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Maternal prenatal state anxiety symptoms and birth weight: A pilot study

Research Article

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Abstract: Many women suffer from new or worsening anxiety during pregnancy. In this pilot study, we investigated the effect of timing and severity of prenatal state anxiety symptoms on reduced birth weight. We hypothesized that: (1) Women with state anxiety symptoms during mid-gestation would deliver newborns with lower birth weight in comparison to participants with symptoms in early gestation and (2) compared to women with lower anxiety symptoms (< 50th percentile), women with medium-to-high state anxiety symptoms (> 50th percentile) would have lower birth weight offspring. The sample consisted of the first 30 pregnant women who agreed to participate in this pilot study. We assessed anxiety symptoms, using the State-Trait Anxiety Inventory during early and mid-gestation. We obtained birth weight from clinical charts. A hierarchical multiple regression showed that, after controlling for covariates, state anxiety symptoms in mid-gestation were associated with lower infant birth weight [$F(9, 7) = 20.30$, $p<.001$]. However, birth weight did not differ as a function of the severity of maternal state anxiety [$F(1, 23)=.14$, $p=.71$ and $F(1, 24)=1.76$, $p=.20$., respectively]. Clearly, our pilot data need replication. Once statistical significance is established with larger samples, it will be informative to examine the clinical significance of those findings.

Keywords: *Prenatal state anxiety symptoms • Early gestation • Mid-gestation • Birth • Weight*

1. Introduction

Anxiety is a stress-related mood state with physiological and psychological parameters [1]. Specifically, state anxiety symptoms refer to how anxious a person feels at a particular temporary moment [2]. Experiencing occasional anxiety is a part of life. However, when anxiety symptoms interfere with daily activities or persist, they can be disturbing. Many women suffer from new or worsening anxiety symptoms during pregnancy [3]. Furthermore, depression and anxiety symptoms often co-occur [3,4]. Despite this, prenatal anxiety has received less attention than depression, and its prevalence is unknown, based on a recent systematic review [3].

The literature on the effects of prenatal anxiety is scarce and conflicting. A previous study found a relationship between prenatal trait anxiety symptoms and low birth weight [5]. More specifically, Hosseini et al. (2009) [5] found that when pregnant women were anxious during mid and late gestation, there was a reduced birth weight. Furthermore, the authors found that anxiety symptoms in early-to-mid gestation significantly predicted reduced birth weight but only when they were severe. In contrast, other studies found no relation between prenatal anxiety and low birth weight [1]. It is thus important to clarify this relationship, especially because it can have detrimental health consequences for infants. For example, restricted fetal growth, expressed by low birth weight, may be associated with insulin resistance [6,7] and non-insulin dependent diabetes mellitus [8]. However, the precise mechanisms underlying these predispositions are still unclear.

Newborns are considered to be of low birth weight when their weight is below 2500g at birth [5]. Many factors may contribute to low birth weight (e.g., smoking [9-12], illicit substance abuse [10,12], depression [12,13], maternal Body Mass Index (BMI) [14], socioeconomic status (SES) [15] and maternal age [14-16]). We adjusted for these potential covariates in this study.

To clarify the relationship between maternal prenatal state anxiety symptoms and newborns' low birth weight,

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we followed pregnant women prospectively until birth. We investigated whether the timing (early vs. mid-gestation) and severity (high vs. low) of maternal prenatal state anxiety symptoms were associated with reduced birth weight. Based on Hosseini et al.'s findings [5], we hypothesized that: (1) Pregnant women who have state anxiety symptoms during mid-gestation will give birth to newborns with lower birth weight in comparison to participants whose anxious symptoms occurred in early gestation and (2) Using a comparison group of women with low anxiety symptoms (in the bottom 50th percentile), we hypothesized that women with medium-to-high anxiety symptoms (in the top 50th percentile) would have lower birth weight infants.

