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Factors associated with the frequency of manic and depressive episodes in bipolar disorder: a multicenter study in China

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Abstract

Background Mania and depression are the predominant mood episodes in bipolar disorder (BD), and their frequency significantly affects the long-term prognosis of patients.

Method This is a multicenter, longitudinal cohort study in China. Sociodemographic and clinical characteristics of patients were statistically analyzed. Poisson regression analyses were performed to identify factors associated with the frequency of manic and depressive episodes.

Results A total of 520 BD patients were enrolled in this study. Poisson regression model analysis showed that shorter years of education (OR = 1.03, $P = 0.03$), mixed polarity of the first episode compared to mania (OR = 2.33, $P < 0.01$) or depression (OR = 1.79, $P = 0.01$), earlier age at diagnosis (OR = 1.03, $P = 0.01$), comorbid substance use disorder (OR = 1.41, $P = 0.02$), presence of psychotic symptoms (OR = 1.18, $P = 0.04$), use of antidepressant medication (OR = 1.52, $P = 0.01$), and non-use of mood stabilizers (OR = 1.57, $P<0.01$) are positively associated with the frequency of manic episodes. Being male (OR = 1.22, $P = 0.01$), the use of mood stabilizers (OR = 1.47, $P<0.01$) and a diagnosis of bipolar II disorder (BD-II) compared to bipolar I disorder (BD-I) (OR = 1.27, $P = 0.01$) are positively associated with the frequency of depressive episodes.

Conclusion The study highlights the critical association of clinical and sociodemographic factors with the frequency of manic and depressive episodes in BD patients. Addressing these factors may improve long-term outcomes for individuals with bipolar disorder.

Keywords Bipolar disorder, Manic episodes, Depressive episodes, China, Multicenter study

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Background

Bipolar disorder (BD) is a chronic mental disorder clinically characterized by recurrent episodes of depression and mania/hypomania, primarily classified into bipolar I disorder (BD-I) and bipolar II disorder (BD-II). Epidemiological data indicate that the global lifetime prevalence of BD is approximately 4.4% [1]. Nearly half of the patients will relapse within one year, often with recurrent episodes [2, 3]. Frequent mood episodes complicate treatment [4], hinder work, study, and daily life, and lead to the chronicity of BD, personality changes, and impaired social functioning [5]. Comorbid conditions, such as substance use disorder, further exacerbate the societal burden [6].

In BD, mania and depression are the predominant mood episodes [4]. Recently, the concept of "predominant polarity" (PP) has been introduced to characterize patterns of mood episodes, referring to the dominance of manic episodes, depressive episodes, or the absence of a clear polarity [7]. A recent meta-analysis found that male gender, psychotic features, and manic onset are associated with manic predominant polarity, whereas depressive onset, a higher number of mood episodes, and a history of suicide attempts are linked to depressive predominant polarity [8].

Previous studies have explored several factors affecting episode frequency. One study found a significant correlation of episode frequency with familial history, early onset age, BD-II, presence of hallucinations or delusions, alcohol abuse, and suicidal behaviors [9]. Another study highlighted that a longer untreated period before the first manic episode leads to worse clinical outcomes, evidenced by more frequent episodes [10]. Additionally, delayed diagnosis, poor medication compliance, and the use of antipsychotics were associated with more frequent mood episodes, particularly in patients aged 36–55 years. Other factors, such as antidepressant use and gender, may also influence BD relapse [11, 12]. A study from Taiwan further demonstrated that BD at index hospitalization, earlier onset of mood episodes, and a higher number of previous hospitalizations were associated with shorter time to rehospitalization [13]. However, similar studies in mainland Chinese populations remain limited, highlighting the need for further research in this area.

This study aims to identify the factors associated with the frequency of manic and depressive episodes in Chinese patients with BD. By examining sociodemographic characteristics, clinical features, and medication use through a large-scale, multicenter survey in China, we hope to fill this research gap and provide guidance for future treatment and management strategies.

Methods

Study design and data collection

This study utilized data from the "Observational Study of Clinical Management of Bipolar Disorder in China," conducted across seven hospitals in six cities: Beijing Anding Hospital of Capital Medical University, the Sixth Hospital of Peking University, Shanghai Mental Health Center, the Second Affiliated Hospital of Zhejiang University, Shenzhen Kangning Hospital, Xijing Hospital, and the First Affiliated Hospital of Kunming Medical College. Patients were enrolled between February 2013 and June 2014, with each sub-center enrolling 50–150 patients.

