

# A comparative study of clinical features of major depressive episode in major depressive disorder and bipolar disorder at tertiary care centre of Saurashtra region

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## ABSTRACT

**Background:** Robust clinical research data are available distinguishing clinical features of the major depressive episode between bipolar depression and major depressive disorder (MDD). Depression is having a highly heterogeneous clinical presentation. MDD and bipolar depression show a significant difference in terms of epidemiology, natural course, genetics, outcome, treatment, and disability thus becoming the major areas of rising concern which need to be addressed. **Objectives:** The aim was to study and compare clinical features of the major depressive episode in MDD and bipolar disorder. **Materials and Methods:** We compared 40 patients with bipolar depression (all 40 patients had bipolar I disorder) and 40 patients with MDD using semi-structured pro forma, DSM-5 criteria for diagnosis, Hamilton rating scale for depression (HRSD-17), Montgomery-Asberg depression rating scale (MADRS), and mood disorder questionnaire. **Results:** Patients with bipolar depression had early age of onset of illness, positive family history of bipolar disorders in family members, longer illness duration, greater rates of any lifetime suicide attempt, higher percentage of hypersomnia, psychomotor retardation, delusions, social withdrawal, and leaden paralysis and scored higher on individual depressive symptoms of the MADRS items in apparent sadness, reported sadness, concentration difficulties, lassitude, inability to feel and of the HRSD in work and interest, and retardation compared to the patients with MDD. **Conclusions:** Subtle differences in phenomenological presentation of unipolar and bipolar depression indicate requirement of a large multicentre, long term prospective and comparative study.


**KEY WORDS:** Bipolar Depression; Major Depressive Disorder; Mania

## INTRODUCTION

Mood disorders previously known as affective disorders are divided into major depressive disorder (MDD) which is characterized by a single mood pole of major depression

and bipolar disorders, having 3 distinct phases; the depressed phase, which mimics the clinical picture of major depression (lower pole), the manic or hypomanic phase (upper pole), and euthymia, or the asymptomatic phase.<sup>[1,2]</sup> Depression has a wide clinical presentation and has various subtypes such as melancholic depression, atypical depression, seasonal depression, dysthymia, and cyclothymia.<sup>[3]</sup>

The first episode in the majority of bipolar patients is a depressive one. Irrespective of diagnosis, patients currently meet criteria for a major depressive episode are straightforward but bipolar patients who first faced with depressive symptoms are extremely difficult for the

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clinician to validate the depression as stemming from bipolar disorder.<sup>[4]</sup>

If current scenario continues in terms of demographic and epidemiological transitions, the burden of depression increases manifold, and it would become the second leading cause of disability life adjusted years by year 2020, second only to ischemic heart disease.<sup>[5]</sup> So far, in India, there has been limited research on the comparative phenomenology of MDD and depressive episode in bipolar disorder. Studying this with the objective of comparing the clinical features of both would help us to determine the distinctive presentation and predictors of these two disorders.

## MATERIALS AND METHODS

A comparative cross-sectional study of inpatients and outpatients with MDD, bipolar I disorder (BID), and bipolar II disorder (BIID) who consulted psychiatry department of a tertiary care medical college between September 1<sup>st</sup> 2014 and September 1<sup>st</sup> 2015. After the Institutional Ethics Committee approved the study for its ethical aspects, 40 patients with bipolar depression (all 40 patients had BID) and 40 patients with major depression were enrolled.

A specially designed semi-structured pro forma is used to determine the sociodemographic and clinical characteristics. Both MDD and bipolar patients were assessed using Hamilton rating scale for depression-17 (HRSD-17) items, Montgomery-Asberg depression rating scale (MADRS), and mood disorder questionnaire.<sup>[6-8]</sup>

### Data Analysis

All data thus collected were tabulated and analyzed using statistical software Epi Info Version 7.0 and Statistical

Package for the Social Sciences for Windows, Version 20.0. Descriptive statistics were showed as mean  $\pm$  standard deviation or median for continuous variables. Association between categorical variables was evaluated using Pearson's Chi-square test. The Mann-Whitney U-test was used to evaluate the significance of the difference between groups in terms of median values. For each item of the MADRS and the HRSD, the study groups were compared using analysis of covariance, with the total MADRS score as the covariate. For all data of result analysis, statistical significance was set at  $P < 0.05$  two-tailed.