2. Materials and methods

2.1 Demographic and clinical characteristics of participants

Thirty pregnant women participated in this prospective study entitled "*Feelings Matter in Pregnancy: A pilot study*" directed by the first author. Participants were recruited from the prenatal clinic of the Cumberland Regional Health Care Centre (CRHCC) (Amherst, Nova Scotia, Canada). Table 1 describes the sample in details. None was taking a prescription drug for depression and/or anxiety. In addition, none suffered from systemic diseases such as hypertension, preeclampsia, lupus or gross placental abnormalities. There were nine smokers in the sample. Mean cotinine level was 66.87 ng/mL (SD = 15.70). Participants were assessed twice during pregnancy: (1) At T1 during the first prenatal visit and (2) at T2 during mid-gestation. There were no drop-outs from T1 to T2. No woman suffered from a chronic or inflammatory illness. The study received ethics approval from the health authority's and Mount Allison University's Research Ethics Boards. All participants provided written informed consent at the onset of the study.

Table 1. Descriptive data of the pregnant women and their newborns (N = 30).

Mothers	
Age (in years)	24.40 (± SD = 4.43)
Body mass index (BMI)	29.61 (± SD = 8.98)
Serum cotinine (in ng/mL)	66.87 (± SD = 15.70)
Education	48% had some high school education 52% had some college/university
Gross family income[a]	65% < $40,000 35% > $40,000
Ethnic/Linguistic Background[b]	100% Caucasian & English-speaking
State Anxiety (STAI-Y1), early gestation	39.46 (± 11.64)
State Anxiety (STAI-Y1), mid-gestation	38.68 (± 10.85)
Newborns	
Birth weight	3293.81 g (± SD = 603.32g
Gestational age at birth (in weeks)	39.34 (± 2.82)
Normal and healthy at birth	100%

[a] *Most mothers were of low socio-economic status (SES)*
[b] *All mothers were Canadians.*

2.2 Experimental procedures

We collected data at three time points throughout pregnancy: at early gestation (T1 = 10 weeks of pregnancy), at mid-gestation (T2 = 26 weeks of pregnancy), and at delivery (T3 = birth time).

2.3 Main measures

2.3.1 State-Trait Anxiety Inventory (STAI)

We measured state anxiety symptoms at T1 (early gestation) and again at T2 (mid-gestation). We chose the STAI because: 1) it is one of the most commonly used reliable and valid instruments for measuring anxiety [17]; 2) it requires 5-10 minutes to be completed and 3) it has been translated into French [18], the language of a large number of the participants of the larger study. The STAI measures anxiety both as a current state (transitory), and as a trait, with 20 items respectively. Participants reported *how they currently feel* (state anxiety) as well as the *general propensity to experience anxiety* (trait anxiety), as a control variable (see below). The STAI test-retest reliability correlations range from 0.59 (state anxiety) to 0.86 (trait anxiety) [19]. The highest possible STAI score on the scale is 80, indicating higher anxiety, and the lowest score is 20, indicating lower anxiety.

2.3.2 Newborns' birth weight

We extracted birth weight from the participants' medical charts.

2.4 Potential confounders

We identified possible risk factors for low birth weight from the literature a priori. Because these factors can act as potential confounders of the results, we measured them as continuous variables in order to take them into account in the analyses. These potential confounders were: (1) Depressive symptoms, measured with the *Patient Health Questionnaire-9* (PHQ-9) at T1 and T2. We chose this instrument because the PHQ-9 is a widely used reliable and valid instrument to screen for depression in primary care, namely with ethnically diverse populations and has a French version [20]; (2) Perceived stress was measured using the *Perceived Stress Scale* (PSS-10) [21] at T1 and T2. The PSS-10 assessed the

participants' perceived stress over the past month. Test–retest reliability is good and internal consistency is high, with Cronbach's α ≥ 0.85 [21,22]; (3) Smoking status was assessed with a *serum cotinine* test measured at T1, using an orasure- 1124E kit; (4) Maternal age and socio-economic status (SES) was measured at T1 with a Demographic Questionnaire, which asked questions about demographic maternal characteristics, medical conditions as well as substance use and finally (5) Gestational Age (GA) at birth, which was extracted from medical charts at T3.

