Examining the Factors Associated with Recurrence of Bipolar Disorder in Patients Hospitalized in Ibn Sina Psychiatric Hospital in Bandar Abbas

Farah Moayed1, MD. Najme rastikerdar2, MSC. shahrzad dahtaei1,3

1. Psychiatrist ,Department of Psychiatry, Behavioral and Neurosciences Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, IR Iran
2. Psychologist ,Department of Psychiatry, Behavioral and Neurosciences Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, IR Iran
3. Student Research Committee, Hormozgan University of Medical Sciences, Bandar Abbas, IR Iran

*Corresponding author : shahrzad dahtaei

ABSTRACT: Introduction: Bipolar mood disorder is a common, severe, and persistent mental disease with periods of major mania and depression. Given the high prevalence and increasing incidence of this disease, the study aimed to identify and assess the effects of multiple risk factors on recurrence of this disease.

Methods: This is a retrospective study conducted in 2015 on 100 patients with bipolar I disorder (BP-I) with at least twice admissions in psychiatric hospital of Ibn Sina in Bandar Abbas. Patients were divided into two groups and all required information was gather by the researcher-made checklist. Finally, all collected data were entered into SPSS version 19 and analyzed using descriptive statistics (average percentage, etc.) as well as Chi-square test, correlation, regression, and ANOVA with repeated measures.

Results: Regarding quantitative factors, the two groups were different only in terms of the number of hospitalizations (t: 2.10, df:98, and α < 0.038). It is worth noting the difference between the two groups was also significant regarding the interval between two consecutive admissions as the grouping index (α: 0.000, df: 98, t: -6.35)

Conclusion: According to the study, previous number of admissions and family history had direct relationship with bipolar disorder recurrence and treatment completion had indirect correlation with the relapse.

Keywords: Assessment, Risk factors, Recurrence, Bipolar Disorder

INTRODUCTION

Bipolar mood disorder is a common, severe, and persistent mental disease with periods of major mania and depression (1). Globally, lifetime prevalence of bipolar disorder is around 0.3 to 1.5 percent. In a cross-sectional study of 61,000 adults in 11 countries, Yutzy et al. (2002) reported the increased prevalence of BP-I and II in recent years. According to this study, the prevalence of this disease was between 0.4% to 1.6% between 1970-2000, and its prevalence increased about 5-7% during late 1990s until 2000 (2).

In bipolar mood disorder or manic-depressive illness, mortality rate is significant. About 25-50% of people with bipolar disorder attempted suicide and 11% had a successful suicide. In addition, a study in the UK (2011) showed that mortality rate in these patients one year after discharge was higher than rates of natural mortality in general population (3). 40 to 50% of patients experience another manic episode in the first 2 years after the initial attack. Symptoms are controlled only in 50-60% of patients under treatment. In 7% of these patients, symptoms do not recur. 45% of patients experience more episodes and 40% of them advance towards a persistent disorder. Shifts between depression and mania are often expedited with increased age. Some studies have considered the following as weak prognostic factors of this disease: bad employment history, drug abuse, psychotic features, depression characteristics interspersed with periods of mania and depression, previous depression, male gender, manic depression pattern with natural mood. On the contrary, factors such as low length of manic phase, late age of onset, low number of suicidal ideations, low number of psychotic symptoms, and low number of medical problems are considered as better prognostic factors (4, 5).

In our current society, paying attention to mental health problems and their treatment is very important and necessary. In fact, providing mental health represents the level of community health. We decided to do a study to determine the factors associated with recurrence in patients with bipolar disorder admitted in Ibn Sina psychiatric hospital of Bandar Abbas with regard to the following factors: high prevalence and increasing
incidence of this disease, high mortality, complications of the recurrence for patients and their families as well as health care costs frequently imposed on families and health care systems due to disease recurrence.

**METHODOLOGY**

This is a retrospective study conducted in 2015 to determine the factors associated with recurrence in patients with bipolar disorder admitted in psychiatric hospital of Ibn Sina in Bandar Abbas. Our target population consisted of patients with BP-I with at least twice admissions in psychiatric hospital of Ibn Sina.

