

## Comorbidity of Anxiety Disorders and Substance Abuse with Bipolar Mood Disorders and Relationship with Clinical Course

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**Objective:** Patients with bipolar mood disorder constitute a relatively large number of individuals hospitalized in psychiatric hospitals. This disorder is highly comorbid with other psychiatric disorders and may effect their clinical course. The goal of this study was to determine the co-occurrence rate of anxiety disorders and substance abuse with bipolar mood disorders and their impact on clinical course.

**Methods:** 153 bipolar patients (type I) were selected among the hospitalized patients at Razi Psychiatric Hospital in Tabriz, Iran, from September 2007 to October 2008 through convenience sampling method. The participants were evaluated by a structured clinical interview based on DSM-IV criteria (SCID), Hamilton Rating Scale for Depression (HRSD) and Young Mania Rating Scale (YMRS).

**Results:** Co-morbidity of anxiety disorders was 46.15%. Occurrence of anxiety disorders was 28% for obsessive-compulsive disorder, 26.6% for generalized anxiety disorder, 4.2% for phobia and 2.1% for panic disorder. Co-morbidity of substance abuse was 7.7% and the highest occurrence of substance abuse was 5.6% for alcoholism and 4.2% for opium. No significant difference was observed between the severity of disease and duration of hospitalization in bipolar patients with or without anxiety disorder. The severity of disease and duration of hospitalization in bipolar patients with substance abuse was higher compared to bipolar patients without substance abuse ( $P < 0.05$ ).

**Conclusions:** This study suggests that there is a high co-morbidity between anxiety disorders and substance abuse with bipolar disorder. Further, this study suggests that co-occurrence of substance abuse disorder with bipolar disorder increases the severity of the disease and duration of hospitalization.

**Key Words:** Anxiety Disorders, Substance Abuse, Bipolar Disorder, Comorbidity, Severity of Disease

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**B**ipolar disorders are among the most common psychiatric disorders which usually become recrudescence and chronic (1). As bipolar disorders may lead to major consequences, psychiatrists attempt to use effective therapies while facing different therapeutic problems. Bipolar mood disorder is influenced by different problems such as psychological stresses (2), co-occurrent diseases (3, 4) and substance abuse (5). Co-occurrence of anxiety disorders and substance abuse are of diagnostic and therapeutic importance because they may complicate the clinical symptoms, decrease treatment response (6, 7), and provide for the establishment of another psychological disorder (8). According to several studies, co-existence of an anxiety disorder with bipolar disorder intensifies the severity of the diseases (9- 11). It is also determined that co-occurrence of substance abuse with

bipolar disorder increases the duration of hospitalization (12). However, Henri C et al (13) obtained converse results which indicate that co-occurrence of anxiety disorders are not related to the severity of bipolar disease and duration of hospitalization. Overall, concurrent substance abuse disorder and anxiety disorders increase the chronicity, disability, and mortality of bipolar disorders.

Co-morbidity of anxiety and substance abuse disorders has many adverse effects on patients with bipolar disorders. The co-occurrence of anxiety disorders with bipolar disorder was 10.6-62.5% for panic disorder, 7.8-42.5% for social phobia, 3.2-35% for obsessive-compulsive disorder, 7-37.8% for post-traumatic stress disorder and 32.7% for generalized anxiety disorder. (14). In addition, co-occurrence of anxiety disorders with bipolar disorder was reported 55.8%, and generalized anxiety disorder and panic disorder had the

highest rate of co-occurrence with bipolar disorder. Another study also reported higher rate of this occurrence (15, 10).

