Psychiatry Research 275 (2019) 373–378

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

# Studying the predictive factors of suicide attempts in patients with type 1 bipolar disorder

Maryam Mazaheri[a], Banafsheh Gharraee[a,*], Amir Shabani[b], Mozhgan Lotfi[c]

[a] Clinical Psychology Department, School of Behavioral Sciences and Mental Health (Tehran Institute of Psychiatry), Iran University of Medical Sciences, Tehran, Iran
[b] Mental Health Research Centre, Mood Disorders Research Group, Iran University of Medical Sciences, Tehran, Iran
[c] Department of Mental Health, School of Behavioral Sciences and Mental Health (Tehran Institute of Psychiatry), Iran University of Medical Sciences, Tehran, Iran

ARTICLE INFO

*Keywords:*
Bipolar disorder
Suicide attempt
Quality of life
Stressful life events
Axis I comorbidity
Medication adherence

ABSTRACT

Bipolar disorder has the highest suicide attempt rate among psychiatric disorders. Many factors are associated with the risk of suicide attempt in patients with type 1 bipolar disorder, but the relation between them has still not been explicitly stated. This study aimed to examine the predictability of suicide attempt risk in BID patients based on quality of life, stressful life events, comorbidity of axis I disorders and medication compliance. We selected 140 inpatients with type 1 bipolar disorder by convenient sampling. Then they completed the WHOQOL-BREF questionnaire, Paykel's stressful life events scale and the medication adherence report scale (MARS). Logistic regression analysis showed that bipolar patients with axis I comorbidity are 40 times more likely to attempt suicide than those without axis I comorbidity. The higher the patients' quality of life, the lower the chance of attempt of suicide. Higher medication compliance reduces the likelihood of suicidal attempt in these patients. And, the increase of stressful life events would raise the risk of suicide attempts, but the relationship wasn't significant. So it can be concluded that quality of life, stressful life events and axis I comorbidity can predict the risk of suicide attempts in patients with type 1 bipolar disorder.

## 1. Introduction

Bipolar disorder is one of the most chronic, severe and recurrent psychiatric disorders. Despite advancements of effective drugs, bipolar disorder is still one of the major causes of death and functional decline which contributes significantly to the quality of life of affected people (Wang et al., 2015). Among psychiatric disorders, bipolar disorder has the highest rate of suicide attempts (Goldstein et al., 2012). Rates of attempted suicide in these patients are higher than 30% (Novick et al., 2010) and the ratio of attempted suicide to completed suicide among patients with bipolar disorder is 5:1, while this ratio in the general population is 20:1 (Baldessarini et al., 2006).

Therefore, it is necessary to investigate the factors associated with suicide attempts in these patients. A study suggests that the quality of life in bipolar patients has been greatly damaged. Quality of life is markedly impaired in patients with bipolar disorder even when they are in their euthymic mood (Michalak et al., 2005). There are several meta-analyses confirming that most patients with bipolar disorder show neurocognitive dysfunction, even during euthymia (Bourne et al., 2013; Bortolato et al., 2015), which counts as a critical factor in their psychosocial disability and lower quality of life (Fountoulakis et al., 2016). Studies have shown that the symptoms of depression are associated with severe impairment in facets of daily life, such as at the workplace and in their social life, which seems to be the affecting factor on quality of life in bipolar patients (Gazalle et al., 2007; Vojta et al., 2001). The study that was done based on the SF-36 scores and DSM-III-R criteria in the Netherlands, showed that patients with type 1 bipolar disorder had lower significant scores in mental health, social functioning and pain, compared to patients with anxiety disorders and substance abuse disorders (ten Have et al., 2002).

One of the reasons that lead to the development of disorder episodes in patients with type 1 bipolar disorder is lack of medication adherence. Poor treatment compliance is one of the main challenges for controlling symptoms and preventing recurrence of mood episodes in patients with bipolar disorder (Leclerc et al., 2013). Non-adherence with medication in patients with bipolar disorder range from 12 to 64% (Gonzalez-Pinto et al., 2010). In a systematic review and meta-analysis done by Cipriani et al. in 2013, the result indicated that with a minimum duration of at least three months treatment, Lithium was more effective than placebo in reducing suicide rates and deaths due to other causes (Cipriani et al., 2013). Comorbidity of alcohol misuse and other drugs (especially cannabis) is one of the strongest factors associated with treatment non-

* Corresponding author.
*E-mail address:* gharraee.b@iums.ac.ir (B. Gharraee).

https://doi.org/10.1016/j.psychres.2019.04.012
Received 16 September 2018; Received in revised form 7 April 2019; Accepted 8 April 2019
Available online 08 April 2019
0165-1781/ 

compliance in patients with type 1 bipolar disorder (Barraco et al., 2012). Patients with comorbid obsessive-compulsive disorder also have more treatment non-compliance than other bipolar patients (Baldessarini et al., 2008). Comorbid disorders in axis I leads to a more long-term course of bipolar disorder (Soreca et al., 2009) and an early onset (Feske et al., 2000).

Research shows that the most comorbidities with bipolar disorder occur with anxiety disorder and substance use. The prevalence of any anxiety disorder in patients with type 1 bipolar disorder who attempted suicide once or more was 74.6%, And the dependency or abuse ratio of alcohol was 48.8%, and the rate of other substance abuse in these patients was 32.3% (Bobo et al., 2018). The presence of substance abuse disorders and anxiety may worsen the prognosis and significantly increase the risk of suicide attempts in these patients. In bipolar disorder, men are more likely to experience substance abuse disorder, and women are more prone to eating and anxiety disorders (Sadock and Sadock, 2011).

