

Factors Affecting the Risk of Mental Disorders in Patients With Bipolar Disorder in the West of Iran

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Abstract

Background: Drug addiction, obsessive compulsive disorders (OCD), and other anxiety disorders are the disorders most commonly found in patients with bipolar disorder.

Objectives: The purpose of this study was to identify the factors affecting the risk of drug addiction, obsessive compulsive disorders, and other anxiety disorders in patients with bipolar disorder.

Patients and Methods: In this retrospective cohort study, the medical records of 400 patients with bipolar disorder hospitalized in Hamadan, Iran, between 2008 and 2014 were examined. Patient information, including demographic characteristics and comorbidity, was collected. A data analysis was performed using a separate logistic regression for each disorder. The statistical package used was STATA software version 11. A P-value of less than 0.05 was considered statistically significant.

Results: The mean (SD) age of the patients with bipolar disorder was 34.62 (1.68) years. Of the 400 patients with bipolar disorder, 135 (33.75%) patients had anxiety disorders, 67 (16.8%) patients suffered from drug addiction, and 45 (11%) patients had OCD. An association was established between drug addiction and OCD, and gender ($P \leq 0.05$). The ORs of anxiety disorders, drug addiction, and OCD were 1.05 (95% CI = 0.65 - 1.68), 0.26 (95% CI = 0.10 - 0.63), and 2.33 (95% CI = 1.21 - 4.48) for women, and 0.92 (95% CI = 0.52 - 2.13), 3.01 (95% CI = 1.64 - 5.55), and 0.64 (95% CI = 0.25 - 1.62) for the patients who smoked, respectively. In addition, there was no significant association between the different disorders and age, marital status, history of relapse, and history of suicide.

Conclusions: The results showed that there was a greater risk of anxiety disorders with bipolar disorder than other disorders. While women with bipolar disorder were at higher risk of anxiety disorders and OCD, men were at greater risk of drug addiction.

Keywords: Anxiety Disorders, Bipolar Disorder, Comorbidity, Drug Addiction, Obsessive Compulsive Disorder, Logistic Regression

1. Background

Bipolar disorder is both a chronic and acute disease characterized by severe and recurrent episodes of depression, mania, and hypomania (1). Although bipolar disorder exists throughout the world, different studies have shown that the lifetime prevalence of this disorder is variable. The lifetime prevalence of bipolar I disorder, for instance, is between 1.6 - 0.2% and 3 - 7% for the full spectrum of the disorder (2). Bipolar disorder usually starts between 15 and 19 years of age (3). There is a 60% risk of patients experiencing a recurrence of bipolar disorder in the first two years, and this risk escalates to around 75% beyond 5 years (4, 5). The World Health Organization reported that bipolar disorder is the sixth leading cause of lifelong disability worldwide among persons aged 15 - 44 years (6).

There is a high rate of comorbid psychiatric disorders in patients with bipolar disorder (7-9). In the study con-

ducted by McElroy et al. involving 288 patients with bipolar disorder, 42% patients suffered from anxiety disorder and 42% were reported to have drug addiction (10). Similarly, Provencher et al. (11) found that 50% - 75% of patients with bipolar disorder have a comorbid anxiety disorder. According to a study carried out in the United States, the prevalence of anxiety disorders and drug addiction is high in patients with bipolar disorder. Anxiety associated with bipolar disorder causes disease onset at an early age as well as more relapses at shorter intervals (12). The results of a study by Surendran and Chakrabarti (13) reiterated the common occurrence and adverse consequences of comorbidities in patients with comorbid bipolar disorder and anxiety disorders. They further showed the usefulness of adjunctive psychosocial treatment. In a European study, almost all patients with bipolar I disorder suffered from comorbid disorders during their lifespan: over two-thirds of the patients had a history of anxiety disorders and 70% had

a history of drug addiction (14).

de Graaf et al. (15) applied a logistic regression to compare subjects with a diagnosis of pure and comorbid disorders. They concluded that female gender, younger age, lower educational level, and unemployment were associated with comorbid anxiety and mood disorders.