Inclusion criteria: (1) Signed written informed consent; (2) Age ≥ 18 years old of any gender; (3) Diagnosis of BD-I or BD-II according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria; (4) Presence of mood episodes (depression, mania/hypomania, or mixed) according to DSM-IV within 3 to 12 months prior to enrollment. Exclusion criteria: (1) Inability to complete the questionnaire; (2) Participation in another interventional clinical study within the past year. The study was approved by the Ethics Committee of Beijing Anding Hospital affiliated with Capital Medical University (Approval No.: 2013 Clinical Review No. 1) and was registered at chictr.org.cn (identifier: NCT01770704, date of registration: first posted on January 18, 2013). All participants provided written informed consent.

The project leader unit was responsible for the organization of the project, quality control, and training in study implementation. Trained psychiatrists at each subcenter screened patients, collected data, and instructed them to complete relevant assessments. The diagnosis of BD was conducted by experienced, uniformly trained psychiatrists at the attending level or above, based on DSM-IV criteria. The Case Report Form (CRF) was completed by researchers through structured patient interviews and a thorough review of clinical records.

The study design and procedure are shown in Fig. 1. At time point 0 (patient enrollment), informed consent was obtained, and baseline assessments were conducted. Sociodemographic data, including age, gender, education, employment status, and residency, were collected alongside clinical characteristics, such as BD type, family history of mental disorders, comorbid substance use disorder, anxiety disorders, psychotic symptoms, polarity of the first mood episode, age of onset, age at diagnosis, and prior treatments. Mood episode data included both retrospective data (covering the 12 months prior to study initiation) and prospective data (spanning the 9-month follow-up period). Manic and depressive episodes were defined in accordance with DSM-IV criteria. Diagnoses of substance use disorder, anxiety disorders, and psychotic symptoms were also made based on DSM-IV

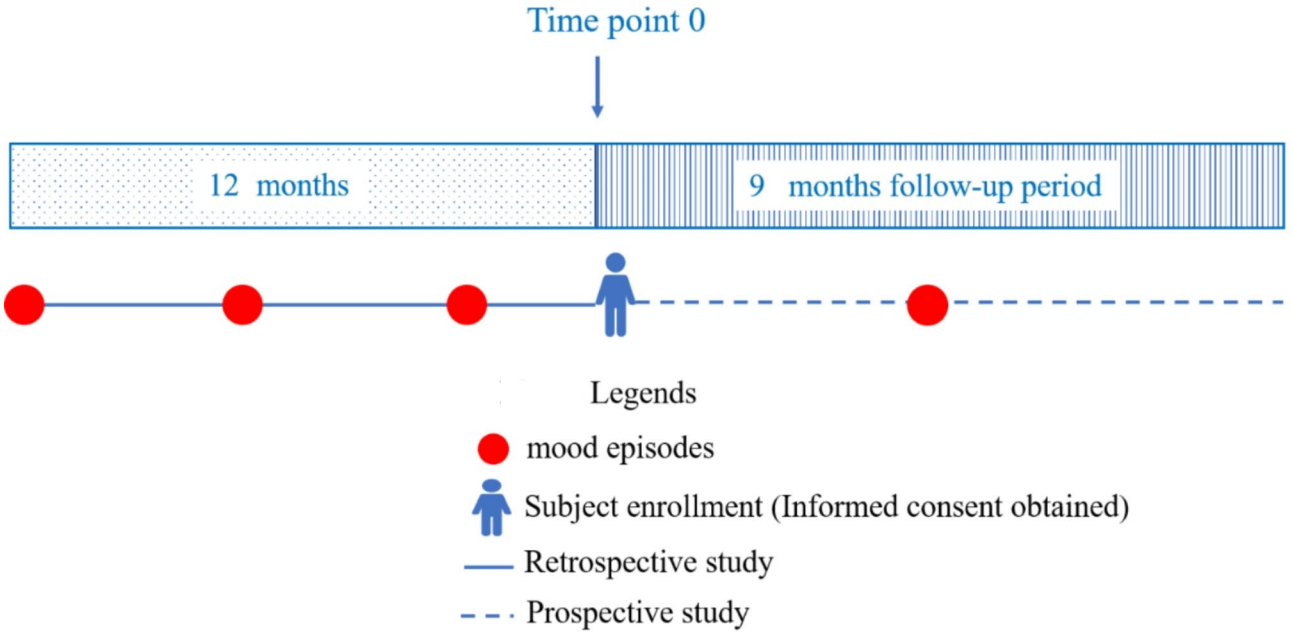

Fig. 1 Study design and procedure

criteria. Family history of mental disorders was defined as a diagnosis of mental illness in first-degree relatives (parents, children, and siblings) or second-degree relatives (grandparents, uncles, aunts, and cousins).

