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ORIGINAL ARTICLE

Misdiagnosis of Bipolar Disorder: Rare or Frequent?

Bipolar Bozuklukta Önceki Yanlış Tanıların Sıklığı

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ABSTRACT

Background: Much as there have been limited number of studies which have examined misdiagnosis of bipolar disorder, it is so difficult to say that there is enough systematic research to identify the diagnostic rate of bipolar disorder. In our literature search, we could not find any study in our country about misdiagnoses before diagnosis of bipolar disorder. Therefore, we planned our study.
Methods: The present study was done at xxx University, School of Medicine, Department of Psychiatry. Patients who were from both out-patient and in-patient clinics were included in the study. After a selection process, 171 patients with bipolar disorder were enrolled. In this group of patients, misdiagnosis of bipolar disorder were investigated.
Results: Of the patients, 56.14 % had misdiagnosis of bipolar disorder. The most frequent misdiagnosis was fetermined to be major depressive disorder (in fifty cases, 54.3%). Followings were schizoaffective disorder (in 18 cases, 24.3%), schizophrenia (in 13 patients, 24.3%), delusional disorder (in 13 patients, 24.3%), dysthymic disorder (in 10 cases, 15.9%), generalized anxiety disorder ((in 10 cases, 15.9%), obsessive compulsive disorder (in seven cases, 12.6%), paranoid personality disorder (in two cases, 4.1%).
Conclusions: The results of the study suggest that bipolar disorder is frequently misdiagnosed and that the most frequent misdagnoses were major depressive disorder and following psychotic spectrum disorders. Clinicians should be aware of frequent misdiagnosis in patients with bipolar disorder.

Keywords: Bipolar disorder; misdiagnosis, frequency

ÖZ

Amaç: Bipolar bozukluğun yanlış tanısını inceleyen sınırlı sayıda çalışma olmasına rağmen, bipolar bozukluğun tanı oranını belirlemek için yeterli sistematik araştırma olduğunu söylemek çok zordur. Yaptığımız literatür araştırmasında Ülkemizde bipolar bozukluk tanısı almadan önce koyulan yanlış tanılarla ilgili bir çalışmaya rastlamadık. Bu sebeplerle çalışmamızı planladık.
Metod: Bu çalışma xxx Üniversitesi Tıp Fakültesi Psikiyatri Anabilim Dalı'nda yapıldı. Hem ayaktan hem de yatan hasta kliniklerinden gelen hastalar çalışmaya dahil edildi. Bir seçim sürecinden sonra bipolar bozukluğu olan 171 hasta alındı. Bu hasta grubunda bipolar bozukluk yanlış tanısı araştırıldı.
Bulgular: Hastaların yüzde 56,14'ünde bipolar bozukluk yanlış tanısı vardı. En sık yanlış tanı majör depresif bozukluk olarak belirlendi (elli vakada %54,3). Bunu şizoaffektif bozukluk (on sekiz hastada %24,3), şizofreni (on üç hastada %24,3), sanrılı bozukluk (on üç hastada %24,3), distimik bozukluk (10 olguda %15,9), yaygın anksiyete bozukluğu (on olguda %15,9), obsesif kompulsif bozukluk (yedi olguda %12,6), paranoid kişilik bozukluğu (iki olguda %4,1).
Sonuç: Çalışmanın sonuçları, bipolar bozukluğun sıklıkla yanlış teşhis edildiğini ve en sık yanlış tanıların majör depresif bozukluk ve ardından psikotik spektrum bozuklukları olduğunu göstermektedir. Klinisyenler bipolar bozukluğu olan hastalarda sık görülen yanlış tanıların farkında olmalıdır.

Anahtar Kelimeler: Bipolar bozukluk, yanlış tanı, sıklık

Introduction

Bipolar disorder is a chronic mood disorder that is characterized by depressive, manic or mixed episodes, in which the person is in complete or near-complete well-being and may lead to functional impairment (1).

The term bipolar was introduced into the field of psychiatry by Jules Falret as a clinical entity called the folie circulaire (cyclical insanity), characterized by episodes of depression and heightened moods. This clinical entity has been called maniacal depressive psychosis. This clinical antity was given a name of maniac depressive psychosis (2). The third edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III) in 1980 changed the term maniac-depressive disorder to bipolar disorder (3). In DSM-IV-TR, the use of bipolar disorder continued, with several changes (4). DSM 5 made some minor changes compared to the DSM IV-TR (5). Although the lifetime prevalence of bipolar disorder is 1% when considered as a broad spectrum, this rate rises to 5%. (6) The mean lifetime prevalence for bipolar disorder type 1 was 0.8%, and 0.5% for bipolar disorder type II. While bipolar disorder type 1 is seen with similar frequency in men and women, bipolar disorder type 2 is more common in women than men. Features such as rapid cycling, mixed episodes, and manic shift with antidepressants are also more common in female patients. A bimodal age model is also recommended for the incidence of bipolar disorder, with an average onset in the 20s. Two peaks are observed between the ages of 15-24 and 45-54 in terms of the distribution of age at onset.

