Prevalence of Metabolic Syndrome in Spanish Patients with Schizophrenia and Overweight. The CRESSOB Study

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Introduction: Metabolic syndrome (MS) (visceral obesity, dyslipidemia, hyperglycemia, and hypertension), has become one of the major public-health challenges worldwide. Patients with schizophrenia are more likely to suffer from MS than the general population.

Objective: The primary aim of this study was to analyze the prevalence of MS in Spanish patients with schizophrenia and overweight and to compare the best method to calculate the MS prevalence in this population. A secondary aim of the CRESSOB study was to determine whether the presence of the metabolic syndrome (MS) is associated or not with clinical remission of schizophrenia.

Methods: The Control of Metabolic and Cardiovascular Risk in Patients with Schizophrenia and Overweight (CRESSOB) study is a 12-month, prospective, naturalistic study including 110 community mental health clinics selected at random. Each site enrolled four consecutive patients with a diagnosis of schizophrenia, according to DSM-IV TR criteria, and who were overweight (Body Mass Index (BMI) >25 kg/m^2). To assess the prevalence of MS we analyzed the baseline results of the CRESSOB study. The National Cholesterol Education Program (NCEP-ATP III), the International Diabetes Federation (IDF) and the American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI) definitions were used to establish the presence of MS. The Positive and Negative Syndrome Scale (PANSS) was used to determine the percentage of patients in remission. Psychosocial functioning was measured by the Global Assessment of Functioning (GAF) scale.

Results: A total of 391 patients were enrolled in the study (mean age 40.5 years, 63.8% men). 75.9% of the patients did not meet criteria for remission, using the selected PANSS items. The mean GAF score was 52.7 (Standard Deviation (SD) 15.4). Overall, 59.0% of males and 58.3% of females fulfilled the NCEP-ATP III criteria, 71.1% of males and 65.8% of females fulfilled the IDF criteria and 70.1% of males and 65.1% of females fulfilled the AHA/NHLBI criteria. The patients who fulfilled remission criteria were younger, had a lower BMI, and a higher GAF score.

Conclusions: MS is highly prevalent in Spanish patients with schizophrenia who are overweight. Given that metabolic syndrome is an important risk factor for cardiovascular disease, these patients should receive appropriate clinical monitoring for this syndrome.

Key Words: Schizophrenia, Metabolic Syndrome, Overweight, Cardiovascular Disease

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PREVALENCIA DEL SÍNDROME METABÓLICO EN PACIENTES ESPAÑOLES CON ESQUIZOFRENIA Y SOBREPESO. EL ESTUDIO CRESSOB

Introducción: El síndrome metabólico (SM) (obesidad visceral, dislipemia, hiperglucemia e hipertensión) se ha convertido en uno de los mayores retos de salud pública en todo el mundo. Los pacientes con esquizofrenia son más propensos a sufrir SM que la población general.

Objetivos: El objetivo principal de este estudio fue analizar la prevalencia del SM en pacientes españoles con esquizofrenia y sobrepeso y comparar el mejor método para calcular la prevalencia de SM en esta población.

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Un objetivo secundario del estudio CRESSOB fue determinar si la presencia del síndrome metabólico (SM) está asociada o no con la remisión clínica de la esquizofrenia.

Método: El estudio de control del riesgo metabólico y cardiovascular en pacientes con esquizofrenia y sobrepeso (CRESSOB) es un estudio a 12 meses, prospectivo y naturalístico, que incluye 110 centros de salud mental seleccionados al azar. Cada centro seleccionó cuatro pacientes consecutivos con diagnóstico de esquizofrenia, según los criterios DSM-IV TR y que además tuvieran sobrepeso (índice de masa corporal (IMC)> 25 kg/m2). Para evaluar la prevalencia del SM se analizaron los resultados de la línea de base del estudio CRESSOB. Se utilizaron las definiciones del programa Nacional de Educación sobre el Colesterol (NCEP-ATP III), de la Federación Internacional de Diabetes (FID) y de la Asociación Americana del Corazón, el Pulmón y la Sangre (AHA/NHLBI) para establecer la presencia de SM. La escala de los Síndromes Positivo y Negativo (PANSS) se utilizó para determinar el porcentaje de pacientes en remisión. El funcionamiento psicosocial se midió mediante la Evaluación Global de Funcionamiento (GAF).

