



# Comorbidities of Major Depressive Disorder and Bipolar Disorders in Patients with Substance Use Disorder in Iran Psychiatric Hospital: A Cross-sectional Study

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Received: 20 Jun 2022

Published: 7 Feb 2023

## Abstract

**Background:** Mood disorders are the most common psychiatric comorbidities in substance users. Mood disorders and substance use disorders are 2 intertwined processes in which treating one aid in treating the other. Depression and substance use disorder are now regarded as major mental health issues due to their widespread incidence.

The study was designed to investigate the prevalence of major depressive disorder (MDD) and bipolar I and II disorders in patients with substance use disorder.

**Methods:** The participants of this cross-sectional study were 320 patients with substance use disorder based on the DSM-5 (diagnostic and statistical manual of mental disorders 5th edition) criteria in Iran Psychiatric Hospital in 2020, who were assessed using the SCID-5-CV (Structured Clinical Interview for DSM-5 disorders-clinician version), and the demographic and clinical variables questionnaire considering familial and substance use history. The chi-square, Fisher, independent t test, and logistic regression were used to analyze the data.

**Results:** Of the patients, 32.8% (n = 105) had mood disorders. The most common mood disorder was MDD (16.9%, n = 54), followed by bipolar I (12.5%, n = 40) and bipolar II (2.8%, n = 9) disorders. Methamphetamine was the most commonly used substance (47.5%, n = 152). Also, 62.5% (n = 200) of participants consumed 2 or more substances simultaneously. The chance of having a mood disorder in married and divorced patients was 2.12 and 2.04 times more than in single patients, respectively.

**Conclusion:** The lifetime prevalence of bipolar I disorder in patients with substance use disorders is several times more than the general population, thus psychiatrists should pay more attention to mood comorbidities diagnosis and treatment in substance users.

**Keywords:** Substance Use Disorder, Comorbidity, Mood Disorders

**Conflicts of Interest:** None declared

**Funding:** None

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**Cite this article as:** Oladikalarijani M, Shabani A, Soraya S, Ahmadkhaniha H. Comorbidities of Major Depressive Disorder and Bipolar Disorders in Patients with Substance Use Disorder in Iran Psychiatric Hospital: A Cross-sectional Study. *Med J Islam Repub Iran.* 2023 (7 Feb);37.3. <https://doi.org/10.47176/mjiri.37.3>

## Introduction

Substance dependency is a chronic, recurrent, and debil-

itating disorder. With a prevalence rate of 6% to 15% in

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### ↑What is “already known” in this topic:

Substance dependency is one of the most important health issues, and mood disorders are the most common psychiatric comorbidity in substance users. Treating one of the entwined processes will help in treating the other. However our knowledge about the comorbidity of these 2 disorders in Iran is limited.

### →What this article adds:

The lifetime prevalence of mood disorders in patients with substance use disorder was 32.8% and the lifetime prevalence of bipolar I disorder in these individuals was several times more than the general population.

The current study's findings revealed that the prevalence of bipolar disorder among methamphetamine and opioid-dependent individuals was high.

several Western countries (1), this health issue imposes a significant economic burden on society, particularly in the areas of health care, criminal justice, and workplace productivity (2). Comorbidity of mental illness with substance use disorders is a quite common phenomenon. According to epidemiologic studies, more than half of people with substance use disorders also have mental disorders. On the other hand, 15% to 40% of people with mental disorders have substance use disorder (3).

Mood disorders (major depressive disorder [MDD], bipolar disorder) are the most common psychiatric comorbidities in substance users (4). Mood and substance use disorders are 2 intertwined processes in which treating one aids in treating the other (5). It is especially difficult to differentiate between substance use disorder and mood and anxiety disorders since the symptoms of substance intoxication and mood and anxiety disorders are very similar (6). Self-medication with alcohol, tobacco, or other substances to mitigate the symptoms of depression or mania is common, but it can make symptoms worse in the long term. When someone becomes addicted to alcohol, tobacco, or any other substance, or even when they quit using it, these symptoms worsen (7). For example, in patients with a history of bipolar disorder, opioid withdrawal may trigger the recurrence of symptoms (8).

Drug and alcohol use is common among people with bipolar disorder, which may lead to functional disability, poor lithium response, worsened depressive symptoms, poor prognosis and compliance, rapid recurrence, experience mood symptoms at a younger age, and an increased risk of suicide, accidents, and hospitalization (9-11).