2. Objectives

There is evidence of the comorbidity of drug addiction, OCD, and other anxiety disorders in patients with bipolar disorders; however, no research has been done to determine the factors affecting the comorbidity of these common disorders in patients with bipolar disorder in Hamadan, which is in the west of Iran. This study was therefore conducted to identify the factors affecting drug addiction, OCD, and other anxiety disorders in patients with bipolar disorder.

3. Patients and Methods

This retrospective cohort study was conducted in Hamadan Province in the west of Iran from April 2008 to September 2014. The population of this study comprised patients with bipolar disorder and more than one relapse leading to hospitalization at Farshchian hospital, which is the only psychiatric hospital in Hamadan Province. Rapid cycling patients were excluded from the study. The data were extracted from the patients' records using a checklist of items that reflected the content parameters of the patients' records and a clinical examination by psychiatrists. The checklist thus included data on demographic variables (age, sex, and marital status) and comorbid disorders (anxiety disorder, drug addiction, and OCD). The data analysis was performed using a separate logistic regression for each disorder. The adjusted odds ratio (OR) was reported to address the association between the comorbidity and the associated predictors. The statistical package used was STATA software version 11 (STATA Corp, College Station, TX). The significance level was established as $P < 0.05$.

4. Results

The study involved 400 patients with bipolar disorder of which 288 (72%) were men. The age range was 15 - 66 years, and the mean (SD) age was 34.62 (11.68) years. Of the 400 patients with bipolar disorder, 135 (33.75%) had anxiety disorders, 67 (16.8%) suffered from drug addiction, and 45 (11%) had OCD. The characteristics of the patients with bipolar disorder and comorbidities are detailed in Table 1.

The results of the separate logistic regression for each disorder are shown in Table 2. With increasing age, the risk of anxiety disorders and OCD increased. Compared to the male patients, the female patients had ORs of 1.05 (95% CI = 0.65 - 1.68), 0.26 (95% CI = 0.10 - 0.63), and 2.33 (95% CI = 1.21 - 4.48) for anxiety disorders, drug addiction, and OCD, respectively. Compared to the married patients, the single, widowed, and divorced patients were at higher risk of anxiety disorders, drug addiction, and OCD; however, the associations were not statistically significant. The risk of anxiety disorders, drug addiction, and OCD for the patients with no history of suicide compared to the patients with a history of suicide was not significant ($P > 0.05$).

Compared to the patients who were non-smokers, there was not a significant association between anxiety disorders and OCD for the patients who smoked ($P > 0.05$), but there was a significant association between smoking and drug addiction ($P < 0.05$). The ORs of anxiety disorders, drug addiction, and OCD in the patients with a history of being hospitalized more than twice were 1.01 (95% CI = 0.64 - 1.53), 1.75 (95% CI = 0.95 - 3.23), and 1.02 (95% CI = 0.52 - 1.99), respectively, compared with those patients who had been hospitalized twice.

5. Discussion

The present study showed that the patients with bipolar disorder treated at Farshchian hospital were at a higher risk of anxiety disorders than other disorders. Additionally, women with bipolar disorder were at a higher risk of anxiety disorders and OCD, while men with bipolar disorder were at greater risk of drug addiction. It was also demonstrated that more men with bipolar disorder were hospitalized than their female counterparts. This is consistent with the results of the studies by Thompson et al. and Rosca et al. (16, 17).

According to previous studies, mood disorders are highly comorbid with other mental disorders, and most often with anxiety. Similarly, in our study anxiety disorders were the most common disorders in patients with bipolar disorder (18, 19). Kim et al. (20) showed that the comorbidity of anxiety disorders in patients with bipolar disorder has a negative effect on the clinical course of the disease. Singh and Zarate (21) reported a 55% rate of anxiety disorders in patients with bipolar disorder (22). The results of our study indicated that the prevalence of anxiety disorders in patients with bipolar disorder was 33.75%. Anxiety disorders have been associated with an increased risk of depression relapse. According to our results, the risk of relapse was more than twice as high in patients with anxiety disorders, drug addiction, and OCD, which can be at-

Table 1. Characteristics of the Patients With Bipolar Disorder and Comorbid Disorders