2.5 Statistical methods

We performed statistical analyses using SPSS 16.0 for Windows (SPSS Inc., Chicago, IL). We set statistical significance at $p < 0.05$. To address the first hypothesis, we used hierarchical regressions to predict the variance in birth weight, which is a continuous dependent variable, from blocks of related independent variables, including the potential confounders mentioned above. The aim of this analysis was to examine additive and unique effects of prenatal state anxiety symptoms at two times during pregnancy (early and mid-gestation). Prior to analyses, data were screened and regression assumptions were met. To address the second hypothesis, we used a comparison group of women with low anxiety symptoms. Based on a median split (50th percentile), we performed a one-way ANOVA to compare birth weight of offspring born to mothers with medium-to-high anxiety symptoms to those born to mothers from the comparison group.

3. Results

3.1 Descriptive analyses: maternal anxious symptoms and newborns' mean weight

Maternal anxiety symptoms scores ranged between 39 and 60 in early gestation and between 20 and 60 in mid-gestation (see Table 1 for means and standard deviations). Most of the newborns had a normal birth-weight (2598-3998 g). The mean birth weight of the newborns was 3293.81 g (SD = 603.32 g). One newborn had a low birth-weight (2400 g), one had very low birth-weight (1140 g) while another newborn had a high birth-weight (4150 g).

3.2 Did women with state anxiety symptoms during mid-gestation give birth to newborns with lower birth weight in comparison to participants who had state anxiety symptoms in early gestation?

Gestational age was the first predictor entered into the hierarchical regression analysis (first block). This block yielded a significant overall model [$F(1, 15) = 5.34$, $p=.04$] and accounted for 26% of the variance in birth weight. The second block of the hierarchical regression analysis included depressive symptoms in early and mid-gestation, maternal age, SES indexed by gross family income, alcohol use and smoking status on top of gestational age. This second model yielded overall significant results [$F(7, 9) = 16.98$, $p<.001$] that accounted for 67% of the variance in birth weight. As Table 2 shows, maternal age, gross family income

Table 2. Hierarchical linear regression model for the prediction of low birth weight.

Predictor variable	B (SE)	β	95% CI		ΔR^2
			Lower	Upper	
Block 1					.26*
Gestational Age	182.02 (78.73)	.51*	14.21	349.3	
Block 2					.67**
T1 Depressive Mood	10.66 (26.61)	.09	-50.25	71.58	
T2 Depressive Mood	-2.54 (21.43)	-.02	-51.02	45.95	
Maternal Age in Years	31.82 (10.15)	.36*	8.87	54.77	
Gross Family Income	130.96 (26.61)	.60**	70.76	191.16	
Alcohol History	-624.56 (156.34)	-.59**	-978.22	-270.89	
Smoking History	-63.52 (126.62)	-.05	-349.96	222.91	
Block 3					.03**
T1 State Anxiety	2.68 (4.96)	.07	-9.05	14.41	
T2 State Anxiety	-22.88 (9.17)	-.54*	-44.55	-1.20	

*CI = Confidence Interval, *p<.05 **p<.01*

and alcohol history were all significant predictors of infant low birth weight, after controlling for gestational age. The final model included maternal prenatal state anxiety symptoms in early and mid-gestation as predictors on top of all the previously found predictors. This final overall model yielded significant results [$F(9, 7)=20.30$, $p<.001$] and accounted for an additional 3% of the variance in birth weight. However, this final model was not significantly better than the second model, $\Delta R^2=.03$, $p=.10$. As Table 2 indicates, maternal state anxiety in mid-gestation was a significant predictor of birth weight, after adjustment for all the covariates listed previously. We found that when there was only a one maternal state anxiety point increase in mid-gestation, there was a decrease in infant birth weight of 22.88 g.

3.3 Did women with medium-to-high anxiety symptoms have lower birth weight infants than women with lower anxiety symptoms?

We performed a median split (50th percentile = 38.5) to assign participants into two groups: The first group included women with lower prenatal state anxiety symptoms (< 38.5). The second group included those with medium-to-high state anxiety symptoms (≥ 38.5). Means and standard deviations can be found in Figure 1. The results of ANOVA showed that birth weight did not differ as a function of the severity of maternal state anxiety symptoms [$F(1, 23)=.14$, $p=.71$ and $F(1, 24)=1.76$, $p=.20$., respectively].