**Sampling was conducted as follows**

Referring to the Health Information Management of Ebn-e Sina hospital, records of 100 patients with a diagnosis of BP-I were gained. From 2015 onward, 100 cases were selected as backward, such that the latest admitted patients with a history of at least two admissions were selected. All needed information of the above patients were recorded until the first half of 2015 in researcher-made checklists including quantitative variables such as the patient's age, age at onset, number of years of education, the interval between incidence of symptoms to seeking treatment, number of admissions, and the average interval between two consecutive admissions as well as qualitative variables such as gender, employment status, marital status, place of residence, type of episode I, addiction, suicidal thoughts, history of suicide, receiving ECT, psychosis symptoms, dominant episode, family history, and the period completion. In this study, disease duration is defined as the beginning of the time when the disease is diagnosed by a psychiatrist. Readmission time intervals are the average time intervals per the number of admissions. Age of onset is when the disease is diagnosed by a psychiatrist. Completion of admission time means discharging a patient by a psychiatrist with general good condition. The interval between the disease onset and the first episode treatment is a period between observing initial symptoms of the disease by relatives of the patient and beginning treatment by psychiatrist. Psychotic symptoms include positive symptoms such as hallucinations, delusions, inappropriate speech and behavior as defined in DSM-V book. Study inclusion criteria: patients diagnosed as BMD-I by a psychiatrist based on DSM IV TR criteria, patients with first admission episode at this center and at least one previous admission.

Exclusion criteria: unrecoverable distorted case information, patients with DSM-II including personality disorder and mental retardation.

Finally, the collected data were entered into SPSS version 19 and analyzed using descriptive statistics (average percentage, etc.) as well as chi-square test, correlation, regression, and ANOVA with repeated measures.

**RESULTS**

**Demographic Findings**

Population of this study included 100 patients with bipolar disorder who were admitted in psychiatric hospital of Ebn-e Sina in Bandar Abbas and had a file there. They were divided into two groups based on the average interval of less than and over 16 months between two consecutive admissions. Descriptive findings related to the interval between two consecutive admissions in both groups and the total population are presented in Table 1.

<table>
<thead>
<tr>
<th>Descriptive group/ Findings</th>
<th>No</th>
<th>Mean</th>
<th>SD</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (the average interval between two consecutive admitted less than 16 months)</td>
<td>50</td>
<td>9.7</td>
<td>3.09</td>
<td>2</td>
<td>15.4</td>
</tr>
<tr>
<td>Group 2 (the average interval between two consecutive admitted more than 16 months)</td>
<td>50</td>
<td>46.93</td>
<td>41.29</td>
<td>16</td>
<td>200</td>
</tr>
<tr>
<td>Total population</td>
<td>100</td>
<td>28.32</td>
<td>34.62</td>
<td>2</td>
<td>200</td>
</tr>
</tbody>
</table>

**Research findings related to quantitative variables**

The minimum and maximum age in group 1 were respectively 20 and 68 years. The minimum and maximum age in group 2 were respectively 20 and 62 years. Minimum age of onset in group 1 and 2 were respectively 17 and 15. Maximum age of onset in group 1 and 2 were respectively 54 and 52. Maximum number of educational years in group 1 and 2 were respectively 16 and 14 years. The minimum number of admissions in both groups were twice and the maximum number of admissions in groups 1 and 2 were respectively 8 and 10 times. Minimum interval between onset of symptoms and admission in the first period in groups 1 and 2 were respectively 4 and 3 days, and the maximum interval between onset of symptoms and admission in the first period in groups 1 and 2 were respectively 180 and 300 days.
Findings related to qualitative variables

The variables of gender, episode type in the first admission, and place of residence had changed and variables of job, marital status, and addiction had not changed in any of the subjects during various periods of admission. However, variables such as suicidal ideation, suicide attempt, family history, receiving shock, completing the course of hospitalization, and psychotic symptoms were different during different periods of admission. Accordingly, the variables were examined in all subjects and were re-coded in 5-degree Likert regarding the trend of each mentioned item. The coding was as follows: all admission courses (always): 1, most of the time: 2, half of admission cases: 3, rare admission cases: 4, and no cases: 5.

