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Research paper

Factors associated with onset timing, symptoms, and severity of depression identified in the postpartum period

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ABSTRACT

Background: Unipolar and bipolar depression identified in the postpartum period have a heterogeneous etiology. The objectives of this study are to examine the risk factors that distinguish the timing of onset for unipolar and bipolar depression and the associations between depression onset by diagnosis, and general and atypical depressive symptoms.
Methods: Symptoms of depression were assessed at 4- to 6-weeks postpartum by the Structured Interview Guide for the Hamilton Depression Rating Scale-Atypical Depression Symptoms in an obstetrical sample of 727 women. Data were analyzed using ANOVA, Chi-square, and linear regression.
Results: Mothers with postpartum onset of depression were more likely to be older, Caucasian, educated, married/cohabitating, have one or no previous child, and have private insurance in contrast to mothers with pre-pregnancy and prenatal onset of depression. Mothers with bipolar depression were more likely to have a pre-pregnancy onset. Three general and two atypical depressive symptoms distinguished pre-pregnancy, during pregnancy, and postpartum depression onset, and the presence of agitation distinguished between unipolar and bipolar depression.
Limitations: The sample was urban, which may not be generalizable to other populations. The study was cross-sectional, which excludes potential late onset of depression (after 4–6 weeks) in the first postpartum year.
Conclusions: A collective set of factors predicted the onset of depression identified in the postpartum for mothers distinguished by episodes of unipolar versus bipolar depression, which can inform clinical interventions. Future research on the onset of major depressive episodes could inform prophylactic and early psychiatric interventions.

1. Introduction

Postpartum depression (PPD) occurs in approximately 13% of mothers (O'Hara and Swain, 1996) and has major implications for the mother's functioning, interpersonal relationships, parenting behaviors, and her offspring's health and developmental outcomes. However, depression identified in the postpartum period is a heterogeneous disorder with a variety of etiologic contributions and no singular phenotype. Postpartum depression includes a mix of symptoms including typical (e.g., low mood, appetite loss, difficulty falling asleep) and atypical symptoms (e.g., weight gain, hypersomnia).

An episode of depression identified during the postpartum period has one of three possible onset times: prior to pregnancy, during pregnancy, or during the postpartum period (Wisner et al., 2013). Very few investigators have evaluated the rates of onset of major depressive disorder according to these time points. In a sample of depressed women identified at 3–5 weeks postpartum (Yonkers et al., 2001) reported onsets prior to pregnancy (25%), during pregnancy (25%), and 4–5 weeks postpartum (50%) (Yonkers et al., 2001). In addition, Stowe et al. (2005) reported onsets during pregnancy (11.5%), early postpartum (within the first 6 weeks postpartum; 66.5%), and late postpartum (after 6 weeks postpartum; 22.0%) in mothers identified during the first year postpartum.

A larger body of research has examined differential risk factors for the onset of major depressive disorder during the pre-pregnancy, prenatal, and postpartum periods to determine the

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psychosocial characteristics associated with onset in each period. History of depression is the strongest predictor of depression in the postpartum period, which includes history of depression prior to and during pregnancy (Beck, 2001; Lee et al., 2007; Leigh and Milgrom, 2008; Leung and Kaplan, 2009; O'Hara et al., 1984; Rich-Edwards et al., 2006). Similarly, a history of depression is a strong predictor of depression during pregnancy (Rich-Edwards et al., 2006). Depression associated with sensitivity to reproductive hormone fluctuation (e.g., premenstrual dysphoric disorder) increases the risk for PPD (Bloch et al., 2005; Soares and Zitek, 2008). Women are also more likely to experience perinatal depression if they have elevated levels of prenatal or postpartum anxiety (Da Costa et al., 2000; Lee et al., 2007; Leigh and Milgrom, 2008; Leung and Kaplan, 2009), or other psychiatric disorders (Bernazzani et al., 1997; Leung and Kaplan, 2009). Women with a negative cognitive style (Leigh and Milgrom, 2008), low self-esteem (Leigh and Milgrom, 2008), and poor coping skills (e.g., escape-avoidance coping) (Gotlib et al., 1991) are also less able to cope with perinatal stressors and are more vulnerable to depressive symptoms.

Depression during the perinatal period is also predicted by psychosocial risk factors. Younger mothers are at greater risk for prenatal and postpartum depression (Akdeniz et al., 2002; Gotlib et al., 1989; Reck et al., 2008; Rich-Edwards et al., 2006; Skowron et al., 2013), which may be a proxy indicator for other stressors that accompany having a child at a young age (e.g., financial hardships, unwanted pregnancy, and lack of a partner) (Rich-Edwards et al., 2006). Other demographic variables, such as less years of education (Gotlib et al., 1989; Reck et al., 2008), unemployment (Gotlib et al., 1989), and low socioeconomic or occupational status (Bernazzani et al., 1997; Leigh and Milgrom, 2008), are also associated with perinatal depression. Various types of stressors have been associated with depression during the perinatal period including stress and medical problems during pregnancy (Akdeniz et al., 2002; Da Costa et al., 2000; Gotlib et al., 1991; Josefsson et al., 2002), difficult childbirth (Cox et al., 1993; Righetti-Veltema et al., 1998), multiparity and greater number of children in the home (Gotlib et al., 1989; Righetti-Veltema et al., 1998; Yonkers et al., 2001), childcare responsibilities (O'Hara et al., 1984), deleterious life events (Bernazzani et al., 1997; Leigh and Milgrom, 2008; Righetti-Veltema et al., 1998), history of abuse (Leigh and Milgrom, 2008), lower marital satisfaction (Gotlib et al., 1991; Leung and Kaplan, 2009), and lack of a partner, support from a partner, or general social supports (Leigh and Milgrom, 2008; Leung and Kaplan, 2009; Milgrom et al., 2008; Yonkers et al., 2001). In all, psychiatric history and various socio-environmental factors are associated with perinatal depression, but little is known about the factors associated with onset timing of depression relative to pregnancy.