Variables	Anxiety Disorder		Drug Addiction		OCD ^a	
	Yes	No	Yes	No	Yes	No
	135 (33.8)	265 (66.3)	67 (16.8)	333 (83.3)	45 (11.3)	355 (88.8)
Sex						
Men	95 (70.4)	193 (72.8)	61 (91.0)	227 (68.2)	24 (53.3)	264 (74.4)
Women	40 (29.6)	72 (27.2)	6 (9.0)	106 (31.8)	21 (46.7)	91 (25.6)
Marital status						
Married	64 (47.4)	126 (47.5)	27 (40.3)	163 (48.9)	19 (42.2)	171 (48.2)
Single	54 (40.0)	110 (41.5)	33 (49.3)	131 (39.3)	19 (42.2)	145 (40.8)
Divorced/widowed	17 (12.6)	29 (10.9)	7 (10.4)	39 (11.7)	7 (15.5)	39 (11.0)
History of relapse						
Twice	49 (36.3)	96 (36.2)	18 (26.9)	127 (38.1)	16 (35.6)	129 (36.3)
More than twice	86 (63.7)	169 (63.8)	49 (73.1)	206 (61.9)	29 (64.4)	226 (63.7)
History of suicide						
No	121 (89.6)	236 (89.1)	62 (92.5)	295 (88.6)	41 (91.1)	316 (89.0)
Yes	14 (10.4)	29 (10.9)	5 (7.5)	38 (11.4)	4 (8.9)	39 (11.0)
Smoker						
No	108 (80.0)	209 (78.9)	41 (61.2)	276 (82.9)	39 (86.7)	278 (78.3)
Yes	27 (20.0)	56 (21.1)	26 (38.8)	57 (17.1)	6 (13.3)	77 (21.7)

^aObsessive compulsive disorder.

tributed to a lower age of onset and the increased severity of the disease (23).

We found that the risk of anxiety disorder among women was greater than in men, but this was not statistically significant. Although Bruffaerts et al.'s study (24) also showed a higher risk of anxiety disorders among women than men, the association was found to be significant. Among the patients in the study by Mohammadi et al. (25), the risk of anxiety disorders was higher among those who were divorced or widowed than among the married patients. This finding was also consistent with the results of our study.

The prevalence of OCD in patients with bipolar disorder is reported to be between 9% and 35% (26), while in our study, 11% of the patients had OCD. Moreover, among the patients with OCD, the OR for women was significantly higher than that for men.

In Tohen et al.'s study (27, 28), 18.7% of the patients suffered from drug addiction, while 32.2% of the patients in Conus et al.'s research were addicted to drugs, with 6.9% having experienced alcohol abuse and dependence. The results of the present study showed that the comorbidity of drug addiction was 16.8% lower than the rates indicated in the aforementioned studies for patients with bipolar dis-

order. Furthermore, the risk of drug addiction was higher in men than in women, which supports the results of the studies by Chien et al. and Bruffaerts et al., both of which were conducted using study samples of patients with psychiatric disorders (24, 29).

In our study, the risk of drug addiction was higher in patients who smoked. This can be attributed to the association between a history of smoking in patients with a more severe course of illness and the increased risk of substance use disorder (30).

A limitation of this study was the lack of information about the severity of the comorbid disorders in the patients with bipolar disorder. In spite of this limitation however, the current study demonstrated that the risk of disease relapse was higher in patients with bipolar disorder who suffered from anxiety and OCD. The results of this study may therefore be beneficial to psychiatrists and psychologists to prevent disease relapse.

5.1. Conclusion

The results of this study showed that the risk of anxiety disorders among patients with bipolar disorder was higher than the risk of other disorders. Additionally, while the risk of anxiety disorders and OCD was higher in women

Table 2. The Results of the Analysis of Risk Factors for Anxiety Disorders, Drug Addiction, and Obsessive Compulsive Disorder in Bipolar Disorder Using a Logistic Regression Model

