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ASSOCIATION BETWEEN METABOLIC SYNDROME RATE AND CONCURRENT PSYCHIATRIC DIAGNOSIS IN PATIENTS WITH BIPOLAR DISORDER*

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ABSTRACT
Objective: Bipolar disorder (BPD) patients were determined to have shorter survival than the general population due to reasons such as early cardiovascular diseases and obesity and this causes a decrease in quality of life and an increase in healthcare costs. Considering this, we aimed to determine the MS rate and the presence of concurrent psychiatric diagnosis in BPD patients who admitted to the outpatient clinic of the Psychiatry Department of Canakkale Onsekiz Mart University Medical Faculty.
Materials and Methods: Eighty euthymic patients with BPD diagnosis were included in the study. Patients were evaluated with Hamilton Depression Rating Scale, Young Mania Rating Scale and SCID I and II. The diagnosis of MS was made according to ATP III criteria.
Results: While 22.2% of the patients (n=6) of 18-35 years of age had MS, MS was present in 45% of the patients (n=21) of 35 years or older. The rate of MS was significantly higher in the patients under 35 years of age compared to the patients 35 years or older ($p<0.05$). The SCID-I evaluation revealed that 20 of the 80 patients (25%) with the diagnosis of BPD had concurrent psychiatric diagnosis. BPD patients with concurrent psychiatric diagnosis had a higher rate of MS compared to the whole study group, while the difference was not statistically significant.
Conclusion: The rate of MS was higher in BPD patients compared to the general population. BPD patients with concurrent psychiatric diagnosis had a higher rate of MS compared to the whole study group, while the difference was not statistically significant. Our results show the importance of implementing a multidisciplinary approach and investigation of MS components in BPD.
Key Words: Bipolar disorder (BPD), Psychiatric Diagnosis, Metabolic Syndrome

1. INTRODUCTION

There are studies showing that patients with bipolar disorder (BPD) have a high prevalence of metabolic syndrome (MS), insulin resistance findings and risk of cardiovascular disease and early mortality (1). BPD patients have a 10- to 20-year shorter life expectancy due to cardiovascular, gastrointestinal and respiratory diseases as well as obesity, metabolic syndrome and malignancies (2,3). MS is defined as a multisystem disorder. The main components of this syndrome are impaired glucose tolerance, a high triglyceride level, a low HDL (high-density lipoprotein) cholesterol level, hypertension and abdominal obesity (4).

These endocrine and cardiovascular conditions may be caused by bipolar disorder itself or by its treatment. Regardless of the drug side effects, it is believed that there is a pathophysiological connection between bipolar disorder and MS criteria (5,6). In addition, psychotropic drug use, sedentary lifestyle, immobilization and decreased functioning contribute to an increased rate of MS (6).

On the other hand, the presence of concurrent psychiatric diagnoses (e.g., anxiety disorder) in BPD further complicates the treatment due to various factors, including increased use of health services, impairment in functioning, risk of increased aggressive behaviors, and unresponsiveness to treatment (7,8).

In this respect, we believe that protecting patients from MS and identification and treatment of patients with MS are important. Thus, our primary objective was to investigate the frequency of MS in BPD patients and our secondary objective was to determine if MS rate increases in the presence of a concurrent psychiatric diagnosis in BPD patients.

2. MATERIALS AND METHODS

Study Population

All patients with the diagnosis of BPD admitting to the outpatient clinic of the Psychiatry Department of Canakkale Onsekiz Mart University Medical Faculty between January 2012 and March 2013 who were under regular outpatient follow-up, taking regular medication, and in euthymic phase for at least 3 months and who agreed to participate were invited to participate in the study. Eighty-eight patients were invited and 82 agreed to participate in the study. Two of these patients were excluded for not fulfilling the diagnostic criteria for bipolar disorder. All patients received a demographics questionnaire containing questions including name, age, gender, marital status, educational level, occupation and socio-economic status. Patients with a diagnosis of type 1 and type 2 bipolar disorder according to DSM-IV-TR diagnostic criteria followed up at the outpatient clinic of the Psychiatry Department of Canakkale Onsekiz Mart University Medical Faculty who were in the euthymic phase were included in the study. Included patients were 18- to 65-year-old adults. Written informed consent was obtained from all participants. Patients who were unable to read or write signed the consent form after being read the written information. Exclusion criteria were being in the

manic/hypomanic/depressive/mixed phase and a psychiatric disease or an additional disease that can affect metabolic parameters.