Few studies have examined the onset of perinatal bipolar depression and the factors that increase the risk of an episode during the perinatal period. Doyle et al. (2012) found that 47% of women referred for treatment during pregnancy for bipolar disorder had a postpartum episode (21% mania/hypomania, 9.3% mixed state, 9.3% depressive mood with or without psychosis, and 7% psychosis not otherwise specified) (Doyle et al., 2012). The factors that increased the risk for a postpartum episode included being symptomatic prenatally, being younger, having an unplanned pregnancy, previous perinatal bipolar episodes, and a family history of bipolar disorder (Doyle et al., 2012). Freeman et al. (2002) found that mothers with bipolar disorder were not usually diagnosed until after the first pregnancy and 67% of women who had bipolar disorder had a postpartum episode after a birth. Every mother who had a postpartum mood episode after a first pregnancy had an episode following the subsequent pregnancies, of which most episodes were depressive (Freeman et al., 2002). The main factors that predicted postpartum episodes were prenatal depressive symptoms (Freeman et al., 2002). The limited data on the predictors of depressive episodes in mothers with bipolar disorder results in a limited understanding of the course of bipolar disorder during the perinatal period and throughout parenthood. In addition, unipolar and bipolar depression share genetic and environmental risk factors (Laursen et al., 2007; McGuffin et al., 2003), but may have differential risk factors that need to be explored in perinatal women.

The focus of this study is on the time of onset of depressive episodes identified in the postpartum period. The objectives of this study are to examine: 1) risk factors that distinguish unipolar or bipolar depression onset during the pre-pregnancy, prenatal, and postpartum periods based on a mother's psychosocial and psychiatric profile, 2) the association of depression onset with general and atypical perinatal depressive symptoms, and 3) the differential effect of the unipolar versus bipolar diagnosis on depression onset and general and atypical perinatal depressive symptoms. The aim is to explore the differences in clinical characteristics based on the time of onset of the depressive episode, which compliments the US Preventive Services Task Force recommendation for depression screening for perinatal women (UPSTF, 2014). This study is novel in that it was conducted with an obstetric population rather than a psychiatric population, which provides generalizable information to the larger population of childbearing women.

2. Methods

2.1. Participants

Participants were part of a larger screening study (Wisner et al., 2013). Mothers were recruited on the maternity unit of a women's hospital (from 2006 to 2012) by a nurse or social worker who provided education about PPD and offered a phone screen at 4- to 6-weeks postpartum. This time period was selected because women normally attended their post-birth obstetrics evaluations at 6-weeks postpartum and the 4–6 week epoch is associated with the highest depression onset (Munk-Olsen et al., 2006). Mothers who were non-English speaking, under 18 years of age, or did not have a telephone were excluded from the study.

In total, 727 postpartum mothers completed the screening and follow-up psychiatric interview. Mothers were primarily Caucasian (66.4%) and African-American (27.5%), with a mean age of 27.6 (SD=5.83). Over half of the mothers were single (54.0%) and 29.2% had a college degree or higher.

2.2. Procedure

A screening program for PPD was implemented at the obstetrics department of Magee Womens Hospital in Pittsburgh, Pennsylvania (Wisner et al., 2013), which was part of a PPD intervention study that targeted women in an urban setting. This paper focuses on episode onset timing. The Edinburgh Postnatal Depression Scale (EPDS) was used as the screening measure for PPD and assessed symptoms during the past 7-day period. The EPDS was chosen as a screening instrument because it is brief and validated in a wide variety of socioeconomic and ethnic groups, acceptable to patients as a screening measure, and the prevailing measure for assessment of PPD. An EPDS cutoff score of 10 or more was defined as a positive screen.

College and graduate students were trained to administer the EPDS by telephone and were supervised by master's-level psychiatric clinicians. The telephone screeners made a concerted effort to contact mothers and collect as many responses as possible between the 4- to 6-weeks postpartum, including daytime and evening phone calls. If contact was not made within the first

3 days, then a postcard was sent to the mother that requested she contact the research team. Contact ceased if the mother was not screened by the 6-week postpartum cutoff.

Mothers who had a positive screening for PPD based on the EPDS cutoff score were asked to complete an in-home psychiatric diagnostic assessment. The psychiatric assessment included primary diagnosis of mood disorders (major depression and bipolar disorder) and secondary diagnoses of co-occurring anxiety, dysthymic, eating, and substance use disorders. The target timing for in-home diagnostic assessment was conducted within 2 weeks of the initial positive screen. Any endorsement of suicidal ideation or an EPDS score greater or equal to 20 resulted in an immediate interview by a supervising clinician to conduct a safety assessment and establish a plan for intervention. The study was approved by the University of Pittsburgh institutional review board. Subjects were compensated with $40 after the completion of the home-visit.

2.3. Instruments

The EPDS (Cox et al., 1987) is a 10-item, self-report scale specifically designed to screen for postpartum depressive symptoms, with higher scores indicating increased risk for depression (score range: 0–30). Depression symptoms that may be part of normal maternal postpartum experiences (e.g., weight/appetite changes, fatigue) are not included in this measure. The EPDS has good internal reliability (Boyd et al., 2005) and test-retest reliability (intraclass correlation coefficient $=0.92$) (Kernot et al., 2014). It has been validated against the diagnostic criteria of the DSM (III, III-R, and IV) and ICD-10 and also against clinician-administered assessments of major depression, including the Structured Clinical Interview for DSM-IV (Eberhard-Gran et al., 2001; Navarro et al., 2007). The EPDS has acceptable sensitivity (range: 65–100%) to detect major depression in postpartum women.

The complete Structured Clinical Interview for DSM-IV (SCID) for Axis I disorder was administered. The SCID has good interrater reliability for Axis I disorders ($K=0.60$–0.83), with the kappa value for major depression being 0.66 (Lobbestael et al., 2011). The SCID has been found to be a valid measure of psychiatric disorders and more effective than standard clinical interviews (Basco et al., 2000). It was administered by master's level clinicians who were trained by viewing standard videotaped diagnostic modules, testing on the information, and completing an assessment with an experienced SCID interviewer. Each diagnostic assessment was reviewed by a board-certified psychiatrist for accuracy.

The Structured Interview Guide for the Hamilton Depression Rating Scale-Atypical Depression Symptoms (SIGH-ADS$_{29}$) is a 29-item, clinician-administered depression assessment that was used to assess depressive symptom severity (Williams and Terman, 2003). The SIGH-ADS$_{29}$ incorporates the 21-item Hamilton Rating Scale for Depression (HRSD) with eight atypical neurovegetative symptoms of depression that are common amongst pregnant women that include: reproductive-related, acute onset non-seasonal and seasonal, and chronic depression. Atypical symptoms are more common in individuals with bipolar disorder (Perugi et al., 1998).

2.4. Statistical analysis

Descriptive statistics for continuous measures are presented as means and standard deviations, and as frequencies and percentages for categorical measures. Between-group comparisons were tested with ANOVA when continuous measures were normally distributed and the non-parametric Kruskal-Wallis test was used when the measures were not normally distributed. For categorical measures, between-group comparisons were made with the Chi-Square test. The onset timing of major depression and bipolar disorder was compared according to the pre-pregnancy, prenatal, and postpartum categories (Table 2). Comorbid disorders associated with these mood disorders were also evaluated to determine whether there was a comorbid condition that differentially affected onset timing of the primary mood disorder. Post-hoc pairwise comparisons for continuous measures were made with Student's t or Mann-Whitney *U* tests for normal and non-normal distributions respectively. The comparisons were made with the Chi-Square test for categorical measures. All pairwise comparisons employed the Bonferroni correction.