In medicine, the accurate diagnosis is important to effectively manage and treat the patient. Misdiagnosis leads to ineffective treatment periods, loss of time and workpower, and money. For this reason, incorrect

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and untimely diagnosis is regarded as so important in medicine. In daily practice of psychiatry, because of the fact that there have not been patognomonic signs and laboratory test, misdiagnosis can be seen widely. On the other hand, it is hard to diagnose bipolar disorder in its early periods particularly when it starts in early ages. In a study, it was found that the misdiagnosis rate for bipolar disorder could reach as high as 69 percent (7).

It has been reported that only twenty percent of patients with bipolar disorder who already have a depressive episode were diagnosed with bipolar disorder during the first year of treatmen It was also emphasized in this study that it took five to ten years to confirm the diagnosis of bipolar disorder (8). Misdiagnoses of bipolar disorder usually consist of schizophrenia, anxiety disorder, borderline personality disorder, major depressive disorder, or substance dependence (9). Sometimes, because of concomitant psychotic symptoms, bipolar disorder is misdiagnosed as subtance related psychotic disorders, or other psychotic disorders including schizophrenia (10). Bipolar II disorder is another clinical antity which has dominantly depressive symptoms. Therefore, it can be misdiagnosed as depressive disorder beacuse of ignoring hypomanic symptoms. Probably, these hypomanic symptoms are evaluated as normal human experiences instead of any pathological state (11). Also, clinicians do not always ask depressed patients about hypomania, and some depressed patients have not yet experienced a manic or hypomanic episode. As a result, patients with BD, particularly BD-II, are frequently misdiagnosed with major depressive disorder (MDD) and may receive inadequate or inappropriate treatment. Thus, early identification of BD is of crucial importance.

Since there have been limited number of studies which have examined misdiagnosis situation of bipolar disorder so far, it is very difficult to say that there are enough systematic research to identify the diagnostic rate of bipolar disorder. On the other hand, we did not find any research in Turkiye. Clinical practice in psychiatry can vary from country to country as can be expected. Therefore, we were curious about the misdiagnosis of bipolar disorder in our country, and planned this study. For these reasons, patients who were confused with other psychiatric disorders were compared with correctly diagnosed bipolar patients in terms of available sociodemographic and clinical data.

Materials and Methods

The study was approved by the Ethics Committee of xxx University (22.03.2016 date, 06/19). The procedures were in line with the ethical standards of the Institutional and National Human Experiments Committee and the Declaration of Helsinki (12).

Patients with bipolar disorder who were from both out-patient and in-patient clinics between 01.04.2016 and 01.04.2017 were included in the study. We gathered totally 212 patients at baseline. However, 41 patients were excluded because patients newly diagnosed with bipolar disorder according to the Diagnostic and Statistical Manual of Mental Disorders, 4th version, text revised (DSM-IV-TR) were included in our study within the specified dates, so a total of 171 patients were included. Meanwhile, although this was a retrospective designed investigation, patient anonymity was strictly continued. As mentioned above, totally 171 patients were included in the analysis. Out of them, 96 were diagnosed as bipolar disorder at first interview. Seventy-five patients were mistakenly diagnosed as other psychiatric disorders and followed, and then they were diagnosed as bipolar disorder. Inclusion criteria consisted of followings: (i) meeting the diagnostic criteria for bipolar disorder according to DSM-IV-TR; (ii) not having a past diagnosis of BD , (iii) being over 18 years old; (iv) not having any severe medical illnesses; (v) not having mental retardation; (vi) not having bipolar disorder induced by organic brain problems; (vii) inexistence of psychoactive and alcohol abuse or dependence according to the DSM-IV-TR; or (viii) existence of complete clinical data for necessary information. The present study was designed in cross-sectional and retrospective manner. All data were gathered by the professional senior psychiatry resident and specialists. When obtaining clinical information about patients with bipolar disorder, it was benefited from both automated information web of our university hospital organized by data processing center of the same hospital and manual medical records of them kept in hospital archive. In case of requirement, accessible patients' relatives were asked for completing incomplete data.

