Original Article

Prevalence and Clinical Features Associated with Unrecognized Bipolar Disorder among Outpatients with Depressive Disorder in Thailand

Aree Hinphet MD[1], Fasinee Arunrodpanya MD[1], Janpen Kwansirikul MD[1], Sukanya Rakkhajeekul MD[2], Piraya Rajsanthia MD[3]

[1] Department of Psychiatry, Faculty of Medicine, Naresuan University, Phitsanulok, Thailand

[2] Division of Psychiatry, Buddhachinaraj Phitsanulok Hospital, Phitsanulok, Thailand

[3] Division of Psychiatry, Phichit Hospital, Thailand, Pichit, Thailand

Objective: To determine the prevalence of unrecognized bipolar disorder and explore the clinical features of outpatients with depressive disorder associated with bipolar disorder.

Materials and Methods: The present study was a cross-sectional study. One hundred six volunteer participants, diagnosed with depressive disorder at Naresuan University Hospital, Buddhachinaraj Phitsanulok Hospital, and Phichit Hospital participated in this study. Psychiatrists interviewed the participants to collect basic data and clinical characteristics to determine unrecognized bipolar disorder using the Thai version of the Mini International Neuropsychiatric Interview (MINI).

Results: The results showed that the prevalence of unrecognized bipolar disorder was 18.9%. When multivariable logistic regression was used, it was found that there were two statistically significant factors associated with unrecognized bipolar disorder. These factors were a history of self-harm or suicide attempts (AOR 4.40, 95% CI 1.24 to 15.60), and atypical depression seen with overeating and hypersomnia (AOR 11.73, 95% CI 2.32 to 59.35).

Conclusion: There are several misdiagnoses of patients with bipolar disorder because the patients are usually in a depressive state when they decide to consult a doctor. Therefore, doctors should further probe especially in patients with atypical depression, history of self-harm or attempted suicide.

Keywords: Bipolar depression; Bipolar disorder; Diagnosis; Epidemiology; Prevalence

Received 29 June 2021 | Revised 6 October 2021 | Accepted 6 October 2021

J Med Assoc Thai 2021;104(11):1821-7

Website: http://www.jmatonline.com

Bipolar disorder is a disease that affects the quality of life of the patients and their families. The World Health Organization (WHO) stated that it is one of the world's leading causes of disability[1,2]. Furthermore, patients with bipolar disorder have a suicide rate of 10% to 30% compared to the general population rate[3]. Moreover, patients with an early onset of bipolar disorder may have a poor prognosis[4]. However, 10% to 22% of patients with bipolar disorder are often misdiagnosed as unipolar depression, resulting in the delay of treatment[4-6]. Although antidepressants have a good therapeutic effect in treating unipolar depression, they are ineffective and could induce mania or hypomania when used in patients with bipolar disorder[7].

Approximately 67% of the patients diagnosed with bipolar disorder had depressive episodes as the first onset of the disease, notably in bipolar II disorder[8]. Most of the patients seek medical attention during depressive episodes wherein they only recognize symptoms of depression but not mania and hypomania[9]. A previous study showed that 46.4% of the patients with major depressive episodes had seen their doctors for more than four years from their first consultation before being diagnosed with bipolar disorder[10]. As a result, many patients with bipolar disorder were not appropriately given proper treatment due to a misdiagnosis, which is usually unipolar depression or major depressive disorder.

Correspondence to:

Hinphet A.

Department of Psychiatry, Faculty of Medicine, Naresuan University, Phitsanulok, 65000, Thailand.