Individual symptoms from the SIGH-ADS$_{29}$ were dichotomized as "absent" and "present." Two logistic models were then fit to each dichotomized symptom: one with timing of onset only and another with timing of onset as well as characteristics that were associated with the timing of onset (age, race, education, insurance, marital status, and parity) (Table 3). Linear regression models were estimated for the subscale and total scores. Because the dichotomized versions of race, education, insurance, and marital status were also statistically significant, they were used as covariates to reduce degrees of freedom. The referent for timing of onset for all models was "during pregnancy." For the last set of linear models (Table 4), symptoms and scale scores were regressed on timing of onset within each subsample of women (unipolar or bipolar) and then again for the entire sample with an interaction term for onset and unipolar versus bipolar depression. Due to null cells for certain symptoms among the bipolar women, logistic models were not estimated.

3. Results

In total, 15,172 women were screened for the study, of which 2033 screened positive for PPD based on the EPDS score of 10 or above. Of mothers screened, 1197 were enrolled in the study and received a home visit and 814 had clinically significant depression based on a SIGH-ADS score of greater than or equal to 18. A sample of 727 mothers met the criteria for inclusion in these analyses by having a diagnosis of unipolar or bipolar depression on the SCID (see Fig. 1), of which 181 (24.9%) had an onset of depression prior to the pregnancy, 267 (36.7%) had an onset of depression during the 9-month period of pregnancy, and 279 (38.4%) had an onset of depression between birth and 4–6 weeks postpartum (see Fig. 2).

The sociodemographic factors associated with the onset of the depressive episode are described in Table 1. Age, race, education, type of medical insurance, and marital status were associated with the onset of depression. The average age (pre-pregnancy: 27.0 (5.9), prenatal: 27.3 (5.8), postpartum: 28.4 (5.7), $p<0.05$) was significantly higher among mothers with onset during the postpartum period compared to those with an onset during the pre-pregnancy or prenatal periods, though there was no significant difference between the pre-pregnancy and prenatal onsets. The distribution of race, education, medical insurance, and marital status differed significantly between depression onset in the postpartum period and onset prior to parturition (pre-pregnancy, prenatal), but not between the pre-pregnancy and prenatal periods. The difference in onset based on race was driven by a higher proportion of Caucasians (and lower proportion of African-Americans) in the postpartum group. The postpartum group had a higher proportion of mothers who were married/cohabiting and had private insurance.

The onset timing of major depression and bipolar disorder and comorbid diagnoses was compared between pre-pregnancy, prenatal, and postpartum (Table 2). The proportion of mothers with bipolar depression was significantly higher among mothers with onset during the pre-pregnancy period (38.7%) compared to those

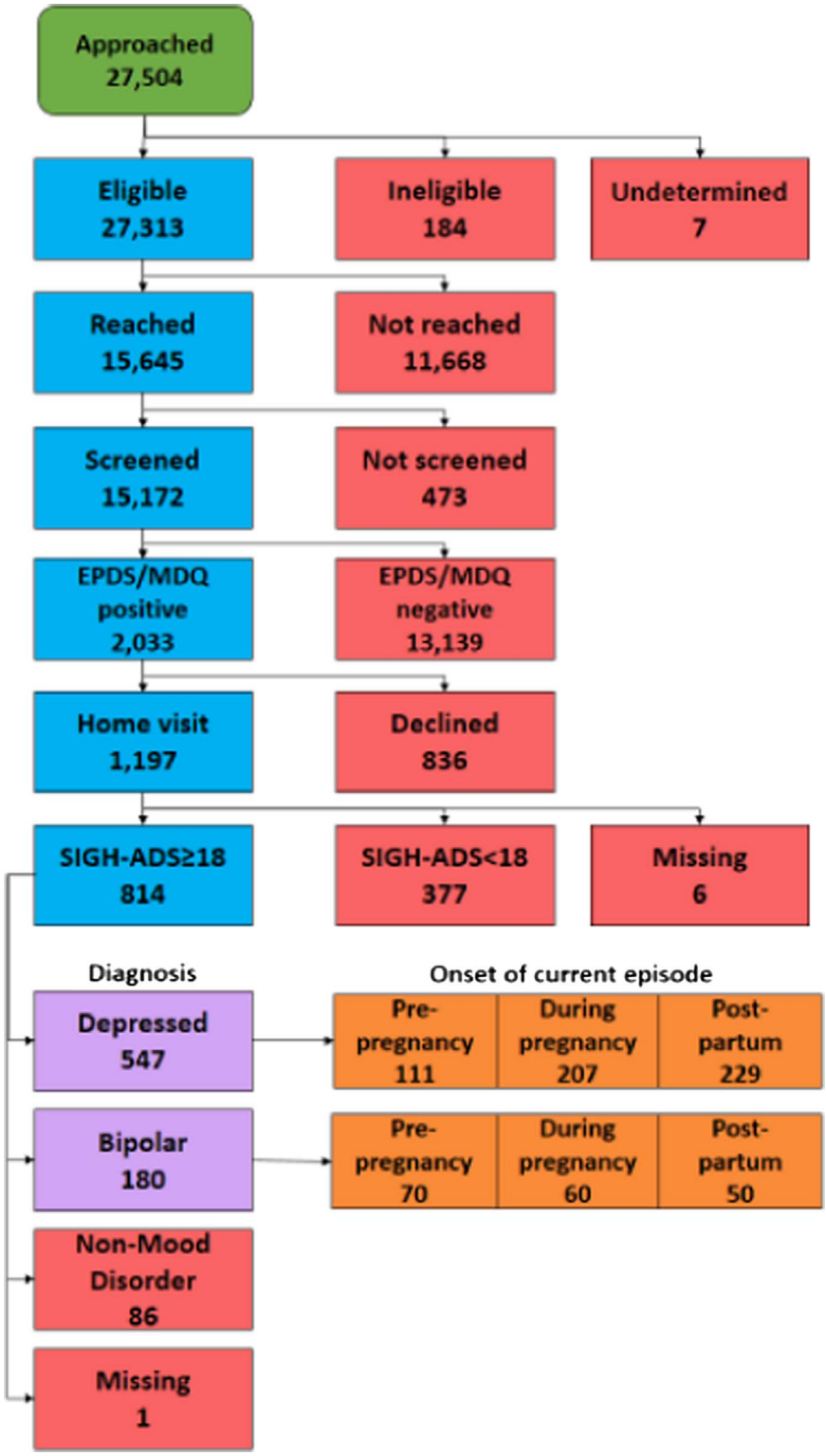

Fig. 1. Consort chart of women who were approached, screened, and participated in the study.

with prenatal (22.6%) and postpartum onset (17.9%). The onset timing of major depression and bipolar disorder did not differ based on the presence of comorbid anxiety, dysthymic, eating, or substance use disorders.