Bipolar patients who also have substance use disorder are at a higher risk of suicide attempt, and attempt suicide six times more than other patients throughout their lives. Also, the risk of completed suicide in these patients is higher than patients with type 1 bipolar disorder without substance abuse. Comorbidity of anxiety disorders with bipolar disorder would cause its early-onset and will increase the risk of attempted suicide and drug use in these patients. This comorbidity increases the number of mood episodes and their severity, and negatively affects the therapeutic response of these patients to lithium (Cardoso et al., 2016).

A recent study shows that the number of stressful events during childhood and before the onset of the first episode is significantly higher in bipolar patients with symptom severity (Maniglio, 2013). The results of several other studies also show that the immensity of stressful life events is associated with suicide attempts in both healthy people and psychiatric patients (Fjeldsted et al., 2017; Golshiri et al., 2017). Severe stressful events are the important risk factors for suicide attempts and completed suicide (Buchman-Schmitt et al., 2017; Paykel and Dowlatshahi, 1988). In bipolar disorder, stressful life events are related to the onset of the first episode (Dunner et al., 1979) and its recurrence (Kennedy et al., 1983). Eighty percent of patients with bipolar disorder experienced at least one stressful event during the three months prior to a suicide attempt, and 57% of patients had also experienced a stressful event (Isometsä et al., 1995) during the week prior to a suicide attempt.

Also according to the literature, the bipolar disorder type 1 in the Iranian sample mostly begins with a manic episode, unlike in Western countries, which begins with depression. For example, in a study by Ghanbari Jolfaei et al. in 2015, it was found that the course of 65% the bipolar type 1 disorders started with a manic episode versus 30% that started with depression (Jolfaei et al., 2015). Or in one study only 32% of the patients' disorders started with depression (Shabani et al., 2006); and in another study, 78% of patients with bipolar disorder type 1 had mania for their first episode (Shabani et al., 2013). Moreover the methods of choice for suicide among Iranians are different than that of patients in more developed countries. Drugs are the most common method of attempting suicide (65.0%), Self-burning and poisoning are the second and third most common methods (15.0% and 12.0% respectively), the rate of hanging is 9.1% and suicide with firearms is 6.0%.(Shirazi et al., 2012).

Hence, according to the research evidence and the relations between the quality of life, comorbid disorders in axis I, stressful life events and medication adherence with the severity of the symptoms and with higher rates of suicide attempts and given the differences in the course of the disorder and suicide methods between Iranians and more developed countries, the present study sought to investigate if these factors had a predictive role in attempting suicide among Iranian patients with type 1 bipolar disorder.

## 2. Method

### 2.1. Participants

We asked 140 patients with type 1 bipolar disorder hospitalized in "Iran psychiatric hospital" and the psychiatric ward of "Rasool-e-Akram" hospital in Tehran to participate in the research. Five of these patients refused to participate in the study and data from 15 patients who participated in the study were excluded because of incomplete information, discharge from the hospital prior to completing the research, receiving Electro-convulsive therapy and in one case, a patient's death due to myocardial infarction. Finally, data collected from 120 patients was analyzed. Patients were divided into two groups based on their suicide attempts in the past year, a group of patients with suicide attempts ($n = 54$) and a group of the patients with no suicide attempts ($n = 66$). The group with no suicide attempts includes patients with no suicidal thoughts as well as patients who decided and planned their suicide, but never acted upon it; either they changed their minds or their plan were interrupted by others. Inclusion criteria were: being diagnosed with type 1 bipolar disorder based on DSM-IV-TR diagnostic criteria with any current mood episode, 18 years of age or over, and being able to read and write in Persian.

### 2.2. Procedure

This cross-sectional study was conducted within 6 months in 2017 in Tehran. Patients were invited to participate in the study after being provided with a comprehensive description of the research plan. If they were willing to participate in the study, they were asked to sign a consent form. Then, an SCID-I interview was conducted to confirm the diagnosis of bipolar disorder type 1 and to investigate the comorbid disorders in axis I. Afterwards, a 30-minute break with refreshments was given to the patients. Then, they were asked to fill in the demographic information checklist, WHOQOL-BREF questionnaire, Paykel's stressful life events scale and the medication adherence report scale. Patients were evaluated when acute symptoms subsided and they were able to participate in the interview and were qualified to sign consent forms. This study was approved for obtaining a Master's degree in Clinical Psychology, in Iran University of Medical Sciences, with the approval of the University's Ethics Committee with the code IR.IUMS.REEC 1395.9311556009.

### 2.3. Measures

#### 2.3.1. Demographic information checklist

This checklist is made by the authors and the characteristics it measures include: age, gender, education, marital status, occupation, history of attempted suicide and current mood episode. The tendency for suicide has been considered as the presence or absence of a suicide attempt. The question that was asked to assess suicide attempts and its history was, "Have you attempted to take your life in the past year?"

