Sensitivity and Specificity of the Mood Disorder Questionnaire as a Screening Tool for Bipolar Disorder During Pregnancy and the Postpartum Period

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ABSTRACT

Background: Previous studies have shown that one-quarter of women with bipolar disorder relapse during pregnancy, and nearly half of bipolar women relapse during the postpartum period. The perinatal period is also associated with an elevated risk for new-onset mood disorder. Bipolar disorder is often unrecognized, and there is often a significant delay between illness onset and proper diagnosis and treatment. The objective of this cross-sectional psychometric study was to investigate the use of the Mood Disorder Questionnaire (MDQ) as a screening tool for bipolar disorder in a community-based population of pregnant and postpartum women.

Method: 150 women with a mean age of 30.1 years (standard deviation = 5.5 years; range, 17–43 years) who had been referred to a women's mental health program for psychiatric assessment during pregnancy (n = 95) or the postpartum period (n = 55) were enrolled between June 2010 and December 2011. All women completed the MDQ on the day of their first assessment, and the sensitivity and specificity of the MDQ were calculated against *DSM-IV*–based clinical diagnoses provided by experienced psychiatrists.

Results: A total of 18 women (12% of the sample) were diagnosed with bipolar disorder (6 with bipolar I disorder, 10 with bipolar II disorder, and 2 with bipolar disorder not otherwise specified). The traditional scoring of the MDQ yielded poor sensitivity (39%) and excellent specificity (91%). The best-fitting model was a modified scoring algorithm using cutoff scores of 7 or more symptoms on the MDQ without the supplementary questions, yielding excellent sensitivity (89%) and specificity (84%).

Conclusions: The MDQ is a useful instrument for screening for bipolar disorder during both pregnancy and the postpartum period. Considering that perinatal women have an elevated risk of both first-onset and relapse of bipolar disorder, particularly during the postpartum period, routine use of screening tools in perinatal programs is encouraged.

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It has been long recognized that the perinatal period is associated with high risk for mood instability, particularly for women with bipolar disorder.[1] A recent large study[2] evaluating 2,252 pregnancies of women with bipolar disorder and major depressive disorder (MDD) showed that 23% of women with bipolar disorder relapse during pregnancy and that this rate increases to 52% during the postpartum period.[2] These findings are in contrast with the 4.6% and 30.0% relapse rates found in women with MDD during pregnancy and the postpartum period, respectively. Among 120,378 women with first-time psychiatric inpatient or outpatient contact, those who had their first-ever psychiatric contact within the first year after childbirth (N = 2,870) were 3 times more likely to be diagnosed with bipolar disorder after 15 years of follow-up.[3] Another large study[4] involving 10,218 mothers reported that a diagnosis of bipolar disorder was the strongest predictor of hospitalizations between days 10 and 19 of the postpartum period (relative risk = 37.22; 95% CI, 58.00–102.04). In this latter study,[4] 26.9% of mothers with bipolar disorder were hospitalized within the first year postpartum. Several lines of evidence suggest that bipolar disorder is particularly associated with more severe forms of psychopathology during the postpartum period, including rapid onset, presence of psychotic symptoms, suicide, and infanticide.[5–7] A study[7] evaluating mothers who were admitted to a forensic psychiatric unit after killing or attempting to kill their children demonstrated that the majority of cases diagnosed with MDD at admission (64.7%) were rediagnosed with bipolar disorder at discharge. Of note, the majority (63%) of the cases rediagnosed from MDD to bipolar disorder had a history of prior treatment with unopposed antidepressants.[7] Data from the United Kingdom showed that suicide is the leading cause of maternal mortality, accounting for 28% of deaths.[8] These data are consistent with a large prospective study[9] showing that bipolar disorder is the second leading psychiatric condition associated with completed suicide in women.

Despite the fact that untreated bipolar disorder is associated with poorer outcomes, bipolar disorder is often unrecognized.[10,11] Results from the 2-year prospective Bipolar Comprehensive Outcomes Study[12] revealed that there is on average a 9-year and 6-year delay in diagnosing bipolar disorder after the first depressive and manic episode, respectively. Many factors contribute to this delay in diagnosing bipolar disorder, including lack of awareness or insight by affected subjects, difficulties with access to proper health care, and a lack of systematic assessment of manic/hypomanic symptoms on the part of the clinicians.[13] The majority of cases of unrecognized bipolar disorder are misdiagnosed as unipolar MDD.[14] Since most perinatal mood episodes are depressive

