Mood Symptoms and Other Maternal Factors in Pregnancy and Adverse Neonate Outcomes

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Research article

Keywords: Antenatal women, Mood symptoms, Other maternal factors, Neonatal outcomes

Posted Date: September 3rd, 2020

DOI: https://doi.org/10.21203/rs.3.rs-61702/v1

Abstract

Background Antenatal women experience a higher level of mood symptoms, which have negative effects on mothers' mental and physical health and their newborns. The relation of maternal moods including depression and anxiety and other maternal factors in pregnancy and neonate outcomes are well-studied with inconsistent findings. Although antenatal women experience a higher level of mood instability (MI), the association between antenatal MI and neonatal outcomes has not been investigated. We aimed to address this gap and to contribute to the pregnancy-neonate outcomes literature by examining the relationship between antenatal mood symptoms and other maternal factors and neonatal outcomes.

Methods A prospective cohort of women (*n* = 555) participated in this study at early pregnancy (T1, 17.4 ± 4.9 weeks) and late pregnancy (T2, 30.6 ± 2.7 weeks). The Edinburgh Postnatal Depression Scale (EPDS) was used to assess antenatal depressive symptoms, the EPDS anxiety subscale was utilized to measure anxiety symptoms, and mood instability was measured using a visual analogue scale. These mood states together with stress, social support, as well as healthy and unhealthy behaviours were also examined in relation to neonatal outcomes using chi-square tests and logistic regression models.

Results Depression and MI were unrelated to adverse neonatal outcomes and anxiety was related to Apgar score with marginal statistical significance. Higher stress, lack of partner support, smoking, and primiparous status were associated with some adverse outcomes.

Conclusions The current study identified no associations between antenatal mood symptoms and neonatal outcomes. Our findings further support and extend previous evidence on smoking abstinence or cessation, and the provision of resources for stress management and social support that could help prevent or alleviate adverse neonatal outcomes.

Background

Pregnancy and childbirth are often viewed as joyful events, but they can also be overwhelming and challenging for some mothers. Becoming a mother is a vulnerable period for women to develop mood symptoms, including perinatal depression, anxiety (1, 2), postpartum blues, baby pinks (3), and mood instability (MI) (4, 5). Perinatal women often experience the highest euphoric, irritable, and depressed moods in early pregnancy and again around the time of giving birth (6, 7). This phenomenon is thought to be triggered by the large hormonal fluctuations occurring at these times (6, 8, 9).

Many studies have found that not only does maternal depression and anxiety adversely affect a mother's physical and mental health, but also the infant's physical and cognitive development, and the mother-infant relationship, all of which endure into childhood and beyond (10). The impact of antenatal depression or anxiety on neonatal outcomes has been investigated extensively in both developing and developed countries. However, the findings are incongruent. Some studies have found a significant relationship between antenatal depression or anxiety and low birth weight (LBW), preterm birth (PTB), small for gestational age (SGA), or low Apgar score (11-14), while others have not (15-18). These

divergent findings could result from differences in the measuring tools, gestational ages, and sample characteristics. Although significant correlations between MI and an array of psychiatric disorders including depression and anxiety have been reported in clinical and general populations (19, 20), and a strong link between MI and depression in perinatal women has been documented (21), the relation of antenatal MI to neonatal outcomes has been less studied, which can partly be explained by the transdiagnostic nature of MI or because MI is seen to be a normal part of women's pregnancy that resolves itself (22).

Maternal mental health and their association with infant outcomes may be related to psychosocial factors and lifestyle in pregnancy. For example, Nylen and colleagues found that women with unsupportive partners had babies with lower Apgar scores compared to those with supportive partners (23). The perception of partner support, they found, partly offsets the adverse effect of maternal depression. Other studies have shown that stress in pregnancy is associated with lower birth weight and pre-term birth (17, 24, 25). These stressors tended to be major life events, disasters, or chronic conditions such as poverty, but not the usual daily hassles (25). Behaviors in pregnancy such as smoking and alcohol use are associated with childhood cognitive and emotional regulation deficits (26), but relatively few studies have reported neonatal outcomes. Alcohol use in pregnancy is associated with lower birth weight (LBW), pre-term birth (PBW) (27, 28), and small for gestational age (SGA) (28). Cotinine levels collected in pregnancy showed an inverse associated with birth weight (29, 30). Generally, no relation between exercise and infant outcomes has been found (31) but there is evidence for positive maternal outcomes, such as cardiovascular health and prevention of gestational diabetes (32, 33).