Statistical analysis

Data analysis was conducted using SAS 9.4 statistical software. Categorical data were presented as counts and percentages, while continuous variables were expressed as mean ± standard deviation (mean ± SD). The full analysis set (FAS), comprising patients who met the inclusion criteria, did not meet any exclusion criteria, and had at least retrospective data available, was analyzed using Poisson regression modeling to identify factors associated with the frequency of depressive or manic episodes. The following variables were analyzed: age, gender, years of education, comorbid substance use disorder, living alone, BD type, family history of mental disorders, comorbid anxiety disorders, occupational status, polarity of the first episode, age at onset, age at first BD diagnosis, presence of psychotic symptoms, and use of medications. Polarity of the first episode (mania/mixed/depression) was treated as a categorical variable and analyzed using dummy coding to avoid multicollinearity. Multicollinearity was further assessed for all variables, with variance inflation factor (VIF) values consistently below 10, indicating no significant multicollinearity. All statistical tests were two-tailed with a significance level set at $P<0.05$.

Results

Sociodemographic and clinical characterizations

A total of 555 patients were screened for this study, of which 35 did not pass the screening process, resulting in 520 patients being included. Among these, 398 patients had BD-I and 122 had BD-II, with 48.46% being male and 51.54% female. The mean age of the patients was 35.65 ± 13.23 years, and the average years of education was 13.10 ± 3.40 years. The mean age at first onset was 30.39 ± 12.21 years, and the mean age at diagnosis was 32.28 ± 12.46 years. The first episode polarity was mania in 33.08%, hypomania in 3.65%, depression in 59.04%, and mixed in 4.23%. Additionally, 41.73% of the patients experienced psychotic symptoms since onset. Detailed information is provided in Table 1.

Types of mood episodes and medications

During the retrospective and prospective follow-up periods, there are a total of 1258 mood episodes, including 383 manic episodes, accounting for 30.45% of all episodes, 187 hypomanic episodes (14.86% of the total), 579 depressive episodes (46.02% of the total), and 109 mixed episodes (8.67% of the total). Medication usage during manic episodes was 68.33%, with 65.84% using traditional mood stabilizers, 66.90% using antipsychotics, 6.05% using antidepressants, 12.10% using anxiolytics, and 6.76% using other medications. During depressive episodes, medication usage was 69.09%, with 62.63% using traditional mood stabilizers, 54.84% using antipsychotics, 49.19% using antidepressants, 19.09% using anxiolytics, and 5.65% using other medications. Detailed information is provided in Tables 2 and 3.

Table 1 Sociodemographic and clinical characteristics of BD-I and BD-II disorders

