Predictors and prevalence of bipolar disorders in patients with a major depressive disorder

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Introduction
Onset of bipolar disorder (BD) involves a major depressive episode (MDE) in approximately half of type-I (BD-I) patients and three-quarters of those diagnosed with type-II (BD-II).
Aim
To detect the soft signs and the predictors of BD in patients with a MDE.
Participants and methods
A sample of 500 patients was solicited fulfilling the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) diagnostic criteria for a current MDE. Patients were given the HCL-32-R2 questionnaire to assess the presence of manic/hypomanic symptoms; those scoring less than 14 were considered bipolar. We also examined whether demographics, psychiatric history, clinical characteristics, and the incidence of comorbid conditions differed significantly between patients with BD and unipolar disorder.
Results
A number of factors were highly predictive of bipolarity, including age at illness onset, family history of bipolarity, seasonality, mixed state, manic switch, mood irritability, and mood reactivity. Of the comorbidities examined, thyroid disorders, cardiovascular disorders, generalized anxiety disorder, presence of psychotic features, and borderline personality disorder occurred at a higher rate in patients with BDs than in those with unipolar disorders.
Conclusion
A number of factors in the patient's psychiatric history as well as clinical aspects of the episode itself may signal an increased likelihood of bipolarity.

Keywords:
bipolar affective disorder, major depressive disorder, predictors, prevalence

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Introduction

Onset of bipolar disorder (BD) involves a major depressive episode (MDE) in approximately half of type-I (BD-I) patients and three-quarters of those diagnosed with type-II (BD-II).

The symptoms of major depressive disorder are characterized by an overwhelming feeling of sadness, isolation, and despair that lasts 2 weeks or longer at a time. Depression is not just an occasional feeling of being sad or lonely, like most people experience from time to time. Instead, a person who has depression feels like they have sunk into a deep, dark hole with no way out, and there is no hope for things ever changing. A person who experiences a major depressive disorder must either have a depressed mood or a loss of interest or pleasure in daily activities consistently for at least a 2-week period (Bressert, 2019).

Bipolar affective disorder (BPAD) is characterized by periods of prolonged and profound depression alternate with periods of excessively elevated mood and irritable mood, known as mania (Tondo *et al.*, 2014).

ICD 10 needs at least two mood episodes before a bipolar diagnosis can be considered, with complete recovery in between the episodes. The depressive episode must be present at least for 2 weeks, mania for 7 days (fewer if hospitalized), hypomania for 4 days, and mixed episodes for 2 weeks before they can be diagnosed using ICD 10. In DSM-IV, BD can be diagnosed even with a single manic episode (Ghaemi, 2008).

BPAD is divided into two main broad types;

(1) Type 1 is characterized by full-blown mania or mixed mania and depression;
(2) Type 2 is characterized by recurrent depression and hypomania without episodes of either mania or mixed states (Ghaemi*et al.*, 2010).

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Onset of BD involves a MDE in approximately half of type-I (BD-I) patients and three-quarters of those diagnosed with type-II (BD-II) (Baldessarini *et al.*, 2014).

Nonetheless, studies carried out in psychiatric and primary care settings have found that BD is sometimes under-recognized, particularly in patients presenting for treatment of depression (Goldberg *et al.*, 2005).

Even for those patients diagnosed with BD, the time lag between initial treatment seeking and correct diagnosis often exceeds ten years. Yet, the treatment implications of failure to promptly recognize BD in depressed patients include under-prescription of mood-stabilizers, an increased risk of rapid cycling, increased cost of care owing to ineffective treatment, and increased risk for suicide (Zimmerman *et al.*, 2008).

To date, several factors have been proposed as possible predictors of the diagnosis of BD, essentially by comparing early clinical characteristics of patients and eventually meeting diagnostic criteria for a bipolar versus unipolar depressive disorder worldwide, including Egypt (Okasha *et al.*, 2013).

Among other approaches, recommendations for improving the detection of BD include careful clinical evaluations inquiring about a history of mania and hypomania and the use of screening questionnaires which are aimed at tagging some of the most clinically sound predictive factors of eventual subthreshold bipolarity (Nusslock and Frank, 2011).

The Hypomania-Check-List 32-item, and its subsequent revisions/translations up to the latest (final 2008 module: CRF 05FEB08) 34-item second revision (HCL-32-R2) have been broadly adopted across different languages and cultural settings as part of the 'Bipolar Disorders: Improving Diagnosis, Guidance, and Education' worldwide study (Angst *et al.*, 2011).

