



Factors related to suicidal behavior in patients with bipolar disorder: the effect of mixed features on suicidality



Hye-Jin Seo, M.D., Hee-Ryung Wang, M.D., Ph.D., Tae-Youn Jun, M.D., Ph.D., Young Sup Woo, M.D., Ph.D., Won-Myong Bahk, M.D., Ph.D.*

Department of Psychiatry, Department of Psychiatry, Yeouido St. Mary's Hospital, College of Medicine, The Catholic University of Korea, 10 63-ro, Yeongdeungpo-gu, 150-713 Seoul, Republic of Korea

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ABSTRACT

Objectives: The aim of the present study was to investigate various risk factors of suicidal behaviors, including the mixed features specifier, in patients with bipolar disorder.

Methods: We retrospectively reviewed medical charts from 2005 to 2014. A total of 334 patients diagnosed with bipolar disorder using the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* were enrolled. Subjects were categorized into two groups according to their history of suicidal behavior and the demographic and clinical characteristics of the groups were compared, including the mixed features specifier. We reevaluated the index episode using *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)* criteria and classified subjects into an index episode with mixed features group and an index episode without mixed features group. Logistic regression was performed to evaluate significant risk factors associated with suicidal behavior.

Results: Suicidal behavior had an independent relationship to mixed features at the index episode using *DSM-5* criteria [odds ratio (OR)=3.39; 95% confidence interval (CI): 1.57–7.34] and number of previous depressive episodes (OR=1.62; 95% CI: 1.34–1.95) in bipolar patients. The mixed feature specifier was the strongest risk factor for suicidal behavior in the present study.

Conclusions: This study may help clinicians understand potential risk factors and manage bipolar disorders with suicidal behaviors. Clinicians should carefully monitor patients with bipolar disorder who exhibit numerous depressive episodes or mixed features for suicidal behavior.

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1. Introduction

Among psychiatric disorders, bipolar disorder is one of the leading causes of suicidal behaviors. This is a major issue in the management of the disease. Patients with bipolar disorder are at equally elevated risk for suicidal ideation, attempt, and fatality [1]. The estimated rate of suicide deaths among people with bipolar disorder is 0.2–0.4 per 100 person-years [2]. Rates of suicide attempts are also very high, with an estimated annual risk of 0.9% per year, and a lifetime risk of up to one-half of patients with bipolar disorder [2]. A 2003 Korean study of bipolar patients found that the prevalence of suicide attempts in patients with bipolar disorder was 7.5% and was higher for patients with bipolar II disorder (26.5%) than for those with bipolar I disorder (5%) [3]. A review has estimated the risk of suicide in bipolar patients to be 20–30 times higher than that of the general population [4]. This risk is greater than in other psychiatric disorders, substance use and general medical disorders, and major depressive disorder across its broad range of severities [5]. Furthermore, suicidal behavior is much more lethal in bipolar disorder than in the general population [6].

Completed suicide occurs once for every 30 attempts in the general population, while it occurs once for every 3–4 attempts in patients with bipolar disorder [7]. Relative to the risk in the general population, bipolar disorder is associated with an increased risk of suicidal behavior in women and a higher lethality in men [8]. Compared with unipolar patients, suicide attempts in bipolar patients tend to be more lethal, particularly in men [9]. Therefore, all suicidal behaviors in bipolar patients need to be considered to have high potential for lethality [10].

Several studies have reported an association between suicidal behavior in patients with bipolar and previous suicidal attempts [11], more lifetime episodes of major depression [12,13], more mixed states [1,5], rapid cycling [11], earlier age at onset [13], comorbid substance or alcohol use disorder [14], a family history of suicide attempts [13] and comorbid anxiety disorders [15].

In particular, bipolar patients with mixed states have been shown to have a higher risk of suicide than those without mixed states. A mixed state is a clinical state in which symptoms of depression and mania concurrently occur and are characterized by the simultaneous presence of both depressive and manic symptoms [16]. Different definitions and terminology have been used over time according to changes in diagnostic criteria or based on the study. Compared with the restrictive definition in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth*

* Correspondence author. Tel.: +82 2 3779 1250; fax: +82 2 780 6577.
E-mail address: wmbahk@catholic.ac.kr (W.-M. Bahk).

Edition, Text Revision (DSM-IV-TR), which requires the overlap of full manic and depressive episode symptoms [17], the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)* has introduced a broader definition and the use of “mixed features” has become a specifier [18].

The association between mixed features as defined by the *DSM-5* criteria and suicidality has not been well studied. It is unclear whether or not the mixed feature specifier in the *DSM-5* plays a role in predicting suicidal behaviors in bipolar patients.

Therefore, the present study investigated various risk factors of suicidal behavior, including the mixed features specifier, in patients with bipolar disorder.