Resultados: Se incluyeron en el estudio un total de 391 pacientes (edad media 40,5 años, 63,8% de hombres). El 75,9% de los pacientes no cumplía los criterios de remisión, utilizando los elementos seleccionados de la PANSS. La puntuación media del GAF fue de 52,7 (desviación estándar (DE) de 15,4). En total, el 59,0% de los varones y el 58,3% de las mujeres cumplían los criterios del NCEP-ATP III, el 71,1% de los varones y el 65,8% de las mujeres cumplieron con los criterios de la FID y el 70,1% de los varones y el 65,1% de las mujeres cumplieron con los criterios de la AHA/NHLBI. Los pacientes que cumplieron los criterios de remisión fueron más jóvenes, tenían un índice de masa corporal más bajo y una puntuación superior en el GAF.

Conclusiones: El SM es altamente prevalente en pacientes españoles con esquizofrenia que tienen sobrepeso. Dado que el síndrome metabólico es un factor de riesgo importante para la enfermedad cardiovascular, estos pacientes deben recibir una monitorización clínica adecuada para este síndrome.

Palabras clave: Esquizofrenia, Síndrome metabólico, Sobrepeso, Enfermedades cardiovasculares

Table 1 Diagnostic Criteria for Metabolic Syndrome

RISK FACTOR	NCEP/ATP III	IDF	AHA/NHLBI
Abdominal obesity			
-Males	>102 cm	>94 cm	>102 cm
-Females	>88 cm	>80 cm	>88 cm
Fasting * Triglycerides	≥150 mg/dl	≥150 mg/dl	≥150 mg/dl
HDL *			
-Men	<40 mg/dl	<40 mg/dl	<40 mg/dl
-Women	<50 mg/dl	<50 mg/dl	<50 mg/dl
Blood Pressure**	≥130/85 mmHg	≥130/85 mmHg	≥130/85 mmHg
Fasting Glucose***	≥110 mg/dl	≥100 mg/dl	≥100 mg/dl

Three or more criteria must be present to establish diagnosis
*Or specific treatment for this lipid abnormality
**Or on antihypertensive medication
***Or on insulin or hypoglycemic medication

Metabolic Syndrome (MS) is defined by a cluster of clinical features that include increased abdominal or visceral adiposity, atherogenic dyslipidemia, hypertension, and glucose dysregulation or diabetes mellitus (DM). MS has been discussed in cardiology and endocrinology for over two decades, but in recent years there has been an sudden increase of publications in this area. The causes of MS are not fully understood but a central role is played by visceral adiposity and insulin resistance[1].

Different diagnostic criteria may be used to evaluate MS, and there is no consensus regarding the criteria of reference for schizophrenia patients. The most commonly used definitions for MS are the Adult Treatment Panel III (ATP III) of the National Cholesterol Education Program[2] and the modified ATP III criteria of the American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI), lowering the threshold for impaired fasting glucose from 100 to 100 mg/dl[3]. A more recent definition by the International Diabetes Federation (IDF) stressed the importance of waist circumference, using both more stringent and ethnic/race specific criteria[4]. (Table 1).

More than 30 studies have become available since the first paper on MS in patients with schizophrenia was published in 2003. The studies with the larger samples showed a prevalence of MS between 44.6% (n=240) (Cohn et al., 2004) and 35.8% (n=1231)[5] using ATP III criteria, and 33.9% (n=2270)[6] and 28.8% (n=508)[7] using AHA criteria, (see[1] for details).

In Spain, three studies on MS prevalence have been published to date, two of them specifically studying schizophrenia patients. In the first one, in which patients in an in-patient unit were included, MS prevalence was 19%[8]. In another study, the rate among outpatients was 24.6%[9]. The third study found a 27% prevalence of MS among psychiatric patients with diverse diagnoses[10]. In all three cases, an ATP III criterion was used. Compared to the general

population, schizophrenia patients have two or three times the risk of suffering MS[11,12]. Prevalence of MS is also high in patients with various other psychiatric disorders, such as bipolar disorder, (see[13] for a review).

The factors that reportedly increase the risk of MS among schizophrenia patients include: genetic risk factors[14], inactive lifestyle[15], poor dietary choices, lower level of adiponectin[16], high Body Mass Index (BMI)[17] and prolonged illness duration[7,18]. Some of the second-generation antipsychotic drugs cause, to a varying extent, dyslipidemia, weight gain, and diabetes, especially clozapine and olanzapine[9,19-23], but not ziprasidone[24,25].