## RESULTS

### Sociodemographic Characteristics

The mean age of persons with MDD was 47.85 years with while in persons with BID mean age was 38.05 years. The gender ratio (Male:female) among persons with MDD and BID was found 1:1.3 and 2.6:1, respectively [Table 1].

### Clinical Characteristics

The median age's at the interview, 1<sup>st</sup> mood (depressive or manic or hypomanic) episode, 1<sup>st</sup> depressive episode, most severe depressive episode for the BID group was early than MDD group. Three or more lifetime depressive episodes were found to be less in persons with MDD compared to BID [Table 1].

### Treatment Characteristics

MDD group was significantly associated with less hospitalization. A higher proportion of subjects reporting never hospitalized in their lifetime compared to the BID group. Considering electroconvulsive therapy (ECT), more

**Table 1:** Sociodemographic and clinical characteristics of MDD and BID groups

Variables	MDD, n=40 (%)	BID, n=40 (%)	Test statistic	P value
Gender, n (%)				
Male	17 (42.5)	29 (72.5)	7.36 <sup>a</sup>	0.006
Female	23 (57.5)	11 (27.5)		
Age (years): Median (IQR)				
At interview	49.5 (36.5–59.5)	35 (28.5-45)	477.5 <sup>b</sup>	0.002*
At 1 <sup>st</sup> mood (depressive or manic or hypomanic) episode	33 (27–48)	21.5 (27–48)	319.5 <sup>b</sup>	0.000*
At 1 <sup>st</sup> depressive episode	33 (27–48)	26 (20–33)	438.5 <sup>b</sup>	0.000*
At most severe depressive episode	37 (27.25–49.5)	26 (18–35)	414 <sup>b</sup>	0.000*
No. of lifetime depressive episodes, n (%)				
Three or more episodes	8 (20)	15 (37.5)	2.99 <sup>a</sup>	0.083
Duration of most severe depressive episode, n (%)				
<3 months	14 (35)	12 (30)	0.23 <sup>a</sup>	0.63
3–6 months	16 (40)	15 (37.5)	0.05 <sup>a</sup>	0.81
>6 months	10 (25)	13 (32.5)	0.55 <sup>a</sup>	0.45

IQR: Interquartile range, a: Chi-square test; b: Mann-Whitney U-test; \* $P < 0.05$ , MDD: Major depressive disorder, BID: Bipolar I disorder

patients of bipolar received ECT during their lifetime, irrespective of depressive or manic or hypomanic episode. Rates of hospital admission for depressive episode in persons with MDD were less than BID [Table 2].

### Suicidal Behavior

Persons with BID were significantly associated with greater rates of any lifetime suicide attempt compared to persons with MDD. A higher proportion of the subjects with BID reporting at least 1 suicide attempt compared to the subjects with MDD [Table 2].

### Family Factors

We found a significant association in the family history of BID between two groups. We observed BID was more common among the family of the subjects with BID compared to MDD.

### Illness Duration

We see more number of patients of a BID than MDD in our psychiatric consultation of >10 years of total duration of illness.

### Substance Dependence

Axis I comorbidity is exclusively associated with psychoactive substance dependence. Nicotine dependence and alcohol dependence were found to be more in patients with bipolar disorder than MDD.

### Medical Comorbidity

Nearly 37.5% of MDD group had Axis III comorbidity, in contrast to 22.5% of BID group. Hypertension and diabetes mellitus were the predominantly reported medical illnesses.

### Clinical Symptoms

The persons with BID had a higher percentage of hypersomnia, psychomotor retardation, delusions, social withdrawal, and leaden paralysis, while the persons with MDD had a higher percentage of initial insomnia, early morning awakening, anger or irritability, tearfulness, subjective restlessness, and anxiety [Table 3, Figures 1 and 2].

### DISCUSSION

Our study found significant symptoms and signs as well as treatment and course variables to differentiate major depressive episode in the persons with MDD and bipolar depression. On comparing the two groups, we observed that the subjects with bipolar depression had early age of onset of illness, positive family history of bipolar disorders in family members, longer illness duration, greater rates of any lifetime suicide attempt, higher percentage of hypersomnia, psychomotor retardation, delusions, social withdrawal, and leaden paralysis compared to the subjects with MDD.