In this study, we examined the association of antenatal mood symptoms and other maternal factors with five neonate outcomes measured shortly after birth.

Methods

Participants and procedure

The current study was a secondary data analysis of the Feelings in Pregnancy and Motherhood Study (FIP). The FIP is a longitudinal cohort study of maternal mental health and the associated factors from 2006 to 2014. Women were recruited in the early pregnancy from a variety of community settings including doctors' offices, prenatal classes, maternity stores, and responders to radio and newspaper advertisements. The inclusion criteria were English speaking women in early pregnancy (gestation $\leq$ 20 weeks), and having a residence in one of two health regions in Saskatchewan. Data were collected by trained research assistants in a face-to-face interview at two-time points during pregnancy: T1 (early pregnancy: 17.4 ± 4.9 weeks), and T2 (late pregnancy: 30.6 ± 2.7 weeks). Information regarding children's neonatal outcomes was obtained from the mothers and linked with hospital discharge records, with permission. If a woman screened positive for depression, she was referred with her permission to her family doctor and given information about local mental health services. If she was deemed at risk of self-

harm or harming others, immediate help was provided. Our sample size for this analysis was 555 mothers and the same number of infants.

Ethics approval for the research protocol was obtained from the Behavioural Research Ethics Board at the University of Saskatchewan. All participants gave written informed consent.

Measures

We assessed the symptoms of three constructs known in the literature to be closely related: depression, anxiety, and mood instability (34, 35), making use of thresholds for clinical relevance.

Depression. Depressive symptoms were measured using the Edinburgh Postnatal Depression Scale (EPDS) at T1 and T2 (36). The EPDS is the most widely used self-report measure for screening postnatal depression (37). Respondents select one of four possible responses (0-3) to each of ten questions to indicate how they felt in the previous week. Ratings for each item are summed for a possible maximum score of 30 (range 0-30; 0 = not depressed, 30 = highest score for depressive mood). Validation studies of the EPDS have been conducted in different cultures, languages, and settings, including in Saskatchewan (38, 39). The EPDS has been found to have a sensitivity of 80% and specificity of 87% (40). In this study, attaining a score ≥ 12 at either T1 or T2 was indicative of clinically significant depression (41-43). In our sample, EPDS had a Cronbach alpha of .83

Anxiety. Anxiety symptoms were measured at T1, and T2 using the EPDS anxiety subscale (items 3, 4, and 5) (44-47) with a range of 0 to 9. Jomeen and Martin (48) found that the anxiety subscale has an acceptable internal consistency (Cronbach α = .77) (49). In our sample, the anxiety subscale had Cronbach alpha of .72. We followed the recommended cut-off score of ≥ 6 for community samples (50). As with the total EPDS score, women were categorized in the high anxiety group if they met the cut-off at either T1 or T2.

Mood instability. Mood instability was measured using five questions that were answered on a Visual Analogue Scale (VAS): 1 “mood frequent ups and downs”, 2 “mood swings occur for no reason”, 3 “other people complain about your mood swings”, 4 “having trouble following through with plans because of mood swings”, and 5 “not making commitments because moods might change”. Women were asked to mark an “X” on a 10 cm line to indicate their level of MI. The length of the segment from the origin to the X mark was measured by a trained research assistant, randomly audited by another. This length of the segment was then translated into a score that ranged from 0 to 50. We dichotomized MI scores into above and below the mean. This was done by calculating the average of T1 and T2 scores separately. If a woman scored above the mean in either period, her MI symptom was coded 1 “High MI” and 0 “Low MI” otherwise.