The frequencies of individual symptoms of depression by time of onset were compared (Table 3). Specifically, mothers with onset during the prenatal and postpartum periods had lower risk of difficulty falling asleep and paranoid symptoms compared to mothers with pre-pregnancy onset. Mothers with onset during the prenatal period had lower risk of obsessive compulsive symptoms compared to those with pre-pregnancy onset, while those with an onset during the postpartum period had increased risk. The overall severity of typical depressive symptoms (the 21 HRSD items) was statistically significant, though the significance was lost after adjusting for possible confounding characteristics.

Of the atypical symptoms of depression (Table 3), hypersomnia

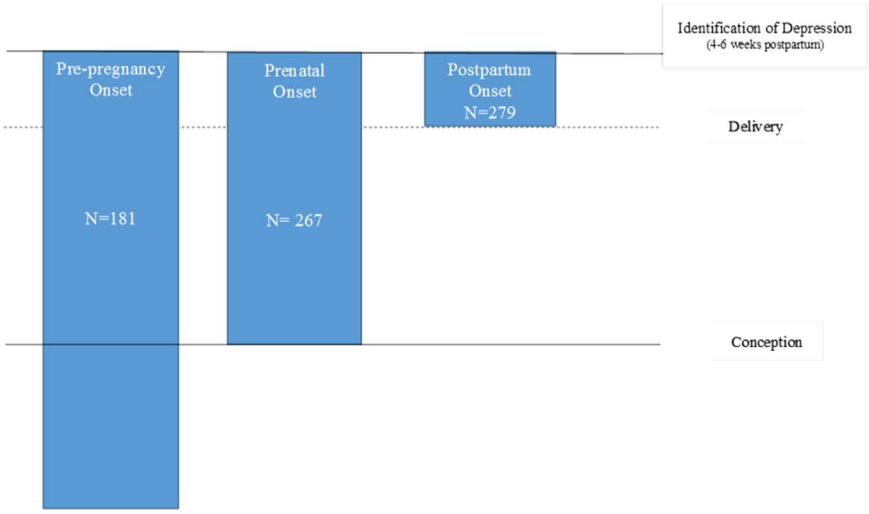

Fig. 2. The number of women who had a pre-pregnancy, prenatal or postpartum onset of depression.

Table 1
Demographic measures by onset in relation to pregnancy.

Measure	Total (N=727)	Onset in relation to pregnancy			Analysis				
		Pre (N=181)	During (N=267)	Post (N=279)	Test statistic	p	Pairwise comparison		
							Pr v D	Pr v Po	D v Po
Age	27.6 ± 5.83	27.0 ± 5.92	27.3 ± 5.84	28.4 ± 5.69	F(2,0)=3.63	0.0270	0.593	0.015*	0.035
Race					$\chi^2(4)=23.1$	0.0001	0.876	< 0.001*	< 0.001*
Caucasian	482 (66.4)	107 (59.1)	161 (60.5)	214 (76.7)					
African-American	200 (27.5)	61 (33.7)	89 (33.5)	50 (17.9)					
Other	44 (6.1)	13 (7.2)	16 (6.0)	15 (5.4)					
Caucasian	482 (66.4)	107 (59.1)	161 (60.5)	214 (76.7)	$\chi^2(2)=21.7$	< 0.0001	0.765	< 0.001*	< 0.001*
Hispanic	19 (2.7)	7 (4.3)	5 (1.9)	7 (2.6)	$\chi^2(2)=2.30$	0.3170			
Education (level)					$\chi^2(8)=45.7$	< 0.0001	0.053	< 0.001*	0.001*
< High school	70 (9.6)	29 (16.0)	24 (9.0)	17 (6.1)					
High school	189 (26.0)	54 (29.8)	81 (30.5)	54 (19.4)					
Some college	255 (35.1)	69 (38.1)	93 (35.0)	93 (33.3)					
College	128 (17.6)	17 (9.4)	42 (15.8)	69 (24.7)					
Graduate school	84 (11.6)	12 (6.6)	26 (9.8)	46 (16.5)					
College education	212 (29.2)	29 (16.0)	68 (25.6)	115 (41.2)	$\chi^2(2)=36.4$	< 0.0001	0.016*	< 0.001*	< 0.001*
Medical insurance					$\chi^2(2)=43.1$	< 0.0001	0.139	< 0.001*	< 0.001*
Private	312 (43.9)	52 (30.2)	98 (37.1)	162 (58.9)					
Public	399 (56.1)	120 (69.8)	166 (62.9)	113 (41.1)					
Marital status					$\chi^2(4)=33.8$	< 0.0001	0.236	< 0.001*	< 0.001*
Single	392 (54.0)	119 (65.7)	158 (59.4)	115 (41.2)					
Married/cohabiting	313 (43.1)	59 (32.6)	98 (36.8)	156 (55.9)					
Divorced/separated	21 (2.9)	3 (1.7)	10 (3.8)	8 (2.9)					
Married/cohabiting	313 (43.1)	59 (32.6)	98 (36.8)	156 (55.9)	$\chi^2(2)=31.1$	< 0.0001	0.356	< 0.001*	< 0.001*
Parity	1.15 ± 1.22	1.36 ± 1.49	1.21 ± 1.16	0.97 ± 1.04	H(2)=9.98	0.0068	0.463	0.004*	0.014*
Parity					$\chi^2(6)=12.7$	0.0482	0.720	0.011*	0.062
0	239 (32.9)	54 (29.8)	80 (30.1)	105 (37.6)					
1	274 (37.7)	62 (34.3)	103 (38.7)	109 (39.1)					
2	137 (18.9)	39 (21.5)	51 (19.2)	47 (16.8)					
3+	76 (10.5)	26 (14.4)	32 (12.0)	8 (6.5)					

Data presented as mean ± SD, n (%N). Descriptive statistics based on available data.