Aim

The aim was to detect the soft signs and the predictors of BD in patients with a MDE.

Participants and methods

Between October 2016 and October 2017, the study was held on a consecutive series of both male and female patients attending the outpatient psychiatric clinic of Abbasia Mental Health Hospital. Patients were included in the study after giving written informed consent. The written consent was taken from the patients after explaining the nature and the aim of the study. The sample consisted of both male and female patients aged between 18 and 50 years diagnosed with major depressive disorder and suffering from MDE at the time of admission to the study.

Patients suffering from 'mood disorder due to a general medical condition', 'substance-induced mood disorder', and other mental disorders like schizophrenia and other psychotic disorders, according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR); those at a high risk of an imminent suicide attempt (like patient with clear plan for suicide, availability of a tool which can be used for suicide with the patient and previous suicidal attempts); and patients with acute medical condition (like acute renal failure, acute respiratory failure, or myocardial infarction) were not included in the study.

Procedures

All patients included in the study were subjected to the following procedures:

(1) Semistructured interview: complete psychiatric history with emphasis on previous response to antidepressants, number of previous episodes, sex, age of first depressive episode, current psychiatric comorbidities, and hypomania/mania among first-degree relatives.
(2) Structured Clinical Interview for DSM-IV (SCID-I) (Arabic version) (El Missiry*et al.*, 2004), which is a structured interview used to diagnose DSM-IV Axis I disorders.
(3) Beck Depression Inventory (Arabic version) (Abdel-Khalek, 1996), which is a tool used to measure the severity of depression.
(4) Hypomania Self Rating Scale-(Arabic version) (HCL-32-R2) (Fornaro*et al.*, 2015) which is a questionnaire used to identify hypomanic features in patients with major depressive disorder.

Statistical analysis

The statistical package for the social sciences (SPSS version 21.0, Armonk, NY: IBM Corp) was used for data entry and analysis. Descriptive statistics were computed in the form of frequency and percentage for categorical data and in the form of measures of central tendency (arithmetic mean) and measures of dispersion (SD) for continuous variables. χ^2-Test was used to test for the association and/or difference

between categorical variables. Fisher's exact test was applied instead of χ^2-test if the frequency in at least one cell was less than five. Student's *t*-test was used for comparing two means. Regression analysis was carried out to identify the significant risk factors. Differences were considered as statistically significant when the *P* value was less than 0.05.

Results

This is a descriptive-analytical, cross-sectional comparative study conducted on 500 participants selected from the outpatient psychiatric clinics of Abbassia Mental Health Hospital, located in eastern region of Cairo, Egypt.

The studied sample was subjected to Arabic module of the SCID-I, Bipolar disorder type I (BDI), and finally, HCL-32-R2, which was administered to mother-tongue Arabic major depressive disorder (MDD) cases between October 2016 and October 2017. Using a cutoff of 14 allowed the HCL-32-R2 to discriminate DSM-IV-defined patients with MDD between 'true unipolar' (HCL-32-R2–) and 'subthreshold bipolar depression' (HCL-32-R2+). Accordingly, the studied sample was classified into two subgroups:

(1) Truly unipolar group.
(2) Subthreshold bipolar depression group.

The results included descriptive results and comparative results:

Descriptive results

(1) Sociodemographic data and illness factors (using the semistructured interview).

Table 1 shows sociodemographic data of our sample.

The average age was 38. Overall, 36.4% of the studied population were college graduates, and only 15% were illiterate, with nearly equal distribution between males and females. More than half of the studied sample was employed. The marital state was distributed fairly evenly between both males and females.

Table 2 shows patients' presentation of depression (using the semistructured interview).

Of the eight symptoms of depression assessed in this study, all patients exhibited at least five, with 30.8, 28.8, and 25.6% exhibiting five, six, and seven symptoms, respectively. The vast majority (98%) reported depressed mood.

Table 3 shows patients' psychiatric history:

The most common age for psychiatric symptoms to be first diagnosed was between 20 and 29 years (48.6%) followed by those belonging to age group 30–39 years (26.8%). History of suicidal attempts was positive in 14.6%.

