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Examination of premenstrual symptoms as a risk factor for depression in postpartum women

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Abstract

PURPOSE—Postpartum depression (PPD) is a significant public health concern with prevalence of major and minor depression reaching 20% in the first three postpartum months. Sociodemographic and psychopathology correlates of PPD are well-established; however, information on the relationship between premenstrual disorders and the development of PPD is less well-established. Thus, the aim of this study was to examine the role of premenstrual syndrome (PMS)/premenstrual dysphoric disorder (PMDD) as a risk factor for PPD.

METHODS—Premenstrual symptoms were assessed retrospectively using the Premenstrual Symptoms Screening Tool (PSST) and depression was diagnosed according to DSM-IV criteria and assessed using the HDRS. A two-stage screening procedure was applied. In the first stage, the PHQ-9 was employed. In the second stage, women endorsing 5 symptoms on the PHQ-9 were administered the SCID, HDRS, and PSST.

RESULTS—Hierarchical linear regression showed that history of depression and PMS/PMDD contributed an additional 2% of the variance ($p < .001$), beyond that of sociodemographic factor effects. The full model accounted for 13% of the variance in postpartum depressive symptoms. Using logistic regression, a significant association also emerged between PMS/PMDD and PPD (OR=1.97).

CONCLUSIONS—The findings of this study suggest that PMS/PMDD is an important risk factor for PPD. Women endorsing a history of PMS/PMDD should be monitored during the perinatal period.

Keywords

Postpartum depression; Risk factors; Premenstrual syndrome (PMS); Premenstrual dysphoric disorder (PMDD); Premenstrual symptoms screening tool (PSST)

Introduction

Approximately 1 in 5 women will experience depression in the postpartum period (Gavin et al. 2005). The symptom profile of postpartum depression (PPD) is similar to that of a major depressive episode outside the postpartum period and is characterized by low mood, loss of

interest in enjoyable activities, fatigue, sleep and appetite disturbance, feelings of guilt, poor concentration and irritability, and suicidal ideation (DSM-IV-TR; American Psychiatric Association 2000). If left untreated, PPD can have deleterious effects on a woman's psychological functioning (O'Hara et al. 2000) and quality of life (DaCosta et al. 2006). Further, there may be both short and long term negative consequences for exposed children, as evidenced in empirical support for impaired maternal-infant interactions (Murray and Cooper 1997), and poor cognitive (Whiffen and Gotlib 1989) and emotional functioning in infants (Murray et al. 2003). Because of the potentially chronic and recurring nature of PPD, children continuously exposed to the effects of depression may be vulnerable to the onset of externalizing disorders (e.g. conduct disorders), and major depression later in life (Weissman and Jensen 2002).

Given the significant impact of PPD on mothers and their children, it is important to further explicate risk factors for PPD to comprehensively inform screening procedures and treatment. A wealth of empirical research suggests that factors such as age, education, marital and breastfeeding status, and psychopathology (e.g., history of depression) may be significantly associated with PPD (Beck 2001; McCoy et al. 2006; Robertson et al. 2004). Nonetheless, risk factor data are relatively less established for menstrual cycle-related variables including premenstrual syndrome (PMS) and premenstrual dysphoric disorder (PMDD) (Bloch et al. 2006). These data may inform etiologic hypotheses for PPD and current strategies for identifying women at a heightened risk for experiencing depression in the postpartum period.