Clinical Points

- Screening for bipolar disorder during pregnancy and the postpartum period has been largely ignored.
- The Mood Disorder Questionnaire is a useful screening tool for perinatal women.
- Correct identification of past history of hypomanic symptoms can prevent the negative consequences of undiagnosed and untreated bipolar illness in perinatal women.

or subsyndromal in nature and since in the vast majority of perinatal cases psychiatric illness precedes the pregnancies,[2] a careful investigation of lifetime manic/hypomanic symptoms is critical in diagnosing or ruling out bipolar disorder in pregnant and postpartum women. Research on proper screening procedures for bipolar disorder in perinatal populations is scarce, and psychometric information is very limited.[15] Sharma and Xie[16] recently published the only study measuring sensitivity and specificity of a screening tool that assesses the presence of lifetime manic/hypomanic symptoms in a sample of 125 women with MDD, bipolar I disorder, or bipolar II disorder.[16] In that study, subjects completed the Mood Disorder Questionnaire (MDQ)[17] and the Structured Clinical Interview for *DSM-IV* Axis I Disorders[18] within 2–4 weeks of childbirth. The authors found that the best sensitivity (0.87; 95% CI, 0.76–0.94) and specificity (0.85; 95% CI, 0.74–0.92) scores were obtained using alternative scoring of the presence of 8 symptoms, excluding the supplementary questions. However, positive and negative predictive values and the chance-corrected level of agreement (κ) were not reported.

The objective of this cross-sectional psychometric study was to investigate the use of the MDQ as a screening tool for bipolar disorder in pregnant and postpartum women referred for psychiatric consultation in a women's mental health outpatient program.

METHOD

Study Participants

We enrolled 150 consecutive pregnant and postpartum women referred for psychiatric consultation at the Women's Health Concerns Clinic, St. Joseph's Healthcare Hamilton, Hamilton, Ontario, between June 2010 and December 2011. The majority of the referrals came from family doctors and obstetric and midwifery clinics in Hamilton, Ontario. On the day of initial assessment, all women completed the MDQ before meeting with a certified psychiatrist for diagnostic assessment and treatment recommendations. Demographic data including age, marital status, parity, and level of education were recorded. Clinical variables included psychiatric diagnoses and MDQ scores. Sensitivity and specificity of the MDQ as a screening tool for bipolar disorder were calculated against clinical diagnoses provided by experienced psychiatrists on the basis of *DSM-IV* criteria. This study was approved by the local research ethics board.

Statistical Analysis

Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and chance-corrected level of agreement (κ) were obtained using the statistical package R, version 2.13.1 (R software and documentation available at http://www.r-project.org). Complementary figures were produced using the software Microsoft Excel, version 14.0 (Microsoft Corporation, Redmond, Washington). For the purpose of our main outcome measure, we took a conservative approach and classified all patients with psychiatric diagnoses of "rule out," "possible," "probable," or "query" bipolar disorder as bipolar negative. As an exploratory analysis, we also measured the sensitivity and specificity of the MDQ, including all cases initially diagnosed as "rule out," "possible," "probable," or "query" bipolar disorder as bipolar positive. Psychometric data were interpreted according to the following criteria: > 0.80 = excellent or highly correlated, 0.80–0.70 = good or adequately correlated, 0.69–0.50 = fair or fairly correlated, and < 0.50 = poor or poorly correlated.[19]

RESULTS

Demographics

Demographic information is shown in Table 1. The mean ± SD age of our sample was 30.1 ± 5.5 years (range, 17–43 years), and the majority of the women were married (n = 87, 58.0%), pregnant (n = 95, 63.3%), and multiparous (n = 92, 61.3%) and had received postsecondary education (n = 81, 54.0%). Of the 150 women evaluated, 18 (12.0%) were diagnosed with bipolar disorder after a psychiatric interview. Bipolar II disorder was the most common subtype (n = 10, 55.6%), followed by bipolar I disorder (n = 6, 33.3%) and bipolar disorder not otherwise specified (NOS) (n = 2, 11.1%).

Psychometric Data for the MDQ Using Traditional Scoring

The sensitivity and specificity of the MDQ were first calculated using the traditional scoring criteria originally proposed by Hirschfeld et al[17] (presence of 7 symptoms plus supplementary questions). Using this scoring algorithm, the MDQ showed poor sensitivity (0.39; 95% CI, 0.17–0.64), excellent specificity (0.91; 95% CI, 0.85–0.95), PPV of 0.37 (95% CI, 0.16–0.62), NPV of 0.92 (95% CI, 0.85–0.96), and κ of 0.29 (95% CI, 0.02–0.55) (Figure 1). Lowering the number of symptoms necessary for a positive screen to 6 did not improve the test properties beyond a sensitivity of 0.44 (95% CI, 0.22–0.69) and a specificity of 0.85 (95% CI, 0.78–0.91).