Variables	Adjusted OR (95% CI)		
	Anxiety Disorders	Drug Addiction	OCD ^a
Age	1.01 (0.99 - 1.04)	0.97 (0.93 - 1.01)	1.02 (0.99 - 1.05)
Sex			
Men	1.00	1.00	1.00
Women	1.05 (0.65 - 1.68)	0.26 (0.10 - 0.63) b	2.33 (1.21 - 4.48) b
Marital status			
Married	1.00	1.00	1.00
Single	1.25 (0.72 - 2.19)	1.06 (0.51 - 2.22)	1.73 (0.73 - 4.10)
Divorced/widowed	1.06 (0.52 - 2.13)	1.21 (0.46 - 3.15)	1.66 (0.64 - 4.33)
History of relapse			
Twice	1.00	1.00	1.00
More than twice	1.01 (0.64 - 1.53)	1.75 (0.95 - 3.23)	1.02 (0.52 - 1.99)
History of suicide			
No	1.00	1.00	1.00
Yes	0.93 (0.47 - 1.84)	0.78 (0.28 - 2.14)	0.73 (0.24 - 2.18)
Smoker			
No	1.00	1.00	1.00
Yes	0.92 (0.52 - 2.13)	3.01 (1.64 - 5.55) ^b	0.64 (0.25 - 1.62)

^aObsessive compulsive disorder.

^bSignificant (P < 0.05).

with bipolar disorder, men were at a higher risk of drug addiction.

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References

- Sadock BJ, Sadock VA. Kaplan and Sadock's synopsis of psychiatry. Lipincott Williams & Wilkins; 2011.
- Angst J, Marneros A. Bipolarity from ancient to modern times: conception, birth and rebirth. *J Affect Disord.* 2001;**67**(1-3):3-19. [PubMed: 11869749].
- Goodwin F, Jamison K. Suicide, in manic-depressive illness. New York: Oxford University; 1990.
- Gelenberg AJ, Kane JM, Keller MB, Lavori P, Rosenbaum JF, Cole K, et al. Comparison of standard and low serum levels of lithium for maintenance treatment of bipolar disorder. *N Engl J Med.* 1989;**321**(22):1489-93. doi: 10.1056/NEJM198911303212201. [PubMed: 2811970].
- Gitlin MJ, Swendsen J, Heller TL, Hammen C. Relapse and impairment in bipolar disorder. *Am J Psychiatry.* 1995;**152**(11):1635-40. doi: 10.1176/ajp.152.11.1635. [PubMed: 7485627].
- Murray CJ, Lopez AD. The global burden of disease and injury series: a comprehensive assessment of mortality and disability from diseases, injuries, and risk factors in 1990 and projected to 2020. 1. Cambridge; 1996.
- Frias A, Palma C, Farriols N. Comorbidity in pediatric bipolar disorder: prevalence, clinical impact, etiology and treatment. *J Affect Disord.* 2015;**174**:378-89. doi: 10.1016/j.jad.2014.12.008. [PubMed: 25545605].
- Parker GB. Comorbidities in bipolar disorder: models and management. *Med J Aust.* 2010;**193**(4 Suppl):S18-20. [PubMed: 20712555].
- Amerio A, Stubbs B, Odone A, Tonna M, Marchesi C, Ghaemi SN. The prevalence and predictors of comorbid bipolar disorder and obsessive-compulsive disorder: A systematic review and meta-analysis. *J Affect Disord.* 2015;**186**:99-109. doi: 10.1016/j.jad.2015.06.005. [PubMed: 26233320].
- McElroy SL, Altshuler LL, Suppes T, Keck PJ, Frye MA, Denicoff KD, et al. Axis I psychiatric comorbidity and its relationship to historical illness variables in 288 patients with bipolar disorder. *Am J Psychiatry.* 2001;**158**(3):420-6. doi: 10.1176/appi.ajp.158.3.420. [PubMed: 11229983].

