

# Influence of misdiagnosis on the course of bipolar disorder

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**Abstract. – BACKGROUND:** It is very common that the diagnosis of bipolar disorder comes with several years of delay. This premise is supported by the fact that this diagnosis is almost always set after longitudinal monitoring of symptoms and by the fact that this disorder is often unrecognized or misdiagnosed.

**AIM:** The aim of this study was to determine the incidence of misdiagnosed bipolar disorder and to explore its influence on the further course of the disorder.

**PATIENTS AND METHODS:** The research was provided as a naturalistic study, which included 65 bipolar patients admitted to the Hospital. We examined medical records of the first episode and five-year follow-up of the course of the disease. The average number of episodes was compared between the group with properly diagnosed first episode and the group with wrongly diagnosed first episode in the observed five-year period. T-test was used in this study, in addition to descriptive parameters, mean, median, standard deviation and coefficient of variation.

**RESULTS:** In the sample over which the survey was conducted 52% of the first episodes of bipolar disorder were wrongly diagnosed. We found a statistically significant difference ( $t = 1.84$ ;  $p < 0.05$ ) in the number of episodes that followed the first episode between patients whose first episode was appropriately diagnosed and patients whose first episode has not been properly diagnosed.

**CONCLUSIONS:** There is a high number of unrecognized and misdiagnosed bipolar disorders. Inadequate diagnosis leads to inadequate treatment of the disorder. Number of next episodes in period of follow up is statistically significantly connected with the adequacy of diagnose.

*Key Words:*

Bipolar disorder, Disease progression, Observational study.

It is very common that the diagnosis of bipolar disorder comes with several years of delay<sup>2</sup>. This premise is supported by the fact that this diagnosis is almost always set after longitudinal monitoring of symptoms and by the fact that this disorder is often unrecognized or misdiagnosed. Much of the difficulty in diagnosis of bipolar disorder is consequent to the changing illness expression of the disorder, inherent in the characteristic mood instability of the illness. Therefore, rather than expect to make a conclusive diagnosis cross-sectionally, it is often advisable to explain the fluctuating course to the patient and an involved family member<sup>3</sup>.

The lifetime prevalence of bipolar affective disorder, according to the World Health Organization, is between 1% and 2.5%<sup>4</sup>. Taking these data into account there is at least 3.2 million people suffering from this disorder in Europe<sup>5</sup>.

The significance of mood disorders is seen in high rate of morbidity and mortality, comorbidity with other mental and physical illnesses and disabilities, as well as in social and economic consequences for the patient, their family and the whole society. Bipolar disorder is the sixth leading cause of disability in the world. Functional recovery in depression is limited as well as in chronic diseases such as diabetes mellitus or cardiovascular diseases<sup>6</sup>.

The lifetime risk of suicide in patients with a diagnosis of bipolar disorder ranges from 8% to 20%<sup>7</sup>. Suicide rates, averaging 0.4% per year in men and women diagnosed with bipolar disorder, are more than 20-fold higher than in the general population. Prospective and retrospective studies<sup>8,9</sup> clearly support the evident clinical observation that if patients with major mood disorder commit or attempt suicide, they do it mostly during their depressive episode (78-89%) and less frequently in dysphoric mania (11-20%), but very rarely during euphoric mania and euthymia (0-7%), indicating that suicidal behaviour in patients with mood disorder is a "state-dependent" phenomenon. Therefore, to adequately diagnose

## Introduction

Bipolar disorder often causes disability and significant functional impairment with considerable consequences on the quality of life not only of the patients themselves, but also of their family members and other in their environment<sup>1</sup>.

and to treat acute mood episodes effectively is essential for suicide prevention.

The aim of this study was to determine the prevalence of misdiagnosed bipolar disorder and to explore its influence on the further course of the disorder.

## Patients and Methods

### Study Procedure

This research is a naturalistic study that was conducted at the Clinic for Psychiatry, Clinical Centre of Vojvodina in Novi Sad, Serbia.

At study intake, raters interviewed subjects about their current and past psychiatric history, and then reviewed medical records and, whenever feasible, interviewed other informants. Diagnoses were then made according to International Classification of Diseases, 10<sup>th</sup> revision (ICD-10) diagnostic criteria.

Only the past diagnoses of the first episodes that were placed into the diagnostic framework of affective disorders (F 30.0-33.9 according to ICD-10) were considered adequate. After examining the medical records from the first episode/hospitalization and five-year follow-up of the course of the disease we performed the re-diagnosis (validation of diagnosis established in the past, after the first hospitalization) – all inadequate diagnosis were replaced with the appropriate diagnosis of bipolar disorder episodes according to the clinical presentation at that time and longitudinal course of the disorder.