MS is being increasingly recognized as a major cause of cardiovascular disease-related mortality and morbidity, both in general population and in people with schizophrenia[3,5,8,26,27]. MS is associated with a four times higher risk of developing diabetes[28] and a three-fold increase inrisk of dying from coronary heart disease[29]; it has been even associated with cognitive impairment[30]. In short, MS is considered to be a complex disease very difficult to control and with poor prognosis. Thus, special attention regarding MS should be paid to patients with severe mental illness.

The objective of this cross-sectional analysis is to determine the prevalence of MS in a subgroup of high-risk Spanish patients who suffer both from schizophrenia and overweight and analyze the differences in prevalence depending on the diagnostic criteria used for MS.

A secondary aim of this analysis is to study whether the presence of MS was associated or not with cross-sectional clinical remission of schizophrenia.

METHODS

Patients

The Control of Metabolic and Cardiovascular Risk in Patients with Schizophrenia and Overweight (CRESSOB) study is a 12-month, observational, prospective, open-label, multicenter, naturalistic study including 110 community mental health clinics selected by geographic population density in order to represent the entire country. The study was conducted from June 2007 to June 2009. We excluded patients younger than 18 years of age and those suffering from mental retardation or severe cognitive impairment. All the patients included gave written informed consent, as stated in the protocol for patients approved by the Institutional Review Board of the University Clinic of Navarra, after the procedures had been fully explained. This study complied with the principles of the Declaration of Helsinki regarding medical research in humans[31]. The study did not interfere with the investigators' decision on the most appropriate treatment for the patients.

Assessment Instruments and Procedures

Each site enrolled four consecutive patients with a diagnosis of schizophrenia, schizophreniform or schizoaffective disorder assessed at each interview using the clinician version of the Structured Clinical Interview[32], as determined by the criteria listed in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR)[33] and overweight (defined as BMI>25 kg/m^2) at the study entry. BMI was calculated following criteria from the National Institutes of Health (NIH)[34] (Clinical WHO guidelines, 1998) and four groups were established: underweight (BMI <18.5), normal weight (BMI 18.5-24.9), overweight (BMI 25-29.9) and obesity (BMI $\geq$30).

Sociodemographic and Clinical Variables

At the baseline interview, the following information was collected: socio-demographic data (gender, age, marital status, number of siblings and children, years of formal education, occupation and occupational status) and clinical data (age at onset, age at diagnosis and duration of illness), medical history, personal and family history of cardiovascular risk, substance abuse (tobacco, alcohol and illegal drugs), health habits (dietetic habits and physical activity), physical examination (weight, height, waist circumference, measured at the umbilicus level, and blood pressure). A fasting blood sample was drawn to evaluate glucose, total cholesterol, high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol and triglycerides. A cross-sectional analysis of baseline visit data was performed in order to determine the prevalence of MS. The National Cholesterol Educational Program (NCEP/ATP III) definition was the main criteria to consider presence of MS in this study. The International Diabetes Federation (IDF) and American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI) criteria were also used (Table 1).

Clinical severity was determined using the Spanish version[35] of the Positive and Negative Symptoms Scale (PANSS) for schizophrenia[36]. The PANSS scale was also used to determine cross-sectional remission[37]. The new remission criteria of the PANSS scale correspond to the score in all the following items $\leq$ 3 (using the scale from 1 to 7). The time component was excluded because analysis was cross-sectional.

- Psychoticism: P1: Delusions; P3: Hallucinatory behavior; G9: Unusual thought content
- Disorganization: P2: Conceptual disorganization; G5: Mannerisms and posturing.
- Negative Symptoms: N1: Blunted affect; N4: Passive/apathetic social withdrawal; N6: Lack of spontaneity and flow of conversation.

The Global Assessment of Functioning (GAF) is a numeric scale used for rating the social, occupational and psychological functioning of patients. It has just one item, to be scored between 1 and 100. A score ≥ 60 was considered as the threshold for proper functioning[38].

Statistical analysis

Statistical analysis was performed using the SAS version 8.2 statistical package. Sample size was calculated on the basis of the primary endpoint (prevalence of MS). A sample size of 450 patients was estimated using a two-tailed test with a 95% confidence interval and normal distribution for large samples. The observed percent of patients monitored in the different modifiable risk factors, would thus have a precision no lower than ± 4.6% with respect to the anticipated percentage of 50% (percent that maximizes the sample size).