Phone: +66-55-9655312

Email: areeh@nu.ac.th

How to cite this article:

Hinphet A, Arunrodpanya F, Kwansirikul J, Rakkhajeekul S, Rajsanthia P. Prevalence and Clinical Features Associated with Unrecognized Bipolar Disorder among Outpatients with Depressive Disorder in Thailand. J Med Assoc Thai 2021;104:1821-7.

doi.org/10.35755/jmedassocthai.2021.11.13102

In Thailand, the scope of unrecognized bipolar disorder patients has not been studied. The Mini International Neuropsychiatric Interview (MINI) is a structured questionnaire created according to the criteria set by the American Psychiatric Association and the WHO to assess psychiatric disorders particularly highlighting manic or hypomanic episodes throughout the patient's life. It was developed by psychiatrists and medical groups in America and Europe[11] and was translated into many languages including Thai. In a study conducted in 2007 using the Thai version of the MINI, it was revealed that the diagnostic set of manic or hypomanic episode, lifetime and present, had high consistency, reliability, and validity (kappa 0.78, sensitivity 0.89, specificity 0.94, positive predictive value 0.78, negative predictive value 0.97)[12].

The primary aim of the current study was to determine the prevalence of unrecognized bipolar disorder utilizing the MINI as the standard tool used by psychiatrists in diagnosing patients with previous diagnosis of depressive disorders such as major depressive disorder, adjustment disorder with depressed mood, adjustment disorder with mixed anxiety and depressed mood, dysthymia, and postpartum depression. The secondary aim was to explore characteristics and other factors associated with unrecognized bipolar disorder.

Materials and Methods

Participants

In the present cross-sectional study, the participants were patients aged 20 to 60 years old, diagnosed with a major depressive disorder, adjustment disorder with depressed mood, adjustment disorder with mixed anxiety and depressed mood, dysthymia, and postpartum depression that visited the outpatient psychiatric department of Naresuan University Hospital, Buddhachinaraj Phitsanulok Hospital, and Phichit Hospital between June 1, 2019 and January 18, 2021. Based on ICD-10 and DSM-V diagnoses, the patients had good awareness and could read, write, and respond in Thai. In contrast, the authors excluded patients diagnosed with bipolar disorder, schizophrenia, schizoaffective disorder, neurodevelopmental disorders such as intellectual disabilities, autism spectrum disorder, and ADHD, neurocognitive disorders including delirium and dementia, stroke, traumatic brain injury, patients with a mood stabilizer such as antiepileptic drugs and lithium, patients with antipsychotic prescriptions, patients with a psychiatric emergency requiring urgent treatment, patients with psychoses, and patients that have used drugs or stopped using drugs in less than one month.

The sample size was calculated using the population proportion formula: $n = z^2_{1-\alpha/2}\, p(1-p)/d^2$[13] recognizing the 50% prevalence of bipolar disorder in patients with depression from a previous study[14], a 95% confidence interval (CI), and a 10% precision error. Ninety-seven participants were required in the study; thus, an additional 8% was added to account for the missing data. Participants who met the inclusion requirements were enrolled using the convenience sampling procedure, yielding 106 participants for analyses.

Instrument and procedure

All procedures in the present study were approved by the Naresuan University Institutional Review Board (IRB No. 0165/62) and the Research Ethics Committees of Buddhachinaraj Phitsanulok Hospital and Phichit Hospital and followed the Ethical Principles for Medical Research Involving Human Subjects (Declaration of Helsinki). Patients signed the informed consent before participating in the study.

Psychiatrists gathered the sociodemographic information and clinical symptoms from all participants. Using the Thai version of MINI[12], the participants were interviewed to assess the past and current episodes hypomania or mania.

Data analysis

Data were analyzed using the Stata, version 12.0 (StataCorp LP, College Station, TX, USA). Preliminary data were analyzed using descriptive statistics as frequency, percentage, mean, and standard deviation to describe the characteristics of the samples. Chi-square test (χ^2)/Fisher's exact test was used to compare differences between groups. The p-values of less than 0.05 were considered statistically significant.

Univariable logistic regression was employed and followed by multivariable logistic regression to find the associations between the various factors and those who were diagnosed with bipolar disorder. To analyze with multivariable logistic regression, the criteria for selecting variables from univariable logistic regression that had a p-value of less than or equal to 0.2 was utilized. Odds ratios (OR), adjusted odds ratio (AOR), and 95% CI were reported from the logistic regression models. The p-values of less than 0.05 were considered statistically significant.