Twenty-nine patients (58%) in group 1 were male and 21 of them (42%) were female. In group 2, 33 patients (66%) were male and 17 of them (34%) were female. In general, 59% and 41% of patients respectively lived in urban and rural areas. Urbanization rate was higher in group 2. 61% of patients with bipolar disorder were unemployed and 39% of them were employed. 69% of patients were married and 31% were single. The most narcotic substance used was cigarette and addiction to hookah, tobacco, opium, alcohol and crystal meth were next in degrees.

In general, drug addiction rates were higher in group 1 compared to group 2. The shocks given for treatment of patients were almost the same in both groups and 11% of patients in all admission types required shock and 27% of patients did not receive any shock for treatment. 31 patients (31%) suffered mania in the first episode of their disease; 45 patients (45%) suffered depression in the first episode, and 24 patients (24%) suffered both mania and depression. In general, mania and depression were respectively more prevalent in groups 2 and 1. Half of the patients with BP-I had a family history of this disease and the other half had no family history of it. As well, family history of this disease was higher in group 1 than in group 2. Thirty-three percent of patients had suicidal thoughts in most admission cases and 17% of them had suicidal thoughts in all admission cases. And 17% had no suicidal thoughts at all. Such suicidal thoughts were higher in group two than in group one. 33% of patients had attempted suicide in half of admission cases. And 15% of patients had a history of suicide attempt in all cases of admission. 49% of patients had positive psychotic symptoms all admission cases, and these figures were higher in group 2 than group 1.

Frequency percentage in patients with BP-I based on dominant episode was as follows: 51% of patients had no certain dominant episode and in 37% of cases, the dominant episode was depression. In 7% and 5% of cases, dominant episodes were respectively mania and mixed. Frequency percentage in people with BP-I based on completion of admission period was as follows: 25% of patients in all inpatient cases had passed total admission period and only 5% of them had not completed hospitalization period in any of the cases.

Analytical findings

In order to compare the two groups in terms of quantitative variables, independent T-test was used and to compare the two groups in terms of qualitative variables, chi-square test was used. Regarding quantitative factors, the two groups were different only in terms of admission numbers (t=2.10, df: 98, a=0.038). Based on independent t-test, there was no significant difference between the two groups in terms of age, age at onset, years of education, and the interval between outbreak of symptoms and seeking treatment in the first period of admission.

Lack of significant differences between these variables indicates comparability and match between the two groups. It is worth noting that the difference between two groups regarding the interval between two consecutive admissions as the grouping index was also significant (t=6.35, DF= 98, α=0.000 ). (Table 2)

<table>
<thead>
<tr>
<th>Variable</th>
<th>T</th>
<th>df</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-1.7</td>
<td>98</td>
<td>0.28</td>
</tr>
<tr>
<td>Age of onset</td>
<td>1.09</td>
<td>98</td>
<td>0.27</td>
</tr>
<tr>
<td>years of education</td>
<td>0.97</td>
<td>98</td>
<td>0.33</td>
</tr>
<tr>
<td>Interval between onset</td>
<td>0.98</td>
<td>98</td>
<td>0.32</td>
</tr>
<tr>
<td>symptoms and seeking treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of admissions</td>
<td>2.10</td>
<td>98</td>
<td>0.03</td>
</tr>
<tr>
<td>The mean interval between</td>
<td>-6.35</td>
<td>98</td>
<td>0.00</td>
</tr>
<tr>
<td>consecutive admissions</td>
<td></td>
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</tbody>
</table>

DISCUSSION

In previous studies, three major categories predicting the recurrence of the disorder were identified. The first category belongs to demographic predictors. Most studies on mood disorders in children and adolescents have suggested that age, gender, race, and socio-economic status do not predict the outcome (6). The second category are psychosocial predictors. In this field, research have focused mainly on life events and stressful factors which affect episodes of depression and mania. These factors include changes in the financial condition of the family, death of a family member or a close friend, conflicts between parents or parental
psychotic disorders (6-8). Research on psychosocial variables as predictors of bipolar disorder outcome are not complete yet. In this study, all patients experienced at least one recurrence. Baldessarini et al. (1990) (9) included the findings of 15 articles in their study which suggested short intervals between illness recoveries, worsening of the illness, and higher recurrence in patients with BP-I. In a study by Salvator et al. (1999) (10), recurrence of BP-I occurred during the first 2 years in 57% of patients. In a study by Amini et al. (11) 21.4% of patients experienced recurrence and readmission during the first year. In another research by Shabani et al. conducted in 2012 (12), 31.8% of patients had a recurrence in the first year.