Diagnosis of Metabolic Syndrome

The diagnosis of MS was assessed according to ATP III criteria. Blood pressure and waist circumference measurements were performed and fasting blood glucose, HDL cholesterol and triglyceride values were obtained from laboratory data of the patients. The ATP III diagnostic criteria require meeting 3 criteria. The criteria were considered to be met when the measurements were over the defined thresholds or, in addition, the criteria for blood pressure, blood glucose, TG level, and HDL were considered to be met if the patient was receiving antihypertensive treatment, insulin or hypoglycemic treatment, TG lowering medication, or HDL-elevating agents, respectively. (9)

Table I. MS components

At least three of the following should be met
• Abdominal obesity (waist circumference: men > 102 cm, women > 88 cm
• Hypertriglyceridemia (≥150 mg/dl)
• Low HDL cholesterol (men < 40 mg/dl, women < 50 mg/dl)
• Hypertension (blood pressure ≥ 130/85 mmHg)
• Hyperglycemia (fasting blood glucose ≥ 110 mg/dl)

Statistical Analysis

Study data were transferred into SPSS 19.0 statistical software and data control and analyses were performed using this software. Chi-square test and t-test were used to compare groups. A p value of <0.05 was considered statistically significant.

3. RESULTS

In our study, 37.5% of BPD patients had MS.

The age range of the included patients was 18-54 years and the mean age of the patients was 41.3±11.5 years.

While 22.2% (n=6) of the patients of 18-35 years of age had MS, MS was present in 45% (n=21) of the patients of 35 years or older. The rate of metabolic syndrome was was found to be significantly higher in individuals over 35 years of age compared to individuals under 35 years of age ($p<0.05$) (Table II).

Table II. Association between age of the patients and MS

	Metabolic Syndrome					
	Yes		**No**		**Total**	
Age	**n**	**Percentage***	**n**	**Percentage***	**n**	**Percentage****
18-35 years	6	22.2	21	77.8	27	33.7
> 35 years	24	45.3	29	54.7	53	66.3
p***	**0.04**				**80**	**100.0**

*: Row Percentage

**: Column Percentage

***: T-test

No significant difference was found according to gender in the patients in the study group (M, 46.7%/ F, 31.3%).

MS was present in 20 BPD patients and again 20 BPD patients had a history of concurrent psychiatric diagnosis. Concurrent psychiatric diagnosis was panic disorder in 4 patients (5%), generalized anxiety disorder in 4 patients (5%), obsessive-compulsive disorder in 4 patients (%5), alcohol dependence syndrome in 3 patients (3.75%), only alcohol abuse in 2 patients (2.5%) and posttraumatic stress disorder in 2 patients (2.5%). Only 2 patients had multiple concurrent diagnoses. One of these patients had panic disorder and alcohol abuse, while the other had posttraumatic stress disorder and alcohol and substance abuse as concurrent diagnoses.

Of the 80 patients included in the study, 8 (40%) of 20 patients with psychiatric comorbidity had metabolic syndrome and 12 (60%) did not. Although the rate of metabolic syndrome was higher in patients with psychiatric comorbidity than in all patients, it was not statistically significant. (Table III).

Table III. Association between Concurrent Psychiatric Diagnosis and MS

	Metabolic Syndrome					
	Yes		**No**		**Total**	
Concurrent diagnosis	**n**	**Percentage***	**n**	**Percentage***	**n**	**Percentage****
Yes	8	40.0	12	60.0	20	25
No	22	36.7	38	63.3	60	75
p***	**0.790**				**80**	**100.0**

*Row percentage

**: Column Percentage

4. DISCUSSION

In our study, 37.5% of BPD patients had MS. BPD and MS were seen to affect each other's disease course reciprocally.

