) (f = 9, m = 11)	35.0%	50.0%	60.0%	33.3%	55.6%	66.7%	36.4%	45.5%	54.5%
≥ 50 (n = 12) (f = 10, m = 2)	50.0%	58.3%	75.0%	50.0%	60.0%	70.0%	50.0%	50.0%	100%

F: Number of females; m: number of males: ATP III: Third Adult Treatment Panel; ATP III-A: Third Adult Treatment Panel criteria revised by the American Heart Association; IDF: International Diabetes Federation, MS: metabolic syndrome.

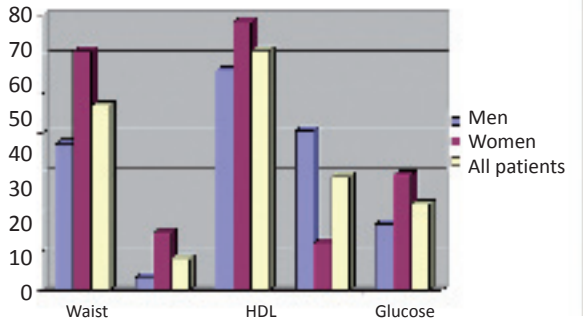

Figure II. Frequency of positive MS Criteria for ATP III (%).

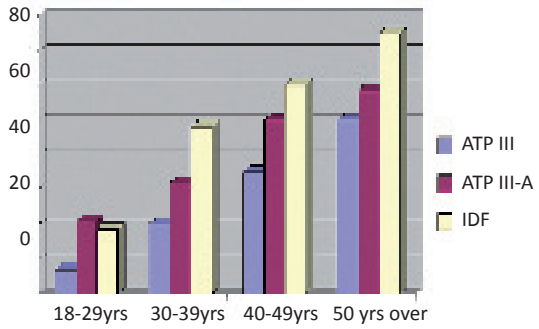

Figure III. Prevalence of MS for age group (%).

phrenic patients was 21% according to ATP III, 34% according to ATP III-A, and 41% according to IDF. The prevalence of MS according to ATP III was lower than previously reported in patients with schizophrenia in Turkey and other countries. There might be several reasons for this finding: The first might be the low mean age of our patients (34.65 ± 11.92 years). In the present study 43% of our participants were younger than 30 years of age. The prevalence of MS was 31.6% among the 57 patients over 30 years of age. Another reason might be that 39% of our patients met only 2 positive criteria for a diagnosis of MS and, thus, were not diagnosed with MS. This situation might also have been related to the percentage of young participants in our sample. Furthermore, when we used more flexible diagnostic definitions, i.e. ATP III-A and IDF, the prevalence of MS sharply increased to levels similar to other studies that utilized the same definitions. This highlights the fact that subclinical metabolic problems could be common.

Waist circumference and HDL were the most commonly observed positive MS criterias. In other words, mean waist circumference was high and mean blood

Table VIII. Comparison of the demographic and clinical characteristics of the patients with and without MS, according to ATP III.

	Patient with MS (n = 21)	Patient without MS (n = 79)	P
Age (years, mean ± SD)	41.90 ± 11.15	32.72 ± 11.43	0.001
Sex (n)			
Female	11	30	
Male	10	49	0.233
Illness duration (months, mean ± SD)	183.90 ± 110.40	104.87 ± 82.55	< 0.001
Treatment duration (months, mean ± SD)	154.19 ± 120.92	83.88 ± 74.33	0.001
Drug type (n)			
Atypical	14	53	
Typical	7	26	0.971
Smoking (n)			
Present	10	41	
Not Present	11	38	0.727
Diabetes in Family (n)			
Present	7	34	
Not Present	14	45	0.422
Hypertension in Family (n)			
Present	13	41	
Not Present	8	38	0.414
Obesity in family (n)			
Present	17	44	
Not Present	4	35	0.035

ATP III: Third Adult Treatment Panel; MS: metabolic syndrome.

HDL level was strikingly low. Waist circumference measurement indicates central obesity. Kato et al. (2004) posited that the relationship between MS and central obesity was stronger than the relationship between MS and obesity (as determined by body mass index). That is, fat level was less important than the distribution of fat in the body. Therefore, Kato et al. (2004) pointed out that waist circumference measurement alone was a good indicator of MS.