Depression and substance use disorder are now regarded as major mental health issues due to their widespread incidence. There is evidence that the stated conditions are connected with a high rate of completed suicides, and when they are comorbid, the risk of suicide increases (12). As a result, assessing secondary or minor mental disorders in people with substance use disorder would reduce the likelihood of self-harming behaviors (13).

There are studies indicating that the course of mood disorders is different in Iranian patients (14), as genetic differences and environmental effects would alter the predominant course of bipolar disorder in different countries. Several studies in Germany, Spain, and the United States have found that depression is the most common phase of bipolar disorder. There have also been studies in India, Fiji, and Nigeria that show the manic phase to be the most prevalent (15).

Iran occupies a unique geographic position as a crossroads between East and West, as well as a transit point for substances. The vicinity of Afghanistan, the world's largest producer of opium (16), has made substance use one of Iran's top psychiatric research priorities. Because of cultural and social differences between Iran and other countries, a lack of comprehensive local information, changes in the prevalence and pattern of disease over time, and the high cost of treatment, studies on substance use disorders and psychological problems in Iran may provide valuable information to health professionals and improve the effectiveness of addiction treatments.

Given the limited studies on the comorbidity of major mood disorders and substance use disorders in our country, as well as not using an interview-based diagnostic instrument, such as the SCID-5-CV (17) (Structured Clinical Interview for DSM-5 disorders-clinician version) in previous studies, the primary goal of this study was to assess the prevalence of major mood disorders in people with substance use disorders in Iran psychiatric hospital, a university-affiliated hospital and a referral center with numerous patients from all regions of Iran.

## Methods

### Participants

Patients with substance use disorders in Iran psychiatric hospitals in 2020 were the participants of this cross-sectional study. Ages 18 to 64 years, a DSM-5 (diagnostic and statistical manual of mental disorders 5th edition) diagnosis of substance use disorder, and written informed consent to participate in the study were the inclusion criteria. Incomplete questionnaire answers and refusal to participate in the study were also criteria for exclusion. A total of 320 outpatients referred to the substance dependence treatment clinic of Iran Psychiatric Hospital were evaluated using the SCID-5-CV and a demographic and clinical variables questionnaire.

### Instruments

#### • Demographic and clinical variables questionnaire

The demographic and clinical variables questionnaire to collect data included the following variables: age, gender, marital status, education level, employment status, family history of substance use, family history of psychiatric disorder, type of substance and method of use, using more than one type of substance, the age of first use, and cigarette smoking.

#### • Structured clinical interview for the DSM-5 disorders-clinician version (SCID-5-CV)

All patients referred to this hospital were examined by psychiatrists and those who were diagnosed with substance use disorder based on the DSM-5 criteria were included in the study. The Persian version of the SCID-5-CV clinical interview—the “mood episodes” section—was used to diagnose major mood disorders (18). The interviewer (a psychiatry resident) was trained by a psychiatrist fluent in the Structured Clinical Interview for DSM-5 (SCID) interviewing.

The SCID is a structured clinical interview used to diagnose psychiatric disorders. The diagnostic agreement of the SCID-5-CV (Persian version) for bipolar disorder, depressive disorder, substance use disorder, and obsessive-compulsive disorder was high (kappa 0.76 to 0.80) and the diagnostic agreement between the SCID interview and the diagnostic gold standard was high (19).

### Data Analysis

SPSS statistical software Version 24 was used to analyze the data. The mean and standard deviation were used to report quantitative data, whereas qualitative data were reported as frequency (percentage and number). Statistical tests used included the chi-square, Fisher, independent t

test, and logistic regression. Statistical significance was defined as  $P < 0.05$ .

### Ethical Considerations

The research process was designed in accordance with the Helsinki and Tokyo Declarations, and all of the project's researchers evaluated ethical issues in various domains, including confidentiality. All participants signed informed written consent after receiving complete information about the study. If any of the patients declined to participate in the trial, they were not deprived of medical care and continued to receive routine treatment. Patients were also assured that their information would be kept private and solely utilized for research purposes. This study did not include any intervention on patients.

### Results

In this study, data were collected from 320 participants. The mean age ( $\pm$ SD) of the participants was  $34.87 \pm 9.19$  years and the mean age at first use was  $23.02 \pm 7.44$  years. Sociodemographic variables are shown in Table 1.