Qualitative and quantitative variables were analyzed using measures of central tendency (mean, median) and dispersion (95% confidence interval [CI]). Qualitative variables were defined according to their absolute and relative frequencies. Dimensional variables and frequencies were compared by parametric or non-parametric tests, as appropriate. The individual prevalence of MS was estimated by the direct method, calculating the corresponding 95% confidence intervals. Association between demographic and clinical variables and MS and its components was examined using chi-square and Student's *t*-test. All statistical tests were two-tailed and p≤0.05 was considered statistically significant.

Binary logistic regression was used to analyze the association between the condition of a positive MS diagnosis with clinical and course-of-illness variables. All logistic regression models fit well according to the Hosmer-Lemeshow goodness-of-fit test[39].

RESULTS

Demographic and Diagnostic Characteristics

A total of 391 patients were enrolled in the study. Seven patients were excluded from the analysis because their BMI was <25 kg/m^2. In the end, 384 were considered evaluable. Of the evaluable patients, 77.7% met diagnosis criteria for schizophrenia, 18.8% for schizoaffective disorder and 3.4% for schizophreniform disorder. Mean age was 40.5 years (SD 10.6) and 63.8% were male. Demographic characteristics of patients are shown in Table 2.

According to the World Health Organization (WHO) classification (Clinical WHO guidelines, 1998), 66.7% of the patients were obese (obesity class I [BMI=30.0-34.9 kg/m^2]: 40.0%, class II [BMI=35.0-39.9 kg/m^2]: 17.6%, and class III [BMI≥40.0 kg/m^2]: 9.1%). Physical parameters of patients are shown in Table 3.

Metabolic Syndrome

Data to determine prevalence of MS (NCEP/ATP III) was available for 251 patients (65.5%). In that subgroup, the prevalence of MS was 59.5% (NCEP/ATP III). The percentages of subjects with MS in the schizophrenia and the schizoaffective disorder groups were 61.2% and 60.8%, respectively. No significant differences were observed between groups. Figure 1 shows the prevalence of risk factors in patients with or without MS (NCEP/ATP III) (p<0.0001 for all factors). The most highly-met criterion was abdominal obesity. The prevalence of MS components (NCEP/ATP III) by gender and for the total sample is showed in Table 4. This table also shows the MS prevalence calculated

Table 2 Demographic Characteristics of Patients

	TOTAL (384)
Age[1]	*349*
Mean Years (SD)	40.5 (10.6)
<30	56 (16%)
30-40	120 (34.4%)
40-50	105 (30.1%)
>50	68 (19.5%)
Gender[1]	*367*
N (%) Male	234 (63.8%)
Years of Schooling[1]	*338*
Mean Years (SD)	11.2 (4.3)
Occupational Status[1]	*374*
Active	67 (18.0%)
Unemployed	62 (16.6%)
Disability Pension	162 (43.3%)
Others	83 (22.1%)
Disease Duration[1]	*318*
Mean Years (SD)	13.7 (9.1)
Smoking[1]	*383*
N (%)	206 (53.8%)
Substance Abuse[1]	*379*
N (%)	41 (10.8%)
Diet Habits1	*376*
Controlling Calories	77 (20.5%)
Controlling Salt	28 (7.5%)
Avoiding Fat/Chol.	103 (27.2%)
Consuming Dietary Fiber	154 (41.4%)
Physical Exercise1	*378*
None	109 (28.8%)
Light	167 (44.2%)
Mild	77 (20.4%)
Intense	18 (4.8%)
Highly Intense	7 (1. 9%)

