

Correlates of current suicide risk among Thai patients with bipolar I disorder: findings from the Thai Bipolar Disorder Registry

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Background: The Thai Bipolar Disorder Registry was a prospective, multisite, naturalistic study conducted in 24 hospitals across Thailand. This study aimed to examine the correlates of current suicide risk in Thai patients with bipolar I disorder.

Methods: Participants were adult inpatients or outpatients with bipolar disorder, based on the *Diagnosis and Statistical Manual of Mental Disorders*, fourth edition. All were assessed by using the Mini International Neuropsychiatric Interview (MINI), version 5. The severity of current suicide risk was determined by using the total score of the MINI suicidality module. Mood symptoms were assessed by using the Young Mania Rating Scale and the Montgomery Asberg Depression Rating Scale.

Results: The data of 383 bipolar I disorder patients were included in the analyses. Of these, 363 (94.8%) were outpatients. The mean (standard deviation) of the MINI suicide risk score was 1.88 (5.0). The demographic/clinical variables significantly associated with the MINI suicide risk scores included age, number of overall previous episodes, the Young Mania Rating Scale score, the Montgomery Asberg Depression Rating Scale scores, and the Clinical Global Impression Severity of Illness Scale for Bipolar Disorder mania score, depression score, and overall score. The variables affecting the differences of suicide risk scores between or among groups were type of first mood episode, a history of rapid cycling, anxiety disorders, and alcohol use disorders. The stepwise multiple linear regression model revealed that the Montgomery Asberg Depression Rating Scale score ($\beta=0.10$), a history of rapid cycling ($\beta=6.63$), anxiety disorders ($\beta=2.16$), and alcohol use disorders ($\beta=2.65$) were significantly correlated with the suicide risk score (all $P<0.01$).

Conclusion: A history of rapid cycling, severity of depressive episode, current anxiety disorders, and current alcohol use disorders correlate with current suicide risk among Thai bipolar I disorder patients. Further studies in larger sample sizes are warranted.

Keywords: Asian, bipolar disorder, correlates, risk, suicide, Thai

Introduction

Bipolar disorder (BD) is associated with marked premature death, with a mortality rate two to three times higher than the general population.¹ Although this increased mortality is in part due to accidents, medical illnesses, and alcohol abuse, the greatest part of excessive death mainly results from suicide.² BD patients are at higher risk of attempted and completed suicide than patients with other mental disorders.^{3–5} Researchers estimate that 21%–54% of BD individuals will attempt suicide at least once in their lifetime, and 10%–18% of them will have premature death.^{5,6}

Previous suicide research in BD patients has highlighted a number of correlates and risk factors. These may include family history of suicide or mood disorders,

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early negative life events, previous suicide attempts, early in the illness course, early onset of illness, a long duration of untreated illness, rapid cycling, psychosocial stressors, comorbid Axis I and II disorders, serious medical illness, lack of medical treatment, lack of social or family support, extent of depressive symptoms, increasing severity of mood episodes, psychotic symptoms, atypical features, the presence of mixed affective states, and abuse of alcohol and drugs.^{7–9} While suicidal ideation and a history of attempted suicide are among the most important risks for suicide,^{10,11} only a few studies have taken into account both suicidal ideas and attempts in assessing the risk factors.

While suicidal behaviors may be different among ethnic groups, little is known about the suicide risk in Asian BD patients. A study carried out in the UK also found that suicide ideas were less common in South Asians (Indian, Pakistani, and Bangladeshi), as well as Black Caribbean and Black Africans, compared with White British.¹² For those living in a community, Asians have a higher suicide rate, lower male-to-female suicide gender ratio, and higher elderly-to-general-population suicide ratios than Caucasians.¹³ In addition, acute life stress (eg, family conflicts, job and financial security issues) plays a more important role than mental illness in causing suicidal behavior. Although there have been some studies of suicide risk in Asian BD patients, only one study has examined a comprehensive list of risk factors in 101 Taiwanese BD patients with attempted suicide.¹⁴ This study found that early age of onset, interpersonal problems, occupational problems, and a large number of episodes were predictors of suicide attempts. Interestingly, the risk factors of interpersonal and occupational problems found in this study were rarely found in Western studies. These results suggest that predictors of suicide attempts in Asian BD patients may differ from those of Westerners.