The age of onset of a first mood episode in persons with BID was earlier (11 years) compared to persons with MDD which is consistent with the findings of Weissman *et al.* and Perlis *et al.* had estimated mean difference of 6 years and 8 years, respectively.<sup>[9,10]</sup> We found that the median age of onset for MDD and bipolar disorder was 33 years (27–48 years) and 21.5 years (17–32.25 years), respectively. The study findings are inconsistent with the study of Kessler *et al.*<sup>[11]</sup>

We found that the gender ratio (male:female) among persons with MDD and BID was found 1:1.3 and 2.6:1, respectively. Bromet *et al.* reported that the male:female ratio in MDD patients was about 1:2.<sup>[12]</sup> The results are higher than our study. Poongothai *et al.* reported that the overall prevalence of depression was 15.1% and was higher in females (females

**Table 2:** Treatment characteristics and suicide history

Variables	MDD, n=40 (%)	BID, n=40 (%)	Test statistic	P value
Treatment characteristics				
Drug naive	4 (10)	1 (2.5)	0.85 <sup>a</sup>	0.35
Help from professional	26 (65)	29 (72.5)	0.52 <sup>a</sup>	0.47
Help from faith-healer and professional both	10 (25)	11 (27.5)	0.06 <sup>a</sup>	0.79
Received ECT	3 (7.5)	10 (25)	3.3 <sup>a</sup>	0.06
Never hospitalized	33 (82.5)	8 (20)	31.26 <sup>a</sup>	0.00*
Hospitalized for depression	7 (17.5)	3 (7.5)	1.02 <sup>a</sup>	0.31
Suicide history				
Attempted suicide	1 (2.5)	10 (25)	6.74 <sup>a</sup>	0.009*
No. of attempts				
One	1 (2.5)	9 (22.5)	5.6 <sup>a</sup>	0.017*
Two or more	0 (0)	1 (2.5)	0.00 <sup>a</sup>	1

a: Chi-square test; \* $P < 0.05$ , MDD: Major depressive disorder, BID: Bipolar I disorder, ECT: Electroconvulsive therapy

**Table 3:** Distribution of participants according to clinical symptoms

Symptoms	MDD, n=40 (%)	BID, n=40 (%)	$\chi^2$	P Value
Depressed mood	37 (92.50)	38 (95.00)	0.00	1.00
Lack of interest	36 (90.00)	37 (92.50)	0.00	1.00
Loss of appetite	36 (90.00)	37 (92.50)	0.0	1.00
Increased appetite	0 (0.00)	0 (0.00)	0.0	0.0
Weight loss	12 (30.00)	8 (20.00)	1.06	0.30
Weight gain	0 (0.00)	0 (0.00)	0.0	0.00*
Initial insomnia	26 (65.00)	14 (35.00)	7.20	0.00
Middle insomnia	19 (47.50)	17 (42.50)	0.20	0.65
Early morning awakening	23 (57.50)	13 (32.50)	5.05	0.02*
Hypersomnia	0 (0.00)	10 (25.00)	9.25	0.00*
Psychomotor agitation	18 (45.00)	20 (50.00)	0.20	0.65
Psychomotor retardation	11 (27.50)	28 (70.00)	14.45	0.00*
Fatigue/decrease energy	39 (97.50)	37 (92.50)	0.00	0.61
Worthlessness	24 (60.00)	27 (67.50)	0.48	0.48
Low self-esteem	31 (77.50)	29 (72.50)	0.26	0.60
Pessimistic thoughts	17 (42.50)	10 (25.00)	2.73	0.09
Anger/irritability	31 (77.50)	12 (30.00)	18.15	0.00*
Something wrong with body	3 (7.50)	2 (5.00)	0.00	1.00
Pathological guilt	6 (15.00)	7 (17.50)	0.09	0.76
Difficulty thinking or concentrating	30 (75.00)	33 (82.50)	0.67	0.41
Suicidal ideation	23 (57.50)	26 (65.00)	0.47	0.49
Suicidal attempt	0 (0.00)	0 (0.00)	0.0	0.00
Early morning worsening of mood	3 (7.50)	9 (22.50)	2.45	0.11
Delusion	1 (2.50)	8 (20.00)	4.50	0.03*
Hallucination	0 (0.00)	3 (7.50)	0.00	0.240
Tearfulness	32 (80.00)	12 (30.00)	20.20	0.00*
Subjective restlessness	10 (25.00)	2 (5.00)	4.80	0.02
Anxiety	31 (77.50)	6 (15.00)	31.42	0.00*
Tendency to blame others	2 (5.00)	0 (0.00)	0.00	0.493
Social withdrawal	17 (42.50)	28 (70.00)	6.146	0.013*
Panic attack	1 (2.50)	0 (0.00)	0.00	1.000
Generalized anxiety	1 (2.50)	0 (0.00)	0.00	1.000
Derealization	0 (0.00)	0 (0.00)	0.0	0.00
Lead paralysis	6 (15.00)	15 (37.50)	5.23	0.02*