Definition

Unrecognized bipolar disorder was determined after the participants diagnosed with depressive disorder such as major depressive disorder, adjustment disorder with depressed mood, adjustment disorder with mixed anxiety and depressed mood, dysthymia, and postpartum depression, were interviewed using the Thai version of MINI with positive results of either hypomanic or manic episodes. These participants have never been diagnosed with bipolar disorder.

Results

The present study enrolled 116 patients, but 10 were excluded due to antipsychotics or mood stabilizers prescription. From the 106 patients interviewed using the Thai version of MINI, unrecognized bipolar disorder was found in 18.9% (95% CI 11.9 to 27.6), hypomanic episode in 14.1%, and manic episode in 5.7%, as shown in Table 1.

Twenty of the 106 patients met the criteria for unrecognized bipolar disorder, with most of them being females (75.0%), between 20 and 29 years old (60.0%), single (65.0%), bachelor's degree holder (60.0%), and being students (55.0%). Whereas, eighty-six patients had no unrecognized bipolar disorder, with females (87.2%) comprising the majority. Other demographic characteristics for this group included age ranging from 20 to 29 years old (61.6%), single (61.6%), holders of bachelor's degree (62.7%), and being students (44.2%). Although the results revealed similarities in characteristics, no statistical differences could be inferred between the groups with and without unrecognized bipolar disorder, as shown in Table 2.

The results of the clinical data of unrecognized bipolar disorder revealed that the patients' age of onset ranged from 20 to 29 years old (45.0%), and duration of illness was less than five years (65.0%), with only one recorded episode of depression (65.0%). A history of self-harm or suicide attempts (70.0%) was also reported, with most attempts occurring five times or more (35.0%). Additionally, physical comorbidities (25.0%) particularly thyroid disease (10.0%), family history of psychiatric disorders (55.0%), treatment resistant depression (5.0%), and an atypical depression (35.0%) were also documented.

Patients without unrecognized bipolar disorder were found to be between the ages of 20 and 29 years old (34.9%). Most of them had been ill for less than five years (57.0%) with one recorded episode of depression (79.1%). A history of self-harm or suicide attempts (39.5%) with one or two attempts was also reported (20.9%). Physical comorbidities (33.7%) especially allergies (9.3%), family history of psychiatric disorders (33.7%), treatment resistant depression (4.6%), and an atypical depression (4.6%) were revealed in the present study.

Table 1. Prevalence of unrecognized bipolar disorder

Diagnosis	Total (n=106); n (%)	
	Yes	No
Unrecognized bipolar disorder	20 (18.9)	86 (81.1)
Hypomanic episode	15 (14.1)	-
Current	3 (2.8)	-
Past	12 (11.3)	-
Manic episode	6 (5.7)	-
Current	2 (1.9)	-
Past	4 (3.8)	-

One participant had hypomanic episode and currently has manic episode.

Analyses of the clinical data of both groups, with and without unrecognized bipolar disorder, showed a significant difference in terms of history of self-harm or suicide attempts, and atypical depression, as shown in Table 3.

Following a univariable logistic regression analysis to assess the association of the characteristics of unrecognized bipolar disorder with the variables, with p-value less than or equal to 0.2, two factors were found to be significantly correlated to unrecognized bipolar disorder with p-value less than 0.05, namely a history of self-harm or suicide attempts (OR 3.57, 95% CI 1.25 to 10.19), and atypical depression (OR 11.04, 95% CI 2.83 to 43.04), as shown in Table 4.

Subsequently, a multivariable logistic regression analysis was performed. Two factors were found to be significantly associated with unrecognized bipolar disorder with p-value of less than 0.05, namely 1) self-harm or suicide attempts (AOR 4.40, 95% CI 1.24 to 15.60), and 2) atypical depression (AOR 11.73, 95% CI 2.32 to 59.35), as shown in Table 4.