Sociodemographic Data Form

A semistructured form was used to record all sociodemographic and clinical data of all patients with bipolar disorder in detail. This form included following data: age of onset of the disorder, the nature of first mood episode, the period from the onset age to the first application, progress of the disorder itself, the period of between onset of the disorder and confirmed diagnosis, the number of manic and depressive episodes, whether patients with bipolar disorder had mixed episodes, whether they had an history of hospitalization for treatment process, present situation for clinical aspect of the disorder, whether they had a family history of psychiatric disorder or not, whether they had a history of suicide and psychotic symptoms, whether their disorders had any rapid cycling nature, and finally whether they had any comorbid psychiatric conditions.

Patients confused with other psychiatric disorders were compared with correctly diagnosed bipolar patients in terms of available sociodemographic and clinical data.

Statistical Analysis

All statistical variables were analyzed by using the Statistical Package for the Social Sciences for Windows software (SPSS) version 22.0 (SPSS, Chicago, IL). An independent t-test was utilized for continuous

variables while chi-square analyses were applied to categorical comparisons. If it is required, for various correlational relationships, Spearman's correlation analysis test was used. A p value of less than 0.05 was considered statistically significant and less than 0.01 was considered highly statistically significant.

Results

In the present investigation, total 212 patients were enrolled at baseline. After an evaluation in terms of selection criteria, 171 patients were included in the analyses of the present study. Out of them, 96 were diagnosed as bipolar disorder at first interview. As mentioned in the Methods section, 75 patients were mistakenly diagnosed as other psychiatric disorders and were followed- up, and then they were diagnosed as bipolar disorder. In this context, 56.14 percent of patients had misdiagnosis of bipolar disorder. The most frequent misdiagnosis was fetermined to be major depressive disorder (in fifty cases, 54.3%). Followings were schizoaffective disorder (in eighteen cases, 24.3%), schizophrenia (in thirteen patients, 24.3%), delusional disorder (in thirteen patients, 24.3%), dysthymic disorder (in ten cases, 15.9%), generalized anxiety disorder ((in ten cases, 15.9%), obsessive compulsive disorder (in seven cases, 12.6%), paranoid personality disorder (in two cases, 4.1%) (Table 1). Out of these patients, 12 patients had two different misdiagnoses whereas three had three different misdiagnoses and three had been misdiagnosed as different four diagnoses.

We did not find any differences between patients with misdiagnosis and with correct diagnosis in terms of the mean age, gender distribution, living place, socioeconomic status, scale scores, total years of education, number of manic episodes in total, the presence of mixed episodes, family history of bipolar disorder, beginning in postpartum periode, and age of onset (P>0.05) (Table 2). However, there are differences in terms of some clinical variables. First of all, depressive episode as a first episode of the disorder was more prominent in patients with misdiagnosis compared to that of those with correct diagnosis (chi-square= 5.01, p<0.05). On the other hand, during all illness period, patients with misdiagnosis had more depressive episodes compared to those of correct ones (t= 2.39 p<0.05). In the misdiagnosis group, the period between age of onset and receiving treatment firstly was statistically significant and briefer than that of correct diagnosis group (t=2.49, p<0.05). In the misdiagnosis group, the number of hospitalization was more frequent than that of correct diagnosis group (t=1.89, p<0.05). In addition to all, the presence of psychotic symptoms were statistically significant and more prominent in the misdiagnosis group compared to correct diagnosis group (chi-square=4.69 p<0.05). Diagnostic comorbidity was also more frequent in the misdiagnosis group compared to correct diagnosis group (chi-square=4.12, p<0.05). Diversity of used psychopharmacological agents was much more in the misdiagnosis group compared to correct diagnosis group (t=2.46, p<0.05).

Table 1. The distribution of misdiagnoses

Misdiagnosis	n	%
Major Depressive Disorder	50	54.3
Schizoaffective Disorder	18	24.3
Schizophrenia	13	24.3
Delusional Disorder	13	24.3
Dysthymic Disorder	10	15.9
Generalized Anxiety Disorder	10	15.9
Obsessive Compulsive Disorder	7	12.6
Paranoid Personality Disorder	2	4.1