Psychometric Data for the MDQ Using Alternative Scoring

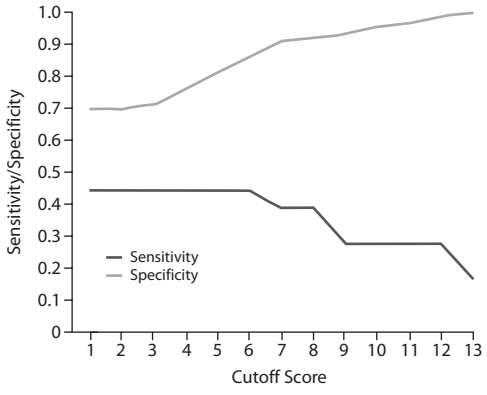
Consistent with other studies in nonperinatal populations,[20–23] a recent report[16] utilizing the MDQ in postpartum

Table 1. Demographic and Clinical Characteristics of the Study Sample (N = 150)

Characteristic	Data
Age, mean (SD), y	30.1 (5.5)
Marital status, n (%)	
Common law	20 (13.3)
Single	39 (26.0)
Married	87 (58.0)
Not available or not reported	4 (2.7)
Education, n (%)	
Incomplete high school	20 (13.3)
High school	25 (16.7)
College degree, 2-year	41 (27.3)
University degree, 4-year	40 (26.7)
Not available or not reported	24 (16.0)
Pregnant, n (%)	95 (63.3)
Postpartum, n (%)	55 (36.7)
Primiparous, n (%)[a]	57 (38.0)
Multiparous, n (%)[a]	92 (61.3)
Primary psychiatric diagnosis, n (%)	
Major depressive disorder	76 (50.7)
Anxiety disorder	26 (17.3)
Bipolar disorder	18 (12.0)
Bipolar I disorder	6 (33.3)[b]
Bipolar II disorder	10 (55.6)[b]
Bipolar disorder not otherwise specified	2 (11.1)[b]
Adjustment disorder	14 (9.3)
Alcohol or substance abuse or dependence	5 (3.3)
Psychotic disorder	3 (2.0)
Attention-deficit/hyperactivity disorder	1 (0.7)
Conduct disorder	1 (0.7)
No lifetime psychiatric disorder	6 (4.0)

[a]Missing data for 1 participant for primiparous or multiparous.
[b]Percentage of bipolar disorder subgroup.

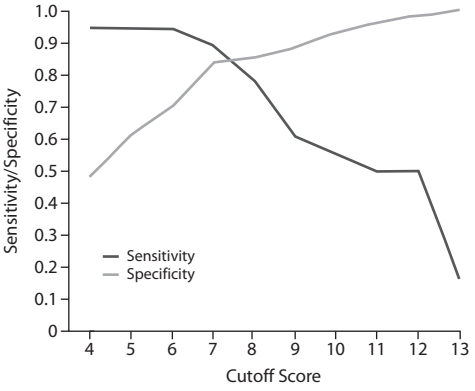
Figure 1. Sensitivity and Specificity of the Mood Disorder Questionnaire Using Traditional Scoring (N = 150)



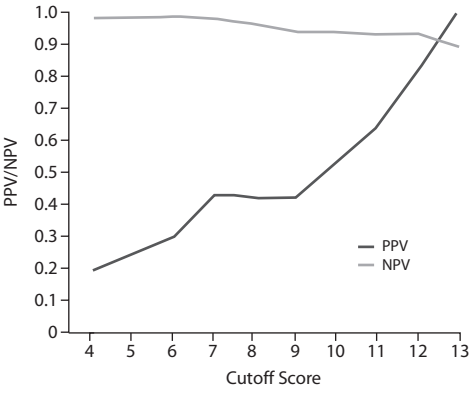
women with affective disorders has also shown weak test properties when using the traditional scoring algorithm. Thus, we repeated the sensitivity/specificity analysis and found that the best-fitting model was the presence of 7 manic/hypomanic symptoms without the supplementary questions, which yielded excellent sensitivity (0.89; 95% CI, 0.65–0.99), excellent specificity (0.84; 95% CI, 0.77–0.89), PPV of 0.43 (95% CI, 0.27–0.60), NPV of 0.98 (95% CI, 0.94–0.99), and κ of 0.50 (95% CI, 0.31–0.68) (Figure 2A and Figure 2B).