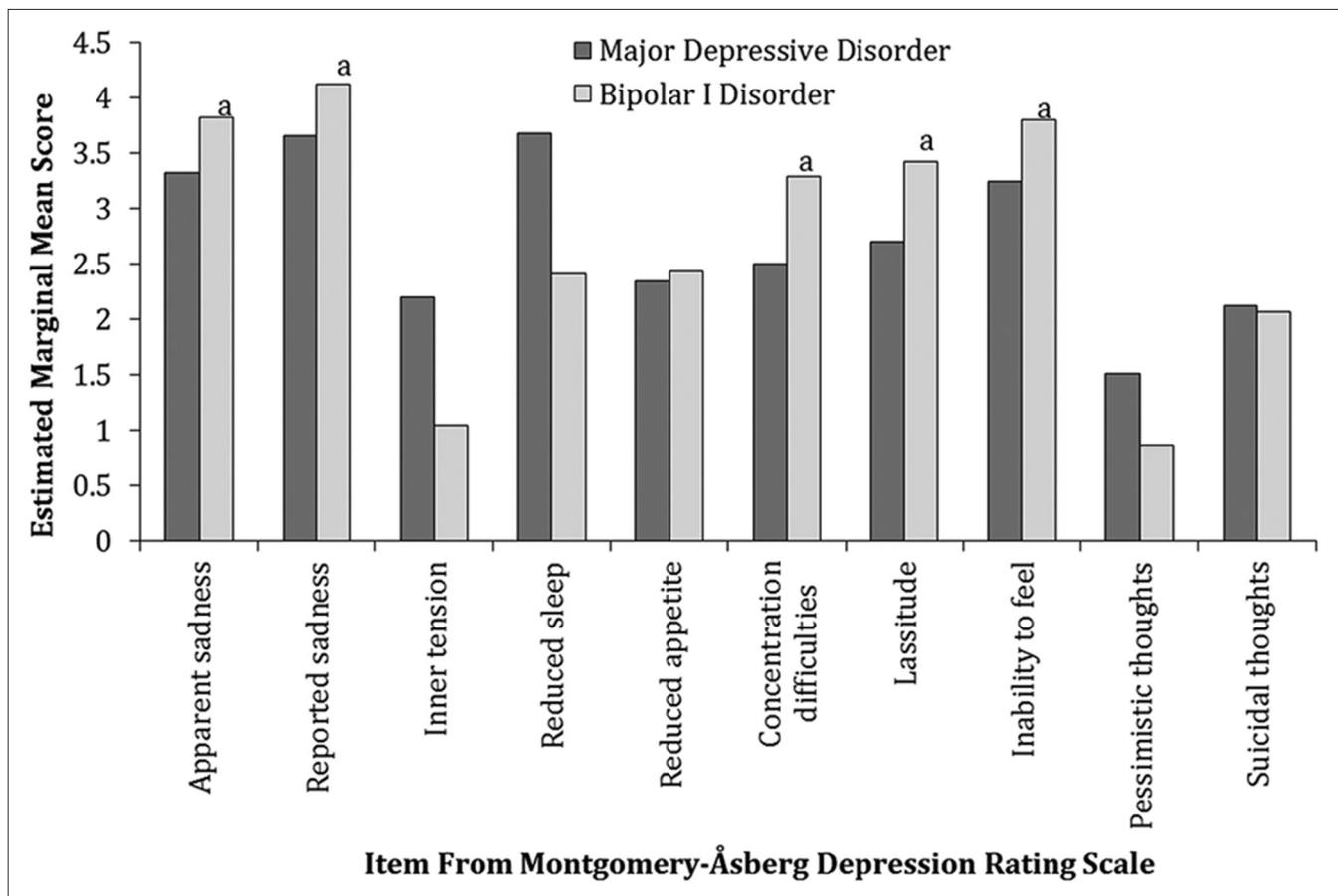
\* $P < 0.05$ , MDD: Major depressive disorder, BID: Bipolar I disorder