[1]=evaluable patients with this data

Table 3 Physical Parameters of Patients

TOTAL (384)	
Weight[1]	*373*
Mean kg (SD)	93.4 (17.9)
BMI[1]	*375*
Mean kg/m² (SD)	32.6 (5.2)
Waist Circumference[1]	*311*
Mean cm (SD)	113.2 (17.0)
Systolic Blood Pressure[1]	*338*
Mean mmHg (SD)	128.8 (16.8)
Diastolic Blood Pressure[1]	*338*
Mean mmHg (SD)	79.3 (10.5)
Blood Pressure[1]	*338*
Optimal (<120 / <80)	64 (18.9%)
120-129 / 80-84	64 (18.9%)
130-139 / 85-89	85 (25.1%)
140-159 / 90-99	101(29.9%)
160-179 / 100-109	19 (5.6%)
≥180 / ≥110	5 (15%)
Total Cholesterol[1]	*325*
Mean mg/dl (SD)	216.4 (48.0%)
HDL Cholesterol[1]	*264*
Mean mg/dl (SD)	51.8 (44.7)
HDL< 40♀-50♂ mg/dl	117 (44.8%)
Triglycerides[1]	*307*
Mean mg/dl (SD)	171.4 (96.0)
TAG ≥ 150 mg/dl	162 (52.8%)
Fasting Glucose[1]	*324*
Mean mg/dl (SD)	101.9 (25.4)
Glucose ≥ 100 mg/dl	139 (42.9%)

[1]=evaluable patients with this data

according to the other MS criteria. The males had a higher proportion of high blood pressure in comparison to females. The prevalence of MS increased significantly with age and weight for both genders (Table 4).

PANSS score was also used to determine the percentage of subject in remission. At baseline the percentage of patients who met the full remission criteria was 22.5% (n=81). We conducted additional analyses to determine if there is an association between the proportion of patients that meet the full remission criteria and the five parameters of MS. We only found differences in one criterion which was a higher proportion of patients with glucose ≥100 mg/dl (or on treatment for diabetes) in the group of patients not meeting remission criteria in comparison with those that met this criteria (59.2% *vs* 45.5%; p=0.026).

Logistic regression analysis failed to find factors (sociodemographic variables, health habits, clinical variables, etc.) that could be associated with MS, using both NCEP-ATP III criteria in the model and IDF as well.

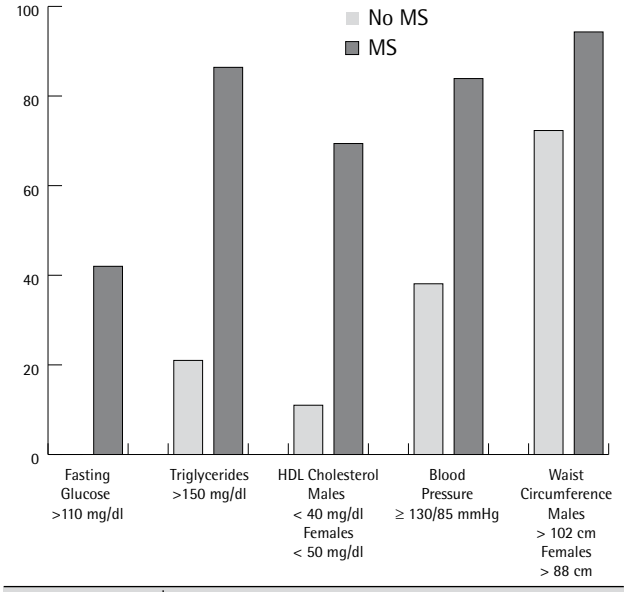

Figure 1 *Prevalence of MS Parameters in Patients with or without MS-NCEP/ ATP III Criteria*

Cross-sectional Remission and Global Assessment of Functioning

Cross-sectional remission was calculated in 352 patients. The proportion of patients who did not meet the full remission criteria was 75.9% (n=267). There are three parameters associated with remission criteria: these patients are younger, weigh less and have a higher GAF scale score (see Table 5).

GAF was evaluated in 343 patients. The mean GAF score was 52.7 (SD 15.4) 95% CI (51.0-54.3); 211 patients (61.5%) had a GAF score under 60.

DISCUSSION

Main Findings, Strengths and Limitations of the Study

MS is highly prevalent among patients with schizophrenia who are overweight. In light of previous findings, we can state that being overweight doubles the risk of suffering from MS. Moreover, NCEP/ATP-III criteria are the least conservative, so that AHA/NHLBI or IDF would point to higher levels. Patients with MS have a very negative effect on the global function of the disease when assessed using the GAF scale. There are no association between the remission criteria and the condition of suffering from MS.