2. Methods

2.1. Subjects

We retrospectively reviewed the medical charts of patients admitted to Yeouido St. Mary's Hospital, College of Medicine, The Catholic University of Korea in Seoul, Korea. All patients hospitalized at this institution were diagnosed using clinical interviews and diagnoses of an Axis I disorder were made by a board-certified psychiatrist in accordance with the *DSM-IV-TR* criteria. All subjects in this study met the *DSM-IV-TR* criteria for bipolar I, bipolar II or bipolar disorder not otherwise specified (NOS) during the period from 2005 to 2014. Inclusion criteria were diagnosis of bipolar disorder with any type of mood episode based on *DSM-IV-TR* criteria and age between 15 and 65 years. Exclusion criteria were insufficient data, a severe comorbid medical or neurological condition that could contribute to mood symptoms, an organic brain lesion that could influence mood symptoms, a thought disorder (such as schizophrenia or schizoaffective disorder) or a cognitive disorder (such as dementia) that could confound the phenomenology of a mood episode.

The charts of 448 inpatients diagnosed with bipolar I, bipolar II or bipolar disorder NOS were initially reviewed and 114 cases were excluded based on the above criteria. Thus, a total of 334 patients were enrolled in the present study and categorized into two groups according to their history of suicidal behavior.

2.2. Assessments

The following demographic and clinical characteristics were collected via chart review: age, gender, marital status, socioeconomic status, employment status, education, age of onset, duration of illness, age at first treatment, number of hospitalization for mood disorder, number of previous mood episodes (number of depressive episodes, number of manic episodes, number of hypomanic episodes, number of mixed episodes), history of rapid cycling, history of psychotic symptoms, age at onset of psychotic symptoms, history of suicidal behavior, alcohol or substance use disorder, psychiatric comorbidity, medical comorbidity, history of using antidepressants, family history of suicide, family history of bipolar disorder, family history of mood disorder and family history of other psychiatric disorders. Number of previous mood episodes including mixed episodes was evaluated according to *DSM-IV-TR* criteria.

We defined suicidal behavior as any suicidal ideation or suicide attempt during the patient's lifetime. Suicidal ideation was defined as thoughts of wishing to be dead, not merely preoccupation with death. Suicide attempts were defined as self-injurious behaviors with some degree of intent to die; self-harm with no suicidal intention was not included. We excluded self-destructive behaviors that the patient denied were done with the intention of dying, such as compulsive self-mutilation to decrease anxiety.

The index episode for each patient was a term used to define any mood episode that led to a hospitalization between 2005 and 2014. If a patient experienced more than one hospitalization during the study period, only data from the most recent admission were analyzed. We

reevaluated the index episode using *DSM-5* criteria and classified the episode as one with a mixed feature or one without mixed features. Two independent psychiatrists who were blinded to the purpose of the study separately evaluated the medical records of the patients for symptoms of the opposite polarity.

The following clinical data from the index episode were obtained: age, marital status, socioeconomic status, employment status and years of education. Clinical characteristics, such as age at first psychiatric treatment, age of onset, number of previous episodes, history rapid cycling, history psychotic symptoms, history of using antidepressants and history of suicidal behavior before the patients visited our hospital, which was retrospectively investigated from the time of the index episode, were also included in the analysis. As this was a retrospective study, all data were obtained during routine psychiatric examinations and treatment.

2.3. Statistical analysis

To compare sociodemographic and clinical characteristics of the two groups, chi-square tests or Fisher's Exact Tests were used for categorical variables and independent *t* tests were used for continuous variables. A multivariate logistic regression model was used to identify factors associated with lifetime suicidal behaviors. Factors with *P* values < .05 at univariate analyses were entered into the model as independent variables. Odds ratios (ORs) with 95% confidence intervals (CIs) were used for observed associations. Two-tailed *P* values with an alpha level of .05 were considered significant, except that a Bonferroni-corrected significance level of *P* < .0026 (0.05/19 tests) was applied to the univariate analysis. All statistical analyses were conducted using IBM SPSS Statistics for Windows (version 20.0; IBM Co., Armonk, NY, USA).

2.4. Ethics

This study was approved using clinical data and secondary data analysis by the institutional review board of Yeouido St. Mary's Hospital in Seoul, Korea and was conducted according to the Declaration of Helsinki. The institutional review board waived the requirement for informed consent because this was a retrospective chart review study.

3. Results

During the study period, 448 patients were discharged with a diagnosis of bipolar disorder. Of these patients, 334 (74.6%) met the eligibility criteria for the study.

3.1. Sociodemographic characteristics at the index episode

A total of 89 (26.6%) patients had a positive history of suicidal behavior and the remaining 245 (73.4%) had no suicidal behavior. The sociodemographic characteristics of the group with suicidal behavior and the group without suicidal behavior are summarized in Table 1. Mean age at the index episode was 37.64 ± 13.65 years in the group with suicidal behavior and 38.44 ± 12.70 years in the group without suicidal behavior. There were no statistically significant differences in mean age between the two groups. We found no significant difference between the groups in the proportions of men and women: women comprised 58.4% ($n = 52$) of the group with suicidal behavior and 55.9% ($n = 137$) of the group without suicidal behavior. Regarding marital status, unmarried patients (57.5%) were the most common in the group with suicidal behavior and married patients (49.6%) were the most common in the group without suicidal behavior, but the groups did not significantly differ in their distribution. Additionally, no significant differences were found between the two groups in terms of other sociodemographic characteristics such as socioeconomic status, employment status and education.

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