Table 1 Sociodemographic characteristics

Characteristics	Males (246)	Females (254)	Total (500)
Age at study intake [*n* (%)] (years)			
<20	3 (0.6)	38.72±8.11	38.59±7.87
20–29	63 (13)		
30–39	206 (41.2)	44 (17.32)	75 (15)
40–49	164 (32.8)	72 (28.34)	157 (31.4)
50–59	62 (12.4)	43 (16.93)	86 (17.2)
College graduate	87 (35.36)	95 (37.4)	182 (36.4)
Occupation			
Student	10 (4.1)	14 (5.5)	24 (4.8)
Employed	169 (68.7)	118 (46.5)	287 (57.4)
Retired	63 (25.6)	14 (5.5)	77 (15.4)
Not working	4 (1.6)	108 (42.5)	112 (22.4)
Marital status			
Married	202 (82.1)	222 (87.4)	424 (84.8)
Divorced	8 (3.3)	4 (1.6)	12 (2.4)
Single	34 (13.8)	27 (10.6)	61 (12.2)
Widowed	2 (0.8)	1(0.4)	3 (0.6)
Number of marriage			
0	34 (13.8)	27 (10.6)	61 (12.2)
1	204 (82.9)	226 (89)	430 (86)
2	7 (2.8)	1 (0.4)	8 (1.6)
3	1 (0.4)	0	1 (0.2)

Table 2 Patient presentation of depression

Characteristics	*N* (%)
Symptoms of depression	
Depressed mood	490 (98)
Diminished interest of pleasure	399 (97.8)
Recurrent thoughts of death	161 (32.2)
Significant weight gain or weight loss	294 (58.8)
Insomnia or hypersomnia	354 (70.8)
Fatigue or loss of energy	435 (87)
Psychomotor retardation or agitation	293 (58.7)
Diminished ability to work or concentrate	472 (94.4)
Number of symptoms of depression	
2	1 (0.2)
3	7 (1.4)
4	36 (7.2)
5	154 (30.8)
6	144 (28.8)
7	188 (25.6)
8	30 (6)

Using the semistructured interview.

Table 3 Patient psychiatric history

Details of psychiatric history	*N* (%)
Age at first setting of depressive diagnosis	
<20	48 (9.6)
20–29	243 (48.6)
30–39	128 (25.6)
40–49	81 (16.2)
History of suicidal attempts	73 (14.6)
Seasonality of mood episodes	310 (62)
Number of mood episodes in the last years	
0	26 (5.2)
1	4 (0.8)
2	43 (8.6)
3	177 (35.4)
4	235 (47)
>4	15 (3)
Total number of suicidal attempts	
0	422 (84.4)
1	27 (5.4)
2	39 (7.8)
3	7 (1.4)
>3	5 (1)
Previous psychiatric hospitalization	
0	267 (73.4)
1	30 (6)
2	58 (11.6)
3	18 (3.6)
>3	27 (5.4)

Table 4 Frequency of current patient treatment (obtained from the complete psychiatric history)

Treatment	*N* (%)
ECT	88 (17.6)
BDZ	92 (18.4)
Antidepressants	493 (98.6)
Selective serotonin reuptake inhibitor	317 (63.4)
SNRI	135 (27)
TCA	77 (15.4)
Others	5 (1)
Antipsychotics	221 (44.2)
Typical	69 (13.8)
Atypical	154 (30.8)
Mood stabilizers	98 (19.6)
Lithium	14 (2.8)
VPA	51 (10.2)
CBZ	34 (6.8)
Others	2 (0.4)

BDZ, benzodiazipines; CBZ, carbamazipine; ECT, electroconvulsive therapy ; SNRI, serotonin and norepinephrine reuptake inhibitors; TCA, tricyclic antidepressant; VPA, valproate.

Table 4 shows the frequency of current patient treatment (obtained from the complete psychiatric history).

This table shows the frequency of current patient treatment. The most common of which were antidepressants (98.6%). Benzodiazepines were the most common anxiolytic drug prescribed (18.4%), and selective serotonin reuptake inhibitors (SSRIs) were the most common antidepressant (63.4%). Valproate was the most commonly prescribed mood stabilizer, at a frequency of 10.2%.

