

Mood State and Severity as a Predictor of Bipolar Disorder Among Antidepressant Non-Responders

Astrid Desrosiers, MD, MPH¹; Robert M.A. Hirschfeld, MD²; Joseph R. Calabrese, MD³; Mark A. Frye, MD⁴; Thomas R. Thompson, MD⁵; Michael L. Reed, PhD⁶; Gary S. Sachs, MD¹

¹Department of Psychiatry, Harvard University, Boston, MA; ²Department of Psychiatry & Behavioral Sciences, University of Texas Medical Branch, Galveston, TX; ³Department of Psychiatry, Case Western Reserve School of Medicine, Cleveland, OH; ⁴Neuropsychiatric Institute and Hospital, Los Angeles, CA; ⁵GlaxoSmithKline, Research Triangle Park, NC; ⁶Vedanta Research, Chapel Hill, NC

ABSTRACT

Objective
This study explored the relationship between mood state, severity and depression symptoms and bipolar disorder (BPD) risk among currently treated patients with depression.

Method
Psychiatrists from community and private practice clinic settings randomly selected patients with unipolar depression who had one or more prior antidepressant (AD) medication failures. Patients with a diagnosis of BPD, OCD, or schizophrenia were excluded. Patient history and AD use were obtained via record abstraction. A self-administered patient survey collected current depression symptoms via the 20-item Center for Epidemiologic Study-Depression (CESD) scale. BPD risk was assessed via the Mood Disorder Questionnaire (MDQ).

Results
Data were collected from 462 females and 140 males. Stepwise logistic regression identified depressive symptoms associated with a MDQ positive (MDQ+) screen for BPD. For females, this included "people were unfriendly" (OR=2.4, p<.002); for males: "felt that people disliked me" (OR=8.8, p<.001), "talked less" (OR=.149, p<.004), "appetite was poor" (OR=3.1, p<.039). Among those with severe CESD depression (n=370), 18.6% screened MDQ+ positive while 29.7% with mild depression (n=64) screened MDQ+ (chi=4.11, p<.04) suggesting that depression may mask recall for manic symptoms.

Conclusions
Gender-specific depressive symptoms may help to identify patients at risk for BPD. Severe depression may mask recall of past mania and manic symptoms. Manic symptom history should be explored during periods of mild or minimal depression to help optimize symptom recall and enhance BPD detection and the likelihood of appropriate treatment.

INTRODUCTION

There is growing evidence that bipolar disorder is frequently undetected or misdiagnosed in patients who consult both primary care professionals and psychiatrists.¹⁻⁴

Misdiagnosis, especially as unipolar depression, is a common problem in patients with bipolar disorder. In the National Depressive and Manic-Depressive Association (NDMDA) study, 69% of patients with bipolar disorder were initially misdiagnosed and 60% of patients were misdiagnosed with unipolar depression.⁵

The aim of the present study was to delineate depressive symptoms that may help identify patients with bipolar disorder currently in treatment for major depression. We also explored the relationship between the severity of depressive symptoms and bipolar disorder risk among patients currently in treatment for unipolar depression.

METHODS

Selection of Subjects

- Psychiatrists from private practice and clinic settings (N=63) were asked to identify their next 10 patients with major depression who had experienced one or more prior medication failure (defined as a change in their depression medication or regimen).
- Patient eligibility criteria:
 - Aged 18+, currently in treatment for major depression
 - Not diagnosed with BPD, OCD, schizophrenia or schizoaffective disorder
 - They had received treatment for major depression for at least three months and had one or more medication changes during their current episode or
 - If treated less than three months, they had changed medications at least three times.

Instruments

- Patient survey:** Demographic and family history form; the Center for Epidemiologic Studies Depression Scale (CES-D); a health care resource use form; the Mood Disorder Questionnaire (MDQ); a co-morbid health problems form; and legal problems were assessed with the legal status section of the Addiction Severity Index (ASI)
- A medical records abstraction form:** Patient and family health history; lifetime history of major depression; current episode of major depression; prescription drug treatment history; number of prior antidepressant medication failures; health care resource use; and outcomes of treatment

Analysis

- Two analyses were conducted. The first looked the association between CES-D depression level (not depressed = score of 0-14; mildly/moderately depressed = 15-21, and severely depressed = 22+) and MDQ status (positive vs. negative). Two-sided Person Chi-Square tests were performed to establish significance. The second analysis used forward stepwise logistic regression and looked at the which CES-D depressive symptoms predicted MDQ positive status separately in males and in females.