Other maternal variables. Demographic, psychosocial, and pregnancy-related variables were also assessed. These included age (< 25 vs ≥ 25 yrs), education attainment (< Grade 12 vs ≥ Grade 12), marital status (with or without a partner), ethnicity (aboriginal or not aboriginal), and annual family

income (≤ 40K vs >40K). The psychosocial variables were sources of social support (1 or less vs 2 or more), the number of stressors (0-2 vs >2), partner support (yes or no), maternal smoking (yes or no), alcohol consumption (yes or no), and physical activity status (yes or no) during pregnancy were assessed. As we did with the mood variables, we classified a woman as having a risk factor if these were reported at either T1 or T2. We also used parity (primiparous vs multigravida) as a maternal variable.

Neonatal outcome variables. Neonatal outcome variables included one- and five-minute Apgar scores, LBW, SGA, and PTB. We dichotomized the Apgar scores based on previous studies [41-44]. Apgar scores reflect a baby's wellbeing at birth by assessing five areas: activity, pulse, grimace, appearance, and respiration (51). Each area is rated from 0 to 2 with a possible score of 10 (scores 7 or above indicate that the baby is doing well). Apgar scores were dichotomized into below normal < 7 or normal ≥ 7 (51). Birth weight was measured in grams (g) and dichotomized into two levels: low < 2500 g or normal ≥ 2500 g (52). SGA was defined as being in the 10^{th} percentile for gestational age (53). Preterm birth is based on the duration of pregnancy in completed weeks from the first day of the last normal menstrual period to birth. The variable was dichotomized into two levels: preterm birth (PTB) (< 37 weeks) and normal term birth (≥ 37 weeks) (54).

Data Analysis

We cross-tabulated nine maternal variables in pregnancy with the five neonatal outcomes. Chi-square or Fisher's exact test was used to examine the association of each maternal variable and each baby outcome (45 tests in all).

For each result that was significant at an α level of 5%, we created a logistic regression model that adjusted for maternal age category and marital status. Each logistic regression model was performed first, with complete cases and then with multiple imputations. Coefficients in logistic regression models were exponentiated to yield odds ratios (OR), and their 95% confidence intervals (CI) were calculated accordingly. Multiple imputation was necessary because five variables (SGA, Apgar 1 minute, Apgar 5 minute, LBW, pregnancy stress, and maternal age category) had missing values that ranged from less than 1 to 17 percent. Multiple imputation is a principled way of avoiding biased estimates that can result from non-random missingness and overly narrow confidence intervals (55).

Statistical analyses were performed using Stata and imputation was carried out using multiple imputation with chained equations (MICE) (56). We created 20 imputed datasets following the recommendation of White and colleagues (57).

Results

Characteristics of the mothers and babies

Mothers had a mean age of 29.0 years (*SD* =4.85), and 38% (n = 212) were first-time mothers. Most of the women lived with a partner, had a Grade 12 or higher education, and had a family income of at least

$40,000. Sixty-eight babies (12%) had a 1-minute Apgar score < 7, while 15 (3%) babies had a 5-minute Apgar of <7. Only 20 (4%) of the baby's birth weight was <2500g, while 39 babies (7%) were SGA. Thirty-two babies were born preterm (6%). The complete demographic, psychosocial, and neonatal outcomes are presented in Table 1.

Table 1. Characteristics of Mothers and Infants (N=555) in the Study

Mothers	n	%
Demographic variables		
Age (≥ 25)	465	84
Living with a partner	504	91
Aboriginal ancestry	42	8
Grade 12 or above	529	95
Family income > $40,000	263	90
Mood symptoms		
Clinically significant depression	109	20
Clinically significant anxiety	118	21
Above-average mood instability	283	51
Psychosocial and behaviour variables		
Engaged in regular physical activity	379	32
Alcohol use	57	10
Cigarettes smoking	72	13
With partner's support	516	93
With a higher level of stress	304	55
First-time mothers	212	38
Infants		
Neonatal outcome variables		
Apgar 1 minute score <7 †	68	12
Apgar 5 minute score <7 †	15	3
Pre-term birth (< 37 weeks)‡	32	6
Low birth weight (<2.5 kg) ‡	20	4
Small for gestational age‡	39	7

† Had 17% missing values ‡ Had 10% missing values

Maternal mood symptoms and other maternal factors and neonatal outcomes

Higher anxiety in pregnancy was associated with a higher proportion of Apgar (5-minute) scores below 7 (X^2=3.78, p = .05) while a higher level of stress was associated with low Apgar (1-minute) scores (X^2=5.09, p = .02). Smoking, lack of partner support, and primiparous status were each associated with SGA (X^2 =10.05, p = .002; X^2 = 7.63, p = .006; X^2 = 13.25, p < .001 respectively). In addition, primiparous status was associated with LBW (X^2 = 4.50, p = .03). Depression, mood instability, alcohol use, and exercise during pregnancy were not associated with any of the neonatal outcomes. PTB was not associated with any maternal mood symptoms and other maternal factors in pregnancy. The complete crosstabulation of maternal variables and neonate outcomes is presented in Table 2.