11. Provencher MD, Guimond AJ, Hawke LD. Comorbid anxiety in bipolar spectrum disorders: a neglected research and treatment issue?. *J Affect Disord.* 2012;**137**(1-3):161-4. doi: [10.1016/j.jad.2011.12.001](https://doi.org/10.1016/j.jad.2011.12.001). [PubMed: [22209124](https://pubmed.ncbi.nlm.nih.gov/22209124/)].
12. Bauer MS, Altshuler L, Evans DR, Beresford T, Williford WO, Hauger R, et al. Prevalence and distinct correlates of anxiety, substance, and combined comorbidity in a multi-site public sector sample with bipolar disorder. *J Affect Disord.* 2005;**85**(3):301-15. doi: [10.1016/j.jad.2004.11.009](https://doi.org/10.1016/j.jad.2004.11.009). [PubMed: [15780700](https://pubmed.ncbi.nlm.nih.gov/15780700/)].
13. Surendran I, Chakrabarti S. Comorbid bipolar, obsessive-compulsive and other anxiety disorders: A patient-report highlighting diagnostic and treatment issues. *Bipolar Disord.* 2016;**2**(107):2.
14. Pini S, de Queiroz V, Pagnin D, Pezawas L, Angst J, Cassano GB, et al. Prevalence and burden of bipolar disorders in European countries. *Eur Neuropsychopharmacol.* 2005;**15**(4):425-34. doi: [10.1016/j.euroneuro.2005.04.011](https://doi.org/10.1016/j.euroneuro.2005.04.011). [PubMed: [15935623](https://pubmed.ncbi.nlm.nih.gov/15935623/)].
15. de Graaf R, Bijl RV, Smit F, Vollebergh WA, Spijker J. Risk factors for 12-month comorbidity of mood, anxiety, and substance use disorders: findings from the Netherlands Mental Health Survey and Incidence Study. *Am J Psychiatry.* 2002;**159**(4):620-9. doi: [10.1176/appi.ajp.159.4.620](https://doi.org/10.1176/appi.ajp.159.4.620). [PubMed: [11925301](https://pubmed.ncbi.nlm.nih.gov/11925301/)].
16. Thompson EE, Neighbors HW, Munday C, Trierweiler S. Length of stay, referral to aftercare, and rehospitalization among psychiatric inpatients. *Psychiatr Serv.* 2003;**54**(9):1271-6. doi: [10.1176/appi.ps.54.9.1271](https://doi.org/10.1176/appi.ps.54.9.1271). [PubMed: [12954945](https://pubmed.ncbi.nlm.nih.gov/12954945/)].
17. Rosca P, Bauer A, Grinshpoon A, Khawaled R, Mester R, Ponizovsky AM. Rehospitalizations among psychiatric patients whose first admission was involuntary: a 10-year follow-up. *Isr J Psychiatry Relat Sci.* 2006;**43**(1):57-64. [PubMed: [16910387](https://pubmed.ncbi.nlm.nih.gov/16910387/)].
18. Angst J. Comorbidity of mood disorders: a longitudinal prospective study. *Br J Psychiatry Suppl.* 1996(30):31-7. [PubMed: [8864146](https://pubmed.ncbi.nlm.nih.gov/8864146/)].
19. Beekman AT, de Beurs E, van Balkom AJ, Deeg DJ, van Dyck R, van Tilburg W. Anxiety and depression in later life: Co-occurrence and communality of risk factors. *Am J Psychiatry.* 2000;**157**(1):89-95. doi: [10.1176/ajp.157.1.89](https://doi.org/10.1176/ajp.157.1.89). [PubMed: [10618018](https://pubmed.ncbi.nlm.nih.gov/10618018/)].
20. Kim SW, Berk L, Kulkarni J, Dodd S, de Castella A, Fitzgerald PB, et al. Impact of comorbid anxiety disorders and obsessive-compulsive disorder on 24-month clinical outcomes of bipolar I disorder. *J Affect Disord.* 2014;**166**:243-8. doi: [10.1016/j.jad.2014.05.017](https://doi.org/10.1016/j.jad.2014.05.017). [PubMed: [25012437](https://pubmed.ncbi.nlm.nih.gov/25012437/)].
21. Singh JB, Zarate CA. Pharmacological treatment of psychiatric comorbidity in bipolar disorder: a review of controlled trials. *Bipolar Disord.* 2006;**8**(6):696-709. doi: [10.1111/j.1399-5618.2006.00371.x](https://doi.org/10.1111/j.1399-5618.2006.00371.x). [PubMed: [17156156](https://pubmed.ncbi.nlm.nih.gov/17156156/)].