16.3% vs. males 13.9%).<sup>[13,14]</sup> The reason for the difference in results could be limited sample size. Weissman *et al.* found nearly equal gender ratio for bipolar disorder and Jolfaei *et al.* reported gender ratio in persons with BID was 2:1.<sup>[9,15]</sup> In our study, males are almost 2.5 times more than females. Again these findings are inconsistent may be due to small sample size or duration of the study.

We found the majority in the MDD group belonged to the age group of 45–54 years while the majority in the BID group belonged to age group of 25–34 years. The above findings are consistent with Shippee *et al.* in which predominant MDD patients belonged to the age group of 45–54 years; however, the values are inconsistent in regard to bipolar disorder.<sup>[16]</sup>

Our study found no significant association with a three or more lifetime depressive episodes in the two diagnostic categories which are to be 20% in persons with MDD while it was 37.5% in persons with bipolar disorder. Mitchell *et al.* reported that bipolar disorder was significantly associated with a greater number of lifetime depressive episodes and a higher proportion of participants with bipolar disorder reporting five or more lifetime depressive episodes compared to the MDD group.<sup>[17]</sup> Perlis *et al.* reported 22.4% and 20.9% of the subjects with bipolar disorder and MDD had 6–25 prior depressive episodes, respectively.<sup>[10]</sup>

Our study findings are different than above mentioned two studies as five or more prior depressive episodes were not



**Figure 1:** Estimated marginal mean scores from individual baseline Montgomery-Asberg depression rating scale items, adjusted for total Montgomery-Asberg depression rating scale score. a - bipolar patients differed significantly from major depressive disorder patients ( $P < 0.05$ ).

reported by any of our study subjects. The possible reasons are that the subjects and their relatives find difficulties in recall depressive episode because patient's symptoms and behavior during a depressive episode may not be distressing to relatives in compared to a manic episode. Although available records with the patients also used to corroborate the history but poor documentation of records leads to misdiagnosis.

Our study found no differences in duration of the most severe depressive episode, patterns of help-seeking and treatment which is consistent with the study of Mitchell *et al.* Although the results are convincing, again, doubt arise on relative's way of conveying information as duration of the most severe depressive episode reported by them is not exact but in approximate value. Majority of participants seek help from a mental health professional, but a minority first or simultaneously sought faith healer. This could be one of the reasons of an under-diagnosed depression in India.

