METABOLIC SYNDROME AND ITS RELATIONSHIP WITH NEGATIVE SYMPTOMS IN FEMALE PATIENTS WITH SCHIZOPHRENIA

Codruta A. Boti¹, Ioana V. Miclutia²

Abstract:
Introduction: High prevalence of metabolic syndrome has been reported in patients with schizophrenia. Factors that contribute to the development of physical and biochemical abnormalities due to this syndrome are: sedentary lifestyle, antipsychotic medication, mental disorder related issues, including negative symptomatology and genetic factors. A significant association between negative symptoms, obesity and metabolic syndrome has been reported in recent studies. Objectives: The objectives of this study were to estimate the frequency of metabolic syndrome and to examine the association between metabolic syndrome and negative symptoms in female patients with schizophrenia.

Methods: Forty for female patients diagnosed with schizophrenia were recruited from psychiatric out-patient clinic. Patients underwent one assessment for metabolic syndrome parameters which included anthropométrical measurements, blood pressure, lipid profile, fasting plasma glucose level. The presence of the metabolic syndrome was determined using the International Diabetes Federation criteria. The Positive and Negative Syndrome Scale was used for characterising symptoms.

Results: Mean duration of illness was 13.93 years and mean duration of education was 13.15 years. Metabolic syndrome was found in 52.27% of the patients (36% with hypertriglyceridemia, 86% with high waist circumference, 59% with low HDL cholesterol, 20.45% with high fasting glucose and 11% with hypertension. The frequency of metabolic syndrome in group patients with predominant negative symptoms was significantly higher (p=0.0026) compared to the group without predominant negative symptoms.

Conclusions: Metabolic syndrome is common in female patients with schizophrenia. Systematically assessment of the various components of metabolic syndrome and adequate treatment should help to reduce the cardiovascular risk and mortality in patients with schizophrenia.

Key words: schizophrenia, metabolic syndrome, negative symptoms

INTRODUCTION

Schizophrenia is a severe mental disorder characterized by positive symptoms (e.g. delusions, hallucinations), negative symptoms (e.g. flattened affect, lack of motivation, social withdrawal) and cognitive impairment, making it one of the first ten causes of chronic disability worldwide with burden in multiple aspects of social, family and professional life (1, 2).

Life expectancy for schizophrenia patients is 15-20 years shorter, and the mortality rate is 2.5-3 times higher compared to the general population correlated with somatic pathology (3, 4). Cardiovascular pathology is the main cause of mortality among patients with schizophrenia (5, 6). According to the third report of the NCEP, metabolic syndrome is an important risk factor for cardiovascular disorders (7). The metabolic syndrome increases the relative cardiovascular risk by 1.2-2 times (8). The metabolic syndrome is a conception that include hyperglycemia, increased blood pressure, elevated triglyceride levels, low high-density lipoprotein cholesterol levels and central obesity (9).

The exact prevalence of metabolic syndrome in patients with schizophrenia is not known, ranging between 11-69 % in treated patients and between 4-26 % in untreated patients; one in three patients fulfill the metabolic syndrome criteria and one in two patients is overweight (10). The prevalence of individual factors that define metabolic syndrome was described by Mitchell et al. in a metaanalysis of 126 studies including 25 692 patients with mean disease duration of 10.4 year: 9.4 % overweight patients, 19.5 % patients with hyperglycemia, 39.3 % with hypertriglyceridemia and 42.6 % with low levels of HDL - Cholesterol, 38.7 % with hypertension, and 10.9 % with diabetes (7).

Risk factors for metabolic syndrome and cardiovascular disorders in people with schizophrenia are complex; they can be divided into three categories: behavioral factors including lack of sufficient physical activity, smoking, substance abuse and unhealthy eating patterns; disease related factors with cardio-metabolic side effects of antipsychotic treatment and low socioeconomic status (11). Also, genetic factors contribute to the high prevalence of metabolic syndrome in these patients (12).