We compared average number of episodes between the group with adequately diagnosed first episode and the group with inadequately diagnosed first episode in the observed five-year period.

### Subjects

The sample for our study included 65 subjects who (1) were admitted to the Clinic of Psychiatry in Novi Sad, Serbia in the period from 01.01.2006. to 31.12.2009, (2) met ICD-10 diagnostic criteria for bipolar disorder (F 31.0-31.9), (3) had more than one hospitalization and (4) were hospitalized for the first time more than 5 years ago.

The study was approved by the Institutional Review Board (Ethics Committee of the Clinical Centre of Vojvodina, Serbia), and the subjects provided written informed consent after receiving a complete description of the study.

### Statistical Analysis

Computer programmes “SPSS” and “Excel” were used for statistical analysis of data.

In addition to descriptive parameters, mean, median, standard deviation and coefficient of variation we used Student’s *t*-test. Prerequisites for the calculation of the *t*-test are nominal distribution and equality of variances of two groups. By convention, statistically significant is considered test in which *p* value is less than 0.05.

The results will be displayed in Tables and Figures.

## Results

In the sample over which the survey was conducted 52% of the patients were wrongly diagnosed during their first episode of bipolar disorder (Table I).

We compared average number of episodes between the group with properly diagnosed first episode and the group with wrongly diagnosed first episode in the observed five-year period. Value 1.84 is obtained using Student’s *t*-test, and this result indicates to a statistically significant difference in the number of episodes that followed the first episode between patients whose first episode was appropriately diagnosed and patients whose first episode was not adequately diagnosed.

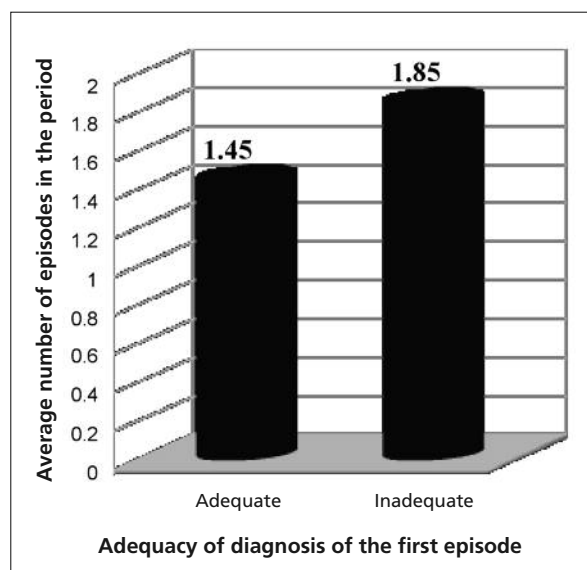
Patients which were wrongly diagnosed during their first episode had significantly more additional episodes of bipolar disorder in observed five-year period (Figure 1).

## Discussion

Results show that 52% of the patients were not diagnosed as mood disorders (F3 according to

**Table I.** Share of specific inadequate diagnoses in the group with inadequately diagnosed first episode.

Diagnosis	F 29	F 20	F 22	F 25	F 41	F 60	F 10	F 98	F 34	F 43	F 53
%	44.12	11.76	11.76	5.88	5.88	5.88	2.94	2.94	2.94	2.94	2.94



**Figure 1.** Average number of episodes in the observed five-year period after the first episode in relation to the adequacy of diagnosis of the first episode.

ICD-10) after their first hospitalization. Some investigators have explored the time to bipolar diagnosis based on previous mental health diagnoses. In the 2000 survey of the National Depressive and Manic-Depressive Association (NDMDA), more than one third of respondents with bipolar disorder were found to have sought professional help within 1 year of the onset of symptoms; however, 69% were misdiagnosed. Patients who were misdiagnosed consulted a mean of 4 physicians before receiving the correct diagnosis and one third waited 10 years or more before receiving an accurate diagnosis<sup>10,11</sup>.

Almost  $\frac{3}{4}$  of inadequately diagnosed patients in our study were diagnosed as a psychotic mental disorders (F29, F20, F22, F25 – according to ICD-10). This indicates that episodes of bipolar disorder with psychotic features are often mistakenly diagnosed as other psychotic disorders. Inadequate diagnosis also often belonged to the group of anxiety disorders, mental and behavioural disorders due to psychoactive substance use or personality disorders. This finding could be explained by the frequent comorbidity of bipolar disorder with some of these groups of disorders and possible overlapping in clinical presentation during the episodes.

