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Disturbed Sleep and Inflammatory Cytokines in Depressed and Nondepressed Pregnant Women: An Exploratory Analysis of Pregnancy Outcomes

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Abstract

Objective—Disturbed sleep and depression are potential risk factors for pregnancy complications. Both conditions are noted to dysregulate biological pathways responsible for maintaining homeostatic balance and pregnancy health. Depression during pregnancy is associated with poor sleep. Thus, we explored whether disturbed sleep was associated with inflammatory cytokines and risk for adverse pregnancy outcomes, as well as whether depression augmented the sleep-cytokine relationship thereby additively contributing to risk for adverse outcomes.

Methods—Interview-assessed sleep and plasma cytokine concentrations were evaluated in a cohort of depressed and non-depressed pregnant women (N= 168) at 20 and 30 weeks gestation. Outcomes evaluated included preterm birth, birth weight, and peripartum events.

Results—Among depressed women, short sleep duration (< 7 hours) was associated with higher IL-8 across time ($\beta=.506$, $p = .001$), poor sleep efficiency (< 85%) was associated with higher IL-6 ($\beta=.205$, $p = .006$), and daytime naps were associated with higher TNF- α ($\beta=.105$, $p = .024$). Aspects of poor sleep were associated with having a lower weight baby ($ps < .053$). Among depressed women, IFN- γ increased risk for preterm birth (OR = 1.175, $p = .032$). Trends for IL-6 and higher birth weight ($\beta = 105.2$, $p = .085$); IFN- γ and lower birth weight ($\beta = -19.92$, $p < .069$); and increased IL-8 and babies weighing < 4000g, (OR = .72, $p < .083$) were observed.

Conclusions—Although speculative, disturbed sleep may disrupt normal immune processes and contribute to adverse pregnancy outcomes. Exploratory analyses indicate depression modifies these relationships.

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Keywords

Sleep; depression; pregnancy; cytokine; outcomes; sleep quality

Introduction

Pregnancy is a period in a woman's life denoted by changes in sleep patterns, including shortened sleep duration, insomnia symptoms and poor sleep efficiency. Evidence indicates that poor and disrupted sleep is associated with a concomitant increase in inflammatory cytokines derived from both plasma and stimulation assays (1-5). Specifically, poor sleep quality (3, 6) fragmented sleep (7, 8), restricted sleep (9, 10), and variability in bed and wake times (11) are associated with higher circulating inflammatory cytokine concentrations (e.g. IL-6, IL-8, TNF- α , and IFN γ). Moreover, longitudinal studies indicate that poor sleep contributes to an elevated inflammatory cytokine profile weeks (12) or even years later (13). Current paradigms indicate that adequate sleep, both in and out of pregnancy, is essential for efficient immune functioning. This is supported by evidence showing that the introduction of a nap or recovery sleep is followed by marked reductions in cytokine concentrations (14-16). It is further theorized that an imbalance in the production of cytokines can compromise the efficiency of the immune system's immediate and long-term ability to ward off disease and maintain health, which may be especially critical during pregnancy.

Cytokines that are dysregulated following disturbed sleep are also the key to a host of normal pregnancy-related processes, including implantation and parturition (17, 18). Of relevance here is that numerous retrospective studies have shown higher inflammatory cytokine concentrations among women with adverse pregnancy outcomes, such as preeclampsia (19-21), intrauterine growth restriction (IUGR) (22, 23), and preterm birth (24-27). Although infection is the primary cause of the excessive inflammation observed in adverse pregnancy outcomes, an infection is identified only in about 50% of adverse outcomes (28, 29). Hence, we suggest that behavioral processes, such as disturbed sleep, may play a role in adverse pregnancy outcomes (30), given the relationship between sleep disturbance and inflammation, and inflammation and adverse outcomes.

Another important correlate to consider during pregnancy is depression, as it is associated with disturbed sleep, increased circulating concentrations of inflammatory cytokines and increased risk for adverse pregnancy outcomes. Depression significantly increases the sleep disruption that women experience during pregnancy compared to non depressed pregnant women (31-34). Higher concentrations of inflammatory cytokines, such as IL-6, IL-8 and TNF- α , are likewise observed in individuals with higher depressive symptoms/major depression compared to individuals with no depression (35-37). This finding has been suggested in both non-pregnant depressed individuals (35, 38) and pregnant women with depressive symptoms (39, 40). Christian and colleagues demonstrated that after adjustment for pre-pregnancy BMI, higher depressive symptoms were related to higher IL-6 and marginally related to TNF- α . While there is a strong correlation between CES-D scores ≥ 16 and clinically determined depression, the association becomes weak when evaluating scores less than 16 (41). Lastly, depression has been independently linked to an increased risk for adverse pregnancy outcomes such as preterm birth and preeclampsia (42-45).