One of the strengths of our study is the high participation rate, due to the fact that we used different diagnostic

Table 4 Prevalence of MS (All Criteria) and its Components (NCEP/ATP III) by Gender and in the Total Sample

	TOTAL (384)			Male (234)			Female (133)			p
Age (years) Mean (SD) 95% CI	**40.5** (10.6) (39.4 ; 41.6) N=349			**39.1** (10.6) (37.7 ; 40.6) N=212			**43.0** (10.4) (41.1 ; 44.8) N=123			**0.0006**
Weight (kg) Mean (SD) 95% CI	**93.4** (17.9) (91.6 ; 95.2) N=373			**99.0** (17.6) (96.7; 101.3) N=225			**84.5** (14.5) (82.0 ; 87.0) N=131			**<0.0001**
	N[1]	n	%[2]	N[1]	n	%[2]	N[1]	n	%[2]	
Waist Circum.	*310*	268	**86.5**	*190*	159	**83.7**	*108*	99	**91.7**	0.0520
Triglycerides	*294*	177	**60.2**	*184*	113	**61.4**	*97*	56	**57.7**	0.5490
HDL	*261*	117	**44.8**	*161*	71	**44.1**	*93*	43	**46.2**	0.7414
Blood Pressure	*341*	225	**66.0**	*211*	151	**71.6**	*115*	64	**55.7**	**0.0037**
Glucose	*294*	72	**24.5**	*181*	43	**23.8**	*101*	25	**24.8**	0.8513
	N[3]	n	%[2]	N[3]	n	%[2]	N[3]	n	%[2]	
NCEP/ATP III	*257*	153	**59.5**	*166*	98	**59.0**	*84*	49	**58.3**	0.9150
IDF	*231*	160	**69.3**	*152*	108	**71.1**	*79*	52	**65.8**	0.4138
AHA/NHLBI	*261*	180	**69.0**	*167*	117	**70.1**	*86*	56	**65.1**	0.4231

N[1]=evaluable patients with enough data to calculate MS (NCEP/ATP III)
%[2] Percentage calculated with respect to the evaluable patients (n/N)
N[3]=evaluable patients with this data
Note: in the male and female groups only appear the data of patients that have been evaluated for the dietetic habits.

Table 5 Cross-sectional Remission

	No Remission (267)	Remission (87)	p
Age (years)[1] Mean (SD) 95% CI	**247** **41.2** (11) (39.8; 42.5)	**75** **38.2** (10.4) (36.0; 40.3)	**0.0258**
Weight (Kg)[1] Mean (SD) 95% CI	**259** **94.7** (18.5) (92.5; 97.0)	**83** **90.2** (15.9) (86.7; 93.7)	**0.0454**
GAF[1] Mean (SD) 95% CI	**258** **48.5** (13.7) (46.8; 50.1)	**81** **65.9** (13.2) (63.0; 68.9)	**<0.0001**

[1]=evaluable patients with this data

criteria to calculate the prevalence of MS in patients with schizophrenia. Furthermore, our study involved a specific sample at high metabolic risk, as we only included those patients with schizophrenia who are overweight.

The limitations of our study include the fact that we only obtained data from 65% of the participants to calculate the prevalence of MS and the fact that it is a cross-sectional study; the longitudinal results will be published in a future research paper.

Prevalence of Metabolic Syndrome

To the best of our knowledge, this is the first study to analyze the prevalence of MS in a specific subgroup of patients with schizophrenia who are overweight. Our ultimate intention is to identify the particular characteristics of such a high-risk subgroup.

The prevalence of MS in our sample is slightly higher than the prevalence reported by many north American studies[21,40] and considerably higher than that reported by other European studies[11,12,41,42]. The prevalence we found (59.5%) is also higher than the findings of previous studies within Spain: 24.6%[9] or 27%[10], using the same diagnostic criteria (ATP III). This leads us to tentatively conclude that Spanish subjects with schizophrenia who are also overweight run twice the risk of presenting MS. If we compare our results to those found for broad samples of Spanish populations, either attending primary healthcare centers (n=4232; prevalence: 22.6%[43]) or the general working population (n=7256; prevalence: 10.2%[44]), the high prevalence seen in our study is very noteworthy, up to six times greater.

In comparison with bipolar disorder in studies realized in American[45,48] and in Spain[49] the prevalence of MS in our study was also remarkably higher.

We found no gender difference regarding the prevalence of MS, unlike other authors[17]. Individual analysis of each one of the MS diagnostic criteria gave differences in terms of blood pressure alone, with hypertension found more frequently in men than in women. A similar finding is reported by Bobes[9].