Variable	BD-I and BD-II *N* (%)	BD-I *N* (%)	BD-II *N* (%)
Sample size	520(100.00)	398(76.54)	122(23.46)
Gender			
male	252(48.46)	197(49.50)	55(45.08)
female	268(51.54)	201(50.50)	67(54.92)
Age (Mean ± SD)	35.65 ± 13.23	35.23 ± 13.08	37.05 ± 13.67
Years of education (Mean ± SD)	13.10 ± 3.40	13.20 ± 3.21	12.76 ± 3.96
Occupational status			
Full-time employment	221(42.50)	166(41.71)	55(45.08)
Part-time employment	69(13.27)	57(14.32)	12(9.84)
Unemployed	230(44.23)	175(43.97)	55(45.08)
Residency status			
Living alone	42(8.08)	31(7.79)	11(9.02)
Co-residence	478(91.92)	367(92.21)	111(90.98)
Current substance use disorder			
Yes	36(6.92)	30(7.54)	6(4.92)
Types of Substance use disorder			
Alcohol	10(1.92)	10(2.51)	0(0.00)
Nicotine	27(5.19)	23(5.78)	4(3.28)
Opioids	1(0.19)	1(0.25)	0(0.00)
Benzodiazepines	2(0.38)	1(0.25)	1(0.82)
Others	2(0.38)	1(0.25)	1(0.82)
Family history of mental disorder			
Yes	151(29.04)	110(27.64)	41(33.61)
Affective disorders	75(14.42)	51(12.81)	24(19.67)
Schizophrenia spectrum disorders	30(5.77)	25(6.28)	5(4.10)
Other mental disorders	62(11.92)	48(12.06)	14(11.48)
Polarity of the first mood episode			
Manic	172(33.08)	172(43.21)	0(0.00)
Hypomanic	19(3.65)	7(1.76)	12(9.84)
Depression	307(59.04)	197(49.50)	110(90.16)
Mixed	22(4.23)	22(5.53)	0(0.00)
Age at diagnosis of BD (Mean ± SD)	32.28 ± 12.46	31.41 ± 12.07	35.13 ± 13.29
Age of onset (Mean ± SD)	30.39 ± 12.21	29.77 ± 11.76	32.41 ± 13.41
Any psychotic symptoms			
Yes	217(41.73)	199(50.00)	18(14.75)

Note: BD-I refers to Bipolar I Disorder and BD-II refers to Bipolar II Disorder. Data are presented as N (%) or Mean ± SD (Standard Deviation). Affective disorders include mood disorder and anxiety disorder

Table 2 Analysis of bipolar disorder episode types

Episode Type	BD-I and BD-II		BD-I		BD-II	
	N	%	*N*	%	*N*	%
Total episodes	1258	100.00	967	100.00	291	100.00
Manic episodes	383	30.45	383	39.61	-	-
Hypomanic episodes	187	14.86	103	10.65	84	28.47
Depressive episodes	579	46.02	372	38.47	207	70.17
Mixed episodes	109	8.67	109	11.27	-	--

Note: BD-I refers to Bipolar I Disorder and BD-II refers to Bipolar II Disorder. Data are presented as N (%)

Factors associated with the number of manic episodes

Poisson regression model analysis identified several factors significantly associated with the number of manic episodes. Positive correlations were found for shorter years of education (OR = 1.03, $P = 0.03$), mixed polarity of the first episode compared to mania (OR = 2.33, $P < 0.01$) or depression (OR = 1.79, $P = 0.01$), earlier age at diagnosis (OR = 1.03, $P = 0.01$), comorbid substance use disorder (OR = 1.41, $P = 0.02$), presence of psychotic symptoms (OR = 1.18, $P = 0.04$), use of antidepressant medication

Table 3 Medication treatment for manic or depressive episodes in bipolar disorder

Medication type	BD-I and BD-II		BD-I		BD-II	
Manic episode medication	***N***	**%**	***N***	**%**	***N***	**%**
Total	192	68.33	191	68.21	1	100.00
Mood stabilizers	185	65.84	184	65.71	1	100.00
Antipsychotics	188	66.90	187	66.79	1	100.00
Antidepressants	17	6.05	17	6.07	0	0.00
Anxiolytics	34	12.10	34	12.14	0	0.00
Others	19	6.76	18	6.43	1	100.0
Depressive episode medication	**N**	**%**	**N**	**%**	**N**	**%**
Total	257	69.09	150	59.29	107	89.92
Mood stabilizers	233	62.63	137	54.15	96	80.67
Antipsychotics	204	54.84	127	50.20	77	64.71
Antidepressants	183	49.19	95	37.55	88	73.95
Anxiolytics	71	19.09	34	13.44	37	31.09
Others	21	5.65	14	5.53	7	5.88

Note: BD-I refers to Bipolar I Disorder and BD-II refers to Bipolar II Disorder. Data are presented as N (%)

Table 4 Factors associated with the number of manic episodes (Poisson regression model)