In total, 152 participants (47.5%) used methamphetamine, 31 (9.7%) cannabis, 40 (12.5%) opium, 78 (24.4%) heroin, 8 (2.5%) methadone, 5 (1.6%) tramadol, and 6 (1.9%) alcohol (Table 2). Also, 96.6% of participants smoked cigarettes.

The most common method of use was smoking. It is noteworthy that 62.5% of the study population and 48.9% of participants with bipolar disorder used more than 1 substance at the same time. Moreover, 28.1% of patients reported a family history of psychiatric disorder.

As shown in Table 2, of the participants, 32.8% had a lifetime mood disorder and 67.2% had no mood disorder. Major depressive disorder (MDD) (16.9%), bipolar I

Table 1. Sociodemographic variables of the study population (N=320)

Characteristics	Number (%)
Gender	Female 28(8.8)
	Male 292(91.2)
Marital status	Single 177(55.3)
	Married 81(25.3)
	Widow 6(1.9)
	Divorced 56(17.5)
Educational level	Illiterate 4(1.3)
	Undergraduate 156(48.8)
	High school diploma 133(41.6)
	Associate degree 3(0.9)
Job status	Bachelor's degree and higher degrees 24(7.5)
	Unemployed 196(61.3)
	Employed 114(35.6)
	Waiting for job 1(0.3)
	Lost job 9(2.8)

(12.5%), and bipolar II disorder (2.8%) were prevalent.

Logistic regression results showed a statistically significant relationship between a family history of psychiatric disorder and mood disorder ( $p < 0.001$ ). The chance of having a mood disorder in patients with a family history of psychiatric disorder was 4.90 times higher than in patients without a family history of psychiatric disorder (Table 3). In addition, the results of the independent t test showed that the difference between the mean age, age at first use, and age of continuous use between the 2 groups with and without mood disorders was not statistically significant ( $p > 0.05$ ).

The results of multinomial regression showed that the chance of having bipolar I disorder in patients who used more than 1 substance was 2.10 times higher than in patients who used only 1 type of substance ( $p = 0.032$ ).

The chi-square test results showed a statistically significant relationship between marital status and mood disorder.

Table 2. Prevalence of mood disorders in association with the used substances

Type of substance		No mood disorder	Major depressive disorder	Bipolar disorder type I	Bipolar disorder type II	Persistent depressive disorder	Total
Methamphetamine	N (%)	107 (70.4)	22 (14.5)	20 (13.2)	3 (2.0)	0	152
Cannabis	N (%)	19 (61.3)	5 (16.1)	5 (16.1)	2 (6.5)	0	31
Opioids	N (%)	76 (64.4)	23 (19.5)	14 (11.9)	4 (3.4)	1 (0.8)	118
Methadone	N (%)	7 (87.5)	0	0	0	1 (12.5)	8
Tramadol	N (%)	4 (80.0)	1 (20.0)	0	0	0	5
Alcohol	N (%)	2 (33.3)	3 (50.0)	1 (16.7)	0	0	6
Total	N (%)	215 (67.2)	54 (16.9)	40 (12.5)	9 (2.8)	2 (0.6)	320

Table 3. Clinical variables in association with having any mood disorder

Variables		With mood disorder	Without mood disorder	P-value	OR (95% CI)
Routs of administration		N (%)	N (%)		
	Smoking	94 (89.5)	193 (89.8)		
	Intravenous	1 (1.0)	1 (0.5)		
	Oral	7 (6.7)	14 (6.5)		
	Smoking/oral	2 (1.9)	4 (1.9)		
More than one substance	Smoking/ iv	1 (1.0)	3 (1.4)		
	Positive	59 (56.2)	141 (65.6)		
Cigarette smoking	Negative	46 (43.8)	74 (34.4)		
	Positive	102 (97.1)	208 (96.7)		
Family history of substance use	Negative	3 (2.9)	7 (3.3)		
	Positive	51 (51.4)	104 (48.4)		
Family history of psychiatric disorder	Negative	51 (48.6)	111 (51.6)		
	Positive	53 (50.5)	37 (17.2)	<0.001*	4.90
	Negative	52 (49.5)	178 (82.8)		(2.91,8.25)