Life-looking study about co-occurrence of substance abuse with bipolar disorder also shows that 57% of patients with type I bipolar disorder were abusing or dependent to one substance, 28.2% were using two substances and 11.3% were abusing three substances. Among the patients with type II bipolar disorder, 39% were abusing or dependent to one substance, 39% were using two substances and 11% were using three or more substances. Alcohol was the most frequently used substance abused by type I and II bipolar patients (16). There are few studies which attempt to evaluate the effect of anxiety disorder and substance abuse on severity of the disease symptoms and duration of hospitalization. Moreover, the conflict between these studies highlights the necessity to conduct a new study. High rates of co morbidity of anxiety disorder and bipolar disorder is a therapeutic and diagnostic warning for effective interventions (17,5) which requires precise understanding and knowledge. Moreover, different occurrences of co-morbidity of psychiatric disorders and substance abuse among different societies and races (18,19) caused this preliminary study to be carried out in Iran.

This study was carried out with the aim of understanding the co-occurrence of anxiety disorders and substance abuse with bipolar disorder and its relationship with the clinical course in an Iranian population.

## Materials and Methods

This was a descriptive-analytic study with a convenience sampling method which was conducted with no gender difference among the patients hospitalized at Razi psychiatric hospital in Tabriz, Iran.

### Participants

The participants were selected among the patients hospitalized from September 2007 to October 2008. 153 bipolar I patients including 105 males and 38 females participated in this study. The patients were recruited according to DSM-TR-TV criteria using standard diagnostic tools for defining bipolar disorders and the accompanying disorders.

The patients were classified into four groups in order to compare the severity of manic and depressive symptoms of patients in the related phases of bipolar disorder:

- 1) Bipolar disorder with Anxiety disorder (BMD+AD);
- 2) bipolar disorder with Substance abuse disorder (BMD+SAD);
- 3) bipolar disorder co morbid with Substance abuse disorder and anxiety disorder (BMD+AD+SAD);
- 4) bipolar disorder without anxiety disorder and substance abuse (BMD+WAD+WSAD).

Inclusion criteria were having bipolar mood disorder based on two psychiatrists' interviews, 18-60 years of age, informed consent and cooperation of the patients and their families. Patients with general medical

conditions (GMC) or psychiatric disorders other than anxiety disorders were excluded from the study.

### Procedures

Demographic data including age, gender, education and occupation were obtained through interview during hospitalization.

### Instruments

#### Structured Clinical Interview for DSM-IV(SCID)

SCID is a widely-used clinical tool for the classification of psychiatric disorders based on DSM-IV criteria (20). The reliability and feasibility of the Persian version of this diagnostic instrument were already determined as fair to good for most diagnostic categories( kappa > 0.6)(21)

#### Hamilton Rating Scale for Depression (HRSD)

Hamilton Rating Scale for depression is a multi-optional scale which evaluates different behavioral, physical, cognitive, and emotional aspects as well as feeling of guilt-, hypochondriasis, suicide, sexual difficulties, and sleep disorders. The scale was used to determine the severity of depression in bipolar disorders in this study. Its validity and reliability have been determined in different studies (22).

#### Young Mania Rating Scale (YMRS)

Young Mania Rating Scale is a multi-optional 11-itemed scale which is used to evaluate the severity of manic symptoms in bipolar disorders for patients from 18 to 60 years of age. The validity and reliability of this scale are determined (23).

### Statistical Analysis

The data were statistically analyzed using SPSS software. Descriptive statistics were used to study the co-occurrence of anxiety disorders and substance abuse. ANOVA test was used to compare the severity of the symptoms of depression and mania in bipolar patients. P-value less than 0.05 was considered to be statistically significant.

## Results

Table 1 shows the demographic characteristics of the studying sample among the three four groups of patients: anxiety disorder with bipolar disorder, substance abuse with bipolar disorder, and bipolar and bipolar disorder without accompanying disease.