Most women of reproductive age experience emotional and physical symptoms premenstrually (Johnson et al. 1988). PMDD is a severe form of this phenomenon, with more frequent symptoms including anger/irritability, anxiety/tension, tired/lethargy, and mood swings (Pearlstein et al. 2005) accompanied by significant functional impairment in social and work domains (APA 2000; Pearlstein et al. 2000). Such symptoms generally onset in the late-luteal phase of the menstrual cycle (e.g., 7 to 10 days prior to menses), and remit within the first three days of menses (Pearlstein et al. 2005). Prospective studies have identified prevalence rates of PMDD ranging from 4.6%–6.4% (Cohen et al. 2002; Sternfeld et al. 2002), consistent with rates identified in retrospective assessments of PMDD (5.1%–6.7%; Steiner et al. 2003b; Wittchen et al. 2002). Moderate to severe premenstrual syndrome (PMS) has a similar symptom profile to that of PMDD and also can lead to impairments in occupational and social functioning, as well as reduced quality of life (Borenstein et al. 2003). PMS, however, is more common as evidenced by prevalence rates ranging from 18.6%–20.7% (Steiner et al. 2003b; Wittchen et al. 2002). Taken together, large retrospective studies assessing PMDD have shown significant functional impairment in both work and interpersonal domains (Steiner et al. 2003b) that is similar in severity to impairment found in major depression and dysthymic disorder (Halbreich et al. 2003; Pearlstein et al. 2000).

The etiology of PPD remains unclear with most research in this area focusing on psychosocial, genetic, and biological factors. Importantly, there is a growing body of literature on the role of ovarian hormones (particularly estradiol) in the modulation of serotonin transmission. This research primarily stems from the hypothesis that a biological mechanism underlies *windows of vulnerability*—periods of hormonal fluctuation when women are at greater risk for experiencing premenstrual disorders and depression during pregnancy, the postpartum, and menopausal transition (Lokuge et al. 2011).

By the end of pregnancy, estradiol levels are as much as 50 times the maximum menstrual cycle level and drop to early follicular phase levels within the first three days following childbirth (Bloch et al. 2003). The rapid decline in estradiol levels immediately following

childbirth may interact with serotonin transmission, leading to a woman's increased susceptibility to experience depression in the postpartum period. This hypothesis finds support in human studies showing changes to 5-HT receptor binding activity in depressed postpartum women, relative to non-depressed women (Moses-Kolko et al. 2008), suggesting that the postpartum hormonal milieu may modulate 5-HT neurotransmission on a functional level. Further support for the estrogen-serotonin interaction is found in recent studies implicating MAO-A activity. Researchers have shown a link between lowered estrogen levels during the first 3 to 4 days postpartum and MAO-A synthesis, identifying elevated MAO-A levels in the early postpartum period as a marker for a monoamine-lowering process that may contribute to the mood dysregulation characteristic of the postpartum blues (Sacher et al. 2010). This estrogen-serotonin interaction model is supported in the PMDD literature as well (Pearlstein and Steiner 2008). For example, a PET study examining 5-HT receptors during the follicular and luteal phases of the menstrual cycle showed serotonergic dysregulation in women with PMDD relative to controls (Jovanovic et al. 2006). Further, PMDD symptoms of poor impulse control, depressed mood, irritability, and increased carbohydrate craving have been characterized as behavioral manifestations of reduced levels of serotonin in the brain (Steiner et al. 2003b). These data findings are consistent with the hypothesized estrogen-serotonin link underlying women's increased vulnerability to experience premenstrual disorders and depression in the postpartum. Improved understanding into the relationship between estrogen and serotonin may inform etiologic biological models for female-related mood disorders more generally, and may have implications for PMS/PMDD as a risk factor for PPD.

The central aim of our study was to investigate PMS/PMDD, assessed using the Premenstrual Symptoms Screening Tool (PSST; Steiner et al. 2003b), as a risk factor for PPD. Based on DSM-IV criteria, the diagnosis of PMDD requires prospective daily symptom charting for two consecutive cycles (APA 2000). Prospective daily charting, however, can be difficult and is time intensive (Smith et al. 2003; Sternfeld et al. 2002). The PSST is an effective screening tool for PMS/PMDD that has been shown to identify a population of women more likely to have clinically significant symptoms from a larger group of women with milder symptoms (Steiner et al. 2003b). To our knowledge, this is the first study to employ the PSST as a measure of PMS/PMDD in the investigation of risk factors for PPD. Our second aim was to further investigate well-established risk factors for PPD, including sociodemographic variables and history of depression, with a sample of women experiencing a range of mild to severe depressive symptoms.