#### 2.3.2. Structured clinical interview for DSM-IV axis I disorders (SCID-I)

SCID is a comprehensive standardized interview for assessing major psychiatric disorders based on DSM-IV definitions and benchmarks that are designed for clinical and research purposes (First et al., 1995). The research version, SCID-I-R,[1] covers all diagnoses and their subtypes and criteria for severity and course of the disorder. The entire SCID-I usually run in a session and lasts between 45 and 90 min. And the suitable age for implementing this interview is at least 18 years old. But it can also be used with minor modifications for those patients under 18 year olds. The minimum educational level required to understand SCID is about

[1] Structural clinical Interview for DSM-IV Axis I Disorder (SCID-I) Research version

**Table 1**
Demographic characteristics of BID patients.

| Variables | Attempters($n$ = 54) | Non-attempters ($n$ = 66) | Parameter ($X^2$ or $t$) | $p$-value |
|---|---|---|---|---|
| Age (mean ± SD) | 34.25 ± 10.22 | 37.66 ± 9.97 | 1.791* | 0.076 |
| Gender *N (%)* | | | | |
| Male | 29 (53.7) | 36 (54.5) | 0.008 | 0.927 |
| Female | 25 (46.3) | 30 (45.5) | | |
| Marital status *N (%)* | | | 8.768 | 0.033 |
| Single | 19 (35.2) | 27 (40.9) | | |
| Married | 14 (25.9) | 28 (42.4) | | |
| Divorced or widowed | 21 (38.9) | 11 (16.7) | | |
| Education *N (%)* | | | 5.925 | 0.432 |
| **Below high school** | 18 (33.3) | 26 (39.4) | | |
| High school graduate | 23 (42.6) | 32 (48.5) | | |
| Bachelor's degree and higher | 13 (24.1) | 8 (12.1) | | |
| Occupational status *N (%)* | | | 3.764 | 0.288 |
| Employed | 19 (35.2) | 15 (22.7) | | |
| Unemployed | 35 (64.8) | 51 (77.3) | | |
| Current mood episode *N (%)* | | | 9.006 | 0.011 |
| Mania | 13 (61.1) | 56 (84.8) | | |
| Depression | 20 (37.0) | 9 (13.7) | | |
| Complex | 1 (1.9) | 1 (1.5) | | |

* For age variable, $t$ statistic has been reported.

8th grade. People with severe disorders or severe psychotic symptoms cannot be evaluated with this interview. The evaluation of the psychometric properties of this interview indicates that its reliability for severe disorders is better than mild disorders, and its validity has been reported in the range of 0.81 to 0.84 (First and Gibbon, 2004). The validity and reliability of this interview in various research has been reported to be acceptable (Groth-Marnat, 2009). The Persian version of this interview was prepared by Sharifi et al. in 2004, and its validity has been reported to be desirable (Sharifi et al., 2009).

#### 2.3.3. Medication adherence report scale (MARS)

This measure was developed by Thompson in 2000 to evaluate patient compliance and includes 10 questions with yes or no answers. The reliability of this scale has been reported by Cook to be optimal (Cook, 2007). The score between zero and seven indicates weak and low compliance, and a score between 8 and 10 represents high compliance. It can be said that MARS is a stable and assured measure and is more reliable than the previous scales used for psychiatric patients (Cook, 2007). In Shiraz, in a research conducted by Hedayati et al. the reliability obtained from the test retest method was 0.91 (Javadpour et al., 2013).

#### 2.3.4. World Health Organization quality of life assessment (WHOQOL-BREEF)

This scale contains 26 questions, and the first question assesses quality of life in general, and the second question assesses the health status in general. The following questions evaluate the quality of life in four areas of physical, psychological, social and the living environment. The questionnaire has been adapted for the Persian language community with a sample population of 5892 of people over 30 years old. Evaluation of its psychometric properties indicates that it has acceptable reliability and validity in Iran in both a clinical and non-clinical population (Nejat et al., al2006).

#### 2.3.5. Paykel's stressful life events scale

This scale was created in 1971 by Paykel and originally consisted of 69 major life events and participants mark events that they personally experienced over the past two years and earlier (in their lifetime). Then, on a scale of 0 to 3 they will rate the severity of their discomfort and the amount of their stress during the event (Paykel et al., 1971). In Iran, Hosseini et al. reported a reliability coefficient of 0.78 through the test retest method (Hosseini et al., 2010).

### 2.4. Statistical analysis

In order to compare the frequency of demographic and clinical characteristics between two groups the Chi-square test was implemented, and to compare the mean of demographic and clinical characteristics in two groups the independent $t$-test was used. Logistic regression test was used to predict suicide attempt in patients with type 1 bipolar disorder based on predictive variables (axis I comorbidity, medication adherence, stressful life events and quality of life).

## 3. Results

### 3.1. Demographic findings

The average age in the group with suicide attempts (SAs) was (34.25 ± 10.22) and in the group with aborted suicide (Non-SAs) was (37.66 ± 9.97) which had no statistically significant difference ($p$ = 0.076). 54.1% of the sample was male. 53.7% of SAs and 54.5% of non-SAs were male, indicating that groups did not differ significantly in terms of gender distribution ($p$ = 0.927). The occupational status of the groups did not differ significantly ($p$ = 0.288), 64.8% of the SAs and 77.3% of non-SAs did not have any job. The groups did not have any significant difference in terms of education ($p$ = 0.432); 75.9% of the SAs group and 87.9% of the non-SAs were high school graduates or lower. But the SAs and non-SAs were significantly different in terms of current mood episode ($p$ = 0.011) and marital status ($p$ = 0.033). So that 61.1% of SAs and 84.8% of non-SAs were currently experiencing symptoms of mania. And 38.9% of SAs were divorced or widowed, and 42.4% of non-SAs were married. See demographic data in more detail in Table 1.