It is revealed that among 143 bipolar patients 66 patients (46.15%) suffered from anxiety disorders, 40 patients (28%) suffered from obsessive-compulsive disorder, 38 patients (26.6%) suffered from generalized anxiety disorder, 6 patients (4.2%) suffered from phobia disorder, 3 patients (2.1%) suffered from panic disorder and 4 patients (2.8%) suffered from other anxiety disorders. The co-occurrence of anxiety disorders was 68.4% for female and 38% for men. Studying the occurrence status of substance abuse indicated that among 143 bipolar patients, while 11

patients (7.7%) abused substances , 8 patients (5.6%) abused alcohol, 6 patients (4.2%) abused opium, 3 patients (1.2%) abused marijuana and 4 patients (2.8%) abused other substances and 83 patients (58%) smoke cigarettes (some patients simultaneously abused several substances). Comorbidity Co-morbidity of substance abuse with bipolar disorder was 2.6% for women and 9.5% for men. Table 2 shows demonstrates the frequencies of co-morbid anxiety and substance abuse disorders in the understudy bipolar patients.

Table 2 3 indicates illustrates the frequency and percentage of bipolar patients in manic phase and depressed depressive phases groups. The average and deviation of Young Mania Rating Scale grades, Hamilton Rating Scale for Depression and duration of hospitalization are presented in table 2 Table 3. The results obtained from ANOVA variance analysis for comparing the severity of mania symptoms using Young Mania Rating Scale in the four groups of patients with anxiety disorder and substance abuse and those without anxiety disorder and substance abuse them revealed that there was no statistically significant difference between these groups (P=0.32).

The severity of manic symptoms among the patients who abused substance and those without anxiety disorder or substance abuse showed a statistically significant difference (P=0.04). There was no significant relation between the severity of manic symptoms and co-occurrence of substance abuse and anxiety disorder among the patients (P=0.96)(Figure 1). Furthermore, There was no statistically significant difference revealed was observed among the groups of patients in considering regarding the average severity of depression symptoms in Hamilton Rating Scale for Depression (P=0.51).

It is notable that there was no statistically significant difference (P=0.37) was observed in from the average duration of hospitalization in the mania manic phase among the four groups of patients with anxiety disorder and substance abuse and those without anxiety disorder and substance abuse them (Table 3, Figure 1). In other words, there was no significant relationship between anxiety disorders and duration of hospitalization in patients this study. There was a significant relationship (P=0.03) in between substance abuse and duration of hospitalization among bipolar

**Table 1. Demographic Characteristics of Bipolar Mood Disorder Patients**

| Characteristics    |                       | BMD + AD<br>N (%) | BMD + SAD<br>N (%) | BMD      | BMD + AD +<br>SADN (%) |
|--------------------|-----------------------|-------------------|--------------------|----------|------------------------|
| Age groups (years) | 18-32                 | 37 (56.1)         | 6(54.5)            | 37(52.1) | 3(60)                  |
|                    | 33-46                 | 21(31..8)         | 3(27.3)            | 23(32.4) | 1(20)                  |
|                    | 47-60                 | 8(12.1)           | 2(18.2)            | 11(15.5) | 1(20)                  |
| Gender             | Male                  | 41(62.1)          | 8(73.7)            | 59(83.1) | 3(60)                  |
|                    | Female                | 25(37.9)          | 3(27.3)            | 12(16.9) | 2(40)                  |
| Education          | Illiterate            | 9(13.6)           | 3(27.3)            | 13(18.3) | 2(40)                  |
|                    | Primary school        | 22(33.3)          | 3(27.3)            | 16(22.5) | 1(20)                  |
|                    | Junior high school    | 18(27.3)          | 4(36.3)            | 24(33.8) | 2(40)                  |
|                    | Senior high school    | 14(21.2)          | 1(.9)              | 15(21.1) | 0(0)                   |
|                    | Academic              | 3(4.5)            | 0(0)               | 3(4.2)   | 0(0)                   |
| Employment         | Unemployed            | 38(57.6)          | 8(72.7)            | 50(70.4) | 5(0)                   |
|                    | Employed              | 28(42.4)          | 3(27.3)            | 21(29.6) | 0(0)                   |
| Marital status     | Married               | 26(39.4)          | 3(27.3)            | 30(42.2) | 0(0)                   |
|                    | Single                | 34(51.5)          | 5(45.4)            | 33(46.5) | 3(60)                  |
|                    | Divorced or separated | 6(9.1)            | 3(27.3)            | 8(11.3)  | 2(40)                  |