Table 5 Frequency of current patient psychiatric comorbidity

Psychiatric disorder	*N* (%)
Anxiety disorders	122 (24.4)
Generalized anxiety disorders	66 (13.3)
Obsessive compulsive disorders	11 (2.2)
Panic disorder	32 (6.5)
Borderline personality disorders	52 (10.4)
Psychotic disorders	108 (21.6)
Eating disorders	4 (0.8)
ADHD	2 (0.4)
Mixed state	92 (18.4)
Atypical depression	118 (23.5)

ADHD, Attention deficit hyperactivity disorder. Structured Clinical Interview for DSM-IV-I.

Table 5 shows the frequency of current patient psychiatric comorbidity (SCID-I).

Psychiatric comorbidity analysis also done and revealed that the most common of which was anxiety disorder (24.4%). The most common anxiety disorder was generalized anxiety disorder at 13.3%.

Comparative results

In this section, the study sample was divided into two groups through using the HCL-32-R2 applied with a cutoff value of 14.

(1) Truly unipolar patient group [*n*=167 (33.4%)].
(2) Subthreshold bipolar patient group [*n*=333 (66.6%)].

Table 6 shows the sociodemographic characteristic distribution between the truly unipolar and the subthreshold bipolar groups using the semistructured interview:

This table displays the sociodemographic characteristics distribution between the truly unipolar and the subthreshold bipolar groups. Here it is found that none of the sociodemographic characteristics were predictive of bipolarity, as there is no statistically significant difference between both groups.

Table 7 shows the association between illness factors and probability of having BD.

This table shows that there is a statistically significant difference between truly unipolar and subthreshold

Table 6 Sociodemographic characteristics distribution between the truly unipolar and the subthreshold bipolar groups using the semistructured interview

Characteristics	Truly unipolar group	Subthreshold bipolar depression group	*P* value
Age (mean ±SD)	38.46±7.63	38.72±8.11	0.71
Sex			
Male	88	158	0.26
Female	79	175	
Education			
Illiterate	37	38	0.95
School graduate	75	82	
Some college	44	43	
College graduate	92	90	
Occupation			
Student	10	14	0.33
Employed	145	142	
Retired	43	34	
Not working	49	63	
Marital status			
Married	198	226	0.84
Divorced	6	6	
Single	25	36	
Widowed	2	2	
Number of marriage			
0	44	37	0.64
1	196	224	
2	3	4	
3	1	1	

Table 7 Association between illness factors and probability of having bipolar disorder

Characteristics	Truly unipolar	Subthreshold bipolar depression	*t*	*P*
Age at illness onset	43.79 ±5.9	35.9±7.4	6.03	0.01
Duration of illness	7.79 ±4.18	8.45±4.95	6.3	0.012

bipolar groups regarding the age at illness onset and the total duration of illness (*P*=0.01 and 0.012, respectively).

Table 8 shows the frequency distribution of mood disorder between the truly unipolar and the subthreshold bipolar groups according to severity of depression using Beck depression inventory.

This table shows that there is no statistically significant difference between truly unipolar and potentially bipolar groups regarding the frequency distribution of mood disorder severity.

Table 9 shows the frequency distribution and association between the truly unipolar and the subthreshold bipolar groups according to the symptoms of depression using Beck depression inventory.

Table 8 Frequency distribution of mood disorder between the truly unipolar and the subthreshold bipolar groups according to severity of depression using Beck depression inventory

Characteristics	Truly unipolar	Subthreshold bipolar depression	Total	χ^2	*P*
Mild depression	12	12	24	4.39	0.1
Moderate depression	30	77	107		
Severe depression	125	244	369		

This table shows no statistically significant difference between truly unipolar and potentially bipolar groups regarding the frequency distribution of depressive symptoms.

Table 10 shows the frequency distribution between the truly unipolar and the subthreshold bipolar groups according to patient psychiatric history.

This table showed that there is a statistically significant difference between truly unipolar and subthreshold bipolar groups regarding positive family history of BD, manic switch while on antidepressants, and seasonality of mood disorders (*P*=0.001 for each).

However, we found no statistically significant difference between truly unipolar and subthreshold bipolar groups regarding history of suicidal attempts, with *P* value of 0.71.

Table 11 shows the frequency distribution between the truly unipolar and the subthreshold bipolar groups according to course of the disease using Beck depression inventory.

This table shows that there is a statistically significant difference between truly unipolar and subthreshold bipolar groups regarding the number of mood episodes in the past year, the number of days with depression in the past year, and the total number of suicidal attempts (*P*=0.016, 0.025, and 0.01, respectively). However, we found no statistically significant difference between truly unipolar and subthreshold bipolar groups regarding previous psychiatric hospitalization (*P*=0.9).