The negative symptoms, including a reduction of emotional responsiveness, motivation, socialization, speech and movement are included in behavioral factors which contribute to a higher risk of metabolic syndrome in patients with schizophrenia. A significant association 

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association between negative symptoms, obesity and metabolic syndrome has been reported in recent studies (10, 11, 12).

The objectives of this study were to estimate the frequency of metabolic syndrome and to examine the association between metabolic syndrome and psychiatric symptoms in female patients with schizophrenia.

MATERIAL AND METHODS

44 adult female patients (age 18-55) with DSM-IV-TR and ICD-10 diagnosis of schizophrenia followed up in the outpatient service of the University Clinic of Psychiatry, Cluj-Napoca, Romania were included into the study. All patients had a minimum of 8 years of education. Patients were included if (a) acute symptoms were remitted, with no relapse in the last 6 months, (b) patients were stable on antipsychotic medication, using the same dosage for at least 4 weeks before inclusion. Patients were excluded if (a) they had a DSM-IV-TR diagnosis of alcohol dependence or other substance dependence, dementia, mental retardation, history of head trauma, or any current severe medical condition (cardiovascular, neumouscular or endocrine condition), (b) severe cardiovascular disorders diagnosed prior to the diagnose of schizophrenia.

The study was approved by the University of Medicine and Pharmacy Iuliu Hatieganu Ethics Committee and all patients signed an informed consent before being admitted in the study.

Information on age, education, economic status, tabacco smoking status, onset and course of illness, antipsychotic treatment were collected through the clinical interview. The types of antipsychotics were categorized into „clozapine/olanzapine” group and „other antipsychotics” group considering that clozapine and olanzapine may have a higher potential in generating metabolic abnormalities (20). Patients were also assessed for psychopathology using Positive and Negative Syndrome Scale and received anthropometric measurements and a fasting metabolic laboratory screening. The definition for predominant negative symptoms used in this study suggests a baseline score ≥ 4 on at least 3 or ≥ 5 on at least 2 of the 7 negative subscale items and a PANSS positive score of <19.

Sitting blood pressure, systolic (SBP) and diastolic (DBP) were recorded. Waist circumference was measured midway between the lowest rib and the iliac crest. Overnight fasting blood was collected for metabolic profile analysis: fasting level of serum triglyceride (TG), fasting plasma glucose level and serum high-density lipoprotein cholesterol (HDL-Col) level were measured.

The diagnosis of metabolic syndrome was defined according to the modified criteria of the International Diabetes Federation (IDF) , which requires the presence of three or more of the following five criteria: high waist circumference (>94 cm for men and >80 for women), hypertriglyceridermia (>150 mg/dl or on lipid lowering medication), low HDL cholesterol level(<40 mg/dl in men and <50 mg/dl in women), high blood pressure (≥ 130/85 mm Hg or on antihypertensive medication) and high fasting glucose concentration (≥100 mg/dl or on glucose-lowering medication) (9).

The association between clinical and demographic characteristics and metabolic syndrome was performed using chi square and Student's t test. ANOVA test was used to describe the relationship between each component of metabolic syndrome characteristics and clinical and demographic characteristics.

RESULTS

The mean age of the patients was 40.45 years and the mean age of education 13.15 years. The mean duration of illness was 13.93 years. 17 patients (38.63%) were current tobacco smokers. The mean PANSS total score was 63.81, which indicates that symptomatology in the study group was mild. 47.72 % of patients had predominant negative symptoms.

Metabolic syndrome was found in 52.27 % of patients (86% with high abdominal circumference, 59% with low HDL cholesterol, 20.45% with high fasting glucose and 11% with hypertension). Female patients with metabolic syndrome had significantly lower education level (p=0.0017) and a significantly higher duration of illness (p=0.0014) compared to patients without metabolic syndrome. Metabolic syndrome was also found to be associated with olanzapine or clozapine current treatment (p=0.0002). The PANSS negative score was significantly higher in patients with metabolic syndrome (p=0.0079).