RESULTS

Patient Demographics	N	%
Total	602	100%
Females	462	76.74
Age (Mean = 47.9, Median = 48.0)		
18-24	22	3.67
25-44	212	35.33
45-64	316	52.67
65+	50	8.33
Ethnic Background		
African American	51	8.5
Caucasian	512	86.39
Other	31	5.1
Of Spanish or Hispanic heritage	20	3.40
Income		
<\$20,000	254	43.2
\$20,000 to \$39,999	130	22.11
\$40,000 to \$59,999	104	17.69
\$60,000 to \$79,999	46	7.82
\$80,000 to \$99,999	16	2.72
\$100,000 to \$119,999	11	1.87
\$120,000+	27	4.59
MD Practice Characteristics		
Private Practice	409	68.01
Community Mental Health Clinic	116	19.19
Hospital	51	8.55
Research Center	22	3.58
Other	4	0.69

Characteristics of Lifetime Clinical Depression

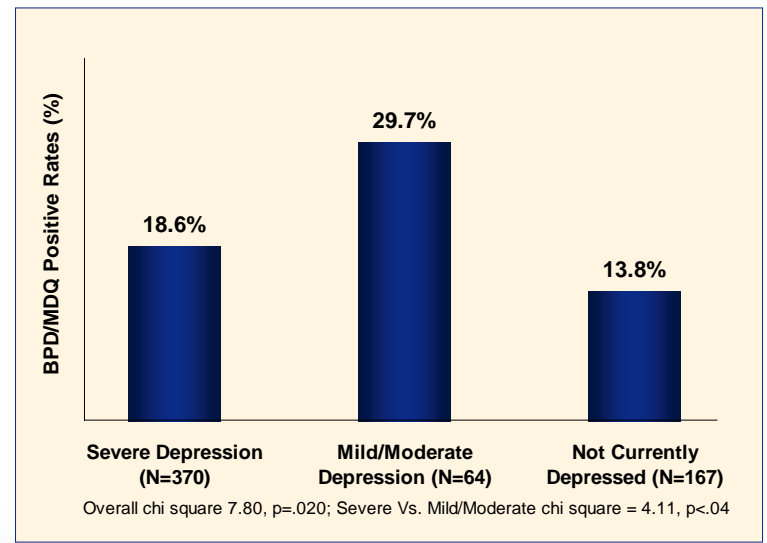
	Total N of Responders	Mean, Median or Percent
Mean age of depression onset (years)	586	27.46
Mean lifetime duration of depression symptoms (years)	585	20.39
Mean age at first MD consultation (age in years)	597	33.16
Median # of lifetime depressive episodes	429	5.00
Median # of lifetime antidepressants taken	559	4.00
Percent reporting prior ECT	600	5.83
If currently reporting depression, mean duration of current episode (years)	381	2.90
If not currently reporting depression, mean duration of most recent episode (years)	188	1.22
Mean # of antidepressants taken for current episode	577	2.68

CES-D Depressive Symptoms Significantly Predictive of MDQ Positive Status

CES-D Variable	Odds Ratio	95% Confidence Interval	Wald	p Value
Females				
People were unfriendly	2.40	1.39-4.14	9.83	.002
Males				
I did not feel like eating; my appetite was poor	3.12	1.06-9.15	4.27	.039
I talked less than usual	0.15**	0.04-0.55	8.08	.004
I felt that people disliked me	8.84	2.70-28.97	12.94	.000

**Odds ratio less than 1 indicates "talked more than usual"

BPD/MDQ Positive Rates by CES-D Depression Status



DISCUSSION

- Nearly 20% of patients who have been prescribed antidepressants for the treatment of unipolar depression screened positive for bipolar disorder risk (MDQ+).
- Bipolar disorder (as indicated by MDQ positive screens) is more prevalent in patients with mild to severe depression than in patients not currently depressed.
- Severe depression may be masking recall for prior manic/hypomanic symptoms to a higher degree than mild to moderate depression.
- We hypothesize that the lower rate of BPD risk among those "not currently depressed" on CES-D is because these are unipolar depressed patients who are responding to AD treatment.
- It seems advisable that manic symptom history should be explored during periods of mild or minimal depression to help optimize symptom recall and enhance the detection of bipolar disorder and the likelihood of appropriate treatment.
- Our analysis identified CES-D depressive symptoms that were significantly associated with a positive bipolar screen on the MDQ.
 - For females, the sole predictive variable was "people were unfriendly"
 - For males the predictive variables were "I felt that people disliked me", "I talked more than usual", and "I did not feel like eating; my appetite was poor".

CONCLUSION

- Gender-specific depressive symptoms may help to identify patients at risk for BPD.
- Severe depression may mask recall of past mania and manic symptoms.
- Manic symptom history should be explored during periods of mild or minimal depression to help optimize symptom recall and enhance BPD detection and the likelihood of appropriate treatment.

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