As suicidal behavior in patients with mood disorder is a “state dependent” phenomenon,¹⁵ it would be of interest to determine the correlates of current suicide risk in BD patients. Together with the aforementioned limitations of evidence in Asian BD patients, the authors proposed to examine the correlates of current suicide risk, taking into account suicidal ideation, suicidal plan, suicidal attempts, and a history of attempted suicide in Thai BD I patients.

Methods

The Thai Bipolar Disorder Registry, implemented in Thailand, was a prospective, national, multisite, naturalistic study conducted in 24 university, public mental, and public general hospitals. Its primary aim was to characterize

the illness course in BD patients. Its details have been published in a recent article.¹⁶ This study did not involve any clinical management of the enrolled participants, and it was approved by the Institutional Review Board or Ethics Committee of each site. Prior to their participation, all participants gave written informed consent after the study details had been fully explained.

Participants

Participants were aged ≥ 18 years old and were inpatient or outpatients with BD I or II. Those participating in other investigational studies and those with travel difficulty were excluded. They were prospectively enrolled from inpatients or outpatients receiving psychiatric treatment at the respective study sites.

Assessment

All participants were assessed at baseline (visit 1) and every 2 months (± 1 month) for 12 months (visit 7). Data collected at baseline were demographic details, history of BD, psychiatric treatment, and physical comorbidity. Assessment at baseline and endpoint included current status of BD and health status. Measures used for evaluating the current status of BD were the Mini International Neuropsychiatric Interview (MINI), version 5,¹⁷ the Young Mania Rating Scale (YMRS),¹⁸ the Montgomery Asberg Depression Rating Scale (MADRS),¹⁹ and the Clinical Global Impression Severity of Illness Scale for BD (CGI-BP-S).²⁰ The health status was assessed by using Rand 36-Item Health Survey (SF-36).^{21,22} Patients with rapid-cycling were defined as having four or more manic, mixed, or depressive episodes in the year prior to baseline assessment.

The MINI suicidality module was used to determine the current suicide risk. It consists of nine questions relevant to suicidal behavior. Each question asked for a yes/no response. The questions (score for a positive response) were as follows: 1) intentional accident (zero points); 2) death wish (one point); 3) self-harm wish (two points); 4) suicide idea (six points); 5) suicide plan (eight points); 6) suicide plan with preparation (nine points); 7) deliberate injuring of oneself (four points); 8) suicide attempt in the past month (ten points); and 9) suicide attempt in lifetime (four points). Of note, as proposed by the developers, the positive response to the first question of intentional accident has no score. The suicide risk scores range from 0–52. Since all questions, except lifetime suicide attempt, are relevant to suicidal behavior during 1 month prior to assessment, the total score of this module therefore reflects the severity of current suicide risk. Although a history of attempted suicide

is not a current condition, it is a risk factor highly ranked for suicide assessed by most psychiatrists.^{10,23} In developing a one-item questionnaire for assessing suicide risk, a history of attempted suicide was found to have high sensitivity (0.80) and very high specificity (0.97) in differentiating between suicidal and nonsuicidal adult inpatients.¹⁰ In addition, it is the strongest and most robust predictor of suicide attempts and suicide completion in mentally ill and BD patients.^{5,7} As proposed by the developers of MINI and the aforementioned rationales, the item of previous attempted suicide of this MINI module was therefore included as a part of the current suicide risk.

Other MINI modules used in this registry included major depressive episode, (hypo)manic episode, panic disorder, agoraphobia, social phobia (social anxiety disorder), obsessive-compulsive disorder, alcohol abuse and dependence, non-alcohol psychoactive substance use disorders, and generalized anxiety disorder. Because only one module of MINI can elicit lifetime mental disorders (ie, panic disorder), only current mental disorders were taken into account.

Statistical analysis

Only baseline data were included in the analysis. Alcohol abuse and dependence were pooled as alcohol use disorders. Panic disorder, agoraphobia, social phobia (social anxiety disorder), obsessive-compulsive disorder, and generalized anxiety disorder were grouped as anxiety disorders. Because only 20 BD II patients were registered and might have a different pattern of suicidal behavior compared with BD I counterparts,²⁴ only the data of BD I patients were included in the analysis.