<table>
<thead>
<tr>
<th>Metabolic syndrome</th>
<th>n</th>
<th>p</th>
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<tbody>
<tr>
<td>No n=21, 47.73%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes n=23, 52.27%</td>
<td></td>
<td></td>
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<tr>
<td>Age, mean value</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40.45</td>
<td>38.56</td>
<td>42.71</td>
</tr>
<tr>
<td>Education, mean value</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13.15</td>
<td>14.1</td>
<td>12.04</td>
</tr>
<tr>
<td>Tabacco smokers, n, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17 (38.63%)</td>
<td>8 (18.18%)</td>
<td>9 (20.45%)</td>
</tr>
<tr>
<td>Duration of illness, mean value</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13.93</td>
<td>10.21</td>
<td>18</td>
</tr>
<tr>
<td>PANSS total score, mean value</td>
<td></td>
<td></td>
</tr>
<tr>
<td>63.81</td>
<td>59.1</td>
<td>68.95</td>
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<tr>
<td>PANSS positive score, mean value</td>
<td></td>
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<tr>
<td>10.84</td>
<td>10.65</td>
<td>11.04</td>
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<tr>
<td>PANSS negative score, mean value</td>
<td></td>
<td></td>
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<tr>
<td>19.29</td>
<td>16.52</td>
<td>22.33</td>
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<tr>
<td>Predominant negative symptoms, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>47.72</td>
<td>52.28</td>
<td>47.72</td>
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<tr>
<td>Current cloz/ olanz treatment, n</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>4</td>
<td>6</td>
</tr>
</tbody>
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P<0.05- statistically significant

Table 1. Demographical and clinical characteristics of the 44 patients with schizophrenia and association with metabolic syndrome (MetS)
Investigating correlations between components of metabolic syndrome and clinical and demographical characteristics, it was found that hypertension has positive correlated significantly with duration of illness.

The frequency of metabolic syndrome in group patients with predominant negative symptoms was significantly higher (p= 0.0026) compared to the group without predominant negative symptoms.

Fig 1 Association between metabolic syndrome and predominant negative symptoms (p=0.0026)

Predominant negative symptoms were found to be associated with higher abdominal circumference (p=0.025). No other component of metabolic syndrome was associated with predominant negative symptoms.

Table 3 Association between components of metabolic syndrome and predominant negative symptoms

<table>
<thead>
<tr>
<th>Component of metabolic syndrome</th>
<th>Predominant negative symptoms (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertriglyceridemia</td>
<td>0.4660</td>
</tr>
<tr>
<td>High abdominal circumference</td>
<td>0.025?</td>
</tr>
<tr>
<td>Low HDL Cholesterol</td>
<td>0.053</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.335</td>
</tr>
<tr>
<td>High fasting blood sugar</td>
<td>0.812</td>
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</tbody>
</table>

P<0.05- statistically significant

DISCUSSIONS

This study assessed the frequency of metabolic syndrome in a Romanian group of women patients diagnosed with schizophrenia, with mild symptomatology. In this sample, a high frequency of 52.27% of metabolic syndrome was observed, despite the fact that this sample was young (mean age 40.48 years). The prevalence of metabolic syndrome in female patients with schizophrenia is not known, ranging between 11-69% in treated patients. Compared with literature data, the metabolic syndrome rate in this sample was higher, Clamors study reported a prevalence of 27.2%, and CATIE study reported a prevalence of 36% (19, 20). The higher rate of metabolic syndrome found in this study may be due to a worse dietary lifestyle and medical care factors, but may also reflect differences in sample characteristics and limited sample size.