Subjects and methods

Study population

Upon receiving approval from the University of Iowa's Institutional Review Board (IRB), potential participants were referred to the study from the University of Iowa Women's Wellness and Counseling Service or identified using the State of Iowa Birth Registry between February 2009 and May 2011. Women identified using the birth registry had given birth in one of seven counties representing both rural and urban populations. Women between the ages of 18 and 50 were sent a letter inviting them to participate in a study regarding their emotional experiences following delivery. Interested women completed an initial questionnaire assessing sociodemographic factors and emotional experiences in one of two ways: by phone or online via the study's website. To participate further, women had to meet the following eligibility criteria: (a) be between 18 and 50 years of age, (b) given birth to a live infant within the last 12 months, (c) able to speak and read English, and (d) endorsed 5 questions at the level of several days or greater on the PHQ-9 (i.e. experiencing at least 5 symptoms of depression at least several days over the last two weeks).

Eligible women were invited to participate in a longer telephone interview. This diagnostic interview included the Structured Clinical Interview for DSM-IV (SCID; First et al., 1995), the Hamilton Depression Rating Scale (HDRS; Hamilton, 1967), and the Premenstrual Symptoms Screening Tool (PSST; Steiner et al., 2003b). See Table 1 for descriptive statistics.

Psychological factors

The Patient Health Questionnaire (PHQ-9; Kroenke and Spitzer 2002) is a 9-item depression scale that consists of the 9 criteria for diagnosing DSM-IV major depression which scores each of the criteria on a scale from 0 (“not at all”) to 3 (“nearly every day”). The PHQ-9 has been found to be an effective tool for diagnosing depression (Huang et al. 2006), monitoring treatment response (Huang et al. 2006), and evaluating depression outcomes (Löwe et al. 2004). Typically a composite score of 10 or greater is used to identify women likely to be experiencing moderate to severe depression. However, this study required women to endorse

5 questions at the level of several days or greater on the PHQ-9 to obtain a sample of women experiencing a wider range of physical and emotional difficulties. Composite scores on the PHQ-9 ranged from 5 to 25 with an average of 9.9 ($SD=4.2$)

The *Structured Clinical Interview for DSM-IV* disorders (SCID; First et al. 1995) was developed to assess major Axis I and II psychiatric disorders based on DSM-IV criteria. Clinician-evaluators conducting the SCID interviews were at least Masters level clinicians who had experience in psychiatric interviewing. To assess inter-rater reliability, the interviews were audio taped, and 10% of them were scored independently by a second interviewer. The kappa value for diagnosis of current MDE and past MDE was 1.00.

The 20-item *Hamilton Depression Rating Scale* (HDRS; Hamilton 1967) is a validated and reliable measure of the severity of current depressive symptoms. The HDRS is a valid indicator of depression severity in PPD accounting for the overlap between somatic HDRS items and typical experiences of postpartum women (Ross et al. 2003).

Premenstrual symptoms

The Premenstrual Symptoms Screening Tool (PSST; Steiner et al. 2003b) is a clinician friendly screening tool that translates categorical DSM-IV criteria into a rating scale with degrees of severity for premenstrual symptoms and impairment (Steiner et al. 2003b). The PSST was administered by a masters-level clinician, and women were asked to retrospectively assess premenstrual symptoms (e.g., irritability, decreased interest in usual activities, concentration difficulties) and functional impairment (e.g., symptoms interfering with interpersonal and work domains) based on their last menstrual cycle pre-pregnancy using a simple 4-point rating (*not at all, mild, moderate, severe*). The PSST provides scoring guidelines for moderate to severe PMS and PMDD. Within this study, 49 women met criteria for moderate to severe PMS. Of those 49 women, 11 also met criteria for PMDD; thus, this group of women characterizes a range of moderate to severe PMS/PMDD. Subjective reporting of severity of symptoms may be the most useful clinical diagnostic indicator of women seeking treatment (Angst et al. 2001), and captures the greatest number of symptomatic women (Smith et al. 2003).