Figure 2. Analyses of the Mood Disorder Questionnaire Using Alternative Scoring (N = 150)

A. Sensitivity and Specificity



B. Positive Predictive Value (PPV) and Negative Predictive Value (NPV)

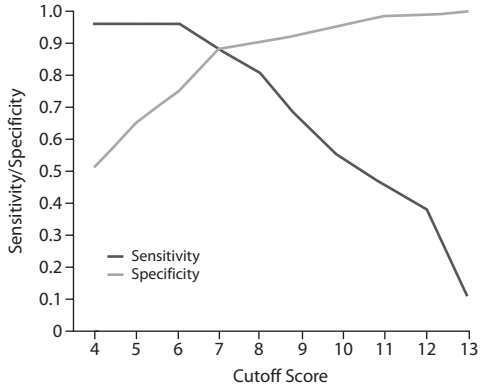


In order to explore the clinical utility of the MDQ as a screening tool for bipolar disorder, including cases for which psychiatrists were unsure about the diagnosis of bipolar disorder after initial assessment, we repeated the analysis including patients initially diagnosed as "rule out," "possible," "probable," or "query" bipolar disorder. After applying this change, the number of bipolar cases increased from 18 to 26. Notably, the best-fitting model remained the same: a cutoff score of 7 symptoms, without the supplementary questions, yielded sensitivity of 0.88 (95% CI, 0.70–0.98), specificity of 0.89 (95% CI, 0.82–0.94), PPV of 0.62 (95% CI, 0.45–0.77), NPV of 0.97 (95% CI, 0.92–0.99), and κ of 0.66 (95% CI, 0.50–0.81) (Figure 3).

Frequency of MDQ Items Among Bipolar and Nonbipolar Patients

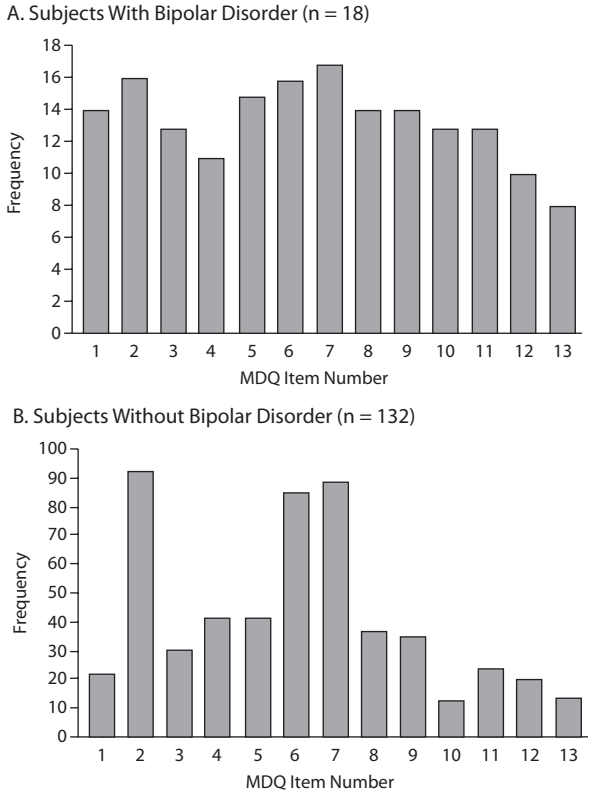
The distribution of manic/hypomanic symptoms endorsed by bipolar and nonbipolar patients was examined using frequency histograms. Bipolar patients (n = 18) showed an even distribution of manic/hypomanic symptoms, whereas nonbipolar patients (n = 132) most frequently endorsed symptoms of irritability, racing thoughts, and difficulty concentrating (Figure 4A and Figure 4B).

Figure 3. Sensitivity and Specificity of the Mood Disorder Questionnaire Using Alternative Scoring, Including Patients With a "Rule Out" Diagnosis of Bipolar Disorder[a]



[a]For this exploratory analysis, all women diagnosed as "rule out," "possible," "probable," or "query" bipolar disorder were considered bipolar cases.