This section describes the information obtained from patients' records of suicidal attempts. Questions were asked about the method of suicide attempt, from the decision to attempting suicide, which are described in Table 2 below. As it can be seen, 74.1% of SAs have impulsively attempted suicide without having any plans. 63% of SAs have reviewed their suicide plan many times in their minds before attempting, while only 15.2% of non-SAs did so. 35.2% of those who attempted suicide had prepared their will before their attempt, while only 4.5% of non-SAs had done the same. 46.6% of SAs and 4.5% of non-SAs had already practiced a suicidal method. 38.9% of the SAs and 4.5% of the non-SAs have had at least one experience in which they were stopped by others. Of course in the case of SAs this refers to the previous situations before attempting. All of the differences between

**Table 2**
Frequency of the attempts, decision making to suicide attempt.

| Variables | Attempters($n = 54$) | non-attempters ($n = 66$) | Parameter ($X^2$) | *p-value* |
|---|---|---|---|---|
| Unplanned or impulsive suicide attempt | 40 (74.1) | 0 (0.0) | 73.33 | 0.0001 |
| Frequent suicide plan review in mind before the attempt | 34 (63.0) | 10 (15.2) | 29.23 | 0.0001 |
| Writing a will before attempting suicide | 19 (35.2) | 3 (4.5) | 18.62 | 0.0001 |
| Practicing suicide method | 23 (46.6) | 3 (4.5) | 25.33 | 0.0001 |
| Beingstopped by others from suicide | 21 (38.9) | 3 (4.5) | 21.89 | 0.0001 |

**Table 3**
Frequency of different suicide methods in SAs by gender.

| Suicide method | Female *N = 25* | Male *N = 29* | $X^2$ | *p-value* |
|---|---|---|---|---|
| Drugs/medication | 8 (14.5) | 11 (16.9) | 4.56 | 0.472 |
| Wrist slitting | 8 (14.5) | 7 (10.8) | | |
| Self-poisoning | 6 (10.9) | 5 (7.7) | | |
| Jumping from height | 2 (3.6) | 3 (4.6) | | |
| Hanging | 0 (0.0) | 3 (4.6) | | |
| Self-burn | 1 (1.8) | 0 (0.0) | | |

the two groups are statistically significant. ($p < 0.0001$).

The frequency of different methods of suicide attempt in SAs divided by gender was reported in Table 3, which, as it can be seen, does not show a significant difference between male and female groups ($p = 0.472$). The most used methods for suicidal attempts were taking drugs (31.4%), or slitting the wrist (25.3%), and only one (1.8%) of these patients attempted to self-burn.

### 3.2. Clinical findings

Findings indicate that the SAs and non-SAs have a significant difference in medication adherence, 68.2% of the non-SAs have high medication adherence, while only 3.7% of SAs have high medication adherence and 96.3% were reported with low medication adherence ($p < 0.0001$). Also, the groups were significantly different in terms of comorbidities in axis I ($P < 0.0001$). 98.1% of the SAs had a comorbid disorder in axis I, 45.5% of the non-SAs had comorbid disorder in axis I while 54.5% of the non-SAs group had no comorbid disorder in axis I. The mean of stressful life events are 58.81 in SAs and 32.32 in non-SAs, The results of the independent *t*-test indicated that the difference between these means is statistically significant ($p < 0.0001$). The mean difference of quality of life between the two groups was also significant ($p = 0.012$). The mean of quality of life was 32.03 in SAs and in 43.78 in non-SAs. Clinical findings in more detail are presented in Table 4.

### 3.3. Logistic regression analysis results

Logistic regression analysis was used to predict the rate of suicide attempts in **patients with type 1 bipolar disorder** based on predicating variables. The results of Hosmer-Lemeshow test confirmed the logistic regression model's goodness of fit ($X^2 = 5.367$, $P = 0.718$) (Table 5).

**Table 5**
Logistic regression analysis results for suicide attempt prediction based on axis I Comorbidity, Quality of life, Medication adherence, and Stressful life events.

| | *P-value* | *OR* | *OR* confidence interval (95%) Lower | Upper |
|---|---|---|---|---|
| Comorbid disorders | 0.003 | 40.618 | 3.584 | 460.359 |
| Quality of life | 0.000 | 0.709 | 0.599 | 0.838 |
| Medication adherence | 0.035 | 0.120 | 0.017 | 0.864 |
| Stressful life events | 0.245 | 1.074 | 0.952 | 1.210 |
| Constant | 0.006 | 5967.460 | | |

The results of logistic regression analysis show that there is a significant relationship between having a comorbid disorder in axis I and suicide attempts, so that those with a comorbid disorder in axis I are 40.6 times more likely to attempt suicide than those with only bipolar disorder (OR = 40.618, $p = 0.003$). The relationship between quality of life and suicide attempts is also significant in these patients ($p < 0.0001$), but the OR = 0.70 is less than one, which means that quality of life can play a protective role, i.e. the higher quality of life, the less likely to attempt suicide. The relation between medication adherence and suicidal attempts is also significant ($p = 0.035$). The OR = 0.12 value is also less than one, which means that medication adherence also can play a protective role that means higher medication adherence reduces the likelihood of attempted suicide. But in the relationship between stressful life events and suicide attempts, more stressful life events increases the chance of suicide attempts, but this relationship is not statistically significant. ($p = 0.245$)

## 4. Discussion

This study sought to investigate the extent to which the variables of quality of life, comorbidity in the axis I, stressful life events, and medication adherence can predict the suicidal attempts in patients with type 1 bipolar disorder. Logistic regression results indicate that quality of life, medication adherence, stressful life events and comorbid disorders in axis I can predict 84% of suicide attempt variance among patients with type 1 bipolar disorder. Low quality of life is related to suicide attempts in both healthy people and patients with psychiatric