* Significant after Bonferroni correction.

remained significant after adjustment for confounding effects. Mothers with onset during pregnancy and postpartum had a lower risk of hypersomnia compared to those with onset during the pre-pregnancy period. The total score of atypical symptoms and the score of the complete SIGH-ADS$_{29}$ (typical and atypical depressive symptoms) differed between groups prior to adjusting for confounding effects, with the pre-pregnancy group having higher scores than the pregnant and postpartum groups, but only the completed SIGH-ADS$_{29}$ remained significant after controlling for confounders.

The effect of the distinction between unipolar versus bipolar depression on the frequency of individual and total depressive symptoms within each point of onset was examined (Table 4). The rate of agitation was similar among mothers with unipolar depression in each group, but mothers with bipolar disorder had higher levels of agitation and more variability in endorsement of agitation between groups. Mothers with bipolar disorder and a prenatal onset of depression had the highest rate of agitation.

4. Discussion

We examined the demographics, depressive symptoms, and onset timing associated with major depression identified during

Table 2
Clinical measures by onset in relation to pregnancy.

Measure	Total (N=727)	Onset in relation to pregnancy			Analysis				
		Pre (N=181)	During (N=267)	Post (N=279)	Test statistic	p	Pairwise comparison		
							Pr v D	Pr v Po	D v Po
Mood Disorder					$X^2(2)=26.5$	<0.0001	<0.001[a]	<0.001[a]	0.178
Depression	546 (75.2)	111 (61.3)	206 (77.4)	229 (82.1)					
Bipolar	180 (24.8)	70 (38.7)	60 (22.6)	50 (17.9)					
Comorbid disorder (current)[b]									
Alcohol abuse	17 (2.3)	4 (2.2)	7 (2.6)	6 (2.2)	$X^2(2)=0.16$	0.9249			
Anxiety	18 (2.5)	5 (2.8)	9 (3.4)	4 (1.4)	$X^2(2)=2.22$	0.3294			
Drug abuse	32 (4.4)	9 (5.0)	12 (4.5)	11 (3.9)	$X^2(2)=0.29$	0.8663			
Dysthymic	17 (2.3)	4 (2.2)	8 (3.0)	5 (1.8)	$X^2(2)=0.90$	0.6383			
Eating	17 (2.3)	4 (2.2)	7 (2.6)	6 (2.2)	$X^2(2)=0.16$	0.9249			
Generalized anxiety	147 (20.2)	33 (18.2)	51 (19.2)	63 (22.6)	$X^2(2)=1.59$	0.4525			
Obsessive-compulsive	40 (5.5)	9 (5.0)	11 (4.1)	20 (7.2)	$X^2(2)=2.54$	0.2808			
Panic	54 (7.4)	20 (11.0)	18 (6.8)	16 (5.7)	$X^2(2)=4.78$	0.0917			
Posttraumatic stress	50 (6.9)	19 (10.5)	17 (6.4)	14 (5.0)	$X^2(2)=5.30$	0.0706			
Social phobia	53 (7.3)	17 (9.4)	18 (6.8)	18 (6.5)	$X^2(2)=1.58$	0.4540			
Specific phobia	46 (6.3)	14 (7.7)	11 (4.1)	21 (7.5)	$X^2(2)=3.43$	0.1796			

Data presented as mean ± SD, n (%N). Descriptive statistics based on available data. Only the mood disorders (major depression; bipolar disorder) are differentiated by onset timing. Chi-square tests were conducted to examine if the comorbid disorders differentiated the onset timing of the mood disorder.

[a] Significant after Bonferroni correction.
[b] Evaluated with the Structured Clinical Interview for DSM Disorders (SCID).

Table 3
Symptomatology measures by onset in relation to pregnancy.

Measure	Total (N=727)	Onset in relation to pregnancy			Odds Ratios (referent: Pre-Pregnancy)					
		Pre (N=181)	During (N=267)	Post (N=279)	Unadjusted			Adjusted[a]		
					Dur	Post	p	Dur	Post	p
HRSD										
Depressed mood	716 (98.6)	178 (98.3)	262 (98.5)	276 (98.9)	1.104	1.550	0.8526	1.098	1.204	0.9767
Feelings of guilt	651 (89.7)	165 (91.2)	238 (89.5)	248 (88.9)	0.824	0.776	0.7311	0.796	0.578	0.2619
Suicide	92 (12.7)	30 (16.6)	35 (13.2)	27 (9.7)	0.763	0.539	0.0939	0.785	0.704	0.4884
Difficulty falling asleep	388 (53.4)	116 (64.1)	133 (50.0)	139 (49.8)	0.560	0.556	0.0044	0.594	0.659	0.0347
Sleep disturbance	653 (89.9)	161 (89.0)	236 (88.7)	256 (91.8)	0.977	1.382	0.4411	0.922	1.111	0.8272
Early morning waking	339 (46.7)	90 (49.7)	128 (48.1)	121 (43.4)	0.938	0.774	0.3462	0.935	0.881	0.8234
Work and activities	697 (96.0)	175 (96.7)	256 (96.2)	266 (95.3)	0.878	0.702	0.7505	0.755	0.622	0.6907
Retardation	228 (31.4)	52 (28.7)	94 (35.3)	82 (29.4)	1.356	1.033	0.2199	1.413	1.343	0.2589
Agitation	194 (26.7)	46 (25.4)	77 (28.9)	71 (25.4)	1.196	1.002	0.5884	1.209	1.159	0.6909
Anxiety - psychic	712 (98.1)	177 (97.8)	260 (97.7)	275 (98.6)	0.979	1.554	0.7490	0.489	0.725	0.6459
Anxiety - somatic	679 (93.5)	171 (94.5)	253 (95.1)	255 (91.4)	1.138	0.621	0.1837	1.200	0.700	0.3255
Somatic symptoms - gastrointestinal	517 (71.2)	132 (72.9)	192 (72.2)	193 (69.2)	0.963	0.833	0.6234	0.889	0.878	0.8331
Somatic symptoms - general	664 (91.5)	168 (92.8)	241 (90.6)	255 (91.4)	0.746	0.822	0.7131	0.758	0.760	0.7086
Genital symptoms	558 (76.9)	136 (75.1)	206 (77.4)	216 (77.4)	1.136	1.134	0.8181	1.193	1.194	0.6953
Hypochondriasis	325 (44.8)	78 (43.1)	122 (45.9)	125 (44.8)	1.119	1.072	0.8464	1.101	1.019	0.8614
Loss of weight	244 (33.6)	58 (32.0)	92 (34.6)	94 (33.7)	1.121	1.078	0.8550	1.068	1.119	0.8719
Insight	41 (5.6)	4 (2.2)	15 (5.6)	22 (7.9)	2.644	3.788	0.0498	2.511	3.547	0.0796
Diurnal variation	444 (61.2)	100 (55.2)	163 (61.3)	181 (64.9)	1.282	1.496	0.1184	1.204	1.061	0.6308
Depersonalization & derealization	247 (34.0)	63 (34.8)	92 (34.6)	92 (33.0)	0.990	0.921	0.8942	0.978	1.029	0.9642
Paranoid symptoms	162 (22.3)	61 (33.7)	70 (26.3)	31 (11.1)	0.703	0.246	<0.0001	0.731	0.359	0.0004
Obsessional/compulsive symptoms	191 (26.3)	50 (27.6)	52 (19.5)	89 (31.9)	0.637	1.227	0.0046	0.711	1.479	0.0022
Total score[b]	17.9 ± 3.75	18.5 ± 3.96	17.7 ± 3.58	17.6 ± 3.73	-0.814	−0.894	0.0277	−0.757	−0.492	0.1134
Atypical depression supplement										
Social withdrawal	620 (85.4)	158 (87.3)	235 (88.3)	227 (81.4)	1.104	0.635	0.0514	1.190	0.767	0.2184
Weight gain	77 (10.6)	24 (13.3)	36 (13.5)	17 (6.1)	1.024	0.424	0.0097	1.099	0.461	0.0181
Appetite increase	119 (16.4)	32 (17.7)	46 (17.3)	41 (14.7)	0.974	0.802	0.6186	0.981	0.763	0.5002
Increased eating	155 (21.3)	41 (22.7)	61 (22.9)	53 (19.0)	1.016	0.801	0.4733	1.051	0.793	0.4110
Carbohydrate craving	451 (62.1)	108 (59.7)	176 (66.2)	167 (59.9)	1.322	1.008	0.2330	1.383	1.117	0.2479
Hypersomnia	48 (6.6)	21 (11.6)	12 (4.5)	15 (5.4)	0.360	0.433	0.0094	0.390	0.518	0.0370
Fatigability	713 (98.2)	178 (98.3)	261 (98.1)	274 (98.2)	0.880	0.924	0.9850	0.571	0.504	0.7271
Diurnal variation	374 (51.5)	108 (59.7)	130 (48.9)	136 (48.7)	0.646	0.643	0.0413	0.680	0.671	0.0967
Total score[b]	6.04 ± 2.37	6.44 ± 2.51	6.15 ± 2.53	5.68 ± 2.06	−0.282	−0.755	0.0023	−0.135	−0.504	0.0660
SIGH-ADS$_{29}$[b]	23.9 ± 4.31	25.0 ± 4.83	23.9 ± 4.13	23.3 ± 4.01	−1.096	−1.650	0.0003	−0.892	−0.996	0.0402