Statistical analysis

Due to insufficient numbers for some of the categories of each sociodemographic variable, the variables were recoded as binary variables representing potential risk factors. Bivariate correlations between potential binary sociodemographic predictors and each of the response variables (HDRS and a diagnosis of PPD) were calculated. Due to the large number of sociodemographic variables, only variables significantly correlated ($p<.05$) with each

response variable were included in the analyses as potential covariates to be controlled for. Age, non-White, low education¹, single and not breastfeeding were all found to be significantly correlated with each of the two response variables (see Table 2). These variables along with moderate to severe PMS/PMDD in the last prenatal menstrual cycle and a diagnosis of past depression were used in the analyses.

A hierarchical linear regression was used to determine the amount of variance in depressive symptoms accounted for by a history of moderate to severe PMS/PMDD and past depression after controlling for significant sociodemographic covariates. The HDRS was the dependent variable. In order to control for the effects of sociodemographic variables significantly associated with the HDRS, age, non-White, low education, single and not breastfeeding were entered into the first block of predictors. To determine if a history of moderate to severe PMS/PMDD and past depression account for additional variance after sociodemographic variables were in the model, PMS/PMDD and past MDE were entered into the second block. The forward entry method was used for each block.

A hierarchical binary logistic regression was used to determine if a history of moderate to severe PMS/PMDD and past depression significantly increased a woman's risk of developing PPD above sociodemographic covariates. A diagnosis of PPD was used as the dependent variable. In order to control for the effects of sociodemographic variables significantly associated with a diagnosis of PPD, age, non-White, low education, single, and not breastfeeding were entered into the first block of predictors. To determine if moderate to severe PMS/PMDD and past history of depression significantly increased a women's risk of PPD after controlling for sociodemographic variables, PMS/PMDD and past history of depression were entered into the second block. The Forward Likelihood Ratio entry method was used for each block, which is a stepwise selection procedure with the entry of a variable being based on the significance of the score statistic and removal based on the probability of a likelihood-ratio statistic. All analyses were conducted using SPSS version 19 (SPSS 2010).

Results

Single, non-White, and low education entered into the first block of the regression and accounted for 11% of the variance ($p < .001$). Past history of depression and moderate to severe PMS/PMDD were entered into the second block and contributed an additional 2% of the variance ($p < .001$). The full model accounts for 13% of the variance in postpartum depressive symptoms as measured by the HDRS. Within the full model, being single, non-White, having a low education, past history of depression and moderate to severe PMS/PMDD significantly predicted postpartum depressive symptoms, whereas age and breastfeeding status did not (see Table 3).

Single (OR=2.43), non-White (OR=2.76) and breastfeeding (OR=1.81) were entered into the first block as significant predictors of PPD. Only moderate to severe PMS/PMDD (OR=1.97) entered into the second block and was significant, whereas history of depression was not. This suggests that moderate to severe PMS/PMDD significantly increased a woman's chances of developing PPD by nearly twofold, independent of the sociodemographic factor effects: being single, non-White, and breastfeeding status. Within the full model, being single, non-White, breastfeeding status, and moderate to severe PMS/PMDD significantly increased a women's risk for experiencing PPD, whereas age, low education and history of depression did not (see Table 4).

¹The low education variable is defined as having at most a high school diploma.

Discussion

Premenstrual symptoms

A significant relationship emerged between moderate to severe PMS/PMDD and PPD in both models after controlling for sociodemographic factors, suggesting that it yielded an independent effect on the development of PPD that was not the result of other factors. Additionally, a history of depression and PMS/PMDD contributed an additional 2% of the variance ($p < .001$) when predicting depressive symptoms based on the HDRS, with the full model accounting for 13% of the variance in postpartum depressive symptoms. This finding is statistically significant; because the PSST is typically utilized as a screening measure rather than as an outcome measure of PMS/PMDD, there are insufficient data in the literature to understand the clinical significance of 2%. Additionally, a history of PMS/PMDD increased a woman's risk of experiencing PPD almost twofold ($OR=1.97$), making this a worthwhile factor for future research. The models supported in this study are consistent with existing empirical data highlighting the role of hormone fluctuations in the onset of PPD (Bloch et al. 2005; Bloch et al. 2006). Such findings are notable when considering the hypothesis that a common etiologic biological mechanism may underlie a *window of vulnerability* for women to experience premenstrual disorders and depression during the postpartum and menopausal transition (Lokuge et al. 2011). There is empirical support for the hypothesis that it is the *abrupt decrease* in hormones following delivery, rather than the *total hormone level*, that is associated with a heightened risk for PPD as evidenced in Bloch et al.'s (2000) work. Women with premenstrual syndrome have demonstrated symptoms as an abnormal response to normal hormonal fluctuations (Schmidt et al. 1998). Further, the effects of estrogen fluctuation on serotonin transmission identified in both animal and human studies have important implications for the *window of vulnerability* hypothesis (Lokuge et al. 2011). Current data findings may lend additional support for the role of an estrogen-serotonin link as a common etiologic biological mechanism among PMDD and PPD. Further research into this area may improve our understanding into the development of postpartum depressive symptoms and foster efficacious prevention and treatment strategies.