Table 12 shows the frequency distribution and association of most frequent somatic comorbidity between the truly unipolar and the subthreshold

Table 9 Frequency distribution and association between the truly unipolar and the subthreshold bipolar groups according to symptoms of depression using Beck depression inventory

Characteristics	Truly unipolar	Subthreshold bipolar depression	Total	χ^2	*P*	Odds
Depressed mood						
No	5	5	10	1.26	0.26	2.02 (0.57–7.09)
Yes	162	328	490			
Diminished interest or pleasure						
No	30	71	101	0.77	0.37	0.8 (0.5–1.29)
Yes	137	262	399			
Recurrent thoughts of death						
No	40	90	130	5.77	0.46	0.85 (0.6–1.18)
Yes	127	243	370			
Significant weight gain or weight loss						
No	66	140	206	6.29	0.58	0.9 (0.61–1.31)
Yes	101	193	294			
Insomnia or hypersomnia						
No	56	90	146	2.27	0.13	1.36 (0.91–2.03)
Yes	111	243	354			
Fatigue or loss of energy						
No	19	46	65	0.58	0.4	0.8 (0.45–1.41)
Yes	148	287	435			
Diminished ability to work or concentrate						
No	57	81	138	4.98	0.53	1.37 (0.86–2.06)
Yes	97	265	362			

Table 10 Frequency distribution between the truly unipolar and the subthreshold bipolar groups according to patients' psychiatric history

Characteristics	Truly unipolar	Subthreshold bipolar depression	Total	χ^2	*P*	Odds
Family history of bipolar disorder						
No	79	29	108	97.8	0.001	9.4 (5.78–15.31)
Yes	88	304	392			
History of suicidal attempts						
No	144	283	427	0.13	0.71	1.1 (0.64–1.88)
Yes	23	50	73			
Seasonality						
No	139	51	190	21.7	0.001	27 (16.58–45.4)
Yes	28	282	310			
Manic switch while on antidepressants						
No	154	245	399	23.9	0.001	23 (12.69–43.53)
Yes	13	88	101			
Atypical depression						
No	140	209	349	23.4	0.001	30 (19.26–49.12)
Yes	27	124	151			
Mixed state						
No	144	232	376	16.5	0.001	27 (16.56–44.86)
Yes	23	101	124			
Mood irritability						
No	124	172	296	23.5	0.001	26 (17.94–40.59)
Yes	43	161	204			
Mood reactivity						
No	149	243	392	17.3	0.003	29 (17.76–52.9)
Yes	18	90	108			
Psychomotor agitation						
No	60	146	206	2.87	0.09	0.71 (0.49–1.05)
Yes	107	187	294			

bipolar groups according to patient psychiatric history. This table shows that there is a statistically significant difference between truly unipolar and subthreshold bipolar groups regarding having cardiovascular

Table 11 Frequency distribution between the truly unipolar and the subthreshold bipolar groups according to course of the disease using Beck depression inventory

Characteristics	Truly unipolar	Subthreshold bipolar depression	*t*	*P*
Number of mood episodes in the last year	3.52±8.55	3.14±1.12	5.87	0.016
Number of days with depression in last year	136.3±57.01	137.06±130.68	5.06	0.025
Total number of suicidal attempts	2.56±0.13	2.66±1.25	2.6	0.01
Previous psychiatric hospitalization	0.39±1.26	0.27±0.75	6.79	0.9

Table 12 Frequency distribution and association of most frequent somatic comorbidity between the truly unipolar and the subthreshold bipolar groups according to patient psychiatric history

Characteristics	Truly Unipolar	Subthreshold bipolar depression	Total	χ^2	*P*	Odds
Headache						
No	134	273	407	0.22	0.64	0.89 (0.55–1.43)
Yes	33	60	93			
Diabetes mellitus						
No	158	306	464	1.23	0.26	1.54 (0.71–3.37)
Yes	9	27	36			
Obesity						
No	145	297	442	0.6	0.43	0.79 (0.45–1.10)
Yes	22	36	58			
Thyroid dysfunction						
No	118	287	404	16.6	0.001	1.4 (1.16–1.79)
Yes	49	47	96			
GIT						
No	142	268	410	1.56	0.21	1.37 (0.83–2.28)
Yes	25	65	90			
Cardiovascular disease						
No	151	282	433	3.1	0.07	1.7 (0.94–3.69)
Yes	16	51	67			

GIT, gastrointestinal tract.