Table 2. Proportion (%) of infants with adverse neonatal outcomes by maternal variables

Variables	Measure	Apgar 1 minute score <7 †	Apgar 5 minute score <7 †	Pre-term birth (< 37 weeks)‡	Low birth weight (<2.5 kg) ‡	Small for gestational age‡
Depression	EPDS < 12	14.78	3.23	6.39	4.36	8.11
	EPDS ≥ 12	14.61	3.37	6.45	2.13	6.52
Anxiety	EPDS Anxiety subscale < 6	13.86	2.45*	6.03	3.72	7.79
	EPDS Anxiety subscale ≥ 6	18.28	6.45*	7.84	4.81	7.92
Mood instability	Below average	14.03	3.62	6.02	4.00	8.84
	Above average	15.48	2.93	6.80	3.91	6.83
Alcohol use	Not at all	14.22	3.61	6.21	4.16	7.98
	Yes, at some point	20.00	0.00	8.33	2.04	6.38
Smoking	No	15.11	3.36	6.05	3.76	6.50*
	Yes	11.36	2.27	9.26	5.45	18.87*
Stress	0-2 stressors	10.75*	3.29	6.99	4.29	9.57
	3+ stressors	18.22*	3.23	5.90	3.65	6.32
Partner support	Yes	14.48	3.22	5.94	3.77	7.01*
	No	19.23	3.85	13.79	6.90	21.43*

Parity (First-time mothers)	No	14.09	3.09	5.71	2.52*	4.46*
	Yes	15.88	3.53	7.57	6.32*	13.51*
Exercise	Yes	14.60	2.84	7.56	4.89	8.72
	No	15.07	4.17	3.85	1.89	5.81

† 17% missing values, ‡ 10% missing values

* p = .05, using a chi-square or Fisher's exact test for cells with small n.

When we adjusted these associations for maternal age category and marital status, five maternal-neonate outcomes remained significant. Smoking, lack of partner support, and primiparous status were associated with SGA. Higher stress was associated with a low Apgar score (1-minute) while being primiparous was linked to LBW. When using complete cases, data analyses results agreed with those using imputed data except for primiparous status and LBW. The results are presented in Table 3.

Table 3. Odds ratios (95% CI's) from logistic regression models of maternal variables for neonatal outcomes (adjusted for mother's age and marital status)

Model	Predictor	Type of analysis	Apgar 1 minute score <7 †	Apgar 5 minute score <7 †	Low birth weight (<2.5 kg) ‡	Small for gestational age‡
1	Higher level of anxiety	Complete cases (n = 461)	–	2.68 (0.98-8.38)	–	–
		Multiply imputed data	–	2.86 (0.94-8.74	–	–
2	Smoking	Complete cases (n = 499)	–	–	–	3.17 (1.36-7.38)*
		Multiply imputed data	–	–	–	3.48 (1.56-7.78)*
3	Lack of partner support	Complete cases (n = 499)	–	–	–	3.34 (1.13-9.89)*
		Multiply imputed data	–	–	–	3.40 (1.16-10.02)*
4	Higher level of stress	Complete cases (n = 461)	1.87 (1.09-3.22)*	–	–	–
		Multiply imputed data	1.88 (1.09-3.25)*	–	–	–
5	Parity (Primiparous)	Complete cases (n = 461)	–	–	2.46 (0.98-6.20)	3.31 (1.66-6.59)*

	Multiply imputed data	–	–	2.52 (1.00-6.29)*	3.27 (1.62-6.62)*

† 17% missing values, ‡ 10% missing values

* $p < .05$

Discussion

In this study, we examined maternal mood symptoms, and psychosocial and behavioral factors in pregnancy with five neonate outcomes. The first main finding is that mood symptoms are not significantly related to neonatal outcomes, or marginally related as in the case of anxiety and low Apgar score at 5 minutes. The second finding is that psychosocial and behaviors factors as well as primiparous status are strongly associated with neonatal outcomes, especially SGA.