**Table 4**
Clinical characteristics of BID patients.

| Variables | Attempters($n = 54$) | Non-attempters *(n = 66)* | Parameter ($X^2$ or *t*) | *p-value* |
|---|---|---|---|---|
| Medication adherence *N (%)* | | | | |
| Low | 52 (96.3) | 21 (31.8) | 51.823 | 0.0001 |
| High | 2 (3.7) | 45 (68.2) | | |
| Comorbid disorders in axis I *N (%)* | | | 51.051 | 0.0001 |
| No disorders | 1 (1.9) | 36 (54.5) | | |
| Anxiety disorders | 20 (37) | 18 (27.3) | | |
| Psychotic disorders | 1 (1.9) | 1 (1.5) | | |
| Substance abuse disorders | 6 (11.1) | 8 (12.1) | | |
| Comorbidity of substance abuse disorders and anxiety disorders | 26 (48.1) | 3 (4.5) | | |
| Stressful life events (mean ± SD) | 58.81 ± 19.20 | 32.32 ± 10.12 | 9.688 | 0.0001 |
| Quality of life (mean ± SD) | 32.03 ± 4.49 | 43.78 ± 5.97 | 12.039 | 0.012 |

disorders (Goldney et al., 2001; Koivumaa-Honkanen et al., 2001). Bipolar disorder is a chronic and progressive disorder that over time significantly affects the various dimensions of an individual's life, including occupation, interpersonal relationships, physical and psychological health of individuals. Finseth et al. study in 2012 showed that low education, unemployment and poor financial status are associated with a poor quality of life in patients with bipolar disorder. As in the present study, most patients are unemployed and have a high school degree or lower that can affect their quality of life. These mentioned factors lead to recurrence of the disorder and suicide attempt through a negative effect on the quality of life of the patients. The presence of comorbidities such as anxiety disorder and substance abuse disorder can affect the quality of life in patients with type 1 bipolar disorder (Hakkaart-van Roijen et al., 2004). As the results of the present study indicate, 48% of the patients concurrently suffer from anxiety disorders and substance abuse disorders, which can affect their quality of life and lead to suicide attempts.

Moderate and high levels of stress is negatively related to quality of life (Kleiveland et al., 2015). Stress and stressful events also increase the risk of suicide (Buchman-Schmitt et al., 2017). It is likely that stressful events, in addition to increasing the likelihood of attempting suicide independently, increase the rates of attempted suicide by reducing the quality of life.

In this study, among the disorders in the axis I, anxiety and substance use disorders have the highest comorbidity with bipolar disorder, and they can predict suicide attempts in these patients. This finding is consistent with the findings of previous studies (Cassidy, 2011; Leverich et al., 2003; Shabani et al., 2013). Anxiety disorders are associated with low quality of life, suicide attempts, higher probability of substance abuse, early onset of the disorder (Simon et al., 2004), more severe symptoms (Otto et al., 2006), short remission periods and more time needed for recovery (Simon et al., 2004). As a result, the patient's functioning and his quality of life is reduced and the likelihood of drug use and suicide attempts in these patients increases. Drug use is associated with early onset of the disorder, more periods of hospitalization, more depression and irritability episodes, and high levels of mood swings (Sonne et al., 1994).

Impulsivity is a common feature in substance users and patients with bipolar disorder that can complicate the course of the disease and its treatment (Swann et al., 2003). It also can lead to suicide attempts. It is likely that the substance use mediates the impact of impulsivity on suicidal attempts. Considering that 74.1% of the patients who attempted suicide in this study also had a background of an impulsive suicidal attempt. It is also possible that the comorbidity of substance use and bipolar disorder result in aggression, impulsivity and violence, which increases the likelihood of acting based on suicidal thoughts (Potash et al., 2000). It should be noted that the pattern of substance use in Iran is different from that of other countries. According to a report by the World Health Organization in 2013, the mean prevalence of global opioid use in the general population was 0.6–0.8%, while the number was three times higher in Iran in 2010, i.e. 2.275% (UNODC, 2016). Therefore the higher rates of suicide attempts in BD patients with comorbid substance use in the present study can be due to the correlation between opioid misuse and suicidal ideation, planning and attempts (Samples et al., 2019).

Also the result show that more stressful life events increases the chance of suicide attempts, but this relationship is not statistically significant. While other studies have confirmed the association between stressful life events and suicidal behaviors (Bryan and Rudd, 2012; Conner et al., 2012; Martin et al., 2013). Stressful life events are one of the important predictors of suicidal attempts in a clinical and non-clinical population (Buchman-Schmitt et al., 2017). Pettit et al. (2004) found that the number of suicide attempts was positively and significantly related to the level of stress that leads to the suicide. In the studied sample, 98.1% of those who attempted suicide had a comorbid disorder in axis I, like anxiety disorders and substance use disorder. These disorders are considered as life-threatening events themselves and act as reasons to experience anxiety and worry in patients with bipolar disorder, and increase the severity of their disorder. Thereby, it affects one's ability to cope with stressful life events and provides grounds for suicide attempt in these patients.

The result also showed that medication adherence can play a protective role in patients with type 1 bipolar disorder, such that higher medication compliance reduces the likelihood of suicidal attempts. But its OR coefficient is less than one (OR = 0.12) which may indicate the medication adherence variable is Indirect, and it affects suicide attempts through other variables. In fact, medication discontinuity can lead to attempted suicide by lowering the quality of life of the patients and exacerbating his comorbid disorders.

Moreover, the findings can have clinical implications for the clinicians who treat bipolar patients. While assessing the suicide probability, clinicians must remain mindful about patients' quality of life, frequency of stressful life events, medical adherence, and axis I comorbid disorders, specifically anxiety and substance use disorders as risk factors of suicidal behavior. Besides, since the higher number of stressful life events increases the risk of suicide, it might be beneficial to include stress management techniques in the treatment plan.