Wrongly diagnosed patients had significantly more episodes than those who were appropriately diagnosed (63 vs. 45,  $p < 0.05$ ) – this is probably consistent with the treatment that was prescribed

in accordance with: diagnosis (non-specific therapy for bipolar disorder), length of treatment (bipolar disorder requires the extension phase and prophylactic therapy), and follow up (frequency of check-ups). Only 52% of US patients with bipolar disorder were fully adherent, according to a recent review<sup>12</sup>.

There is always the question about the cost implications of the time lapse before patients were diagnosed with bipolar disorder. It is found that these delays may result in excess costs both during the time of the delay and after diagnosis<sup>13-15</sup>. This finding may reflect treatment refractoriness in the post-bipolar diagnosis period or more intensive treatment, and also suggests that more aggressive recognition and treatment can reduce healthcare costs.

Future analyses will examine risk factors for misdiagnose of bipolar disorder and will give suggestions for steps to be taken.

#### Conflict of Interest

None to declare.

#### References

- 1) ANGST J, SELLARO R. Historical perspectives and natural history of bipolar disorder. *Biol Psychiatry* 2000; 48: 445-457.
- 2) AGIUS M, MURPHY CL, ZAMAN R. Under-diagnosis of bipolar affective disorder in A bedford CMHT. *Psychiatr Danub* 2010; 22(Suppl 1): S36-37.
- 3) BOWDEN C. Diagnosis of Bipolar Disorder. In: *Handbook of Bipolar Disorder*. Kasper S, Hirschfeld R (editors). Taylor and Francis Group, 2005; pp. 11-20.
- 4) NEDIC A, ZIVANOVI O (editors). *Psychiatry, Novi Sad: University of Novi Sad, Medical Faculty, 2009.*
- 5) DITTMANN S, BIEDERMANN NC, GRUNZE H, HUMMEL B, SCHARER LO, KLEINDIENST N, FORSTHOFF A, MATZNER N, WALSER S, WALDEN J. The Stanley Foundation Bipolar Network: results of the naturalistic follow-up study after 2.5 years of follow-up in the German centres. *Neuropsychobiology* 2002; 46: 2-9.
- 6) GOLDBERG JE, ERNST CL. The economic and social burden of bipolar disorder: a review. In: *Bipolar disorder, vol. 5*. Maj M, Akiskal HS, Lopez-Ibor JJ, Sartorius N (editors). John Wiley and Sons Ltd, 2002; pp. 441-467.
- 7) BOSTWICK JM, PANKRAZT VS. Affective disorders and suicide risk: a reexamination. *Am J Psychiatry* 2000; 157: 1925-1932.

- 8) ISOMETSÄ ET, HENRIKSSON MM, ARO HM, LÖNNQVIST JK. Suicide in bipolar disorder in Finland. *Am J Psychiatry* 1994; 151: 1020-1024.
- 9) VALTONEN H, SUOMINEN K, MANTERE O, LEPPÄMÄKI S, ARVILOMMI P, ISOMETSÄ ET. Suicidal ideation and attempts in bipolar I and bipolar II disorders. *J Clin Psychiatry* 2005; 66: 1456-1462.
- 10) AKISKAL HS. Classification, diagnosis and Boundaries of bipolar disorders: a review. In: *Bipolar disorder*, vol. 5. Maj M, Akiskal HS, Lopez-Ibor JJ, Sartorius N (editors). John Wiley and Sons Ltd, 2002; pp. 1-51.
- 11) HIRSCHFELD RMA, LEWIS L, VORNIK LA. Perception and Impact of Bipolar Disorder: How far have we really come? Results of the National Depressive and Manic-Depressive Association 2000 survey of individuals with bipolar disorder. *J Clin Psychiatry* 2003; 64: 161-174.
- 12) PANI L. The need for individualised antipsychotic drug therapy in patients with schizophrenia. *Eur Rev Med Pharmacol Sci* 2009; 13: 453-459.
- 13) BIRNBAUM HG, SHI L, DIAL E, OSTER EF, GREENBERG PE, MALLETT DA. Economic consequences of not recognizing bipolar disorder patients: a cross-sectional descriptive analysis. *J Clin Psychiatry* 2003; 64: 1201-1209.
- 14) RUSSELL J, HAWKINS K, OZMINKOWSKI RJ, ORSINI L, CROWN WH, KENNEDY S, FINKELSTEIN S, BERNDT E, RUSH AJ. The cost consequences of treatment-resistant depression. *J Clin Psychiatry* 2004; 65: 341-347.
- 16) STANG PE, FRANK C, KALSEKAR A, YOOD MU, WELLS K, BURCH S. The clinical history and costs associated with delayed diagnosis of bipolar disorder. *Med Gen Med* 2006; 8: 18.