Table 2. Sociodemographic and clinical data of the subjects

		Correct Diagnosis	Misdiag-nosis	P
Gender	Female	51	38	p>0.05
	Male	45	37	
Marital status	Single	53	32	p>0.05
	Married	41	42	
	Widowed	2	1	
Education	Uneducated	18	8	p>0.05
	Primary	23	25	
	Secondary	10	8	
	High	29	19	
	University	16	15	
Occupation	Housewife	40	31	p>0.05
	Student	18	11	
	Official	13	5	
	Worker	5	10	
	Others	1	2	
	Unoccupated	16	12	
	Retired	3	4	
Age		34.5±11.4	36.7±11,5	p>0,05
The number of manic episodes		116	102	p>0,05
The number of mixed episodes		43	37	p>0,05
Family history	Yes	35	33	
	No	61	42	
Beginning in postpartum periode	Yes	13	9	p>0,05
	No	83	66	
Age of onset		21.2±6.4	23.4±3.2	p>0,05

Discussion

In the present investigation, after an evaluation in terms of selection criteria, total 171 patients were included. We have obtained some important results that can shed light on the psychiatry professionals in their clinical practice. First of all, in the present study, 56.14 % of patients with bipolar disorder had been misdiagnosed as other psychiatric disorders, so it means tat over half of bipolar patients had misdiagnosis. The most frequent misdiagnosis was determined as major depressive disorder (in 50 cases,

54.3%). Followings were schizoaffective disorder (in 18 cases, 24.3%), schizophrenia (in 13 patients, 24.3%), delusional disorder (in 13 patients, 24.3%), dysthymic disorder (in 10 cases, 15.9%), generalized anxiety disorder (in 10 cases, 15.9%), obsessive compulsive disorder (in seven cases, 12.6%), paranoid personality disorder (in two cases, 4.1%). Considering that bipolar disorder is known as both chronic and disabling, and since the lifetime risk of suicide is 20 times higher than in the general population, the risk of death is high, the importance of accurate diagnosis is understandable.

The accurate and early diagnosis is important in the medicine. By this way, it is possible to manage and treat a patient effectively. Misdiagnosis causes to ineffective treatment periods, loss of time and workpower, and money. For this reason, incorrect and untimely diagnosis is regarded as very important in medicine. In daily practice of psychiatry, because of the fact that there have not been patognomonic signs and laboratory test, misdiagnosis can be seen widely. On the other hand, it is hard to diagnose bipolar disorder in its early periods, particularly when it has started in early ages. There have been limited number of studies examining the rate of misdiagnosis in patients with bipolar disorder. First of all, the reason that we have selected bipolar disorder is that in clinical practice we observe that bipolar disorder seems to be misdiagnosed.

This condition looks like to affect treatment progress of bipolar disorder and to lead to loss of functionality. In fact, these facts motivated us to analyze patients with bipolar disorder for misdiagnosis. In our present study, as aforementioned, 56.14 %, or more than half of patients with bipolar disorder were misdiagnosed with other psychiatric disorders. The rate was obviously high. In fact, this condition seems to be normalized in clinical practice of psychiatry. Previously, Shen et al. (13) examined the reasons for misdiagnosis of bipolar disorder in the outpatient clinic so that psychiatry professionals could distinguish the disorder more clearly and avoid diagnostic errors. They reported that out of 177 patients with bipolar disorder, 136 (76.8%) had been misdiagnosed as other psychiatric disorders. In another study which was performed in China by Hirschfeld et al., it was reported that the rate of misdiagnosis for bipolar disorder could be as high as 69%, and 20% of patients with bipolar disorder who had already had a depressive episode received a confirmed diagnosis within the first year of treatment.

These rates were higher than ours. In fact, those studies were also in retrospective design like ours.

Misdiagnoses that were determined in the present study were major depressive disorder, schizoaffective disorder, schizophrenia, delusional disorder dysthymic disorder, generalized anxiety disorder, obsessive compulsive disorder, and paranoid personality disorder in the rank of frequency. In fact, it is not surprise to see major depressive disorder in the first rank. Because major depressive episodes are already a part of bipolar disorder, it can be easily misdiagnosed and can be overlooked. Individuals with bipolar disorder spend a much greater percentage of their time in depressive rather than manic or hypomanic episodes (14,15). Moreover, in more than half of patients with bipolar disorder, the first episode may be depression, increasing chances of misdiagnosis as a unipolar mood disorder, at least initially. In a study by Shen et al., it was shown that the most common misdiagnosis was major depressive disorder (70,6%)(13). Frye et al. reported that clinicians misidentify bipolar disorder more than half the time. Das et al. reported that 112 (9.8%) of 1.157 adult patients seeking primary care at an urban general medicine clinic serving a low-income population screened positive for lifetime bipolar disorder (16,17). Initial misdiagnosis of patients with bipolar disorder results in delay of appropriate treatment and the potential for mistreatment with antidepressant monotherapy, which may subsequently increase the risk of recurrence and chronicity in this progressive disorder. (18, 19)