### 4.1. Future directions

There is lack of studies about the determining number or types of stressful life events for a patient that can trigger a suicide attempt. But it seems the distinctive key factor between those who consider, but do not attempt suicide, and those who succeed in their suicide attempt is the capability for suicide (Van Orden et al., 2010). According to the studies, both genetic and environmental factors (stressful life events) are responsible for individual differences in suicide capability (Buchman-Schmitt et al., 2017). A longitudinal study might clarify how stressful life events and suicidal behaviors interact.

Also if the patient's medication adherence is studied in a longitudinal study over a longer time period, and also with more detailed and tailored measures, this variable would better foresee suicide attempts.

### 4.2. Limitations of the study

The sample of this study only covers patients admitted to psychiatric centers, so it is necessary to be cautious in generalizing the research findings. This is a cross-sectional study; therefore, there is no possibility of concluding about causality. In this research, only the last mood episode during hospitalization was determined, while determining the type of episodes, especially the number of depression episodes experienced by the patient before attempting suicide, is important for predicting their future behavior. And since this study is retrospective, based on records of suicide attempts in the past, predictive quality of the findings should be considered with caution. The components reviewed in this study are very broad and may be influenced by several factors. For example, quality of life can be influenced by factors such as disorder stigma, spirituality, etc. These issues cannot be addressed using the WHOQOL assessment. Moreover, the participants weren't examined for axis II diagnoses, which could be an important factor in suicidal behavior in any sample. But since this is the case for both compared groups and they both have similar conditions, it factors out from the equation; but there is no doubt that any underlining psychopathology can have some effect on the suicidal behavior.

## Acknowledgments

We would like to show our gratitude to the management and staff of the Iran Psychiatric Hospital and psychiatric ward of Rasool-e-Akram Hospital for their cooperation and encouragement all throughout the implementation phase. This work would not have been possible without

their support.

## References


Baldessarini, R.J., Perry, R., Pike, J., 2008. Factors associated with treatment non-adherence among US bipolar disorder patients. Hum. Psychopharmacol. Clin. Exp. 23 (2), 95–105.

Baldessarini, R.J., Pompili, M., Tondo, L., 2006. Bipolar Disorder. In: Simon, R.I., Hales, R.E. (Eds.), The American Psychiatric Publishing Textbook of Suicide Assessment and Management. American Psychiatric Publishing, Washington, DC, pp. 770.

Barraco, A., Rossi, A., Nicolò, G., 2012. Description of study population and analysis of factors influencing adherence in the observational Italian study "Evaluation of Pharmacotherapy Adherence in Bipolar Disorder"(EPHAR). CNS Neurosci. Ther. 18 (2), 110–118.

Bobo, W.V., Na, P.J., Geske, J.R., McElroy, S.L., Frye, M.A., Biernacka, J.M., 2018. The relative influence of individual risk factors for attempted suicide in patients with bipolar I versus bipolar II disorder. J. Affect. Disord. 225, 489–494.

Bortolato, B., Miskowiak, K.W., Köhler, C.A., Vieta, E., Carvalho, A.F., 2015. Cognitive dysfunction in bipolar disorder and schizophrenia: a systematic review of meta-analyses. Neuropsychiatr. Dis. Treat. 11, 3111–3125.

Bourne, C., Aydemir, O., Balanza-Martinez, V., Bora, E., Brissos, S., Cavanagh, J.T., et al., 2013. Neuropsychological testing of cognitive impairment in euthymic bipolar disorder: an individual patient data meta-analysis. Acta. Psychiatr. Scand. 128, 149–162.

Bryan, C.J., Rudd, M.D., 2012. Life stressors, emotional distress, and trauma-related thoughts occurring in the 24 h preceding active duty US Soldiers' suicide attempts. J. Psychiat. Res. 46, 843–848.

Buchman-Schmitt, J.M., Chu, C., Michaels, M.S., Hames, J.L., Silva, C., Hagan, C.R., et al., 2017. The role of stressful life events preceding death by suicide: evidence from two samples of suicide decedents. Psychiatry Res. 256, 345–352.

Cardoso, T.d.A., Bauer, I.E., Jansen, K., Suchting, R., Zunta-Soares, G., Quevedo, J., et al., 2016. Effect of alcohol and illicit substance use on verbal memory among individuals with bipolar disorder. Psychiatry Res. 243, 225–231.

Cassidy, F., 2011. Risk factors of attempted suicide in bipolar disorder. Suicide Life Threat Behav. 41 (1), 6–11.

Cipriani, A., Hawton, K., Stockton, S., Geddes, J.R., 2013. Lithium in the prevention of suicide in mood disorders: updated systematic review and meta-analysis. BMJ 346, f3646.

Conner, K.R., Houston, R.J., Swogger, M.T., Conwell, Y., You, S., He, H., Gamble, S.A., Watts, A., Duberstein, P.R., 2012. Stressful life events and suicidal behavior in adults with alcohol use disorders: role of event severity, timing, and type. Drug Alcohol Depen. 120, 155–161.

Cook, C., 2007. Models to evaluate patient compliance. Patient Compliance with Medications: Issues and Opportunities. The Haworth Press, Inc, USA, pp. 89–109.

Dunner, D.L., Patrick, V., Fieve, R.R., 1979. Life events at the onset of bipolar affective illness. Am. J. Psychiatry 136 (4B), 508–511.

Feske, U., Frank, E., Mallinger, A.G., Houck, P.R., Fagiolini, A., Shear, M.K., et al., 2000. Anxiety as a correlate of response to the acute treatment of bipolar I disorder. Am. J. Psychiatry 157 (6), 956–962.