Variables were expressed as mean (standard deviation [SD]) and number (%). First, Pearson's correlation coefficients were calculated to determine the significant associations of continuous demographic/clinical variables and the suicide risk scores. For categorical variables, the differences of suicide risk scores between or among groups were examined using Student's *t*-test and one-way analysis of variance, respectively. Stepwise multiple linear regression analysis of the suicide risk score was applied to determine its significant predictors ($P < 0.05$). R^2 and adjusted R^2 were analyzed to evaluate the ratio of the sum of squares explained by a regression model. Coefficient values with 95% confidence intervals were used to quantify the strength of associations. The statistical significance for all tests was set at $P < 0.05$. Statistical analyses were performed using the software package SPSS Statistics 17.0 (IBM Corporation, Armonk, NY, USA).

Results

The data of 383 BD I patients were included in this study. Of these, 233 (60.8%) were female, and 363 (94.8%) were outpatients. The mean (SD) of age and age of onset were 42.3 (12.2) and 31.3 (11.6) years old, respectively. Of 383 participants, 303 currently had no mood episode. Current mood episodes were as follows: manic ($n=31$), major depressive ($n=25$), hypomanic ($n=17$), and mixed ($n=7$). The mean (SD) of YMRS and MADRS scores were 3.8 (5.7) and 4.9 (6.6), respectively. Prevalence of nine suicidal behaviors were as follows: intentional accident (7.3%), death wish (9.9%), self-harm wish (3.7%), suicide ideation (5.2%), suicide plan (1.6%), suicide plan with preparation (0.8%), deliberate injuring of oneself (1.3%), suicide attempt in the past month (2.1%), and suicide attempt in lifetime (20.6%). The mean (SD) of the MINI suicide risk score was 1.88 (5.0).

Tables 1 and 2 show the variables included in the univariate analyses. By using Pearson's correlation coefficient r , the continuous demographic/clinical variables significantly associated with the MINI suicide risk scores were age ($P=0.02$), number of overall previous episodes ($P=0.02$), the YMRS score ($P < 0.01$), the MADRS scores ($P < 0.01$), the CGI-BP-S mania score ($P < 0.01$), the CGI-BP-S depression score ($P < 0.01$), and the CGI-BP-S overall score ($P < 0.01$) (Table 1). The variables affecting the differences of suicide risk scores between or among groups included type of first mood episode ($P < 0.01$), a history of rapid cycling ($P < 0.01$),

Table 1 Sociodemographic/clinical characteristics and their correlations with suicide risk among 383 Thai bipolar I disorder patients

Sociodemographic/clinical characteristics	Mean (SD)	Significant correlation (r, P)
Age (years)	42.3 (12.2)	-0.12, 0.02
Age at onset (years)	31.3 (11.6)	-0.10, 0.05
Years of untreated illness	4.2 (6.9)	-0.04, 0.42
Number of all previous episodes	4.9 (5.0)	0.13, 0.02
Number of previous manic/hypomanic episodes	3.1 (2.8)	0.05, 0.35
Number of previous depressive episodes	1.6 (3.1)	0.14, 0.07
Number of previous mixed episodes	0.2 (1.0)	0.24, 0.15
YMRS score	3.8 (5.7)	0.15, <0.01
MADRS score	4.9 (6.6)	0.30, <0.01
CGI-BP-S mania score	1.7 (1.2)	0.17, <0.01
CGI-BP-S depression score	1.5 (1.0)	0.27, <0.01
CGI-BP-S overall score	1.8 (1.2)	0.23, <0.01

Abbreviations: CGI-BP-S, Clinical Global Impression Severity of Illness Scale for Bipolar Disorder; MADRS, Montgomery Asberg Depression Rating Scale; SD, standard deviation; YMRS, Young Mania Rating Scale.