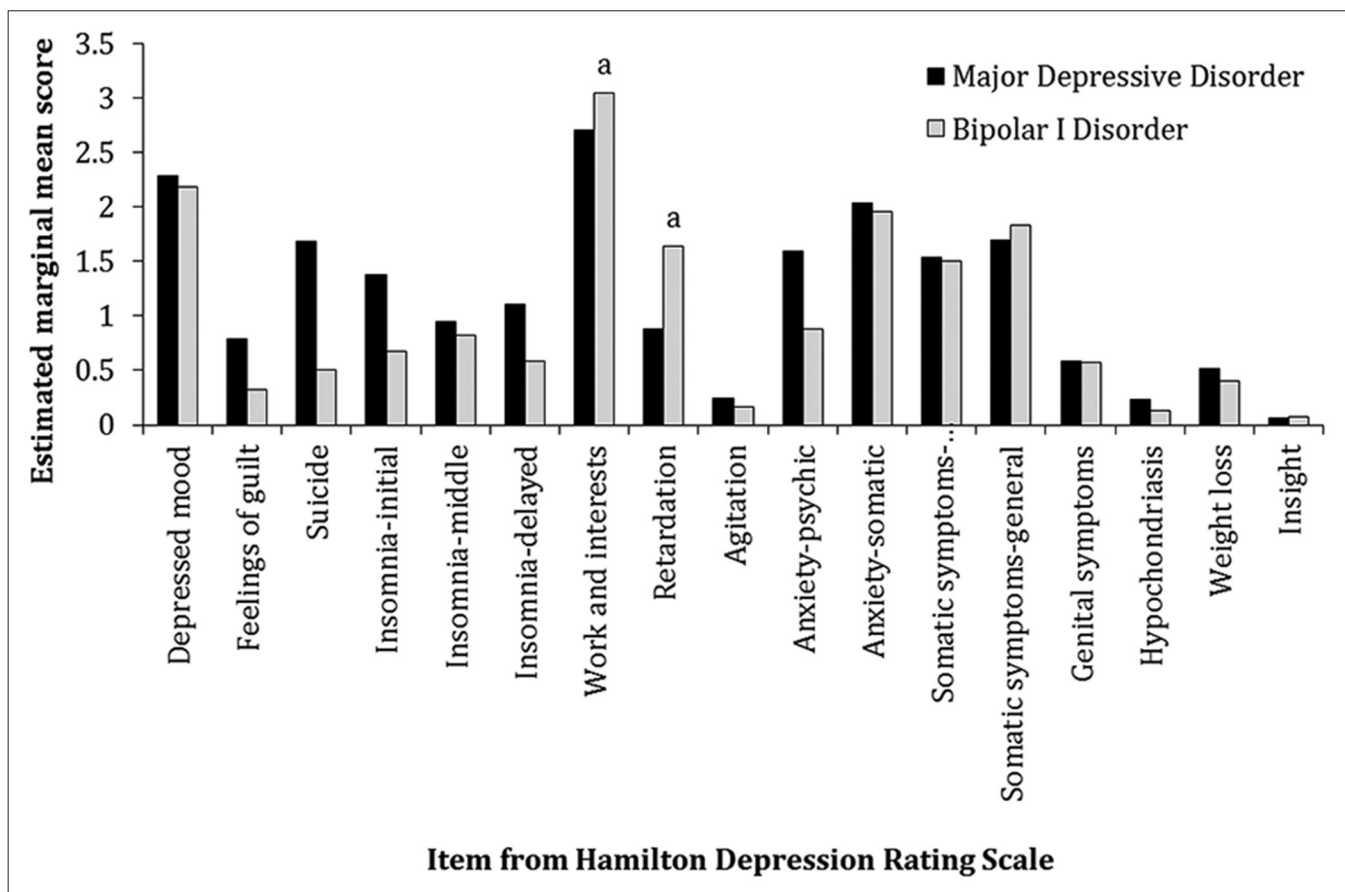
We found persons with BID reported greater rates of any lifetime suicide attempts with a higher proportion reporting at least 1 suicide attempt compared to persons with MDD which is similar to the study of Kessler *et al.* and Chen *et al.* reported the lifetime rates of suicide attempts of persons with bipolar disorder and unipolar disorder were 29.2% and 15.9% (ranges of 26–29% vs. 14–16%), respectively.<sup>[18,19]</sup> We found

that patient and their relatives having difficulties to unfold the history of previous suicide attempt may be due to (1) stigma related to mental illness and (2) concern medicolegal issues.

We also observed that BID was more common among the family members of the subjects with BID compared with MDD which is similar to the study of Benazzi *et al.* reported MDD with family history of bipolar disorder was present in 20.0% of the patients while bipolar disorder with family history of bipolar disorder was present in 53.7% of the patients.<sup>[20]</sup>

We found persons with BID had a higher percentage of hypersomnia, psychomotor retardation, delusions, social withdrawal, and leaden paralysis, while persons with MDD had a higher percentage of initial insomnia, early morning awakening, anger or irritability, tearfulness, subjective restlessness, and anxiety. The study findings are consistent with the study of Mitchell *et al.* reported that subjects with bipolar disorder had a significantly higher prevalence of early morning awakening, morning worsening, psychomotor retardation, difficulty thinking or concentrating, delusions, and hallucinations.<sup>[17]</sup>

