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FREQUENCY OF BIPOLAR AFFECTIVE DISORDER IN PATIENTS WITH MAJOR DEPRESSIVE EPISODE WITH OR WITHOUT PSYCHIATRIC CO-MORBID DISORDERS

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SUMMARY

Background: *Epidemiological studies indicate that only 20% of patients with Bipolar Affective Disorder are diagnosed on time while in 35% of patients diagnosis is 10 years late. Unipolar depression represents the most frequent misdiagnosis.*

Aim: *The aim of this study was to determine the frequency of BAD in subjects diagnosed with Major Depressive Episode with or without co-morbid disorders.*

Subjects: *The study was a part of a large international, multi-center, non-interventional study that was conducted in 14 countries between May and November 2008. Sample in Bosnia and Herzegovina included 200 adult subjects with MDE according to the DSM IV diagnostic criteria who consented to take part in the study, who did not exhibit symptoms of acute somatic condition at the time, and who were capable of filling the HCL-32 checklist.*

Methods: *The following assessment instruments were used: CRF (Case Report Form) that includes general psychiatric assessment, GAF (Global Assessment of Functioning) and HCL-32 (Hypomania Symptom Checklist).*

Results: *Bipolar Affective Disorder was diagnosed in 67.84% of the study subjects, and MDE in 32.16%. At least one co-morbid psychiatric disorder was present in 77.78% of subjects with BAD and in 22.22% of subjects with MDE. Anxiety disorders co-morbidity was present in 61.9% of subjects with BAD and in 38.10% of subjects with MDE.*

Conclusions: *Our results confirm previous research about underdiagnosing of BAD. This has unforeseen consequences on the course and prognosis of the disorder significantly affecting quality of life of the patients.*

Key words: *bipolar affective disorder - unipolar depression - major depressive episode*

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INTRODUCTION

Bipolar affective disorder is a chronic mental health disorder characterized with irregular course during acute episodes, high frequency of inter-episode sub-syndromal symptoms and high prevalence o co-morbid psychiatric disorders. Generally the course of this disorder is marked by repeated occurrence of manic and depressive episodes that occur with varying frequency and intensity. BAD is also characterized with increased risk for suicide, alcohol and psychoactive substance abuse, and a significant impairment in functioning that is eventually reflected in the reduction of quality of life and serious consequences on the socio-economic status of the patients (Sachs 2004, Miklowitz 1997, Wyatt 1995).

Diagnostic and Statistical Manual of Mental Disorders (DSM IV) classification divides affective disorders in Depressive disorders (Unipolar Depression), Bipolar Disorders, Affective Disorders due to general medical condition and Affective Disorders caused by psychoactive substance abuse. Depressive disorders (Major Depressive Disorder, Dysthymia and Depressive Disorder unspecified) can be distinguished from Bipolar Affective Disorder by the absence of history of manic, mixed or hippomanic episode. Bipolar disorders (Bipolar I, Bipolar II, Cyclothymia and Bipolar Disorder unspecified) all include history of manic, mixed or hypomanic episode usually connected with the history of Major Depressive Episode (APA, 2000). The onset of the disorder is most commonly in the period of adolescence and early adulthood. As a consequence of repeated episodes of the illness, one third of affected subjects attempt suicide in the course of their lifetime and 10-15 percent of them commit suicide (Baldesarini & Tonto 2003).

Depression is the most frequent symptom in Bipolar Affective Disorder, 3,5 times more frequent than mania, followed by hypomania, rapid cycling and mixed episodes. According to a number of international studies, people with BAD are depressed 33,2 percent of the time in the course of a year. The duration of manic symptoms during a year of this disorder is three times shorter (Andrade 2003, Kessler 1994, Judd & Akiskal 2003).