In the entire course of bipolar disorder, there were apparently more depressive episodes than manic or hypomanic episodes. In particular the patients with bipolar II disorder had a depressive presentation throughout most of their illness, making the clinical diagnosis even more difficult. (20, 21)

Here are some features that help differentiate bipolar depression from major depressive disorder. Bipolar depression; current or past history of episode of hypomania/mania, more withdrawn and retarded with tendency for hypersomnia, agitation and weight loss less common, relatively young age of onset of symptoms, atypical symptoms of depression more common, family history of bipolar disorder relatively more common, more recurrent pattern of illness and relatively brief episodes, less response to antidepressant therapy, postpartum onset and premenstrual syndrome more common, psychotic features more common, mood lability and seasonal pattern more common, substance use and suicide attempt more common. (22, 23)

During all illness period, patients with misdiagnosis had more depressive episodes compared to those of correct ones ($p<0.05$). In the misdiagnosis group, the period between age of onset and receiving treatment firstly was statistically significant briefer than that of correct diagnosis group ($p<0.05$). The number of hospitalization was more frequent in the misdiagnosed group ($p<0.05$). Until the patients were diagnosed with bipolar disorder, they were treated with misdiagnosis. Since no effective treatment is given for the diagnosis of bipolar, the time until the diagnosis is prolonged and patients experience more depression attacks and more frequent hospitization.

The quality of records might have affected the results. In retrospective designed studies, it is clear that manner of records could directly affect the results of the studies (7). In addition, for a long time, in our university hospital, an automated computer system for the records of patients instead of manual patients records has been used. This can be also another positive factor that could have affected our results.

Because, it is possible that in automated system data can be keep in confidence compared to manual one. On the other hand, relatively low rate of misdiagnosis for bipolar disorder could be associated with other factors that we could identify now.

Following major depressive disorder, the most frequent misdiagnoses were psychotic ones, schizoaffective disorder, schizophrenia, and delusional disorder. This finding is not in accordance with the results of the studies mentioned above. Shen et al. showed that 20.6% of patients with bipolar disorder were mistakenly diagnosed with schizophrenia. (13) However, bipolar disorder itself can include psychotic symptoms in its clinical presentaion. Some studies show that psychotic symptoms are one of the major risk factors for bipolar disorder in patients with depression (24). For this reason, it is not abnormal to misdiagnose as psychotic disorders. But we do not exactly know why our results were different from theirs in terms of misdiagnoses of psychotic disorder. We probably do not have any systematic data on this, but since one of Turkiye's five largest depot hospitals for psychotic disorders is located in our region, the number of patients with schizophrenia is particularly high in our region. Because of the fact that our outpatient and inpatient assisstants and specialists meet a huge number of patients with psychotic disorder particularly schizophrenia, schizoaffcetive disorder and delusional disorder, the number of misdiagnosis of bipolar disorder as schizophrenia, schizoaffective disorder, or delusional disorder may be more compared to the results of studies aforementioned. Apart from this, we do not know any other reason why psychotic disorders as misdiagnosis are so high in the present study.

Before completing the discussion section, we should mention some limitations of the present study. First of all, this was a retrospectively designed study, and this study was as much a chart review as we used information embedded in the automated hospital system. Second, The sample size was small because it was performed in a clinic in a university hospital. Third, this study was a misdiagnosis investigation in patients with bipolar disorder. It is still possible to misdiagnose even for confirmed diagnoses. Finally, this is a retrospective study and all diagnoses were made by various psychiatrists, assistants or lecturers because clinical assessment scales were used in the examinations of patients. Thus, diagnostic reliables may be questioned. This condition can be accepted as another limitation.

Consequently, the present study was first study in our country. The results of the study suggest that bipolar disorder is frequently misdiagnosed one and that the most frequent misdagnoses were major depressive disorder and following psychotic spectrum disorders. Clinicians should be aware of frequent misdiagnosis in patients with bipolar disorder because misdiagnosis can cause ineffective treatment periods, loss of time and workpower, and money.

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Author Contributions

Conception: Ç.Ö., Data Collection and Processing: Ç.Ö., Design: Ç.Ö., Supervision: S.Ş., A.İ., Analysis and Interpretation: Ç.Ö., S.Ş., Literature Review: Ç.Ö., Writer: Ç.Ö., Critical Review: S.Ş., A.İ.

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