In the present study, psychomotor retardation and anxiety as a predominant clinical feature in persons with BID and MDD, respectively, again consistent with the previous



**Figure 2:** Estimated marginal mean scores from individual baseline Hamilton Rating Scale for Depression items, adjusted for total Montgomery-Asberg depression rating scale score. a - bipolar patients differed significantly from major depressive disorder patients ( $P < 0.05$ ).

study of Parker *et al.* suggests bipolar depressed patients were significantly more likely to demonstrate psychomotor disturbance (particularly retardation) and pathological guilt.<sup>[21]</sup>

The study findings are consistent with the study of Mitchell *et al.* reported the retardation subscale score was higher in subjects with bipolar disorder compared to MDD ( $4.6 \pm 4.2$  vs.  $2.8 \pm 3.1$ ) and Newcastle endogenous depression diagnostic index rated 71.8% bipolar patients demonstrated depressed psychomotor activity than MDD patients (41%).<sup>[22]</sup>

Our study findings are inconsistent possibly due to different methodology with the study of Xiang *et al.* reported compared to MDD patients, BID was characterized by more atypical depressive features (increased appetite, increased sleep, and weight gain), more psychotic symptoms while BIID was characterized by more psychotic symptoms.<sup>[23]</sup>

We found that the persons with BID had higher estimated marginal mean score with individual MADRS items in apparent sadness, reported sadness, concentration difficulties, lassitude, and inability to feel while the persons with MDD had a higher score in inner tension, reduced sleep, and pessimistic thoughts. The persons with BID had higher estimated marginal mean score with individual

HRSD items in work and interest and retardation, while the persons with MDD had a higher score in initial insomnia, insomnia delayed, and anxiety-psychic. Our study findings are not consistent with the study by Perlis *et al.* reported the subjects with bipolar disorder were statistically significantly different compared to MDD with individual MADRS items in apparent sadness, inner tension, reduced sleep, pessimistic thoughts, and suicidal thoughts.<sup>[10]</sup> Our study findings are not consistent with it due to the small sample size compared to a large multicenter trial.

Teja *et al.* reported that depressed mood and difficulties in work are present in all cases. Late insomnia, somatic anxiety, initial insomnia, psychic anxiety, suicidal ideations, retardation, loss of insight, middle insomnia, genital symptoms, hypochondriasis, gastrointestinal symptoms, agitation somatic symptoms in general, and diurnal variation are present in >50% of the subjects. Depersonalization, paranoid and obsessional symptoms were reported very infrequently, and guilt was present in about half of the subjects. Again the study findings are inconsistent due to different study design.<sup>[24]</sup>

The total duration of illness of majority of the persons with BID and MDD is >18 years and <3 years, respectively. In our study, we see more number of patients of a BID than

MDD in psychiatric consultation of >10 years of total duration of illness. The study findings are similar to a study of Forty *et al.* reported median illness duration 20 years for the bipolar group, but findings are inconsistent with regard to MDD group.<sup>[25]</sup>

### Strength of the Study

- Subtle differences between the clinical features of major depressive episode in BID and MDD can be detected
- The study includes both qualitative (i.e., gender, clinical symptoms, and sociodemographic characteristics) and quantitative data (i.e., age, total duration of illness, and rating scales) so phenomenology between two diagnostic categories can be identified
- Depressive symptoms such as reverse neurovegetative symptoms (i.e., hypersomnia and increased appetite) and other determinants (i.e., age of onset of illness, family history, suicide, and treatment) were clinically evaluated and recorded.

### Limitation of the Study

- The sample size in the present study is small so results cannot be generalized.
- Retrospective evaluation of facts of a depressive episode is difficult.
- The rating scales (HRSD and MADRS) are clinician rated, so the possibility of observer bias is likely.
- Items of HRSD and MADRS do not assess all the core criterion symptoms particularly reverse neurovegetative symptoms, so they were underscored.

### CONCLUSION

The current symptoms of bipolar depression have been thought by many to be similar to those seen in unipolar depression. Yet it seems that there are subtle differences in the phenomenological representation of unipolar and bipolar depression. Differentiating between unipolar and bipolar depression is consistent with dimensional distinctions between the two disorders. It also offers clinical utility in identifying patients who may warrant further assessment for bipolarity.

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