Bipolar Affective Disorder is a relatively frequent psychiatric disorder with lifetime prevalence of 3.0-6.5 percent with approximately equivalent gender distribution (Weissman et al. 1996, Akiskal, Mallya 1987). Epidemiological studies indicate that only 20% of patients with Bipolar Affective Disorder are diagnosed on time while in 35% of patients diagnosis is 10 years late. This delay is usually a consequence of misdiagnosing Bipolar II as Unipolar depression or Dysthymia or other psychiatric co-morbid disorders (Hirchfeld et al. 2005, Krishnan, 2005). Efficacy of treatment of manic and depressive episodes depends on the timely diagnosis and adequate choice of psychopharmacotherapy.

When trying to define a real challenge in the treatment of BAD it does not appear to be the treatment of individual acute episodes but the effort to develop and design long-term strategies for prophylaxis aiming to

reduce relapse risk and improve the quality of life of these patients between the episodes of illness (Tohen et al. 2004, Miklowitz et al. 2003). Neuronal degeneration and deterioration of cognitive functions that correlate with deterioration of general functioning occur as a part of relatively slow process in the course of bipolar affective disorder (Strakowski et al. 1999).

Our study was a part of a large international, multi-center, non-interventional study that was conducted in 14 countries between May and November 2008 (Angst et al. 2011). This article presents the analysis of results of a sample of 200 subjects from Bosnia and Herzegovina. Likewise, the results of other subsamples have been analyzed and published (Bschor et al 2012).

METHODS

The primary goal of the study was to determine the frequency of BAD in subjects diagnosed with Major Depressive Episode with or without co-morbid disorders. Our secondary goals were to analyze socio-demographic characteristics of the study subjects, to determine the type and number of depressive symptoms, frequency of previously diagnosed Bipolar I and Bipolar II Disorder as well as other psychiatric disorders, to determine the age when first depressive episode was diagnosed and frequency of suicide attempts. We determined the duration of current depressive episode, current medication and level of functioning as well as the presence of co-morbid psychiatric disorders in subjects with unipolar depression and bipolar affective disorder.

The study was multi-centric, non-interventional, with cross-sectional register and it was conducted in the period between May and November 2008 in 14 countries. The sample in Bosnia and Herzegovina was comprised of 200 adult (18 years old or more) subjects with a diagnosis of Major depressive Episode according to DSM IV diagnostic criteria (presence of at least 5 out of 9 symptoms of depression) who consented to participate in the study. The subjects were recruited as a consecutive sample of patients with depression by their treating psychiatrists who participated in this study. The patients who did not meet inclusion criteria were not included in the study. The exclusion criteria were the presence of acute or urgent somatic disorder and the inability to complete a self-assessment Hypomania Symptom Checklist (HCL-32).

The following assessment instruments were used in the study: CRF (Case Report Form) that includes general psychiatric assessment, GAF (Global Assessment of Functioning) and HCL-32 (Hypomania Symptom Checklist).

RESULTS

In the sample of 200 subjects 32.5% were men and 67.5% were women. Their average age was 49. Majority of the subjects were married (60.8%) and the percentage of subjects who were single (17.09%) was bigger than the percentage of the subjects who were divorced (12.56%), Table 1.

Table 1. Socio-demographic characteristics of the sample

Gender	
Male	65 (32.50 %)
Female	135 (67.50%)
Age	46.26 (±10.87)
Marital status	
Married	121 (60.80%)
Divorced	25 (12.56%)
Single	34 (17.09%)
Other	19 (9.55%)

The biggest number of the study subjects were treated as out-patients (64%), and 36% were treated as in-patients. Depressive mood was present in all study subjects, and repetitive thoughts about death were present in 47.5% of the subjects. More than 66% of the subjects had eight or nine symptoms of depression. Bipolar I was previously diagnosed in 15.5% of the subjects, Bipolar II in 12.5%, and other psychiatric disorders were previously diagnosed in 72% of the subjects. First diagnosis of depression was recorded in the majority of subjects between the ages of 30 and 39. Postpartum depression was present in 14.81% of the female subjects, and there was a history of suicide attempt in 28% of the subjects. Average duration of current MDE was 2.8 (±1.1) months, ranging from 1 month to 6 months. Average GAF score was 45.1 (±18.5), ranging from as low as 5 to a high score of 95. (Table 2).