Data presented as mean ± SD, n (%N). Descriptive statistics based on available data.
Abbreviations: HRSD, Hamilton rating scale for depression; SIGH-ADS, Structured interview guide for the Hamilton rating scale for depression with atypical depression supplement.

[a] Adjusted for age, Caucasian race, college education, type of medical insurance. married/cohabiting, and parity.
[b] Parameter estimates are beta coefficients, not odds ratios.

Table 4
Symptomatology measures by onset in relation to pregnancy and unipolar versus bipolar disorder.

Measure	Unipolar				Bipolar				Probability values		
	Total (N=547)	Pre (N=111)	During (N=207)	Post (N=229)	Total (N=180)	Pre (N=70)	During (N=60)	Post (N=50)	Uni-polar	Bi-polar	Inter-action
HRSD											
Depressed mood	538 (98.5)	109 (98.2)	203 (98.5)	226 (98.7)	178 (98.9)	69 (98.6)	59 (98.3)	50 (100)	0.9395	*	*
Feelings of guilt	493 (90.3)	105 (94.6)	185 (89.8)	203 (88.6)	158 (87.8)	60 (85.7)	53 (88.3)	45 (90.0)	0.2250	0.7705	0.2394
Suicide	55 (10.1)	16 (14.4)	22 (10.7)	17 (7.4)	37 (20.6)	14 (20.0)	13 (21.7)	10 (20.0)	0.1309	0.9666	0.4466
Difficulty falling asleep	270 (49.5)	65 (58.6)	93 (45.1)	112 (48.9)	118 (65.6)	51 (72.9)	40 (66.7)	27 (54.0)	0.0745	0.1023	0.2894
Sleep disturbance	500 (91.6)	99 (89.2)	188 (91.3)	213 (93.0)	153 (85.0)	62 (88.6)	48 (80.0)	43 (86.0)	0.4859	0.3905	0.3468
Early morning waking	254 (46.5)	56 (50.5)	100 (48.5)	98 (42.8)	85 (47.2)	34 (48.6)	28 (46.7)	23 (46.0)	0.3164	0.9567	0.8634
Work and activities	528 (96.7)	109 (98.2)	202 (98.1)	217 (94.8)	169 (93.9)	66 (94.3)	54 (90.0)	49 (98.0)	0.1163	0.2638	0.0890
Retardation	162 (29.7)	28 (25.2)	67 (32.5)	67 (29.3)	66 (36.7)	24 (34.3)	27 (45.0)	15 (30.0)	0.3933	0.2353	0.5286
Agitation	117 (21.4)	24 (21.6)	42 (20.4)	51 (22.3)	77 (42.8)	22 (31.4)	35 (58.3)	20 (40.0)	0.8908	0.0086	0.0284
Anxiety - psychic	533 (97.6)	107 (96.4)	200 (97.1)	226 (98.7)	179 (99.4)	70 (100)	60 (100)	49 (98.0)	0.3751	*	*
Anxiety - somatic	509 (93.2)	103 (92.8)	197 (95.6)	209 (91.3)	170 (94.4)	68 (97.1)	56 (93.3)	46 (92.0)	0.2017	0.4573	0.3781
Somatic symptoms - gastrointestinal	378 (69.2)	76 (68.5)	145 (70.4)	157 (68.6)	139 (77.2)	56 (80.0)	47 (78.3)	36 (72.0)	0.9011	0.5721	0.6691
Somatic symptoms - general	499 (91.4)	101 (91.0)	188 (91.3)	210 (91.7)	165 (91.7)	67 (95.7)	53 (88.3)	45 (90.0)	0.9728	0.3040	0.3734
Genital symptoms	426 (78.0)	85 (76.6)	162 (78.6)	179 (78.2)	132 (73.3)	51 (72.9)	44 (73.3)	37 (74.0)	0.9122	0.9904	0.9805
Hypochondriasis	252 (46.2)	46 (41.4)	98 (47.6)	108 (47.2)	73 (40.6)	32 (45.7)	24 (40.0)	17 (34.0)	0.5355	0.4356	0.2535
Loss of weight	192 (35.2)	36 (32.4)	77 (37.4)	79 (34.5)	52 (28.9)	22 (31.4)	15 (25.0)	15 (30.0)	0.6537	0.7085	0.4989
Insight	36 (6.6)	4 (3.6)	11 (5.3)	21 (9.2)	5 (2.8)	0 (0.0)	4 (6.7)	1 (2.0)	0.1108	*	*
Diurnal variation	352 (64.5)	64 (57.7)	132 (64.1)	156 (68.1)	92 (51.1)	36 (51.4)	31 (51.7)	25 (50.0)	0.1673	0.9827	0.5145
Depersonalization & de-realization	178 (32.6)	39 (35.1)	65 (31.6)	74 (32.3)	69 (38.3)	24 (34.3)	27 (45.0)	18 (36.0)	0.8043	0.4233	0.3608
Paranoid symptoms	102 (18.7)	35 (31.5)	49 (23.8)	18 (7.9)	60 (33.3)	26 (37.1)	21 (35.0)	13 (26.0)	<0.0001	0.4222	0.0730
Obsessional/compulsive symptoms	126 (23.1)	24 (21.6)	36 (17.5)	66 (28.8)	65 (36.1)	26 (37.1)	16 (26.7)	23 (46.0)	0.0191	0.1112	0.8778
Total score	17.4 ± 3.54	17.8 ± 3.86	17.2 ± 3.36	17.4 ± 3.52	19.3 ± 4.04	19.6 ± 3.91	19.4 ± 3.81	18.7 ± 4.47	0.3397	0.4157	0.5106
Atypical depression supplement											