Weight and age are the single most important factors associated with a higher prevalence of MS, a point also revealed by previous studies[9]. Surprisingly, when using multivariate analysis by different logistic regression models we did not find an association between clinical variables, including dietary habits and physical exercise, and MS diagnosis. This finding can be explained, at least in part, by the fact that there is not a big difference in these behaviors in the subgroup of patients included in our study (schizophrenia with overweight).

Different Diagnosis Criteria to Measure MS

As may be expected when strict diagnostic criteria are used -such as the IDF or AHA, as opposed to the ATP III (see Table 1)- prevalence rates can increase by around 10%. Such a difference must be taken into account when comparing studies; for instance, the prevalence we report (59%) would be in line with a figure of 69% based on alternative diagnostic criteria.

Other recent studies that apply the ATP III criteria do not arrive at such great differences in prevalence rates, possibly because their sample populations are not restricted to schizophrenic patients who are overweight[11,17]. We might surmise that the differences in MS prevalence (when assessed with different tools) are greater when the study population is limited to psychiatric patients who are also overweight.

According to our results we can say that the IDF and AHA/NHLBI diagnostic criteria, which differ only in the abdominal obesity criteria, show prevalence rates that are almost equal and about 10 percentage points higher than the NECP/ATP III, which is the one that weighs more basal hyperglycemia. This last criterion (basal hyperglycemia) is the most sensitive in diagnosing the SM (none of the patients who did not meet this criterion were diagnosed of SM, see Figure 1), therefore, we believe that although this scale is more conservative, clinicians should use because it includes a higher cutoff for the most sensitive criteria that comprise the metabolic syndrome. According to our results abdominal obesity seems to be overly prevalent but little discriminative in diagnosing the syndrome.

Metabolic Syndrome and Illness Remission

In our sample 75.9% of patients did not fulfill remission criteria, this result is higher than another studies with large samples, like SOHO study (61.8%)[50] and ESFERA study (55.2%)[51], but in that cases they did not include only overweight patients and used different criteria to measure the remission.

We have not found any article that studies the relationship between MS and the condition to fulfill remission criteria. Another study found that schizophrenia patients with MS had more psychopathology (measured with PANSS scale) and more greater severity (measured with CGI) but did not study the remission criteria specifically[52]. The only parameter of MS that can be associated with illness remission is hyperglycemia. Therefore, we can conclude that MS seriously affects physical health but is not overly associated to actual remission criteria (that are based on some parameters of the PANSS scale). We think that it is very important to include some physical parameters in future remission criteria illness, especially in schizophrenic patients who are overweight. Some researchers affirm that the patients who fulfill these criteria have better functional improvement than those who present clinical stability[53].

Although we have not found an association between MS criteria and remission of schizophrenia, our analysis find an association between low weight and remission (see Table 5), the explanation for this finding may be due to methodological limitations of the study. It is possible that patients who do not meet the criteria for remission of schizophrenia are treated with higher doses of antipsychotics (or various combinations of drugs at a time), especially those that are associated with MS, such as clozapine and olanzapine[9,19-23], which could explain the higher weight and greater association with MS. This result is similar to another Spanish study that found a higher risk of coronary heart disease (but not a higher prevalence of MS) in schizophrenia patients with deficit symptoms[54].

In conclusion, our study shows that MS is highly prevalent in a relatively young sample of Spanish patients with schizophrenia who are overweight. Given the fact that MS is an important risk factor for cardiovascular disease, such patients should receive appropriate clinical monitoring for this condition. Different consensus protocols[18,19,22,55] have been developed to help clinicians to ensure that people with schizophrenia do indeed receive appropriate and timely care of their physical disorders. The literature suggests that persons with schizophrenia are less likely to receive the same level of recommended services, such as physical examinations, and are more likely to perceive barriers for care than persons without severe mental illness[8,56,57]. Therefore, all health professionals involved in the care of a patient with schizophrenia, including the treating psychiatrist, can contribute to control metabolic disorders.

CONFLICT OF INTEREST

Prof. Dr M. Bernardo has been a spokesperson for and advisory board member of Bristol-Myers Squibb, Eli Lilly,

Janssen-Cilag, Mylan, Organon and Pfizer. Dr L. Gutiérrez-Rojas has been a spokesperson for and advisory board member of Bristol-Myers Squibb, Janssen-Cilag, Astra-Zeneca and Pfizer. The rest of the authors have no transmitted any conflict of interest.

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