Table 4. Marital status in the study population with/without mood disorder

Marital status	Mood Disorder		95% CI for OR	P-value
	With mood disorder N (%)	Without mood disorder		
Single	45 (42.9)	132 (61.4)	1.00	
Married	34 (32.4)	47 (21.9)	2.12 (1.21,3.70)	0.008*
Widowed	3 (2.9)	3 (1.4)	2.93 (0.57,15.05)	
Divorced	23 (21.9)	33 (15.3)	2.04 (1.08, 3.84)	0.026*

ders ( $p=0.040$ ). Logistic regression results showed the chance of having a mood disorder in married patients to be 2.12 times more than in single patients (odds ratio [OR], 2.12 [95% CI, 1.21-3.70];  $p=0.008$ ). Also, the chance of having a mood disorder in divorced patients was 2.04 times more than in single patients (OR, 2.04 [95% CI, 1.08-3.84];  $p=0.026$ ) (Table 4).

### Discussion

Mood disorders are one of the most common psychiatric comorbidities in substance users (4), and in some cases, using substances as self-medication for mood disorders symptoms is one of the reasons for continuing or relapsing (20). In addition, substance use disorder has an impact on disease diagnosis, treatment, and prescription selection. Failure to diagnose serious depression or bipolar disorder can result in substance use, recurrence of mood disorders, and even increased suicide risk (21). The lifetime prevalence of mood disorders in our study was 32.8%, with MDD being the most common mood disorder (16.9%), followed by type 1 (12.5%) and type 2 (2.8%) bipolar disorders. A study in Kashan declared major depression disorder Bipolar I disorder and bipolar II disorder prevalence in the general population was 8.2%, 2.4%, and 1.8%, respectively (22). Although MDD is the most common mood disorder in our study, bipolar I disorder seems to be almost 5 times more common among these patients than in the general population. It nevertheless demonstrates the significance of treating people with bipolar I disorder as substance users, despite the possibility of referral bias. Furthermore, persistent substance use worsens the symptoms of mood disorders, particularly bipolar disorder and makes these disorders more apparent by changing subclinical symptoms into clinical ones. Another explanation could be that patients with more severe symptoms would refer to psychiatric clinics for treatment more often. It seems that patients who attempted to quit using substances had more signs of mood disorders than those who did not. Our findings were in accordance with recent review research that found MDD to be the most common psychiatric comorbidity among opioid-dependent patients, and substance dependence was most closely linked to depression (21).

A study done in Guilan on visitors of substance use treatment centers using Becks depression inventory found the prevalence of depression to be 48.96%. (23)

It seems that the prevalence of depression is higher in self-reported methods compared with clinical interview ones, which put more strict criteria for identifying depressive disorders rather than depressive symptoms. Although given the likelihood of cognitive impairment in people

with substance use disorder, and even recall bias in reporting past depressive episodes, underdiagnosis of mood disorders in these groups is possible (24).

In our study, 29.7% of patients with methamphetamine use disorder had a mood disorder, with 14.5% having MDD, 13.2% bipolar I disorder, and 2% bipolar II disorder. A study of patients with methamphetamine use disorder in the United States found similar results. However, their study found a lower prevalence of lifetime bipolar disorder (mood disorder, 32.3%; MDD, 12.7%; and bipolar disorder, 5.8%) (25).

A study conducted on the Canadian adult population found a lifetime prevalence of MDD to be 21.2% in drug-dependent patients, which is in accordant with our study (26).

The lifetime prevalence of mood disorder was 34.8% in the population with opioid use disorder (opium and heroin) in the present study (19.5% for MDD, 11.9% for bipolar I disorder, and 3.4% for bipolar II disorder).

Another study in Spain found that 48% of opioid-dependent candidates for opioid agonist therapy had mood disorders, according to the Europe ASI section I (27). Differences in diagnostic tools could explain the increased prevalence of mood disorders in the mentioned study compared to ours.

Research in the United States found that 23% of the general population smoked cigarettes, whereas it was 2 to 4 times higher in those with psychiatric illness and substance use disorder (28). These findings are congruent with our results, which revealed that 310 (96.9%) of the individuals smoked cigarettes. It is important to note that Iran's population aged 15 to 64 has a current smoking prevalence of 12.5% and a daily prevalence of 11.3% (29).

According to the results, 48.9% of participants with bipolar disorder used multiple substances at the same time, and the risk of developing bipolar I disorder was 2.1 times higher in patients who used multiple substances than in patients who only used 1 type of substance. In a study of patients with bipolar disorder in Iran, 46.4% exhibited polysubstance use, which could be related to different substances being used at different phases of the disease (5).