We found that antenatal depression is not related to SGA/PTB/LBW/low Apgar score that is in agreement with prior studies (16, 18, 58, 59), but in contrast to others (12, 60, 61). The major reasons for the divergent findings may be related to differences in the measurement of depression, gestational age, settings, and the samples. For example, a study with 791 women in the US assessed depression using the Center for Epidemiological Studies Depression Scale (CESD) in their early pregnancy (around 10 weeks gestation) (61). Studies found that CESD tends to produce higher scores and more false-positive results in symptomatic pregnant and postpartum women (62-64). In this diverse sample of 38.1% Caucasian, 28.6% Asian or Pacific Island, 21.0% Hispanic, and 6.8% African American women, a positive association between depression and PTB was found. Similar findings were reported in a study including 959 Chinese women in late pregnancy using the Beck Depression Inventory to assess women's depressive status (65). Berle et al. (58) found a negative association between depression and PTB in 680 Norwegian women at 16 weeks gestation by the Hospital Anxiety and Depression Rating Scale. In addition, the positive relationship between antenatal depression and neonatal outcomes in developing countries was proposed to be related to low socioeconomic status in women who face a greater challenge of comorbid risk factors (e.g., maternal undernutrition) (66, 67). A meta-analysis of 29 studies (68) investigated possible moderators of neonatal outcomes, and found the country in which the study was conducted (developed or developing country) was a significant moderator of the association between antenatal depression and LBW. However, Goedhart et al. (2010) conducted a study of 8,050 women at 12 weeks of pregnancy in Holland, and found a positive relationship between perinatal depression and neonatal outcomes. Furthermore, in a study by Nasreen et al. (11), 720 women from two rural subdistricts of the developing country of Bangladesh were assessed in their third trimester using the EPDS to determine depressive status, and a significant relationship between antenatal depression and LBW was found while controlling for poverty and maternal nutritional status. The mechanism of impact of antenatal depression on neonatal outcomes is not well understood, and more research is required.

Among the mood symptoms, elevated anxiety was associated with low Apgar score at 5-minutes although this did not survive signficance when adjusting for maternal age and marital status. Anxiety is closely related to stress, and a higher level of stress was associated with low Apgar score (1-minute) in our study. Potential causal pathways through which prenatal anxiety and stress may lead to adverse neonatal outcomes have been proposed. One potential mechanism was identified as changes in maternal hypothalamic–pituitary–adrenal (HPA) axis activity. Increased maternal HPA axis activity has been observed during the perinatal period (69). However, experiencing elevated levels of anxiety and stress during pregnancy may contribute to an increase in stress hormones, such as cortisol and catecholamines (70). The release of stress hormones has also been found to cause changes in immunologic functioning and uterine blood flow during human pregnancy, thus increasing vulnerability to preterm birth, SGA, and low BW (71-76). However, not all studies found such an association (16, 58), which might be related to the timing of when antenatal anxiety and stress were measured in pregnancy, and what instruments were utilized (77, 78) while others suggest that the mechanisms of the association between stress and neonatal outcomes need to be further investigated (79, 80).

To the best of our knowledge, this is the first study to report the relationship between antenatal MI and neonatal outcomes, and we did not find a significant relationship. It may be that MI affects neonatal outcomes through depression, anxiety, or stress since MI is related to depression, anxiety, and stress as reported in clinical samples (19, 81) and perinatal women (21, 82). To date, the possible role of antenatal MI in fetal intrauterine development remains unexplored. More studies are required in order to understand the relationship between antenatal MI and neonatal outcomes.