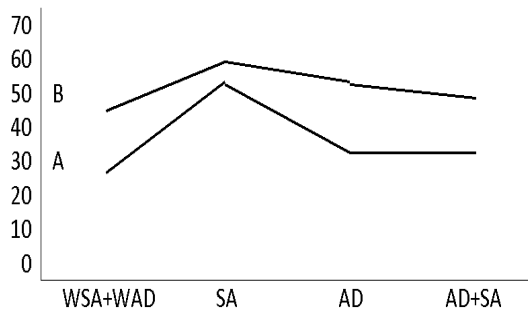
BMD=Bipolar Mood Disorder, AD=Anxiety Disorders, SAD= Substance Abuse Disorders

**Table 2. Frequency of co-morbidities in bipolar patients**

| Anxiety disorders       | N (%)     | Substance Abuse Disorders | N (%)   |
|-------------------------|-----------|---------------------------|---------|
| OCD                     | 40 (28)   | Alcohol                   | 8 (5.6) |
| GAD                     | 38 (26.6) | Opium                     | 6 (4.2) |
| Panic disorder          | 3 (2.1)   | Cannabis                  | 3 (1.2) |
| Phobia                  | 6 (4.2)   | Other substances          | 4 (2.8) |
| Other anxiety disorders | 4(2.8)    |                           |         |

**Table 3. Duration of Hospitalization and Severity of Bipolar Disorder Symptoms**

| Phase                | Groups                            | Number<br>(%) | Symptoms<br>of BD | Days of<br>hospitalization |
|----------------------|-----------------------------------|---------------|-------------------|----------------------------|
|                      |                                   |               | Mean(SD)          | Mean(SD)                   |
| Mania<br>(N=136)     | With anxiety                      | 58(46)        | 55.98(9.97)       | 38.47(19.5)                |
|                      | With substance abuse              | 11(8.7)       | 59.9(11.3)        | 48.5(34.7)                 |
|                      | With anxiety & substance abuse    | 5(7.5)        | 54.2(5.9)         | 38 (21.2)                  |
|                      | Without anxiety & substance abuse | 62(92.5)      | 51.6(12.8)        | 31.3(218)                  |
| Depression<br>(N=17) | With anxiety                      | 8(47)         | 44.75(13.9)       | 29.6(16.3)                 |
|                      | Without anxiety & substance abuse | 9(53)         | 40.89(9.7)        | 21.9(18.4)                 |



**Figure 1. Duration of hospitalization in bipolar patients with and without comorbidities**

**A.** days of hospitalization in patients with anxiety disorder, substance abuse with those without substance abuse and anxiety disorder in depressive phase

**B.** severity of disease in patients with anxiety disorder, substance abuse and those without anxiety disorder and substance abuse in manic phase

patients in the mania manic phase. Hence substance abuse increases the duration of hospitalization among bipolar patients in the mania manic phase. There was also no statistically significant difference ( $P=0.37$ ) in average duration of hospitalization duration in the depression depressive phase. No patient had substance abuse criteria in depression this phase.

## Discussion

It seems that the higher co-occurrence of anxiety disorders and substance abuse with bipolar disorder is a risk factor for bipolar patients, and may expose them to higher rates of psycho-social consequences. Lower quality of life (24, 25, 14), higher rates of committing suicide or suicidal ideations (26-29,14,5), lower probability of improvement (14), low treatment response and increased duration of hospitalization (13) are important findings through several researches.