First, M., Spitzer, R., Gibbon, M., Williams, J., 1995. Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I). 1997. Arlington: American Psychiatric Publishing Incorporated.

First, M.B., Gibbon, M., 2004. The structured clinical interview for DSM-IV axis I disorders (SCID-I) and the structured clinical interview for DSM-IV axis II disorders (SCID-II). In: Hersen, M. (Ed.), Comprehensive Handbook of Psychological Assessment, Volume 2: Personality Assessment 2. pp. 134.

Fjeldsted, R., Teasdale, T.W., Jensen, M., Erlangsen, A., 2017. Suicide in relation to the experience of stressful life events: a population-based study. Arch. Suicide Res. 21 (4), 544–555.

Fountoulakis, K.N., Vieta, E., Young, A., Yatham, L., Grunze, H., Blier, P., et al., 2016. The international college of neuropsychopharmacology (CINP) treatment guidelines for bipolar disorder in adults (CINP-BD-2017), Part 4: unmet needs in the treatment of bipolar disorder and recommendations for future research. Int. J. Neuropsychopharmacol. 20 (2), 196–205.

Gazalle, F.K., Frey, B.N., Hallal, P.C., Andreazza, A.C., Cunha, Â.B.M., Santin, A., et al., 2007. Mismatch between self-reported quality of life and functional assessment in acute mania: a matter of unawareness of illness? J. Affect. Disord. 103 (1), 247–252.

Goldney, R.D., Fisher, L.J., Wilson, D.H., Cheok, F., 2001. Suicidal ideation and health-related quality of life in the community. Med. J. Aust. 175 (10), 546–549.

Goldstein, T.R., Ha, W., Axelson, D.A., Goldstein, B.I., Liao, F., Gill, M.K., et al., 2012. Predictors of prospectively examined suicide attempts among youth with bipolar disorder. Arch. Gen. Psychiatry 69 (11), 1113–1122.

Golshiri, P., Akbari, M., Zarei, A., 2017. Case–control study of risk factors for suicide attempts in Isfahan, Iran. Int. J. Soc. Psychiatry 63 (2), 109–114.

Gonzalez-Pinto, A., Reed, C., Novick, D., Bertsch, J., Haro, J., 2010. Assessment of medication adherence in a cohort of patients with bipolar disorder. Pharmacopsychiatry 43 (07), 263–270.

Groth-Marnat, G., 2009. Handbook of Psychological Assessment. John Wiley & Sons.

Hakkaart-van Roijen, L., Hoeijenbos, M., Regeer, E.J., Ten Have, M., Nolen, W., Veraart, C., et al., 2004. The societal costs and quality of life of patients suffering from bipolar disorder in the Netherlands. Acta Psychiatr. Scand. 110 (5), 383–392.

Hosseini, E., Ghasemi, N., Molayi Gonbadi, G., Rezayi, L., 2010. Comparison of the level of stress and body image among individuals aged 20-30 seeking and not seeking cosmetic surgeries in Ahvaz province. J. Mod. Ind./Organ. Psychol. 1 (3), 75–84.

Isometsä, E., Heikkinen, M., Henriksson, M., Aro, H., Lönnqvist, J., 1995. Recent life events and completed suicide in bipolar affective disorder. A comparison with major depressive suicides. J. Affect. Disord. 33 (2), 99–106.

Javadpour, A., Hedayati, A., Dehbozorgi, G.-R., Azizi, A., 2013. The impact of a simple individual psycho-education program on quality of life, rate of relapse and medication adherence in bipolar disorder patients. Asian. J. Psychiatr. 6 (3), 208–213.

Jolfaei, A.G., Ghadamgahi, P., Ahmadzad-Asl, M., Shabani, A., 2015. Comparison of demographic and diagnostic characteristics of Iranian inpatients with bipolar i disorder to western counterparts. Iran. J. Psychiatry Behav. Sci. 9 (2), e839.

Kennedy, S., Thompson, R., Stancer, H.C., Roy, A., Persad, E., 1983. Life events precipitating mania. Br. J. Psychiatry 142 (4), 398–403.

Kleiveland, B., Natvig, G.K., Jepsen, R., 2015. Stress, sense of coherence and quality of life among Norwegian nurse students after a period of clinical practice. PeerJ 3, e1286.

Koivumaa-Honkanen, H., Honkanen, R., Viinamaeki, H., Heikkilae, K., Kaprio, J., Koskenvuo, M., 2001. Life satisfaction and suicide: a 20-year follow-up study. Am. J. Psychiatry 158 (3), 433–439.

Leclerc, E., Mansur, R.B., Brietzke, E., 2013. Determinants of adherence to treatment in bipolar disorder: a comprehensive review. J. Affect. Disord. 149 (1), 247–252.

Leverich, G.S., Altshuler, L.L., Frye, M.A., Suppes, T., Keck Jr, P.E., McElroy, S.L., et al., 2003. Factors associated with suicide attempts in 648 patients with bipolar disorder in the Stanley Foundation Bipolar Network. J. Clin. Psychiatry 64 (5), 506–515.

Maniglio, R., 2013. Prevalence of child sexual abuse among adults and youths with bipolar disorder: a systematic review. Clin. Psychol. Rev. 33 (4), 561–573.

Martin, J.S., Ghahramanlou-Holloway, M., Englert, D.R., Bakalar, J.L., Olsen, C., Nademin, E.M., Jobes, D.A., Branlund, S., 2013. Marital status, life stressor precipitants, and communications of distress and suicide intent in a sample of United States Air Force suicide decedents. Arch. Suicide Res. 17, 148–160.