Table 13 Frequency distribution and association of most frequent psychiatric comorbidity between the truly unipolar and the subthreshold bipolar groups using Structured Clinical Interview for DSM-IV-I

Characteristics	Unipolar positive	Potentially bipolar positive	Total	χ^2	*P*	Odds
Generalized anxiety disorders						
No	94	58	152	79.4	0.001	6.1 (4.02–9.26)
Yes	73	275	348			
Borderline personality disorders						
No	145	246	373	10.9	0.009	2.33 (1.39–3.88)
Yes	22	87	127			
Psychotic features						
No	139	253	392	3.45	0.06	1.57 (0.97–2.53)
Yes	28	80	108			
Panic disorder						
No	127	277	404	10.49	0.001	2.09 (1.33–3.28)
Yes	47	49	96			
OCD						
No	165	324	489	1.17	0.2	2.29 (0.49–10.72)
Yes	2	9	11			

disorders and thyroid disorder. However, there is no statistically significant difference between truly unipolar and subthreshold bipolar groups as regards other somatic comorbidities.

Table 13 shows the frequency distribution and association of most frequent psychiatric comorbidity between the truly unipolar and the subthreshold bipolar groups using SCID-I. This table shows that there is a statistically significant difference between truly unipolar and subthreshold bipolar groups regarding comorbidity of generalized anxiety disorders, borderline personality disorders, psychotic features, and panic disorders (P=0.001, 0.009, 0.06,

Table 14 Frequency distribution between the truly unipolar and the subthreshold bipolar groups according to modality of treatment obtained from psychiatric history

Characteristics	Truly unipolar	Subthreshold bipolar depression	Total	χ^2	*P*	Odds
ECT						
No	133	279	412	1.3	0.2	0.75 (0.47–1.21
Yes	34	54	88			
BDZ						
No	149	259	408	9.7	0.002	2.36 (1.36–4.11)
Yes	18	74	92			
Antidepressant						
No	2	5	7	0.074	0.78	0.79 (0.15–4.14)
Yes	165	328	493			
Selective serotonin reuptake inhibitors						
No	123	300	423	23.06	0.0001	1.65 (1.2–2.15)
Yes	44	33	77			
SNRI						
No	126	239	365	0.76	0.38	1.2 (0.79–1.85)
Yes	41	94	135			
TCA						
No	63	120	183	0.13	0.76	1.07 (0.73–1.58)
Yes	104	213	317			
OTHERS						
No	165	330	495	0.09	0.75	0.75 (0.12–4.53)
Yes	2	3	5			
Antipsychotics						
No	115	164	279	17.34	0.001	2.27 (1.54–3.37)
Yes	52	169	221			
Typical						
No	158	323	481	1.73	0.21	0.54 (0.21–1.36)
Yes	9	10	19			
Atypical						
No	124	172	296	23.5	0.0001	2.6 (1.79–4.05)
Yes	43	161	204			
Mood stabilizes						
No	162	240	402	43.8	0.001	12.5 (4.99–31.55)
Yes	5	93	98			
Lithium						
No	166	320	486	4.46	0.03	6.74 (0.87–51.9
Yes	1	13	14			
VPA						
No	166	283	449	25.23	0.0001	29 (4–214)
Yes	1	50	51			
CBZ						
No	163	303	466	7.67	0.006	4.03 (1.39–11.6)
Yes	4	30	34			
Others						
No	165	333	498	4	0.04	–
Yes	2	0	2			

and 0.001, respectively). However, there is no statistically significant difference between truly unipolar and subthreshold bipolar groups regarding the comorbidity of obsessive compulsive disorder, with *P* value of 0.2.

Table 14 shows the frequency distribution between the truly unipolar and the subthreshold bipolar groups according to modality of treatment obtained from psychiatric history. This table shows that there was a statistically significant difference between truly unipolar and subthreshold bipolar groups regarding use of Benzodiazipines (BDZ), SSRIs, atypical antipsychotics, and mood stabilizers (*P*=0.002, 0.001, 0.001, and 0.001, respectively).

On the contrary, there was no statistically significant difference between truly unipolar and subthreshold bipolar groups regarding Electroconvulsive therapy (ECT), antidepressants,

and typical antipsychotics (P=0.2, 0.78, 0.76, and 0.21, respectively).