Social withdrawal	461 (84.4)	98 (88.3)	179 (86.9)	184 (80.3)	159 (88.3)	60 (85.7)	56 (93.3)	43 (86.0)	0.0807	0.3521	0.3595
Weight gain	53 (9.7)	12 (10.8)	30 (14.6)	11 (4.8)	24 (13.3)	12 (17.1)	6 (10.0)	6 (12.0)	0.0041	0.4708	0.1150
Appetite increase	91 (16.7)	19 (17.1)	38 (18.4)	34 (14.8)	28 (15.6)	13 (18.6)	8 (13.3)	7 (14.0)	0.5978	0.6713	0.6994
Increased eating	115 (21.1)	25 (22.5)	49 (23.8)	41 (17.9)	40 (22.2)	16 (22.9)	12 (20.0)	12 (24.0)	0.2978	0.8700	0.5202
Carbohydrate craving	332 (60.8)	59 (53.2)	133 (64.6)	140 (61.1)	119 (66.1)	49 (70.0)	43 (71.7)	27 (54.0)	0.1400	0.1059	0.0756
Hypersomnia	34 (6.2)	11 (9.9)	10 (4.9)	13 (5.7)	14 (7.8)	10 (14.3)	2 (3.3)	2 (4.0)	0.1968	0.0532	0.5467
Fatigability	542 (99.3)	110 (99.1)	205 (99.5)	227 (99.1)	171 (95.0)	68 (97.1)	56 (93.3)	47 (94.0)	0.8735	0.5842	0.6652
Diurnal variation	266 (48.7)	65 (58.6)	96 (46.6)	105 (45.9)	108 (60.0)	43 (61.4)	34 (56.7)	31 (62.0)	0.0683	0.8105	0.4861
Total score	5.93 ± 2.27	6.16 ± 2.36	6.18 ± 2.54	5.60 ± 1.91	6.37 ± 2.63	6.87 ± 2.69	6.05 ± 2.51	6.06 ± 2.63	0.0129	0.1225	0.2148
SIGH-ADS$_{29}$	23.4 ± 3.98	24.0 ± 4.65	23.4 ± 3.84	23.0 ± 3.73	25.7 ± 4.81	26.5 ± 4.76	25.4 ± 4.70	24.7 ± 4.90	0.1543	0.0893	0.6020

Data presented as mean ± SD, n (%N). Descriptive statistics based on available data.
Abbreviations: HRSD, Hamilton rating scale for depression; SIGH-ADS, Structured interview guide for the Hamilton: rating scale for depression with atypical depression supplement.

* Inestimable due to null cells.

the postpartum period in a large obstetrical sample. Unipolar versus bipolar depression differentiated mothers by onset timing, with mothers with bipolar disorder having a history of depression that preceded the pregnancy. Of the 29 symptoms of depression, three general (difficulty falling asleep, paranoid, and obsessive compulsive) and one atypical (hypersomnia) symptom differentiated the subgroups of depressed mothers based on onset time. Agitation was the only factor that differentiated mothers with unipolar and bipolar depression, with mothers with bipolar disorder and a prenatal onset depressive episode experiencing greater agitation.

As anticipated, favorable demographic factors are protective against onset of depression before or during pregnancy. The data from the Centers for Disease Control and Prevention demonstrate that a mother who has children when she is older is more likely to be Caucasian, educated, married, have more resources (e.g., health insurance) and have fewer children (Martin et al., 2015; Martinez et al., 2012; Mathews and Hamilton, 2014). The accumulation of these resources supports a more stable environment, opportunities to reduce stressors, and security when stressors arise. These resources reduce the risk that a mother will develop depression prior to the major life changing event of parturition and raising a newborn. Disadvantaged mothers are more likely to develop depression as the result of stressors during the pre-pregnancy or prenatal periods that can be maintained or exacerbated by the challenges that accompany having a newborn (Beck, 2001).

Similarly, the onset timing is indicative of depression severity and course. A depressive episode that predates pregnancy suggests increased vulnerability to symptom worsening postpartum and may also have implications for a sustained trajectory of depression. Depression prior to pregnancy implies a more chronic form of depression that is not related to hormonal change (as for pregnancy/postpartum) or postpartum stressors.