Discussion

More than 50% of patients with bipolar disorder are often misdiagnosed on initial presentation, typically at the onset of depressive episodes[8]. The present study showed 18.9% (95% CI 11.9 to 27.6) prevalence of unrecognized bipolar disorder, which is consistent with the findings of previous studies[4-6,15]. Most of the symptoms as revealed in the present research include hypomanic episodes (14.1%) and were the ones that often happened in the past (11.3%).

Table 2. Sociodemographic data

Variables	Unrecognized bipolar disorder (n=20); n (%)	No (n=86); n (%)	F or χ^2	p-value
Sex			1.89	0.170[a]
Male	5 (25.0)	11 (12.8)		
Female	15 (75.0)	75 (87.2)		
Current age (year)			6.46	0.091[a]
20 to 29	12 (60.0)	53 (61.6)		
30 to 39	4 (20.0)	6 (7.0)		
40 to 49	3 (15.0)	7 (8.1)		
50 and over	1 (5.0)	20 (23.3)		
Mean±SD	29.35±10.23	32.99±13.67		
Current status			2.28	0.319[a]
Single	13 (65.0)	53 (61.6)		
Married	6 (30.0)	18 (20.9)		
Divorced/widowed/separated	1 (5.0)	15 (17.5)		
Education level			6.42	0.318[b]
Uneducated	0 (0.0)	1 (1.2)		
Primary education	1 (5.0)	11 (12.8)		
Secondary education	0 (0.0)	1 (1.2)		
High school/vocational certificate	1 (5.0)	10 (11.6)		
Bachelor's degree	12 (60.0)	54 (62.7)		
Postgraduate	6 (30.0)	9 (10.5)		
Current occupation			5.87	0.421[b]
Unemployed	2 (10.0)	7 (8.1)		
Government service/state enterprise	4 (20.0)	11 (12.8)		
Agriculture	0 (0.0)	1 (1.2)		
Trade	0 (0.0)	9 (10.5)		
Hiring workers	0 (0.0)	10 (11.6)		
Student	11 (55.0)	38 (44.2)		
Others	3 (15.0)	10 (11.6)		

[a] Chi-square test, [b] Fisher's exact test, * p<0.05

When the factors correlated with unrecognized bipolar disorder were analyzed, two of them were found to be statistically significant (p-value less than 0.05), namely 1) atypical depression (AOR 11.73, 95% CI 2.32 to 59.35), and 2) history of self-harm or suicide attempts (AOR 4.40, 95% CI 1.24 to 15.60). The present study shows that the symptoms of atypical depression as overeating and hypersomnia[16,17] are consistent with the results of the other studies[18,19]. Meanwhile, the history of self-harm or suicide attempts identified in the present study coincides with the findings of the other research[4,10,20], which support the notion that a delay in diagnosing bipolar disorder increases the risk of suicide[21]. As a result, increasing awareness of bipolar disorder would help physician to understand and recognize all preliminary indicators of the condition, allowing patients to obtain accurate diagnosis and care as soon as possible, and subsequently minimizing or eliminating the risk of suicide.

The factor of family history of psychiatric disorder provides interesting data because it identifies the nature of the disease. The result of the previous research has shown that having a family history of bipolar disorder is linked to an increased risk of developing the disease[22,23], which contradicts the findings of the present study. The families of the participants in the present study have no reported cases of bipolar disorder but have history of psychiatric disorders with unknown diagnoses.