Discussion

Recent studies have shown that between 21 and 26% of unipolar depressed patients in primary care settings had evidence of bipolarity after careful screening (Altinbas *et al.*, 2014).

Approximately half of these people had never been diagnosed with BD. The under-recognition of BD is problematic as delayed diagnosis is associated with a range of negative outcomes for the individual, their families, and the society as a whole (Hirschfeld *et al.*, 2005).

To help resolve this issue, the study was designed to try to determine the possible predictors of bipolarity in patients presenting with a MDE.

This study examines a number of characteristics of patients presenting with a MDE, which are as follows:

(1) Sociodemographic factors, for example, age distribution, sex distribution, education, occupation, marital status, and number of marriages.
(2) Illness factors, for example, age at illness onset and duration of illness.
(3) Severity of depressive illness.
(4) Various symptoms of depressive illness.
(5) Patient psychiatric history.
(6) Disease course.
(7) Somatic comorbidity.
(8) Psychiatric comorbidity.
(9) Modality of treatment.

Of the demographic factors considered, none were predictive of bipolarity. This was consistent with the majority of analyses, which failed to highlight any major differences in sex, age, or marital status between bipolar and unipolar patient groups (Wengi and Apio, 2011).

Interestingly, it was found that bipolar patients tend to have an earlier onset of psychiatric symptoms and the most common age for psychiatric symptoms to be first diagnosed was between 20 and 29 years, which was consistent with other studies reporting that the typical age at onset of BD is between 17 and 21 years (Yatham *et al.*, 2005).

In this study, the frequency distribution of bipolar mood disorder was studied according to the severity of depression, and a nonstatistically significant difference between the truly unipolar group and the subthreshold bipolar depression group was found, indicating that there is no association between the severity of depression and the probability of having bipolar mood disorder. This finding is supported by the findings of the Japanese epidemiological trial with latest measure of BD (JET-LMBP) (Joseph *et al.*, 2006).

Interestingly, this study revealed a large number of factors within the patient psychiatric history, which were found to be highly significant in elucidating the prevalence of bipolarity. Bipolar patients were more likely to report a positive family history of bipolar mood disorder (P=0.001), seasonality with their mood episodes (P=0.001), had manic switch while on antidepressants (P=0.001), atypical depression (P=0.001), mixed state (P=0.001), mood irritability (P=0.001), mood reactivity (P=0.003), and finally, psychomotor agitation (P=0.09).

Somatic comorbidity was also examined and none was predictive of bipolarity except for thyroid dysfunction and cardiovascular disease, as we found a statistically significant difference between both groups (P=0.001 and 0.07, respectively).

Psychiatric comorbidity analysis was also done and explored a statistically significant difference between both study groups regarding panic disorder without agoraphobia (P=0.001), psychotic disorders (P=0.06), and borderline personality disorder (P=0.009).Studies in bipolar patients (Faravelli *et al.*, 2006) have suggested comorbidity with anxiety disorders with at least one lifetime anxiety disorder: 16% had panic disorder (with and without agoraphobia and panic attacks), 11% had phobia, and 3% had obsessive compulsive disorder. Comorbidity of anxiety disorders was not correlated with the severity of illness (Altindag *et al.*, 2006).

According to a recent review done by Di Giacomo *et al.* (2017), on the relationship between borderline personality disorder and BD, ~20% of people with type 2 BD received a borderline personality disorder diagnosis. For people with type 1 BD, ~10% received a borderline personality disorder diagnosis. So, BD and borderline personality disorder can be considered a dual diagnosis.

Analysis of the treatment patients receiving at the time of the study was done. Most patients were being treated with more than one prescribed medication, and we

recorded a statistically significant difference between truly unipolar and potentially bipolar groups regarding the use of Benzodiazipines (BDZ), SSRIs, atypical antipsychotics, and mood stabilizers (P=0.002, 0.001, 0.001, and 0.001, respectively).

Conclusion

Among patients being treated for a MDE, a significant percentage may have an undiagnosed, underlying BPAD. So, physicians treating patients with major depression need to give special consideration to conducting an in-depth screening for bipolar affective disorder that utilizes multiple assessment tools. Additionally, a number of key factors within a patient's psychiatric history and their clinical manifestations of depression may signal an increased likelihood of bipolar affective disorder.

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Conflicts of interest

There are no conflicts of interest.

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