Risk factors

Regarding the second aim of our study, a significant association was detected between marital status, race, education level and PPD using the HDRS as an outcome measure of depression severity. Further, being single, non-White, and not breastfeeding were significantly associated with a diagnosis of PPD based on DSM-IV criteria. Interestingly, we found a significant association between variables education and race, and PPD. Socioeconomic deprivation indicators such as low income, low education, and unemployment have been identified as risk factors for depression (Robertson et al., 2004). These factors have yielded small but significant effects in the development of PPD; though, race has not emerged as a significant risk factor in previous meta-analytic studies (Beck et al. 2001; Robertson et al. 2004). These disparate findings may be due to the different response variables (continuous versus binary) used in the models. Additionally, a high percentage of women endorsed White as their racial affiliation (95%); thus, generalizations to more diverse populations are limited. In general, the two models represent the more well-established risk factors for PPD. In particular, our findings are consistent with meta-analytic studies showing significant relationships between being single, personal history of depression (Beck 2001; Robertson et al. 2004), breastfeeding status (McCoy et al. 2006) and PPD.

Strengths/limitations

The strengths of the current study include use of the PSST, a clinician friendly tool that translates DSM-IV criteria for moderate to severe PMS/PMDD and provides a severity rating scale for functional impairment (Steiner et al. 2003b). Existing PPD risk factors studies utilize DSM-IV criteria for PMDD with varying definitions of clinically significant premenstrual symptoms to assess PMDD; the PSST is a reliable screening tool that can accurately identify women suffering from PMDD (Steiner et al. 2003b). Second, this study employed a clinician-rated Hamilton Depression Rating Scale and the SCID, a diagnostic interview and the ‘gold standard’, to assess depression. Previous investigations on PMDD as a risk factor for PPD have relied on self-report measures of depression (e.g., Edinburgh Postnatal Depression Scale) (Bloch et al. 2006). Finally, by using less stringent criteria on the PHQ-9, we were able to obtain a sample of women with greater variability in depressive symptoms that is more characteristic of populations seen in a clinical setting.

One limitation of this study was that the PSST reflected the participants’ retrospective recall of their premenstrual symptoms prior to pregnancy, sometimes a year before, while the PSST is designed for the previous menstrual cycle. Additionally, retrospective assessment of premenstrual symptoms is considered less reliable relative to the “gold standard” of prospective daily mood ratings (Meaden et al. 2005). The diagnosis of PMDD by the DSM-IV criteria is based on prospective daily mood charting completed over two consecutive menstrual cycles (APA 2000). Nonetheless, in previous studies it was reported that daily ratings hindered research participation, as evidenced in an epidemiological study in which 30% of the participants refused to participate in data collection and only 50% of those enrolled completed two full cycles of daily ratings (Sternfeld et al. 2002). Second, our sample was primarily Non-Hispanic² (98%) and White (95%). Thus, replication of the current findings is needed in more diverse samples.