Table 2 Sociodemographic/clinical characteristics and suicide risk in Thai bipolar I disorder patients

Sociodemographic/clinical characteristics	N=383 n (%)	Mean (SD)	Significant difference ^a
Sex			$t=-1.51$,
Male	150 (39.2)	1.4 (3.2)	$P=0.09$
Female	233 (60.8)	2.2 (5.8)	
Marital status			$F=1.21$,
Single	132 (34.5)	1.5 (3.6)	$P=0.30$
Married	192 (50.1)	2.3 (6.2)	
Divorced/widowed	59 (15.4)	1.5 (3.0)	
A history of hospitalization ^b			$F=0.58$,
Yes	231 (60.3)	1.9 (4.5)	$P=0.56$
No	124 (32.4)	1.6 (5.3)	
Type of first mood episode			$F=4.95$,
Depression	92 (24.0)	2.9 (6.1)	$P<0.01$
Mania/hypomania	252 (65.8)	1.3 (3.4)	
Mixed	27 (7.0)	4.4 (19.3)	
Undetermined	12 (3.1)	0.7 (1.6)	
A history of rapid cycling ^b			$t=6.94$,
Yes	30 (8.1)	11.0 (19.1)	$P<0.01$
No	342 (91.9)	1.8 (4.7)	
Anxiety disorders (panic, agoraphobic, social anxiety, OCD, PTSD, or GAD)			$t=-2.45$,
Yes	48 (12.5)	4.9 (9.6)	$P=0.02$
No	335 (87.4)	1.5 (3.8)	
Alcohol use disorders (alcohol dependence + alcohol abuse)			$t=-0.68$,
Yes	30 (7.8)	1.61 (4.7)	$P=0.01$
No	353 (92.2)	1.6 (4.7)	
Substance dependence/abuse			$t=-0.53$,
Yes	10 (2.6)	2.7 (5.1)	$P=0.60$
No	373 (97.4)	1.9 (5.0)	
Psychiatric disorder in first-degree relatives			$t=0.74$,
Yes	117 (30.5)	2.2 (6.0)	$P=0.46$
No	266 (69.4)	1.8 (4.5)	

Notes: ^aStudent's *t*-test for between group difference and one-way analysis of variance for among group difference; ^bhistory of hospitalization in 22 patients and history of rapid cycling in eleven patients were undetermined due to missing data.

Abbreviations: GAD, generalized anxiety disorder; OCD, obsessive-compulsive disorder; PTSD, post-traumatic stress disorder; SD, standard deviation.

current anxiety disorders ($P=0.02$), and current alcohol use disorders ($P<0.01$) (Table 2).

The stepwise multiple linear regression model revealed that the MADRS score ($\beta=0.10$), a history of rapid cycling ($\beta=6.63$), current anxiety disorders ($\beta=2.16$), and current alcohol use disorders ($\beta=2.65$) were significantly correlated with the suicide risk score (all $P<0.01$) (Table 3). The model predicted 21% of the suicide risk score ($R^2=0.22$; adjusted $R^2=0.21$; $F=26.17$, $P<0.01$).

Discussion

This prospective study of Thai BD I patients was dominated by outpatients. The low YMRS, MADRS, and MINI

Table 3 Stepwise multiple linear regression of factors predicting the suicide risk (to enter: $P=0.1$; to leave: $P=0.2$)

Risk factor	β	SE (β)	<i>t</i>	<i>P</i>	95% confidence interval	
					Lower bound	Upper bound
Constant*	13.78	2.06	6.68	<0.01	9.73	17.84
A history of rapid cycling	6.63	1.02	6.48	<0.01	8.65	4.62
MADRS	0.10	0.04	2.72	<0.01	0.03	0.18
Anxiety disorders	2.16	0.73	2.97	<0.01	0.73	3.58
Alcohol use disorders	2.65	0.85	3.11	<0.01	0.97	4.33

Notes: * $R^2=0.22$, adjusted $R^2=0.21$, $F=26.17$, $P<0.01$.

Abbreviations: MADRS, Montgomery Asberg Depression Rating Scale; SE, standard error.

suicidality scores suggested that these participants were mildly ill. However, this study still found that a history of rapid cycling, the severity of depressive state, current anxiety disorders, and current alcohol use disorders are the state-dependent risk factors of suicide in this population. Although these four factors correlated well with current suicidality, the low adjusted R^2 of 0.21 suggests that many factors not included in this study also played a role, eg, family history of suicide or mood disorders, early negative life events, psychosocial stressors, serious medical illness, lack of social or family support, psychotic symptoms, atypical features.