Other factors in the present study that contradicted the previous findings include early age at onset of

Table 3. Characteristics of clinical symptoms

Variables	Unrecognized bipolar disorder (n=20); n (%)	No (n=86); n (%)	F or χ^2	p-value
Age of onset of the symptom (year)			1.19	0.756[a]
10 to 19	6 (30.0)	28 (32.6)		
20 to 29	9 (45.0)	30 (34.9)		
30 to 39	2 (10.0)	7 (8.1)		
40 and over	3 (15.0)	21 (24.4)		
Mean±SD	25.25±9.66	27.60±12.86		
Duration of illness (year)			2.50	0.678[a]
Less than 5 years	13 (65.0)	49 (57.0)		
5 years and over	7 (35.0)	37 (43.0)		
The number of episode of depression			1.78	0.410[a]
1	13 (65.0)	68 (79.1)		
2 to 4	5 (25.0)	13 (15.1)		
5 and over	2 (10.0)	5 (5.8)		
History of self-harm/suicide			6.08	0.014[a]*
No	6 (30.0)	52 (60.5)		
Yes	14 (70.0)	34 (39.5)		
Number of self-harm/suicide				
1 to 2	3 (15.0)	18 (20.9)		
3 to 4	4 (20.0)	7 (8.1)		
5 and over	7 (35.0)	9 (10.5)		
Physical comorbidities			0.57	0.452[a]
No	15 (75.0)	57 (66.3)		
Yes	5 (25.0)	29 (33.7)		
• Diabetes	1 (5.0)	1 (1.2)	1.29	0.256[a]
• Hypertension	1 (5.0)	3 (3.5)	0.10	0.749[a]
• Dyslipidemia	0 (0.0)	3 (3.5)	0.72	0.530[b]
• Migraine	0 (0.0)	4 (4.7)	0.97	0.427[b]
• Asthma	0 (0.0)	2 (2.3)	0.47	0.657[b]
• Allergy	1 (5.0)	8 (9.3)	0.39	0.534[a]
• Thyroid disease	2 (10.0)	2 (2.3)	2.63	0.105[a]
• Others	0 (0.0)	9 (10.5)	2.29	0.140[b]
Family history of psychiatric disorders			3.13	0.077[a]
No	9 (45.0)	57 (66.3)		
Yes	11 (55.0)	29 (33.7)		
• Unknown diagnosis	6 (30.0)	4 (4.6)	12.20	<0.001[a]*
• Psychotic disorders	2 (10.0)	3 (3.5)	1.53	0.216[a]
• Depressive disorder	3 (15.0)	14 (16.3)	0.02	0.888[a]
• ADHD	0 (0.0)	3 (3.5)	0.72	0.530[b]
• Others	0 (0.0)	5 (5.8)	1.22	0.344[b]
Treatment resistant depression (not responding to at least three antidepressants)			0.01	0.947[a]
No	19 (95.0)	82 (95.4)		
Yes	1 (5.0)	4 (4.6)		
Atypical depression (overeating and hypersomnia)			16.07	<0.001[a]*
No	13 (65.0)	82 (95.4)		
Yes	7 (35.0)	4 (4.6)		

[a] Chi-square, [b] Fisher's exact test, * p<0.05

Table 4. Factors associated with unrecognized bipolar disorder (univariable and multivariable logistic regression)

Factors	Unrecognized bipolar disorder	
	OR (95% CI)	AOR (95% CI)
Sex		
Male	2.27 (0.69 to 7.50)	3.31 (0 78 to 14.02)
Female	1.00	1.00
Age (year)		
20 to 29	1.00	1.00
30 to 39	2.94 (0.72 to 12.08)	2.11 (0.34 to 13.22)
40 to 49	1.89 (0.42 to 8.40)	2.14 (0.37 to 12.33)
50 and over	0.22 (0.03 to 1.81)	0.11 (0.01 to 1.35)
History of self-harm/suicide		
No	1.00	1.00
Yes	3.57 (1.25 to 10.19)*	4.40 (1.24 to 15.60)*
Family history of psychiatric disorders		
No	1.00	1.00
Yes	2.40 (0.89 to 6.45)	1.84 (0.50 to 6.71)
Atypical depression (overeating and hypersomnia)		
No	1.00	1.00
Yes	11.04 (2.83 to 43.04)*	11.73 (2.32 to 59.35)*