Figure 4. Frequency of Mood Disorder Questionnaire (MDQ) Symptoms Among Subjects With and Without Bipolar Disorder



DISCUSSION

This study is the first to investigate the use of the MDQ as a screening tool for bipolar disorder in a community-based sample of pregnant and postpartum women. We found that, when using an alternative scoring algorithm of the presence of 7 manic/hypomanic symptoms without the supplementary questions, the MDQ is an excellent screening tool for perinatal women seeking psychiatric consultation. Using this scoring system, we obtained high sensitivity (89%) and NPV (98%), which are the most important properties of a screening tool from a clinical standpoint.[24] Screening tools with high NPV are particularly helpful clinically when the test is negative, which would suggest that there is little chance that the disorder is present in a given subject (false negative). The relatively low PPV of the MDQ in screening for bipolar disorder in our population (43%) is in line with previous reports[13,17,25] and indicates that about half of those who scored positive for bipolar disorder using the MDQ were not diagnosed as having bipolar disorder by the clinical interview (false-positives). It is important to keep in mind that the predictive value of a screening test depends on the prevalence of the disease in the sample.[24,26] A study[13] of predictive values of screening tools for bipolar disorder (including the MDQ) showed that lower PPVs are expected when the probability of the disease is low.

Consistent with previous reports,[16,21–23] our results demonstrated that the use of alternative scoring enhances the likelihood for the MDQ to detect milder forms of bipolar disorder (bipolar II and bipolar disorder NOS). Considering that bipolar I disorder is easier to recognize and diagnose than bipolar II disorder and bipolar disorder NOS, we agree with the commentary by Zimmerman et al[24] that the main clinical utility of the MDQ is probably its ability to detect these milder forms of bipolar disorder. This attribute of the MDQ may be particularly relevant to the perinatal population, given that women with bipolar II disorder are just as likely to relapse during pregnancy and the postpartum period as women with bipolar I disorder.[2] Furthermore, detection of subthreshold bipolar symptoms is relevant clinically as the number of hypomanic symptoms during depressive episodes is a strong predictor of later conversion to bipolar disorder.[27,28] This clinical finding is in line with the results from our exploratory analysis showing that the high sensitivity and specificity of the MDQ were retained even when we included the cases for which psychiatrists were suspicious but yet unsure about the diagnosis of bipolar disorder in their initial assessment (the "rule out" cases). It is conceivable that a number of these cases may have been diagnosed with bipolar disorder at discharge.

A frequent clinical question that arises with regard to screening for bipolar disorder during pregnancy and the postpartum period is "When is the best time to screen?"[15] Considering that bipolar women tend to relapse early and at relatively high rates during pregnancy, that in most cases the illness starts before the pregnancy, and that mood instability during pregnancy is one of the strongest predictors of postpartum episodes,[2,29,30] we argue for "the earlier the better." To put this topic in a more general perspective, despite the fact that the prevalence of gestational diabetes (2%–6%)[31] and bipolar disorder (4%)[32] are similar, women are routinely screened for the former, while health care providers largely fail to inquire about symptoms of mania during

pregnancy.[10,33] As mentioned above, the consequences of undiagnosed bipolar disorder during the perinatal period can be devastating for both mothers and infants.[7,11]

The present study should be interpreted in view of its strengths and limitations. One may argue that one of the limitations of our study is the lack of a structured diagnostic interview. We argue that this lack is, in fact, a strength because we tested the usefulness of the MDQ as a screening tool for bipolar disorder in a real clinical setting. The use of psychiatrists for clinical assessments rather than nonclinician raters is regarded as the gold standard in terms of accuracy in diagnosing bipolar disorder, especially bipolar II disorder and subthreshold bipolar disorder.[14,34] Nevertheless, studies directly comparing clinical assessments versus structured research interviews in individuals with bipolar disorder have found high levels of agreement.[35] Another strength of our study comes from the fact that psychiatric services in Canada are 100% publicly insured, which increases the generalizability of our results. There are major efforts underway to screen for perinatal depression. However, screening for bipolar disorder in pregnancy and the postpartum period has been largely ignored.[6] Our findings suggest that the use of a screening tool for bipolar disorder in this population can not only help identify past hypomanic symptoms that would go undetected otherwise, but also ultimately guide appropriate treatment plans and prevent the well-known negative outcomes of undiagnosed illness.

In conclusion, when an alternative scoring of 7 manic/hypomanic symptoms without supplementary questions is used, the MDQ is an excellent screening tool for bipolar disorder in pregnant and postpartum women seeking psychiatric assessment. Future studies investigating the performance of the MDQ in obstetric, midwifery, and general practitioner clinics would shed light on the usefulness of this scale in nonpsychiatric perinatal settings.

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