The definition of MS is expanded to include increasingly broader groups with changes made in the WHO criteria by lowering the threshold values for blood pressure, blood glucose and waist circumference in the ATP-III and IDF criteria (11,12). MS criteria aim to early identify the disease and its risks. The common underlying pathophysiology and physiological risk factors of BPD and MS include, in addition to obesity, glucose and insulin dysregulation, hypothalamic-pituitary-adrenal (HPA) axis and hypothalamic-pituitary-thyroid (HPT) axis disorders and sympathetic nervous system disorders (3,13). In addition, many pharmacological agents used in BPD may cause weight gain and lipid and glucose metabolism disorders and untreated BPD patients have an increased prevalence of obesity (14,15).

This results in an increase in the risk of diabetes, hypertension, dyslipidemia, cardiovascular diseases and MS. MS itself increases the risk of type 2 diabetes five-fold and the risk of death

from coronary artery diseases three- to six-fold. These concurrent medical conditions and obesity are associated with the worse clinical course and early mortality observed in bipolar patients (16).

Many studies found a tendency for MS in BPD and schizophrenia patients irrespective of the use of atypical antipsychotics; because of seasonal, lifestyle, and genetic factors; HPA system axis disorder; immunological factors in disease mechanisms, etc. (17,18,19).

Studies on MS prevalence report varying rates. The SEMT (Society of Endocrinology and Metabolism of Turkey) guidelines report a prevalence of 22% in the general population, while Fagiolini et al. found a rate of 30% in 171 patients, Yumru et al. reported a rate of 53.0% in 60 patients and Correll et al. found a rate of 43.2% in 74 patients (6,20-23). The primary aim of our study was to determine the rate of MS in our study group of patients with BPD. Consistent with the literature, our study found a rate of 37.5%, which is higher compared to population data.

The other aim of our study was to investigate the "concurrent diagnosis" defined as the presence of an additional psychiatric disease in BPD patients and to determine its association with MS. In our study, 40% of the BPD patients with concurrent psychiatric diagnosis had MS. Although not statistically significant, MS rate was higher in patients with concurrent psychiatric diagnosis among BPD patients. In our study, 20% of the patients had concurrent diagnosis, but studies show that the lifetime rate of concurrent psychiatric diagnosis ranges from 50-70% in type 1 BPD patients. It was reported that mood symptoms appear at earlier ages, rapid cycling is more common and the severity of cycles gradually increase in patients with concurrent diagnosis (24,25) and early-onset bipolar disorder is particularly associated with increase in comorbid somatic diseases, poor prognosis, anxiety disorder, substance use disorder, and suicide attempt (24). Missing the concurrent diagnosis may result in misinterpretation of the disease symptoms as indicative of personality pathology, leading to difficulty in the diagnosis and treatment of disease stages (25). In this study, we aimed to remind that patients with BD may have both MS and comorbid psychiatric diagnoses and that a multidimensional evaluation is necessary. We observed in our study that concurrent psychiatric diagnosis causes an increase in not only bipolar episodes, but also MS rate, although there was not a statistical difference as the number of cases was low.

MS rate was statistically significantly higher in patients over 35 years of age than in patients under 35 years of age. In the literature, studies on MS and endothelial damage reported that

more patients over 35 years had endothelial damage and this was associated with mortality (26) This risk will further increase in the aging BPD population (1). In this regard, we think that health expenses will mostly be reflected in the use of inpatient services.

Our study has some limitations restricting the generalizability of the results. Our sample included BPD patients in remission who were not experiencing episodes but the sample size was inadequate. In addition, the absence of a control group does not allow a comparison between patients and healthy individuals. Longer studies with larger samples may provide more insight into this subject.

The coexistence of so many variables related to MS causes different MS rates in different units for the patient, increasing the importance of prevalence studies.

Sound and reliable data for Turkey on bipolar disorder and other psychiatric diseases are required. It is believed that results of studies conducted in different regions of our country will be useful in developing the psychiatric disease profile of Turkey, determining the population-specific characteristics, identifying the risk factors, determining treatment costs and improving mental health services (27).

In clinical practice, screening for metabolic syndrome at an early stage in bipolar disorder will decrease the early mortality risk associated with cardiovascular diseases and increase quality of life.

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