The chances of having a mood disorder were found to be 4.9 times higher in patients with a family history of psychiatric disorder in the present study. Only 8.4% of the participants held an academic degree, while 89.6% were undergraduates. Also, 61% of those who took part were unemployed. Our findings are consistent with the Graph study, which looked at the 12-month risk factors for comorbidity of mood, anxiety, and substance use disorder

and found that the likelihood of comorbidity of substance use and mood disorders was higher in women, low-educated participants, unemployed people, people with a family history of psychiatric illness, and people who had experienced childhood trauma (30). According to a review article, the prevalence of smoking and substance use disorder is higher among the unemployed, and unemployment is an important risk factor for substance use disorders (31).

Our findings revealed a statistically significant relationship between patients' marital status and mood comorbidities, with married patients having a 2.12 times higher likelihood of having mood disorders than single patients, and divorced patients having a 2.04 times higher chance of having mood disorders. Scott et al (32) observed that marriage was related to a lower risk of the first episode of most mental disorders, but divorce was associated with an increased risk of all mental diseases in both sexes in research of 73,099 people from 15 different countries.

The discrepancy between the 2 studies could be due to the fact that in Iran, lower income and financial problems can impact married life, and marriage raises the risk of mental disorders.

Surprisingly, methamphetamine was the most widely used substance, although opioids were the most commonly used substance in the 2 prior studies in Iran, which were conducted on the general population (33, 34).

Opium is extensively used in our country and appears to be more socially acceptable than other substances. It is classified as a soft drug and is taken in social gatherings by individuals from all socioeconomic backgrounds (34). Despite their increasing prevalence, opioid users appear to visit addiction treatment centers less frequently than other substance users.

In a study of 57 patients referred to an addiction treatment center in Mexico, the mean age at first use was 15.7 years, and the most commonly used substances were alcohol and cannabis (12). The mean age of beginning substance usage in our study was 23 years.

Disparities in the results appear to be due to differences in consumption patterns and drug availability. Drug usage in these patients, as well as healthy persons, is influenced by culture and socioeconomic factors. Another factor could be that some patients in Iran intentionally deny using substances due to cultural and legal constraints (5). In general, differences in the results of various studies could be attributed to differences in research methods, study population, the socioeconomic and cultural status of the study population, diagnostic instruments utilized in the study, and study complexity when patients are polysubstance users.

### Conclusion

Mood disorders have significant comorbidity with substance use disorder. The lifetime prevalence of bipolar I disorder in those with substance use disorders is several times more than the general population.

The current study's findings revealed that the prevalence of the bipolar disorder among methamphetamine and opioid-dependent individuals was high, which could be rep-

resentative of Iranian patients with substance use disorder who are under treatment, emphasizing the delicate attention they need, and the presence of psychiatrists in substance dependence treatment centers for screening mood disorders comorbidities and proper treatment. However, additional research is needed to figure out why these people have a higher prevalence of bipolar disorder.

### Limitations

Despite our significant results, the current study was conducted in only 1 outpatient center; thus, we recommend that similar studies be conducted in multiple centers across Iran and on inpatients to evaluate the role of other characteristics and drug use patterns. Due to the low number of participants with alcohol, methadone, tramadol, and cannabis use disorders in this study, the prevalence of mood disorders in these subcategories could not be commented on. The diagnosis of mood disorders in our study was only made by interviewing the participant. Given the likelihood of cognitive impairment in people with substance use disorder and recall bias in reporting past depressive episodes, underdiagnosis of mood disorders in these groups is possible.

### Ethical Issues

The trial was approved by the ethics committee of Iran University of Medical Sciences institutional review board (IR.IUMS.FMD.REC.1399.148) and conducted according to the Declaration of Helsinki and subsequent revisions. Written informed consent was obtained from all participants. Patients were informed that their participation was a voluntary activity and that they had the right to leave the study at any time with no negative effect on their treatment.

### Acknowledgments

This paper was a part of a residency thesis done at Iran Psychiatric Hospital and the authors would like to thank the administrators of Iran Psychiatric Hospital and all the patients who participated in this study.

### Authors Contribution

Study concept and design: Amir Shabani, Hamid Reza Ahmdakhaniha

Analysis and interpretation of data: Mahsa Oladikalarijani, Shiva Soraya

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### Conflict of Interests

The authors declare that they have no competing interests.

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