Current medication of the study subjects included benzodiazepines in 67.5% of the sample, other anxiolytics in 6% of the sample. SSRIs were the most frequently prescribed antidepressants for the study subjects (63.5%), followed by TCA (20%) and SNRI (5.5). First generation antipsychotics were prescribed to 24.5% of the subjects and second generation antipsychotics to 24%. Lithium was the least prescribed mood stabilizers (4%), compared with valproate (7%), carbamazepine (17.5%) and other mood stabilizers (19%). Table 3.

Our results indicate high frequency of Bipolar Affective Disorder in subjects with Major Depressive Episode. BAD was found in 67.84% of the subjects and only 30% of the subjects had previous diagnosis of this disorder.

Higher presence of co-morbid psychiatric disorders was recorded in subjects with Bipolar Disorder (77.78%) compared with subjects with unipolar depression (22.22%). A co-morbid anxiety disorder was present in 61.9% of subjects with Bipolar Disorder and only 38.1% of subjects with unipolar depression.

Table 2. Type of treatment, depressive symptoms, number of depressive symptoms, age at first diagnosis of depression, presence of postpartum depression in the female sample, history of suicide attempt, duration of current MDE and GAF scores

Type of treatment	
Out-patient	128 (64.00%)
In-patient	72 (36.00%)
Depressive symptoms	
Depressed mood	200(100%)
Significantly reduced pleasure in activities	199 (99.50%)
Significant weight loss or gain	169 (84.50%)
Insomnia or hypersomnia	189 (94.50%)
Psychomotor retardation or agitation	170 (85.00%)
Fatigue and loss of energy	189 (94.50%)
Feeling of worthlessness or guilt	171 (85.50%)
Impaired concentration	181 (90.50%)
Repetitive thoughts about death	95 (47.50%)
Number of depressive symptoms	
5	6 (3%)
6	24 (12%)
7	37 (18.50%)
8	67 (33.50%)
9	66 (33.00%)
Previous psychiatric diagnoses	
Bipolar I	31 (15.50%)
Bipolar II	25 (12.50%)
Other	144 (72.00%)
Age at first diagnosis of Depression	
<15	1 (0.51%)
15-19	6 (3.08%)
20-29	49 (25,13%)
30-39	63 (32.31%)
40-49	50 (25.64%)
50-59	26 (13.33%)
>=60	0 (0.00%)
Postpartum depression in female sample (N=135)	20 (14.81 %)
Suicide attempt	56 (28.00%)
Duration of current MDE (months)	2.8 (±1.1) Min: 1 month Max: 6 months
GAF	45.1 (±18.5) Min: 5 Max: 95

Table 3. Current medication

Current medication	
Benzodiazepines	135 (67.50%)
Other anxiolytic agents	12 (6.00%)
Antidepressants	
SSRI	127 (63.50%)
SNRI	11 (5.50%)
TCA	40 (20%)
Other antidepressants	9 (4.50%)
Antipsychotic drugs	
FGA	49 (24.50%)
SGA	48 (24%)
Mood stabilizers	
Lithium	8 (4.00%)
Valproate	14 (7.00%)
Carbamazepine	35 (17.50%)
Other mood stabilizers	38 (19.00%)