The association between current suicide risk and rapid cycling found in this study is consistent with previous findings. In a meta-analysis, rapid cycling increased the odds of attempted suicide for 1.54-fold in BD patients.⁷ However, a recent study found that rapid cycling increased only lifetime suicidal ideation but not lifetime suicide attempts.²⁵

The present findings confirm the association of depression severity and suicide risk. Suicidal behavior is a part of major depression and all measures used for assessing depression severity. Almost 80% of BD suicides occur during a major depressive episode.²⁶ In an 18-month follow-up study, depressive phase at index episode was a predictor of suicide attempts.²⁷ Even mixed mania, a manic episode with limited symptoms of depression, the chance of suicidal behavior also increases 26.7-fold compared with pure mania.²⁸

Anxiety disorders are a noteworthy risk factor for suicide in BD patients. Although the lifetime prevalence of these disorders might be as high as 86.7%,²⁹ the prevalence was only 26.7% in Taiwanese patients with BD.³⁰ The low prevalence of current anxiety disorders in the present cohort (12.5%) might be caused by the use of MINI, which mainly detected current mental disorders, or by nature of the low prevalence

of anxiety disorders in Asian BD patients. However, these findings still replicated the meta-analytic results and suggest that comorbid anxiety disorder increased the risk of suicide attempts in BD I patients.⁷

Alcohol abuse and dependence may be found in 38.0%–56.3% of BD I individuals.²⁹ The results of this study suggest that alcohol use disorders in the past year increase the current risk of suicidality in BD I patients. These findings are in line with the results of a meta-analysis and a recent study in Europe, which found that alcohol use disorders increased lifetime suicide attempts.^{7,31} As lifetime alcohol use disorders may be found in 42.6% of BD patients,³² this common comorbidity may play an important role in increasing the suicidality in BD patients.

Several risk factors shown in previous studies were not found in the present one (eg, early onset of illness,^{33,34} duration of untreated illness,³⁵ substance abuse comorbidity^{36,37}). The present mean age of onset (31.3 years) was later than those of previous findings (18–24 years).³⁸ The mean duration of untreated illness (4.2 years) was also shorter than Western findings (eg, 9.6 years in France).³⁹ As ethnicity did not have a significant influence on the age of onset,⁴⁰ these findings might reflect the unawareness of mild mood disturbance in the early stage of BD. The fact that the substance abuse module of MINI focuses only on the previous year might be a cause of the low prevalence of substance abuse comorbidity.

The present study design and sample were relatively different from those of previous studies, and these issues should be taken into account when interpreting the results of this study. While the key outcomes of most studies were suicides and lifetime suicide attempts, the present one intended to examine the current or the state-dependent suicide risk, taking into account all current suicidal behaviors and a history of attempted suicide. The present findings therefore reflect the more current problem of suicidality. The prevalence of attempted suicide, which was the most common suicidal behavior in this study, was only 20.6% compared with that of European studies (21%–54%).⁶ It is possible that the differences in study design and subjects (mainly Thai outpatients) play an important role in causing the dissimilarities in results.

There were some limitations in this study. First, the sample size of 383 is relatively small for a multivariate study. False negative findings for some risk factors could therefore not be ruled out. Second, this study had multiple testing, which might lead to the problem of false positive findings. However, the high significance ($P < 0.01$) for all

four factors may indicate less cause for concern in regard to this problem. Third, the characteristics of this sample were unique. They were Thai BD I patients, who currently had mild mood symptoms and low suicidality. The present findings may not be able to be generalized to BD I patients with severe mood episodes. Last, some variables (eg, age at onset, number of previous episodes) were based on patients' subjective perception, and therefore include a recall bias.

The present results provide another perspective of suicide risks among BD I patients. While most of the previous studies mainly focused on a long-term course of complete suicide or suicide attempts, the present one adds the evidence of the current clinical features affecting current suicide risk. In addition, these results confirm that some predictors of long-term suicidal behavior, eg, depression, a history of rapid cycling, comorbidity of anxiety/alcohol use disorders, are also correlated with current suicide risk.

Conclusion

A history of rapid cycling, severity of depressive episode, current anxiety disorders, and current alcohol use disorders correlate with current suicide risk among Thai BD I patients. The presence of these clinical features should raise the physician's awareness on the currently high suicidality in these patients. Further studies in larger sample sizes are warranted.

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