AOR=adjusted odds ratio; OR=odds ratio; CI=confidence interval

Adjusted for age, sex, history of self-harm/suicide, family history of psychiatric disorders and atypical depression

* p<0.05

bipolar disorder[4,17,19] and the number of episodes of depression[17,19]. Due to recall bias, participants were unable to recall the exact age at which their symptoms began, as well as the number of depressive episodes they had experienced. The authors included only adults aged 20 to 60, which may introduce selection bias. Similarly, a previous study in pediatrics found that the age of onset did not reach statistical significance for unipolar and bipolar pediatric depressive disorders[23]. Furthermore, treatment resistant depression or depression that is not responding to at least three antidepressants, found in the present study was inconsistent with the other findings[17]. Some participants were given a limited number of antidepressants to choose from and they received the same treatment.

Although major depressive disorder with mixed features is a strong risk factor in developing bipolar disorder[16], the present study enrolled participants who had major depressive disorder regardless of any subtypes and not taking any antipsychotics and mood stabilizers, which are commonly prescribed in patients with major depressive disorder with mixed features[24,25] and bipolar disorder. The authors focused on unrecognized bipolar disorder that fulfilled the criteria for hypomanic or manic episodes.

Conclusion

The present research reveals the predominance of unrecognized bipolar disorder among the patients who present clinical features of depressive symptoms. Patients with atypical depression, and a history of self-harm or suicide attempts should be closely monitored, as these two manifestations are associated with bipolar disorder.

What is already known on this topic?

Patients with bipolar disorder often see a doctor with depressive symptoms, which are complicated to diagnose and make treatment plans properly. Several studies revealed the prevalence of this problem. However, the data concerning the prevalence of unrecognized bipolar disorder is not known in Thailand.

What this study adds?

The results of this study revealed the prevalence of unrecognized bipolar disorder in adults in Thailand consistent with the results of previous studies around the world. This finding reinforces the importance of recognizing the prevalence of this disease in Thailand.

Acknowledgement

The researchers would like to express their gratitude to all the volunteers who participated in the interview. This endeavor has resulted in the discovery of new knowledge that can be used in providing effective treatments for psychiatric patients.

Funding disclosure

The authors have received research grants from the Faculty of Medicine, Naresuan University.

Conflicts of interest

The authors have no conflicts of interest to disclose.

References

1. GBD 2015 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet 2016;388:1545-602.
2. Murray CJ, Lopez AD. The global burden of disease: a