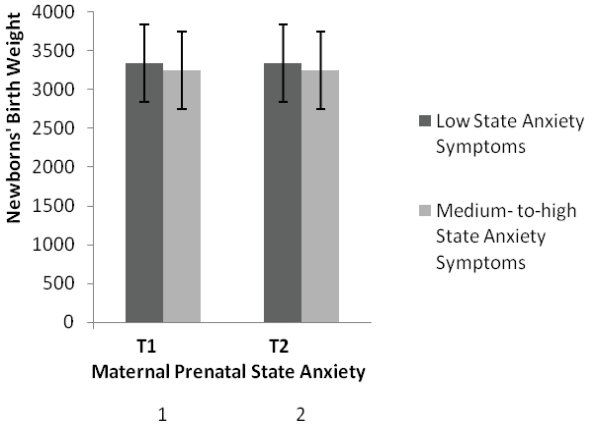

Figure 1. Means and standard deviations of the newborns' birth weight for the timing (T1 in early gestation and T2 in mid-gestation) and severity of maternal prenatal state anxiety.

4. Discussion

Most participating women had moderate state anxiety symptoms while a few of them had medium-to-high levels. Although their mean state anxiety levels were slightly higher than the STAI mean scores of women aged 19-39 years old, the mean values observed were in the reference range of the STAI norm group (36.17, SD = 10.96). As hypothesized, and despite the limited range of anxiety severity in women, we found a significant effect of prenatal state anxiety symptoms on birth weight when symptoms occurred in mid-gestation. More specifically, the timing of state anxiety symptoms during mid-gestation was associated with a 22.88g decrease in the newborns' birth weight. In contrast, state anxiety symptoms in early gestation did not significantly predict reduced birth weight, after adjusting for covariates. These findings followed the same trend previously observed in other studies on trait anxiety [5]. Additionally, birth weight did not appear to differ as a function of severity of prenatal anxiety symptoms. It is then likely that if prenatal state anxiety symptoms are not severe enough, especially in early gestation, a reduced birth weight will not be captured.

It is possible that our first finding may be due to the role of maternal hypothalamic-pituitary-adrenal (HPA) axis in anxiety. Comparable to the effect of prenatal depression, state anxiety symptoms may lead to an increased activity of the maternal HPA axis, which may be translated into elevated cortisol levels (beyond the pregnancy-related normal and transient hypercortisolism) [23]. From animal studies, we know that such an effect could in turn reduce fetal weight and/or lead to alterations in the fetal HPA axis [24]. Since we did not measure maternal prenatal health behaviours in this study, another alternative explanation linking maternal prenatal anxiety to low birth weight could be due to potentially associated poor maternal prenatal health behaviours [25].

Our study helps as a pilot because it sets the stage for a larger-scale investigation (N= 200, based on a priori power analysis) by testing its feasibility and validating its measures. In the larger study, we will investigate whether increased maternal inflammatory parameters during pregnancy would be a plausible biological mechanism linking maternal anxiety symptoms to low birth weight. The forthcoming larger study will keep the same design whilst controlling for additional confounders, namely blood cord immune measures (indicative of prenatal infection).

4.1 Study strengths and limitations

This pilot study has several strengths. First, we adjusted for relevant potential covariates. More specifically, the study prospective design and analyses allowed us to rule out any potential effect of prenatal depressive symptoms on birth weight (even if those symptoms corresponded to "mild" depression). Clinically speaking, this is perhaps the most significant finding as it seems to suggest that maternal prenatal anxiety symptoms may be associated with reduced birth weight. Second, despite the limited sample size, our data were in line with findings from other studies [15,16] in regards to maternal demographic characteristics and reduced birth weight. For example, we also observed that older participants gave birth to larger newborns and newborns born to mothers from higher SES were larger. Despite its strengths, our pilot study is limited by: (1) its small sample size, which restricts the generalizability of the findings and (2) the limited range of anxiety scores (in the moderate levels), which may have reduced the statistical power of analyses to detect differences.

4.2 Conclusion

Due to the small sample size, it is clear that these findings need replication. Once statistical significance is established with much larger samples, it would be informative to establish whether those findings are clinically significant in terms of maternal well-being and/or infant postnatal growth and development.

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