Variable	Wald Z statistic	*P*-value	OR	95%CIL	95%CIU
Age (≥65/<65)	0.01	0.90	0.96	0.51	1.98
Gender (female/male)	0.64	0.42	1.07	0.91	1.25
Years of education (short/long)	4.54	**0.03**	1.03	1.06	1.00
Comorbid substance use disorder (yes/no)	5.84	**0.02**	1.41	1.06	1.84
Residency status (living alone/co-residence)	0.21	0.65	1.08	0.79	1.51
Family history of mental disorder (yes/no)	0.50	0.48	0.94	0.78	1.12
Comorbid anxiety disorders (yes/no)	0.74	0.39	1.14	0.84	1.51
Occupational status (unemployed/employed)	0.31	0.58	1.05	0.89	1.24
First episode polarity (mixed/mania)	12.75	**< 0.01**	2.33	3.85	1.52
First episode polarity (hypomania/mixed)	0.29	0.59	1.31	0.52	3.90
First episode polarity (mixed/depression)	6.06	**0.01**	1.79	2.94	1.16
Age at onset (old/young)	3.49	0.06	1.02	1.00	1.05
Age at first BD diagnosis (young/old)	6.08	**0.01**	1.03	1.05	1.01
Presence of psychotic symptoms (yes/no)	4.16	**0.04**	1.18	1.01	1.39
Use of antipsychotics (no/yes)	1.26	0.26	0.83	0.59	1.14
Use of antidepressants(yes/no)	5.99	**0.01**	1.52	2.17	1.10
Use of mood stabilizers(no/yes)	20.37	**< 0.01**	1.57	1.30	1.92

Note: BD-I refers to Bipolar I Disorder, BD-II refers to Bipolar II Disorder, OR refers to odds ratio. The number of manic episodes includes both retrospective (past 12 months) and prospective (9-month follow-up) counts. 95%CIL and 95%CIU represent the lower and upper limits of the 95% confidence interval, respectively

(OR = 1.52, $P = 0.01$), and non-use of mood stabilizers (OR = 1.57, $P<0.01$). Detailed information is provided in Table 4.

Factors associated with the number of depressive episodes

The Poisson regression model analysis revealed that being male (OR = 1.22, $P = 0.01$), the use of mood stabilizers (OR = 1.47, $P<0.01$) and a diagnosis of BD-II compared to BD-I (OR = 1.27, $P = 0.01$) were significantly positively associated with the number of depressive episodes. Detailed information is provided in Table 5.

Discussion

The hospitalization rate for patients with BD is significantly higher than those with other conditions, thus it is crucial to investigate the factors associated with mood episodes. This study identified several factors associated with the frequency of manic and depressive episodes in BD. Key findings include shorter years of education, mixed first episode polarity, earlier age of diagnosis, comorbid substance use disorder, presence of psychotic symptoms, use of antidepressants, and non-use of mood stabilizers being positively associated with the number of manic episodes. Meanwhile, being male, using mood stabilizers and a diagnosis of BD-II were positively associated with the number of depressive episodes.

Table 5 Factors associated with the number of depressive episodes (Poisson regression model)

Variable	Wald Z statistic	*P*-value	OR	95%CIL	95%CIU
Age (≥ 65/<65)	0.92	0.34	0.80	0.51	1.29
Gender (male/female)	6.67	**0.01**	1.22	1.43	1.05
Years of education (long/short)	0.00	0.94	1.00	0.98	1.02
Comorbid substance use disorder (yes/no)	0.10	0.75	0.95	0.68	1.29
Residency status (living alone/co-residence)	1.85	0.17	0.84	0.65	1.09
BD type (II/I)	6.26	**0.01**	1.27	1.05	1.52
Family history of mental disorder (yes/no)	1.91	0.17	1.12	0.95	1.32
Comorbid anxiety disorders (yes/no)	0.29	0.59	0.92	0.68	1.22
Occupational status (unemployed/employed)	1.00	0.32	1.09	0.92	1.28
First episode polarity (mania/mixed)	1.63	0.20	1.34	0.83	2.06
First episode polarity (hypomania/mixed)	0.00	0.96	1.01	0.56	1.83
First episode polarity (depression/mixed)	1.19	0.28	0.79	0.49	1.18
Age at onset (old/young)	0.24	0.62	1.00	0.99	1.02
Age at first BD diagnosis (old/young)	0.74	0.39	0.99	0.97	1.01
Presence of psychotic symptoms(yes/no)	0.17	0.68	0.96	0.80	1.15
Use of antipsychotics(no/yes)	0.82	0.37	1.12	0.87	1.43
Use of antidepressants(no/yes)	0.15	0.70	1.04	0.85	1.27
Use of mood stabilizers(yes/no)	18.41	**< 0.01**	1.47	1.72	1.23

Note: BD-I refers to Bipolar I Disorder, BD-II refers to Bipolar II Disorder, OR refers to odds ratio. The number of depressive episodes includes both retrospective (past 12 months) and prospective (9-month follow-up) counts. 95%CIL and 95%CIU represent the lower and upper limits of the 95% confidence interval, respectively

The relationship between shorter years of education and increased manic episodes is consistent with previous research. For example, Ramsey et al. found that lower education levels were a risk factor for frequent manic episodes and higher all-cause mortality rates in these patients [14].