comprehensive assessment of mortality and disability from diseases, injuries, and risk factors in 1990 and projected to 2020. Cambridge, MA: The Harvard School of Public Health on behalf of the World Health Organization and the World Bank; 1996.
3. Dome P, Rihmer Z, Gonda X. Suicide risk in bipolar disorder: A brief review. Medicina (Kaunas) 2019;55:403.
4. Bouchra O, Maria S, Abderazak O. Screening of the unrecognised bipolar disorders among outpatients with recurrent depressive disorder: a cross-sectional study in psychiatric hospital in Morocco. Pan Afr Med J 2017;27:247.
5. Chen FZ, Xiang YT, Lu Z, Wang G, Hu C, Kilbourne AM, et al. Characteristics of unrecognised bipolar disorder in patients treated for major depressive disorder in China: general versus psychiatric hospitals. East Asian Arch Psychiatry 2013;23:139-43.
6. Hughes T, Cardno A, West R, Marino-Francis F, Featherstone I, Rolling K, et al. Unrecognised bipolar disorder among UK primary care patients prescribed antidepressants: an observational study. Br J Gen Pract 2016;66:e71-7.
7. Pacchiarotti I, Bond DJ, Baldessarini RJ, Nolen WA, Grunze H, Licht RW, et al. The International Society for Bipolar Disorders (ISBD) task force report on antidepressant use in bipolar disorders. Am J Psychiatry 2013;170:1249-62.
8. Daban C, Colom F, Sanchez-Moreno J, García-Amador M, Vieta E. Clinical correlates of first-episode polarity in bipolar disorder. Compr Psychiatry 2006;47:433-7.
9. Dell'Osso L, Pini S, Cassano GB, Mastrocinque C, Seckinger RA, Saettoni M, et al. Insight into illness in patients with mania, mixed mania, bipolar depression and major depression with psychotic features. Bipolar Disord 2002;4:315-22.
10. Inoue T, Inagaki Y, Kimura T, Shirakawa O. Prevalence and predictors of bipolar disorders in patients with a major depressive episode: the Japanese epidemiological trial with latest measure of bipolar disorder (JET-LMBP). J Affect Disord 2015;174:535-41.
11. Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry 1998;59 Suppl 20:22-33;quiz 4-57.
12. Kittirattanapaiboon P, Khamwongpin M. The validity of the mini international neuropsychiatric interview (MINI)-Thai version. J Ment Health Thai 2005;13:125-35.
13. Ngamjarus C, Chongsuvivatwong V, McNeil E. n4Studies: Sample size calculation for an epidemiological study on a smart device. Siriraj Med J 2016;68:160-70.
14. Akiskal HS, Bourgeois ML, Angst J, Post R, Möller H, Hirschfeld R. Re-evaluating the prevalence of and diagnostic composition within the broad clinical spectrum of bipolar disorders. J Affect Disord 2000;59 Suppl 1:S5-30.
15. Daveney J, Panagioti M, Waheed W, Esmail A. Unrecognized bipolar disorder in patients with depression managed in primary care: A systematic review and meta-analysis. Gen Hosp Psychiatry 2019;58:71-6.
16. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-5). 5th ed. Arlington, VA: American Psychiatric Publishing; 2013.
17. Shabani A, Zolfigol F, Akbari M. Brief major depressive episode as an essential predictor of the Bipolar Spectrum Disorder. J Res Med Sci 2009;14:29-35.
18. Motovsky B, Pecenak J. Psychopathological characteristics of bipolar and unipolar depression - potential indicators of bipolarity. Psychiatr Danub 2013;25:34-9.
19. Xiang YT, Zhang L, Wang G, Hu C, Ungvari GS, Dickerson FB, et al. Sociodemographic and clinical features of bipolar disorder patients misdiagnosed with major depressive disorder in China. Bipolar Disord 2013;15:199-205.
20. Shi L, Thiebaud P, McCombs JS. The impact of unrecognized bipolar disorders for patients treated for depression with antidepressants in the fee-for-services California Medicaid (Medi-Cal) program. J Affect Disord 2004;82:373-83.
21. Dunner DL. Clinical consequences of under-recognized bipolar spectrum disorder. Bipolar Disord 2003;5:456-63.
22. Poon Y, Chung KF, Tso KC, Chang CL, Tang D. The use of Mood Disorder Questionnaire, Hypomania Checklist-32 and clinical predictors for screening previously unrecognised bipolar disorder in a general psychiatric setting. Psychiatry Res 2012;195:111-7.
23. Uchida M, Serra G, Zayas L, Kenworthy T, Faraone SV, Biederman J. Can unipolar and bipolar pediatric major depression be differentiated from each other? A systematic review of cross-sectional studies examining differences in unipolar and bipolar depression. J Affect Disord 2015;176:1-7.
24. Verdolini N, Hidalgo-Mazzei D, Murru A, Pacchiarotti I, Samalin L, Young AH, et al. Mixed states in bipolar and major depressive disorders: systematic review and quality appraisal of guidelines. Acta Psychiatr Scand 2018;138:196-222.
25. Na KS, Kang JM, Cho SE. Prevalence of DSM-5 mixed features: A meta-analysis and systematic review. J Affect Disord 2021;282:203-10.