Conclusions

The current findings suggest that premenstrual syndrome (PMS)/premenstrual dysphoric disorder (PMDD) is a significant risk factor for postpartum depression within the first 12 months following childbirth. These data are in concordance with previous findings implicating PMDD in the development of PPD (Bloch et al. 2005; Bloch et al. 2006). Meta-analytic studies examining PPD risk factors have primarily focused on sociodemographic variables and psychopathology (e.g., history of depression). Our findings lend further support for well-established risk factors including marital and breastfeeding status, and history of depression, and highlights the role of less researched variables—race, education, and premenstrual disorders—as precipitating factors in the onset of PPD. Future research should include replication of PMS/PMDD using the PSST, as well as PMS/PMDD, race, and education as risk factors in a non-treatment seeking population. Notably, according to a panel of experts in women’s mental health formed by the Mood Disorders Work Group for DSM-5, sufficient empirical evidence on the diagnosis, treatment, and indicators of the disorder has been vetted to the point that the disorder should qualify as a category in DSM-5 (Epperson et al. 2012). Clinical implications include the importance of assessing premenstrual symptoms antenatally using the PSST to identify women with a history of PMS/PMDD who may be at a potentially higher risk for developing PPD. These data may inform preventative and therapeutic interventions to better target at-risk women.

²Non-Hispanic was not significantly correlated with each of the response variables thus was not included in the analyses, which may be a function of the low prevalence rate of Hispanics evidenced in the sample.

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Table 1

Descriptive Statistics

	M	SD
Mother's Age	29.6	5.1
# of Weeks Postpartum	8.2	4.3
PHQ-9 Score	9.9	4.2
HDRS	10.3	7.1
	N	%
Race		
Non-White	23	4.9
White	446	95.1
Ethnicity		
Hispanic	9	1.9
Non-Hispanic	469	98.1
Relationship Status		
Single	85	19.1
In a Relationship	360	80.9
Low Education		
Yes	51	10.7
No	424	89.3
Breastfeeding		
Yes	364	76.2
No	114	23.8
PMS/PMDD		
Yes	49	10.3
No	429	89.7
PPD		
Yes	139	29.1
No	339	70.9
Past MDE		
Yes	236	49.5
No	241	50.5

Note. Due to missing data for several variables, the n's range from 469 to 478.

Table 2
Significant Bivariate Correlations Between HDRS, Current MDE, and Predictors

	1a	1b	2	3	4	5	6	7	8
1a. HDRS	.-								
1b. PPD	.-	.-							
2. Mother's Age	-.11 *	-.14 ***	.-						
3. Non-White	.15 ***	.12 *	-.07	.-					
4. Low Education	.25 ***	.18 ***	-.35 ***	.02	.-				
5. Single	.29 ***	.23 ***	-.32 ***	.06	.31 ***	.-			
6. Not Breastfeeding	.17 ***	.16 ***	-.12 ***	-.01	.30 ***	.30 ***	.-		
7. PMS/PMDD	.17 ***	.15 ***	-.06	.05	.08	.14 ***	-.10 *	.-	
8. Past MDE	.11 *	.09 *	.11 *	-.01	-.11 *	.03	-.01	.15 ***	.-

*

p < 0.05

p < .01

Table 3
Hierarchical Linear Regression of Factors Associated with HDRS (Method: Forward). n = 435

	β^a	<i>p</i>	Adj. R^2	ΔR^2	<i>p</i>
Model 1					
Single	0.21	<.001	.11	.11	<.001
Low Education	0.18	<.001			
Non-White	0.12	.010			
Model 2					
Single	0.19	<.001	.13	.02	<.001
Low Education	0.20	<.001			
Non-White	0.11	.013			
Past MDE	0.11	.019			
PMS/PMDD	0.09	.048			

^aStandardized Beta Coefficient

Table 4

Hierarchical Logistic Regression of Factors Associated with PPD (Method: Forward Likelihood Ratio). n = 436

Bivariate Odds Ratio (95% CI)	
	PPD
Non-White	2.76 [*] (1.11–6.88)
Single	2.43 ^{**} (1.42–4.17)
Not Breastfeeding	1.81 [*] (1.10–2.98)
PMS/PMDD	1.97 [*] (1.02–3.79)

*
p < 0.05

**
p < .01