The association between lack of social support during pregnancy and poor neonatal outcomes has been documented according to a systematic review (83). Our findings further support and extend previous evidence on the effect of low social support on the occurrence of adverse neonatal outcomes. During early pregnancy, women experience tremendous changes physically and psychologically which require major adjustments, and social support plays a crucial role to help women cope with the transition to motherhood (84, 85). Lack of social support from partner, family and/or friends can be reflected on lack of social stability and social participation, which has a very negative impact on the psychological well-being of pregnant women (86, 87). While the mechanism of the association between antenatal social support and neonatal outcomes is not fully understood, some proposed that effects of social support on neonatal outcomes maybe by increasing maternal stress, probably via the pathway of biological stress systems including HPA axis activity (88, 89).

Smoking was a risk factor for SGA in the current study, which replicated previous studies (90-92). Antenatal cigarette smoking leads to fetal exposure to nicotine, which crosses the placenta and leads to a 15% higher concentration than in maternal blood (93, 94). Nicotine interferes with normal placental function, and reduces uterine blood flow by an average of 30 to 49%, which causes a deprivation of nutrients and oxygen, resulting in fetal hypoxia and malnutrition, and may lead to intrauterine growth restriction (93, 95).

Our study found that being primiparous was associated with LBW and SGA, which is consistent with some studies (96). A meta-analysis of 41 studies found that being primiparous increased a woman's risk of having a baby with LBW and SGA (96). Parity influences the growth of the placenta and its efficiency, which is related to uterine blood flow, oxygen availability, nutrient exchange, and endocrine regulation of the fetus (97, 98).

There were several limitations to the current study. First, although this is a relatively large sample, the participants were predominantly Caucasian, married, with post-secondary education, and higher family income, which limits the generalization of the findings. According to the 2016 Census of Canada (99), Aboriginal people accounted for 15.6% of the total population of Saskatchewan compared with 7.2% in this sample. Second, the measure of depression, anxiety, MI, and other psychosocial and behaviour variables relied on participants' subjective report, which could be influenced by women's current thoughts, feelings, and consideration of social desirability particularly, reporting antenatal smoking, alcohol consumption, and drug use (100, 101). Third, MI holds a temporal property since mood fluctuations can change from moment to moment, which is unlikely to be recalled accurately, such as which day and what time during the day it occurred (102). Two recent studies reported that paper-and-pen measures of MI do not agree with smartphone measured MI (103, 104). Finally, the VAS used to assess antenatal MI is not previously validated. Due to a lack of validated instruments in measuring perinatal MI, studies often utilize non-validated measures (105, 106). There is a need for validating existing instruments in perinatal women or developing assessment tools that are specifically relevant to perinatal MI.

Conclusion

The current study identified no associations between antenatal mood symptoms and neonatal outcomes. However, our findings further support and extend previous evidence on smoking abstinence or cessation, and the provision of resources for stress management and social support that could help prevent or alleviate adverse neonatal outcomes.

Abbreviations

AGA: Appropriate for gestational age

CESD: Center for Epidemiological Studies Depression Scale

CI: Confidence intervals

EPDS: Edinburgh Postnatal Depression Scale

FIP: Feelings in Pregnancy and Motherhood Study

g: Grams

LBW: Low birth weight

LGA: Large for gestational age

MI: Mood instability

N: Sample size

OR: Odds ratios

PTB: Preterm birth

SD: Standard deviation

SGA: Small for gestational age

T1: Early pregnancy: 17.4 ± 4.9 weeks

T2: Late pregnancy: 30.6 ± 2.7 weeks

T3: Postpartum: 4.2 ± 2.1 weeks

VAS: Visual Analogue Scale

Declarations

Ethics approval and consent to participate

Ethics approval for the research protocol was obtained from the Behavioural Research Ethics Board at the University of Saskatchewan (Beh # 16-267). Written informed consent was obtained from women before they participated in the study.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and analyzed in this study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

This work was supported by the Canadian Institutes of Health Research (Grant # 145179). The funding agency had no role in the design, data collection, analysis, interpretation, and writing of the study.

Authors' contributions

HL overviewed current literature on the topic, analyzed the data, interpreted results, and wrote the initial manuscript draft; AB and NM originally designed the study and gathered the data; AB, RB, and LB provided expertise and appraisal of available data; LB analyzed the data, AB, RB, LB, and NM provided the interpretation of results and provided an overview of current literature on the topic, and AB provided supervision. LB revised the initial draft. All the authors contributed comments and approved the final version.

Acknowledgments

The authors would like to thank the women who participated in this study.

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