Various studies have been conducted to determine the factors affecting recurrence of bipolar disorder (13, 14). Predictor variables are different in some of them. Difference between the identified variables in such studies may be due to different population of patients, differences in sample size and data collection time, differences in the types of investigated variables and the analysis methods selected for evaluation of variables.

The findings showed that the number of previous admissions increases the number of recurrences. The results were in line with the research conducted by Kessing et al. (2004), Altman et al. (1973), De DC et al. and Perlis et al. (2004) (15-18). Their studies also showed that high number of previous periods increases the risk of recurrence events.

This study showed that having mental disorders in first-degree relatives increases the risk of recurrence events. The results are in line with the studies conducted Duffy et al. (2007) (18). Duffy et al. (18) conducted a study on the children of patients with BP-I which showed that 32.36% of children had experienced at least one episode of mood disorder. Their findings showed that the risk of repeated recurrences in patients with a history of PB-I in their parents is high such that the mentioned risk was 61% in 5 years. However, in the study by Perlis et al. (17), family history of recurrence and the risk of recurrence were not correlated.

In the study of bipolar disorder for finding its relation with demographic and clinical factors, it was revealed that age is not associated with recurrence rates. Results of regression analysis showed that age cannot significantly predict this outcome. These findings were consistent with Emslie et al. (1997) (19) but were inconsistent with Goodyer et al. (1997) (20). Lars Vendel Kessing (2000) (21) and Consuelo de Dios et al. (2004) (22) also confirmed these findings in their studies and stated that there is no difference between the effects of age in the early and late episodes. Regarding the impact of age, Gilman et al. concluded in 2012 (23) that exposure to adversity in childhood increases the effects of stressful factors on adulthood euphoria. Their findings showed that social experiences are involved in early development and future course of bipolar disorder. Strober et al. (1995) (24) showed that adolescent bipolar patients respond to treatment better and quicker than bipolar children. Albeit, Perlis et al (17) demonstrated that onset of disease at early ages is associated with a higher rate of anxiety disorders and more recurrences, shorter periods of normal mood, and higher probability of suicide attempts. They also stated that very early onset of disease can lead to chronic state. In this regard, Kowatch et al. (1999) (25) showed that disease duration predicts the treatment outcome such that long-time episodes of the disease have a negative effect on prognosis and are correlated with weak response to the treatment and increased episodes of depression. Kupfer et al (2010) (26) defined the age of 20 as the criterion for higher effects of disease development. The contrast between the results of these studies could be because their target populations were different. Such that in the study conducted by Strober et al. (1995) (24), the study population consisted of adolescents but in Perlis et al. (17), the population included all age groups. In our study, the average age of onset in low and high recurrence groups were respectively 34 and 36 years. Social demands and responsibility of the person rise with age increase and these factors can affect disease recurrence. Albeit, social expectations from newly-discharged patients might be low and hence, they are less affected by age-related stress and their disease relapses are quite similar to those younger than them. A few studies have associated female gender to poor outcome of treatment (19, 20, 27). This is while Brunelle et al (1993) (28) concluded in their study that disease severity and female gender predict the level of recovery. And psychotic features and poor insight predict higher duration of the disease and admission. In this study, there was no significant relationship between gender and disease recurrence which was consistent with the studies conducted by Kessing et al. (29), Kupfer et al. (26).

However, in the study of Qoreyshe et al. (2009) (30) women were exposed to a greater risk of relapse compared to men which was in conflict with our study. Gilman et al. (2012) (23) came to the conclusion that physical and sexual abuse are also significantly associated with higher risks of recurrence. Considering that physical abuse occurs more often in women, he hypothesized that recurrence of bipolar disorder in women might be associated with the sexual abuse imposed on them.