This study found that patients whose first episode polarity was mixed had more manic episodes than those whose first episode was either mania or depression. While there is no direct evidence from previous studies to support this finding, related studies by Kim et al. [15] and Sentissi et al. [16] have shown that patients with mixed episodes are more likely to have a family history of psychosis, comorbid personality disorders, and a history of suicide attempts, as well as exhibiting rapid cycling and a high relapse rate.

The positive correlation between the number of manic episodes and earlier age at diagnosis has been corroborated by Ortiz et al., who found that patients with an earlier age at first episode often presented more frequently with psychotic symptoms, mixed episodes, and greater illness severity [17]. Soni et al. also noted that patients diagnosed at an earlier age had significantly more manic episodes and a higher likelihood of a family history of BD [18].

The association between comorbid substance use disorder and the presence of psychotic symptoms in manic episodes has been well-documented. Leonardo et al. found that patients with psychotic symptoms experienced more frequent manic episodes [19]. Studies have noted that up to 60% of BD patients may experience psychotic symptoms during their lifetime, particularly during mania, and the presence of psychotic symptoms complicates the course of BD, often leading to longer hospitalizations and more frequent manic episodes [20–22]. These episodes tend to be more severe, with lower likelihoods of clinical remission and greater mood instability. Psychotic symptoms are often associated with agitation, anxiety, and aggressive behaviors, which can increase the frequency of episodes and even lead to lifelong mood instability [23].

In our study, we examined the comorbidities of BD-I and BD-II patients and found that the prevalence of comorbid substance use disorder is high, especially in BD-I, where it can be as high as 40% [6]. Substance abuse, such as stimulants, can trigger manic episodes, and severe mania can also lead to substance abuse [24]. Gold et al. found that BD patients with comorbid substance use disorder had higher Young Mania Rating Scale (YMRS) scores and more frequent manic episodes, and this comorbidity leads to a more complex disease course, lower remission rates, and more frequent mood episodes [25]. Patients with BD and substance use disorder share temperamental characteristics such as irritability, hyperarousal, circumscribed mindfulness, and alexithymia, which increase difficulty in managing emotional states and may lead to more frequent and severe mood episodes [24, 26].

Academic conclusions regarding the effect of antidepressants on the number of manic episodes are not uniform. Clinical experience and previous studies generally agree that antidepressants may increase mood instability in BD patients [27]. The results of our study are consistent with this view, supported by Schneck et al.'s large

prospective study, which showed that BD-I or BD-II patients taking antidepressants were 3.8 times more likely to experience rapid cycling [28]. The study by M. Fornaro further confirmed that prior use of antidepressants before admission was associated with prolonged hospitalization, which in turn predicted greater illness severity and increased treatment challenges [29]. Despite the higher risk of switching to mania, antidepressants continue to be used clinically due to the significantly longer duration of depressive episodes in BD [19]. Keita et al.'s follow-up study found no significant association between antidepressant use and the incidence of mania or hypomania over a year [30]. Additionally, the Canadian Network for Mood and Anxiety Treatment (CANMAT) guidelines recommend antidepressant monotherapy as a third-line treatment for BD-II depression [31]. Given the mixed evidence, antidepressant use should be evaluated on a case-by-case basis.

Being male was found to be positively associated with the number of depressive episodes. This finding contradicts Massimiliano et al.'s study, which found a positive correlation between females and the number of lifetime depressive episodes [32]. Differences in results may be due to variations in sample populations, study design, and methodology. Overall, research on gender differences in bipolar depressive episodes is inconclusive, necessitating further studies to provide precise treatment guidelines.