According to the results of this study, the co-occurrence of anxiety disorder and bipolar disorder is 46.15% which is compatible with some other studies (6, 10, 14). The occurrence of anxiety disorders with bipolar disorder in lifetime is reported to be between 24 to 93% in all clinical and epidemiological studies (15). The occurrence of substance abuse with bipolar disorder was 7.7% in this study. Findings of different researches revealed that bipolar disorder is related to substance abuse (5, 7, 30-32). However, this study indicated lower rate of co-occurrence of substance abuse with bipolar disorder in comparison with other researches' reports (6,17, 33-35). Further more, it was revealed that anxiety disorders were more common among women, and substance abuse disorders were more common among men.

In our study, obsessive-compulsive disorder, generalized anxiety disorder, phobia and panic disorder had higher co-occurrence rate with bipolar disorder respectively. This finding is in contrast with the results of a study which emphasized the conformity of neuroanatomy and behavioral process of panic disorder and bipolar disorder (36). Our findings are in

accordance with the results of a study in which the co-occurrence of bipolar disorder and alcoholism has been declared (37).

Based on the present study, there was no significant relationship between anxiety disorders and severity of bipolar mood disorder and duration of hospitalization. This is matched with the study conducted by Henry C et al (13) but is contrary to the results of some other studies (7,10, 11,27, 38).

We showed that substance abuse increases the duration of hospitalization and intensifies the symptoms of bipolar disorder in the manic phase (Figure 1). Weak response to lithium therapy (39), younger age of bipolar disorder onset (40,41), increased duration of hospitalization (12,42), weak psycho-social functioning after discharging from hospital (43) and increased mortality rates are of significant consequences when co-occurrences develop. (9). Therefore, simultaneous treatment of substance abuse and bipolar disorder will have a desirable effect on prognosis and clinical course of bipolar disorder and will be considered cost-beneficial while decreasing the duration of hospitalization (7,6,26).

In this study, most bipolar patients had anxiety disorders and substance abuse during their young ages. This was also replicated by another research (5). It seems that substance abuse in bipolar patients in younger ages may be the result of either emotional effects of bipolar disorder to overcome the arousal states, or the lower age of substance abuse onset in the society. Tranquilizers (alcohol and opium) are the most commonly used substances. The main reason is that the patients' experiences with alcohol and drugs are idiosyncratic. For instance, some patients reported using alcohol and other drugs to enhance or prolong periods of mania while others used alcohol and other drugs to dampen down the effects of mania and comorbid anxiety (44).

## Conclusions

Co-morbidity of anxiety disorders and substance abuse is higher among bipolar hospitalized patients. Obsessive-compulsive disorder and generalized anxiety disorder as well as alcoholism and opium abuse are more common in dual diagnosis bipolar disorder and co-morbid anxiety & substance use disorders. Anxiety disorders are most common among females and substance abuse disorders among males. Co-occurrence of substance abuse disorder intensifies bipolar disorder and increases the duration of hospitalization among bipolar patients. There was no significant relationship between anxiety disorders and duration of hospitalization and severity of disease among hospitalized bipolar mood patients.

The results of this study are in accordance with the results of the previous studies, and emphasize the high co-occurrence of anxiety disorders and substance abuse with bipolar disorder. Therefore, we must consider these results in future studies in order to distinguish the biological factors involved in this co-occurrence. It is

of great importance to pay more attention to simultaneous diagnoses and the possible treatment of co-morbidities as well.

### Limitations

Although we have attempted to control confounding factors, some of them impose important biases which could limit the findings of the study; namely, gender, age, and socio-economic status. As the sample size was small, we could not consider other co-morbidities. Therefore, the number of mixed bipolar states was so small that we excluded them from the study. We suggest developing a prospective cohort study to trace the clinical course and severity outcome of bipolar patients' co-morbidities with anxiety and substance abuse disorders as the ongoing cross-sectional descriptive study is unable to demonstrate the associations between the variables. Further studies in this field with a larger sample size are suggested.

### Conflict of Interest

No conflict of interest is declared.

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