Michalak, E.E., Yatham, L.N., Lam, R.W., 2005. Quality of life in bipolar disorder: a review of the literature. Health Qual. Life Outcome 3 (1), 72.

Nejat, S., Montazeri, A., Holakouie Naieni, K., Mohammad, K., Majdzadeh, S., 2006. The World Health Organization quality of Life (WHOQOL-BREF) questionnaire: translation and validation study of the Iranian version. J. Sch. Public Health Inst. Public Health Res. 4 (4), 1–12.

Novick, D.M., Swartz, H.A., Frank, E., 2010. Suicide attempts in bipolar I and bipolar II disorder: a review and meta-analysis of the evidence. Bipolar Disord. 12 (1), 1–9.

Otto, M.W., Simon, N.M., Wisniewski, S.R., Miklowitz, D.J., Kogan, J.N., Reilly-Harrington, N.A., et al., 2006. Prospective 12-month course of bipolar disorder in out-patients with and without comorbid anxiety disorders. Br. J. Psychiatry 189 (1), 20–25.

Paykel, E.S., Dowlatshahi, D., 1988. Life events and mental disorders. In: Fisher, S., Reason, J. (Eds.), Handbook of Life Stress, Cognition and Health. John Wiley & Sons, New York.

Paykel, E.S., Prusoff, B.A., Uhlenhuth, E., 1971. Scaling of life events. Arch. Gen. Psychiatry 25 (4), 340–347.

Pettit, J.W., Joiner, T.E., Rudd, M.D., 2004). Kindling and behavioral sensitization: are they relevant to recurrent suicide attempts? J. Affect. Disord. 83, 249–252.

Potash, J.B., Kane, H.S., Chiu, Y.-f., Simpson, S.G., MacKinnon, D.F., McInnis, M.G., et al., 2000. Attempted suicide and alcoholism in bipolar disorder: clinical and familial relationships. Am. J. Psychiatry 157 (12), 2048–2050.

Sadock, B.J., Sadock, V.A., 2011. Kaplan and Sadock's Synopsis of Psychiatry: Behavioral Sciences/Clinical Psychiatry. Lippincott Williams & Wilkins.

Samples, H., Stuart, E.A., Olfson, M., 2019. Opioid use, misuse, and suicidal behaviors in a nationally representative sample of US adults. Am. J. Epidemiol kwz061.

Shabani, A., Eftekhar, M., Daneshamouz, B., Ahmadkhaniha, H., Hakim shoushtari, M., Ghalebandi, M., Panaghi, L., 2006. Degree of recurrence of type I bipolar disorder: a 17 month follow-up of patients with first-episode mania. Adv. Cogn. Sci. 8 (3), 33–42.

Shabani, A., Teimurinejad, S., Kokar, S., Asl, M.A., Shariati, B., Behbahani, Z.M., et al., 2013. . Suicide risk factors in Iranian patients with bipolar disorder: a 21-month follow-up from BDPF study. Iran J. Psychiatry Behav. Sci. 7 (1), 16.

Sharifi, V., Assadi, S.M., Mohammadi, M.R., Amini, H., Kaviani, H., Semnani, Y., et al., 2009. A persian translation of the structured clinical interview for diagnostic and statistical manual of mental disorders: psychometric properties. Compr. Psychiatry 50 (1), 86–91.

Shirazi, H., Hosseini, M., Zoladl, M., Malekzadeh, M., Momeninejad, M., Noorian, K., Mansorian, M., 2012. Suicide in the Islamic Republic of Iran: an integrated analysis from 1981 to 2007. EMHJ 18 (6), 607–613.

Simon, N.M., Otto, M.W., Wisniewski, S.R., Fossey, M., Sagduyu, K., Frank, E., et al., 2004. 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 161 (12), 2222–2229.

Sonne, S.C., Brady, K.T., Morton, W.A., 1994. Substance abuse and bipolar affective disorder. J. Nerv. Ment. Dis. 182 (6), 349–352.

Soreca, I., Frank, E., Kupfer, D.J., 2009. The phenomenology of bipolar disorder: what drives the high rate of medical burden and determines long-term prognosis? Depress. Anxiety 26 (1), 73–82.

Swann, A.C., Pazzaglia, P., Nicholls, A., Dougherty, D.M., Moeller, F.G., 2003. Impulsivity and phase of illness in bipolar disorder. J. Affect. Disord. 73 (1), 105–111.

ten Have, M., Vollebergh, W., Bijl, R., Nolen, W.A., 2002. Bipolar disorder in the general population in The Netherlands (prevalence, consequences and care utilisation): results from The Netherlands Mental Health Survey and Incidence Study (NEMESIS). J. Affect. Disord. 68 (2), 203–213.

United Nations Office on Drugs and Crime, 2016. World Drug Report. United Nations Publication Sales No. E.16.XI.7.

Van Orden, K.A., Witte, T.K., Cukrowicz, K.C., Braithwaite, S., Selby, E.A., Joiner, T.E., 2010. The interpersonal theory of suicide. Psychol. Rev. 117, 575–600.

Vojta, C., Kinosian, B., Glick, H., Altshuler, L., Bauer, M.S., 2001. Self-reported quality of life across mood states in bipolar disorder. Compr. Psychiatry 42 (3), 190–195.

Wang, M., Alexanderson, K., Runeson, B., Mittendorfer-Rutz, E., 2015. Sick-leave measures, socio-demographic factors and health care as risk indicators for suicidal behavior in patients with depressive disorders–a nationwide prospective cohort study in Sweden. J. Affect. Disord. 173, 201–210.