Although mood stabilizers are widely regarded as effective in preventing both depressive and manic episodes in patients with BD [33, 34], our study revealed a significant positive correlation between the use of mood stabilizers and the number of depressive episodes. This finding contradicts conventional clinical wisdom and may be attributed to several factors: Firstly, the study sample might include unique subgroups of patients who exhibit a different response to mood stabilizers compared to the general population. These subgroups may have distinct genetic backgrounds or comorbid conditions that diminish the efficacy of mood stabilizers in preventing depressive episodes. Secondly, issues with medication adherence among some patients could lead to subtherapeutic levels of mood stabilizers, thereby reducing their effectiveness. Poor adherence to prescribed medication regimens is a well-documented challenge in the management of bipolar disorder and could explain the observed discrepancy [35, 36].

Limitations

Although this study is a multicenter study and has a large sample size, there are some limitations. First, the study combined retrospective and prospective data to analyze factors associated with mood episodes, allowing for an extended observation period. However, retrospective data are inherently subject to recall bias, which may compromise accuracy. Moreover, the inclusion of retrospective data limits the ability to establish temporal relationships between variables, thereby restricting causal inferences. Additionally, prior mood episodes may influence clinical characteristics such as comorbidities and medication choices, potentially affecting result interpretation. Second, structured diagnostic tools were not employed in this study, which may have affected diagnostic accuracy. Future research should utilize standardized diagnostic interviews, such as the Mini-International Neuropsychiatric Interview (MINI) [37]or the Structured Clinical Interview for DSM Disorders (SCID) [38], to enhance diagnostic consistency and rigor. Third, the DSM-5 has replaced "mixed episodes" with the specifier "mixed features," applicable to both manic and depressive episodes. Consequently, studies based on DSM-IV criteria may be considered outdated, potentially limiting the relevance of the findings in the context of current diagnostic frameworks. Fourth, the metrics included in this study were not comprehensive. Key factors, such as electroconvulsive therapy (ECT) use and medication adherence, were not assessed, which may have limited the scope of the analysis. Finally, the 9-month prospective observation period may inadequately capture neurobiological trajectories associated with illness chronicity, such as kindling-mediated sensitization to recurrence. Future decade-scale cohort studies encompassing broader developmental phases of bipolar disorder are warranted to validate the generalizability of these episode dynamics.

Conclusion

The study highlights the critical association of clinical and sociodemographic factors with the frequency of manic and depressive episodes in BD patients. Key findings include the positive association of shorter educational attainment, mixed first episode polarity, earlier diagnosis, comorbid substance use disorder, psychotic symptoms, antidepressant use, and non-use of mood stabilizers with manic episodes. In contrast, being male and mood stabilizer use were linked to more depressive episodes. Future research should explore these factors in greater depth to optimize treatment options and enhance patients' quality of life.

Abbreviations

BD	Bipolar disorder
BD-I	Bipolar I disorder
BD-II	Bipolar II disorder
PP	Predominant polarity
DSM-IV	The diagnostic and statistical manual of mental disorders, fourth edition
mean ± SD	Mean ± standard deviation
CRF	Case report form
FAS	The full analysis set
VIF	Variance inflation factor
OR	Odds ratio

95%CIL	Lower limits of the 95% confidence interval
95%CIU	Upper limits of the 95% confidence interval
ECT	Electroconvulsive therapy
CANMAT	The Canadian network for mood and anxiety treatment
YMRS	Young mania rating scale
MINI	Mini-international neuropsychiatric interview
SCID	Structured clinical interview for DSM disorders

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Author contributions
Ling Zhang designed the study. Jin-jie Xu conducted a literature review and interpreted the results. Jin-jie Xu, Shuang Liu prepared the manuscript. Xue-quan Zhu analyzed and interpreted the data. Ling Zhang, Bing-bing Fu, Yan-li Pan, Cong-cong Sun, Sheng Li, Gao-ming Xie edited the manuscript. All authors reviewed the manuscript.

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Data availability
The data that support the findings of this study are available from the corresponding author, upon reasonable request.

Declarations

Ethics approval and consent to participate
The experimental protocol was established, according to the ethical guidelines of the Helsinki Declaration and was approved by the Institutional Review Board (IRB) of Beijing Anding Hospital affiliated with Capital Medical University (Approval No.: 2013 Clinical Review No. 1) and was registered at chictr.org.cn (identifier: NCT01770704, date of registration: first posted on January 18, 2013).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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