Depression can be differentiated by onset timing based on unipolar versus bipolar classification. Depression did not have a differential onset based on comorbidity with other psychiatric diagnoses, which suggests that depression onset is influenced by the inherent characteristics of the depression (unipolar versus bipolar) rather than distinct disorders that are commonly associated with depression (Fava et al., 2000; O'Brien and Vincent, 2003; O'Donnell et al., 2004; Swendsen and Merikangas, 2000). Comorbid psychiatric diagnoses may have relevance for women with mood disorders (e.g., recurrence, severity, response to treatment) (Andreescu et al., 2007; Sherbourne and Wells, 1997; Simon et al., 2004), but not for the onset of depression. Notably, the increased likelihood of an onset of a depressive episode during the *pre-pregnancy period* highlights the longevity of depression for mothers with bipolar disorder for several reasons. Individuals with bipolar disorder have a lifetime predisposition to depressive episodes, earlier onset of first depressive episode, and more frequent depressive episodes than unipolar depression (Mitchell et al., 2008). Studies comparing unipolar and bipolar depression have found that bipolar subjects are more likely to experience stressful events (e.g., social rhythm disruptions, severe experiences), which provoke episodes. Depressive episodes are also more likely to occur independent of major life stressors (e.g., transition to parenthood) in individuals with bipolar depression (Hammen et al., 1989; Malkoff-Schwartz et al., 2000). Depressive episodes occurring irrespective of stressors increases the risk of onset occurring prior to the perinatal period. Therefore, a pre-pregnancy onset of depression and the additional stressful events that accompany pregnancy and the postpartum period may extend the chronicity of depression in mothers with bipolar depression.

Although medication is the mainstay of treatment for bipolar disorder, individuals with bipolar disorder tend to have poorer medication compliance than those with unipolar depression (Lingam and Scott, 2002). This may help explain the significant increase in pre-pregnancy onset of depression in women with bipolar disorder observed in this study. Medication noncompliance in bipolar disorder is also due to the discontinuation of medication by expectant mothers and physicians who are hesitant to prescribe in pregnancy (Viguera et al., 2000, 2007; Bonari et al., 2005). Discontinuation of mood stabilizers, as well as antidepressants, during pregnancy increases the risk of symptom recurrence and that symptoms will continue or worsen postpartum (Viguera et al., 2007; Cohen et al., 2006). Viguera et al. (2007) found that the risk of recurrence was 85% for mothers who discontinued their mood stabilizer treatment, with earlier onset of recurrence if the medication was discontinued during pregnancy abruptly or rapidly and a higher likelihood of having a depressed episode (41.3%) than a mixed state (38.1%), hypomanic (11.1%), or manic (9.5%) episode. Furthermore, women with bipolar or unipolar depression who comply with medication treatment often have suboptimal plasma drug concentrations (Clark et al., 2013; Sit et al. 2008; Lingam et al. 2002) due to the physiological changes of pregnancy, which increases the risk of recurrence. In short, women with bipolar disorder are at increased risk for chronic depression that onsets prior to pregnancy and continues into motherhood. Women with unipolar depression are at more likely to experience prenatal and postpartum onset. Continuous screening and specialized psychiatric treatment that targets the perinatal depressive symptomatology is warranted (USPTF, 2014).

The individual symptoms endorsed on the SIGH-ADS$_{29}$ provided a differentiation of the onset timing of depressive episodes: obsessive-compulsive, difficulty sleeping, and paranoid symptoms. Postpartum onset of depression is associated with OCD symptoms (Miller et al., 2015). Similar to depression, a recent meta-analysis by Russell et al. (2013) demonstrated that the highest prevalence of OCD symptoms in a woman's lifetime was during the postpartum period. Postpartum obsessions and compulsions are associated with concerns about the newborn child, including thoughts about imminent danger or contamination, thoughts of hurting the infant, cleaning behaviors, and checking behaviors (Abramowitz et al., 2003; Wenzel et al., 2001; Wisner et al., 1999). The combination of typical and atypical symptoms (SIGH-ADS$_{29}$) rather than either symptom type alone differentiated timing of depression onset, which supports assessing traditional depression symptoms with atypical symptoms for a perinatal population. The pre-pregnancy group had higher severity of total SIGH-ADS$_{29}$ score, which demonstrates that pre-pregnancy onset indicates greater severity. Likewise, paranoid symptoms, which commonly accompany severe depression and psychosis (Tonna et al., 2012; Bentall et al., 2009), were associated with pre-pregnancy onset of depression. In addition, women with onset before pregnancy had a higher likelihood of difficulty falling asleep and hypersomnia. Sleep disturbance tends to precede and be concurrent with major depression, increases depression severity, and influences the longitudinal trajectory of the depression (Franzen and Buysse, 2008), thus being related to an earlier onset. According to the National Comorbidity Survey, atypical symptoms, such as hypersomnia, are more common in women, related to early age of onset, and associated with impairment in functioning (e.g., restricted activity days, increased psychiatric healthcare utilization) (Matza et al., 2003).

4.1. Strengths and limitations

This study has several strengths that support the validity and applicability of the findings. First, the sample was recruited from an obstetrics population and was heterogeneous, which improves the generalizability. The psychiatric assessments were clinician-rated and assessed the spectrum of typical and atypical depressive

symptoms. At the same time, the findings must be interpreted within the context of the study's limitations. For one, the sample of mothers was primarily from an urban setting, which may have differential sociodemographic risks for depression compared to other settings. For instance, the rate of married mothers in this sample was less than the rate in the 2012 U. S. census (64% married) (Vespa et al., 2013). Second, the assessment of depression after birth was cross-sectional. Depression identified early in the postpartum period is associated increased depression throughout the first year postpartum (Beeghly et al., 2002). An examination of the first year postpartum would be informative for screening protocols during the first-year well-child visits to identify mothers with a new onset or persistent depression beyond one month postpartum (Chaudron et al., 2004).

5. Conclusion

The findings from this study emphasize the power of the collective protective and risk factors (age, race, education, marital status, health insurance, parity) on onset of depression in women with unipolar and bipolar depression. Women with pre-pregnancy onset are more likely to have hypersomnia or difficulty falling asleep, paranoid symptoms and higher severity of typical and atypical symptoms during the postpartum period. Agitation is indicative of bipolar disorder and prenatal onset of a depressive episode. Onset timing was relevant for the diagnostic distinction between unipolar and bipolar depression. The varying courses of depression across childbearing suggests that women may also have differential depression trajectories across the first year postpartum, which would have significant implications for the mother and infant's health and development. Future research on the factors predicting the course of women's mood during this sensitive period is warranted.

The findings have clinical relevance for assessment and treatment of depression identified in the postpartum period. The characteristics of a depressive episode identified in the postpartum are heterogeneous based on onset timing. The differentiation of chronic, semi-acute, and acute depression reveals the vulnerability and resiliency of the depression identified in the postpartum. Earlier onset is associated with heightened severity, a longer course of depressive symptoms, and a particular symptom set in the postpartum period. Earlier onset indicates a depressive episode that is more resistant to remission and has an extended chronicity that requires prolonged monitoring and treatment. A comprehensive assessment of onset timing, typical and atypical symptoms, and unipolar versus bipolar disorder is recommended to improve the effectiveness of postpartum treatment.

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