In this sample, a frequency of 86% of high abdominal circumference, a frequency of 59% of low HDL Cholesterol, a frequency of 36% of hypertriglyceridemia, a frequency of 11% of hypertension and a frequency of 20.45% of high fasting glucose were observed. The results were also higher than those reported by Michell et al. in a recent meta-analysis performed on 25 692 patients: 39.3% hypertriglyceridemia, 42.6% with low levels of HDL-cholesterol and hyperglycemia 10.9% (7). Only hypertension was found in a small number of patients in our sample compared to the percentage of 38.7 reported by Michell and al.

A high percentage of patients following treatment with Olanzapine or Clozapine (60%) met the criteria for metabolic syndrome. Metabolic disturbances caused by olanzapine and clozapine are documented by meta-analyses. They are regarded as the most important antipsychotics that cause weight gain, hyperglycemia and dyslipidemia (21).
In this study, there were no significant differences between the metabolic syndrome group and the group without metabolic syndrome group regarding smoking habit and economic level. The rate of smokers found in this sample (37%) was 2.5 fold higher than the rate of 14.4% of female smokers in Romanian population (21). The results are consistent with the literature data which shows that smoking prevalence is almost three times higher among patients with schizophrenia compared with the general population and the number of cigarettes smoked is higher among patients with schizophrenia compared with the general population (22). In a Finnish study conducted in subjects with psychotic pathology, the habit of smoking was described as the most important predictors of mortality to 8 years (23).

Negative symptoms like anhedonia, apathy, associability, decreased interest in their own health, lack of motivation are factors related to lifestyle (diet, physical activity) involved in the etiology of metabolic syndrome. In this study, almost half of patients had predominant negative symptoms (47.72%). The frequency of metabolic syndrome is significantly higher in patients with predominant negative symptoms compared to the group without predominant negative symptoms. Also, abdominal circumference was significantly higher in patients with predominant negative symptoms. Literature data regarding the relationship between the type of symptomatology and metabolic syndrome disturbances are limited and inconclusive. Saddichha et al. (24) and Kirkpatrick et al. (25) showed that negative symptoms correlated with obesity and metabolic syndrome. In a recent study of 1120 patients, 52.2% were found with negative symptoms; the prevalence of metabolic syndrome was significantly higher in the group of patients with negative symptoms (43.9%) compared to the group without negative symptoms (34.9% 0) (26). Metabolic syndrome was significantly correlated with negative symptoms, age and somatic comorbidities. In a study of 372 patients with schizophrenia treated with antipsychotic a longer period of 2 years, Chen et al. showed that negative symptoms were negatively correlated with body mass index and serum triglyceride level and positively with HDL-Col level, authors suggesting that patients with negative symptoms may have a different lipid profile compared to those with no obvious negative symptoms (27). Other studies did not find significant differences in negative symptomatology between patients with and without metabolic syndrome (19).

When the relationship between negative symptoms and metabolic disturbances was investigated, various definitions were choose for negative symptoms. This is one of the reason for the inconclusive conclusions in literature. Future studies and meta-analysis are needed in this field of study.

This study has several limitations. Due to the cross sectional nature of the study, we were unable to investigate the causal nature of the differences observed between the two groups (with and without metabolic syndrome) and also of the associations found between negative symptomatology and metabolic syndrome components. The small sample size is another limitation of this study.

CONCLUSIONS
This study demonstrates that metabolic syndrome and its components (dyslipidemia, obesity, hyperglycemia, hypertension) had a high frequency among young female patients with mild and stable symptoms of schizophrenia compliant to atypical antipsychotics treatment.

Almost half of the study group had predominant negative symptoms. Metabolic syndrome was diagnosed significantly more often in patients with predominant negative symptoms.

These findings highlight the need for systematically anthropometric and biochemical evaluation in order to early detect the metabolic disturbances in patients with schizophrenia. The prevention and treatment of metabolic syndrome should help to reduce mortality and to improve overall prognosis in this population.

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LIST OF ABBREVIATIONS:
PANSS- positive and negative syndrome scale
MetS- Metabolic syndrome
NCEP- National Cholesterol Education Program
HDL- High density lipoprotein

REFERENCES


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