In this study, we did not find a significant relationship between marital status and disease relapses. This is while in the study by Qureshi Zadeh et al. (2009) (30), the rate of recurrence was significantly higher in married patients. In their review, Leslie et al. (2004) (31) referred to interpersonal relationships and concluded that variables of interpersonal relationships are not significant predictors of the disorder recurrence. This means that the presence or absence of a partner has no effect on recurrence. In connection with the effect of marital status, Lars Vendel Kessing et al. (29) stated that there is no difference in the effect of recent divorce on initial and later episodes but it seems that the recent death of spouse has an increasing effect on the course of the
disorder. According to Gilman et al. (23), social experiences are effective in the early development and future course of bipolar disorder. In their opinion, this issue conforms to etiologic models of bipolar disorder reflecting shortages in the ways of response to life stresses.

In this study, there was no significant relationship between recurrence of the disorder and residence location. In a study by Consuelo de Dios et al. (2012) (22), patients who lived in urban-rural areas were exposed to 57% higher risk of recurrence compared to those who lived in cities with over 100,000 inhabitants. It was also found that most episodes in bipolar patients were positively correlated with social function failure (32), weaker response to lithium therapy (33) and probability of recurrence in the future (34).

In a study by Grof et al. in 1993 (33), psychotic symptoms during disorder episodes, long episodes, and occurrence of an episode were the results of depression or mania with weaker outcomes of lithium therapy.

In a study by Strober et al. (1995) (24), the required time for recovery from illness was respectively 9 weeks, 11 weeks, and 15 weeks for people with pure mania, mixed episodes, and those with rotational states. The time required for recovery was longer in depressed patients. In people with rotational or mixed episodes, there were higher risk of recurrence (35). In 2004, Biederman et al. (36) showed in pursuit of a group of adolescent bipolar patients that in mixed subtypes, recurrence rates were higher and the interval between recurrent episodes was shorter.

The disease duration until current admission (onset of recent symptoms until the current admission) had no correlation with recurrence. This finding was not consistent with the results obtained by Kowatch et al. (1999) (25). In their study, they concluded that the longer is the duration of disease until current admission, the higher is the probability of recurrence within 6 months. These findings can be interpreted as such: when patients have acute severe symptoms, they are hospitalized and referred for treatment in a short interval after onset of symptoms. Since severity of the patient's disease was already high, the relapse rate is also high. The contradiction between these findings and foreign investigations can be due to different times of referring for treatment between manic and mixed bipolar patients in our society and foreign samples. Note that clinical experiences in our society showed that bipolar manic patients come earlier for treatment and mixed bipolar patients come later.

In addition, manic periods are pleasant experiences for manic patients and treatment acceptance by them is thus less. However, because of negative experiences of mixed patients in phases of depression, their adherence to medication protocol and treatment acceptance might be higher. This outcome might justify higher severity of mania in manic patients and its low severity in mixed patients.

Episode type I had no effect on relapse of the disease. However, psychosis on early admission was positively correlated with the rate of relapse at 6-month follow-up based on the following studies: Biederman et al. (36), Brunelle et al. (2009) (37), and Grof et al. (1993) (33). Psychotic features in early hospitalization were associated with weak disease outcome.

It seems that the presence of psychotic features associated with lower reality testing have negative effects on some factors affecting treatment efficacy such as the acceptance of treatment, motivation for treatment, collaboration with the physicians and increase severity of the disease and eventually lead to worse outcomes.

In a study by Perlis et al. in 2004 (17), substance abuse disorder at the beginning of study was correlated with increased risk of relapse of manic and anxiety disorder at baseline was associated with increased risk of manic attacks. Anxiety disorder at the beginning of study was associated with increased risk of recurrent bouts of depression.

This is while no relationship was seen in our study between drug abuse and relapse.

CONCLUSION

According to this study, previous hospitalizations and family history had a direct relationship with bipolar disorder relapse and completion of treatment period had an inverse relationship with the relapse. Therefore, these results emphasized the need to assess and regard demographic and clinical features of bipolar patients in making treatment decisions such that they can receive special health care and follow-ups during their treatment in case of existence of prognostic factors at the time of diagnosis.

REFERENCES