MSR indicated that adult blood HDL level was 49 mg/dl on average in Turkey, which was higher than the blood HDL level of our participants in the current study (42.08 ± 11.16 mg/dl). Furthermore, an important finding of the present study was that the mean TG level of the male patients was higher than normal levels (159.20 ± 125.18 mg/dl). Fasting blood glucose level and blood pressure level were infrequently met criteria, but when ATP III-A and IDF definitions were considered, the fasting blood sugar parameter was satisfied twice as often as when the ATP III definition was used (this rate was 22% based on ATP III, and 50% according to ATP III-A and IDF). In the present study the mean fasting blood glucose level was high (106.04 ± 59.30 mg/dl), which is in line with the results of McEvoy et al. (2005), who reported that pre-diabetes and type-II diabetes were frequent among people with schizophrenia.

When we compared patients with MS to those without MS, in terms of demographic and clinical characteristics, we found that the patients with MS had higher mean age, which contradicts earlier reports in the literature (Heiskanen et al., 2003; Kato et al., 2004; Hagg et al. 2006). Metabolic parameters deteriorate with age. In the cited studies the relationship between age and MS did not reach the level of statistical significance. Hagg et al. (2006) and Yazıcı et al. (2005) did not find a coherent relationship between age and MS frequency, but in the present study we found that the frequency of MS increased consistently with age. Moreover, only 1 male patient (3.2%) among 31 male patients under the age 30 years had MS. Yazıcı et al. (2005) found that the frequency of MS was 37% among men under the age of 30 years and 14.3% among those between 30 and 39 years. MS was more prevalent in women according to all 3 definitions, but the rate did not reach the level of statistical significance. Illness and treatment durations of patients with MS were longer than in patients without MS. This might have been related to the combined effects of illness and drug treatment on metabolic problems (e.g. weight gain and high blood pressure) or, the length of illness/treatment duration might have been directly linked to increased age. There is an assumption that atypical antipsychotics can trigger weight gain and related metabolic changes; however, in the present study there wasn't a relationship between the type of drugs used (typical-atypical) and MS diagnoses, which is similar to what was reported by Kato et al. (2004) and Heiskanen et al. (2003). The differential metabolic side effects of atypical antipsychotics should also be considered. For instance, Meyer et al. (2005) reported that within the 20-week period when there was a shift from olanzapine treatment to risperidone, they observed a significant decrease in the frequency of MS among patients. In the current study we examine smoking and metabolic problems, but could not find any significant relationship between them, which is in line with the findings of Hagg et al. (2005) and Kato et al. (2004). Moreover, similar to the findings of Kato et al. (2004), we didn't find a relation between MS and a family history of hypertension or diabetes; however, we did find a significant relationship between MS and family history of obesity, which to our knowledge has not been previously reported.

Schizophrenic patients are at risk of MS and related metabolic problems, which should not be ignored by clinicians. In particular, in the presence of risk factors such as older age, female gender, long duration of both illness and treatment, and family history of obesity, clinicians should evaluate the metabolic condition of patients. We recommend that physicians: 1. Provide suggestions and homework to increase the level of physical activity and improve patient diet (in collaboration to dieticians); 2. Regularly evaluate blood pressure, waist circumference, and blood biochemical analyses, and refer patients to appropriate departments for consultation; 3. Reconsider the use of antipsychotics associated with the risk of metabolic problems. In line with our findings, Kato et al. (2004) suggested that increased waist circumference and problems in the lipid profile were the most significant parameters of MS that should be regularly evaluated.

One strength of the present study was its focus on different definitions of MS while investigating the MS prevalence. In this manner subclinical levels of MS were also taken into consideration. We found that the prevalence of MS was low according to ATP III, while based on the more flexible definitions like ATP III-A and IDF, the prevalence of MS increased. Thus, our findings highlight the fact that clinicians that do not want to ignore subclinical metabolic problems could utilize ATP III-A and IDF diagnostic criteria.

In conclusion, although the present study found that

the prevalence of MS in schizophrenic patients was lower according to ATP III, in comparison to similar studies, it is increased when ATP III-A and IDF were taken into account. High waist circumference and low HDL level were prevalent among the patients. The factors related to MS were age, illness and treatment durations, and family history of obesity. The prevalence of MS was higher among female than males according to all 3 definitions. The major limitation of this study was its small sample size. We recommend further studies with larger schizophrenic samples to be able to generalize the results.

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