22. Perlis RH, Ostacher MJ, Patel JK, Marangell LB, Zhang H, Wisniewski SR. Predictors of recurrence in bipolar disorder: Primary outcomes from the systematic treatment enhancement program for bipolar disorder (step-bd). *Am J Psychiatr.* 2006;**163**(2):217-24. doi: [10.1111/j.1399-5618.2006.00371.x](https://doi.org/10.1111/j.1399-5618.2006.00371.x). [PubMed: [17156156](https://pubmed.ncbi.nlm.nih.gov/17156156/)].
23. Serretti A, Chiesa A, Calati R, Linotte S, Sentissi O, Papageorgiou K, et al. Influence of family history of major depression, bipolar disorder, and suicide on clinical features in patients with major depression and bipolar disorder. *Eur Arch Psychiatry Clin Neurosci.* 2013;**263**(2):93-103. doi: [10.1007/s00406-012-0322-y](https://doi.org/10.1007/s00406-012-0322-y). [PubMed: [22569753](https://pubmed.ncbi.nlm.nih.gov/22569753/)].
24. Bruffaerts R, Sabbe M, Demyttenaere K. Attenders of a university hospital psychiatric emergency service in Belgium - general characteristics and gender differences. *Soc Psychiatry Psychiatr Epidemiol.* 2004;**39**(2):146-53. doi: [10.1007/s00127-004-0708-x](https://doi.org/10.1007/s00127-004-0708-x). [PubMed: [15052397](https://pubmed.ncbi.nlm.nih.gov/15052397/)].
25. Mohammadi MR, Davidian H, Noorbala AA, Malekafzali H, Naghavi HR, Pouretamad HR, et al. An epidemiological survey of psychiatric disorders in Iran. *Clin Pract Epidemiol Ment Health.* 2005;**1**:16. doi: [10.1186/1745-0179-1-16](https://doi.org/10.1186/1745-0179-1-16). [PubMed: [16185355](https://pubmed.ncbi.nlm.nih.gov/16185355/)].
26. Simon NM, Otto MW, Wisniewski SR, Fossey M, Sagduyu K, Frank E, et al. Anxiety disorder comorbidity in bipolar disorder patients: data from the first 500 participants in the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD). *Am J Psychiatry.* 2004;**161**(12):2222-9. doi: [10.1176/appi.ajp.161.12.2222](https://doi.org/10.1176/appi.ajp.161.12.2222). [PubMed: [15569893](https://pubmed.ncbi.nlm.nih.gov/15569893/)].
27. Tohen M, Zarate CJ, Hennen J, Khalsa HM, Strakowski SM, Gebre-Medhin P, et al. The McLean-Harvard First-Episode Mania Study: prediction of recovery and first recurrence. *Am J Psychiatry.* 2003;**160**(12):2099-107. doi: [10.1176/appi.ajp.160.12.2099](https://doi.org/10.1176/appi.ajp.160.12.2099). [PubMed: [14638578](https://pubmed.ncbi.nlm.nih.gov/14638578/)].
28. Conus P, Cotton S, Abdel-Baki A, Lambert M, Berk M, McGorry PD. Symptomatic and functional outcome 12 months after a first episode of psychotic mania: barriers to recovery in a catchment area sample. *Bipolar Disord.* 2006;**8**(3):221-31. doi: [10.1111/j.1399-5618.2006.00315.x](https://doi.org/10.1111/j.1399-5618.2006.00315.x). [PubMed: [16696823](https://pubmed.ncbi.nlm.nih.gov/16696823/)].
29. Chien IC, Chou YJ, Lin CH, Bih SH, Chou P. Prevalence of psychiatric disorders among National Health Insurance enrollees in Taiwan. *Psychiatr Serv.* 2004;**55**(6):691-7. doi: [10.1176/appi.ps.55.6.691](https://doi.org/10.1176/appi.ps.55.6.691). [PubMed: [15175468](https://pubmed.ncbi.nlm.nih.gov/15175468/)].
30. Ostacher MJ, Nierenberg AA, Perlis RH, Eidelman P, Borrelli DJ, Tran TB, et al. The relationship between smoking and suicidal behavior, comorbidity, and course of illness in bipolar disorder. *J Clin Psychiatry.* 2006;**67**(12):1907-11. [PubMed: [17194268](https://pubmed.ncbi.nlm.nih.gov/17194268/)].