DISCUSSION

The study sample consisted of 32.5 percent men and 67.50 percent women. This is in concordance with previous studies stating that depression is approximately two times more frequent in women than in men. Repetitive thoughts about death and dying were present in 47.50 percent of the study subjects, this reflecting the fact that depression is a psychiatric disorder with significant suicide risk (McElroy et al 2006). The finding that majority of the subjects (68%) were treated as out-patients indicate the possibility of adequate treatment and control of symptoms of Major Depression in community mental health centers or in family practice. Subjects with severe depressive symptoms and those with significant suicide risk were treated as in-patients in the Department of Psychiatry of the Clinical Center of the Sarajevo University. Bipolar I was the most frequent previously diagnosed psychiatric disorder in our sample (15.50%), followed by Bipolar II (12.50%), while other psychiatric disorders were present in 72% of the study subjects. Suicide attempts were recorded in 28% of the subjects. A large number of published studies record the prevalence of suicide attempts in bipolar disorder at approximately 35% (Sareen et al 2005). According to Slama et al (2004) suicide risk is related with earlier onset of the disorder, higher frequency of depressive episodes and anti-depressant induced mania, and alcohol abuse, as well as the presence of suicidal behavior in other family members (Angst et al 2005). Same authors did not find the correlation between suicide attempts and the diagnosis of Bipolar I or Bipolar II affective disorders or the gender of patients.

Average duration of current depressive episode was between one and six months in our study. Severity of depressive symptoms and serious impairment of social and occupational functioning of the study subjects are reflected in the average Global Assessment of Functioning score of 45. The analysis of medications prescribed for current depressive episode of the subjects reveals frequent use of benzodiazepines in treatment plans (in 73.50% of the subjects). Selective serotonin reuptake inhibitors (SSRI) were the most frequently prescribed antidepressant drugs (63.50%). First generation antipsychotic drugs were prescribed to 23.50% and second generation antipsychotic drugs in

24%percebt of the subjects. This probably reflects the fact that most of the SGA drugs are not reimbursed by the health insurance companies in Bosnia and Herzegovina. Lithium was the least frequently used mood stabilizer (4.0%). This is probably the consequence of the fact that only a small percentage of study subjects were previously diagnosed with Bipolar Disorder and were hence treated for unipolar depression.

Bipolar affective disorder was recorded in 67.84% of the study subjects and unipolar affective disorder in 32.16%. In the light of the fact that the majority of our subjects were first diagnosed with depression at the age of 30-39, and that the average age of our subjects was 49, our results indicate the difficulties in diagnosing Bipolar II Disorder, which is in accordance with earlier studies of the delay or obstacles for diagnosing bipolar affective the disorders. We recorded at least one co-morbid psychiatric disorder in 77.8% of subjects with bipolar depression and 22.22% of subjects with unipolar depression. Anxiety disorders were recorded in 61.9% of subjects with bipolar depression and 38.1% of subjects with unipolar depression confirming the results of previous studies of psychiatric co-morbidity in bipolar disorders (Chengpappa et al 2000).

CONCLUSIONS

The results of our study indicate high frequency of Bipolar Affective Disorder in subjects with Major Depressive Episode. BAD was found in 67.84% of the subjects and only 30% of the subjects had previous diagnosis of this disorder. This indicates the difficulties in establishing a diagnosis of this disorder, particularly Bipolar II and Bipolar III, leading to inadequate treatment of the patients. The most frequent misdiagnoses are Unipolar depression, Dysthymia, Delusional Disorder and Schizophrenia.

Our results indicate significantly higher presence of co-morbid psychiatric disorders in subjects with Bipolar Disorder (77.78%) compared with subjects with unipolar depression (22.22%). A co-morbid anxiety disorder was present in 61.9% of subjects with Bipolar Disorder and only 38.1% of subjects with unipolar depression.

Delay of the diagnosis of Bipolar Disorder was a frequent finding in our study, particularly so because the first depressive episode was diagnosed in our subjects at the age of 30-39, and their mean age at the time of the study was 49. This confirms the results of previous studies of late diagnosis of Bipolar Disorder and its unforeseen consequences on the clinical course, frequent development of co-morbid psychiatric disorders, neurodegenerative damages to the central nervous system and occurrence of cognitive dysfunction, and the eventual reduction in the quality of life of patients with Bipolar Disorder. The most important prevention of disability in this group of patients is the early diagnosis and treatment using contemporary guidelines for pharmacological and non-pharmacological treatment options. Because of the high incidence of Bipolar Affective Disorder in patients with Major depressive episode, we also recommend routine use of Hypomania Self-rating Scale for patients presenting for treatment of depression.

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