To date, the majority of the evidence has linked disturbed sleep and elevated inflammatory cytokines, depression and inflammatory cytokines, or elevated inflammatory cytokines and pregnancy complications. However, no study has concurrently evaluated all correlates and their possible interactive effect in pregnant women. We suggest that among depressed pregnant women with poor sleep, for example, we would anticipate an augmented

inflammatory response which subsequently increases risk of adverse outcomes as compared to depressed pregnant women with adequate sleep or non-depressed pregnant women with poor sleep. Hence, we sought to explore whether disturbed sleep in pregnancy was associated with inflammatory cytokine concentrations, whether this relationship contributed to adverse pregnancy outcomes, and whether depression moderated these associations.

Methods

Participants

This is a secondary analysis assessing participants who participated in the “Antidepressant Use During Pregnancy” prospective observational study that evaluated whether the presence of depression or antidepressant medication (SSRI) use during pregnancy was associated with adverse pregnancy outcomes. Details of the recruitment process, inclusion and exclusion criteria are described elsewhere (45). Briefly, pregnant women (N = 168) 15-44 years of age, able to speak English, a singleton pregnancy and < 20 weeks gestation were recruited. Women were recruited from two sites: Cleveland between Jan 23, 2000 and Aprils 1, 2001, and Pittsburgh between April 23, 2003 and July 11, 2007. They were assessed at weeks 20, 30 and 36 of pregnancy. Each hypothesis tested had a varying number of participants depending on available data. There were 168 mother/infant pairs included in at least one statistical model. All participants provided written and informed consent. The study was approved by the Institutional Review boards at the Cleveland and Pittsburgh sites.

Procedures

Sleep variables were obtained from the Structured Interview Guide for the Hamilton Depression Rating Scale with Atypical Depression Supplement (SIGH-ADS) (46). We assessed naps, defined as more than 1 minute of reported daytime napping; sleep onset latency (SOL), defined as the amount of time the participant stated it took her to fall asleep; wake after sleep onset (WASO), defined as the total number of minutes spent awake at night; total sleep duration (TSD), defined as total nocturnal sleep excluding time to sleep onset and time spent awake at night but including nap time; time spent in bed; sleep efficiency (SE), defined as the amount of total sleep duration divided by time spent in bed multiplied by 100%; and symptoms of insomnia, defined as difficulty initiating sleep, difficulty maintaining sleep or early morning awakening. In order to make clinically relevant comparisons within groups, we dichotomized the sleep variables as follows: Naps Yes/No; SOL was dichotomized at ≤ 15 minutes; WASO at ≤ 20 minutes; Time in Bed 7-9 hours or not; TSD < 7 hours Yes/No or > 9 hours Yes/No; SE $\leq 85\%$; and Insomnia Yes/No.

Blood samples were collected during each of the maternal assessments (20, 30 and 36 weeks). At the cohort level, collection times were arranged at the convenience of the participant, therefore times varied from 9:00AM – 6:00PM. While there is a recognized circadian rhythm to cytokine production and concentration, levels are lowest during the daytime (47). Due to missing data, time of day could not be controlled for in the statistical analyses. At the individual levels, blood was collected at approximately the same time during each assessment to reduce the influence of intra-individual diurnal variation.

Additional Measures—The presence of clinical depression was determined at enrollment (20 weeks) using the Structured Clinical Interview for DSM-IV (SCID) (48). In the parent study, depression severity was assessed at each time point with the 29-item SIGH-ADS (46). Descriptive data for the sample were collected at 20 weeks and included demographic characteristics, SSRI use, smoking status, alcohol use, and parity. Delivery records were reviewed at 2 weeks postpartum. Outcome measures were recorded onto the Peripartum Events Scale (PES) (49). The PES was developed to quantify stressful events related to

pregnancy, labor, and delivery. Outcomes obtained from the PES and evaluated in this study include preterm birth (< 37 weeks) (yes/no), gestational weight (grams), and scores on the PES. The total PES score is the total number of events from nine subscales. The item scores on the infant subscale of the Peripartum Events Scale (33) assessed 10 problems (pH correction, volume expansion, transfusion, hypoglycemia, hyperbilirubinemia, hypocalcaemia, sepsis, meconium aspiration pneumonitis, other, and other life-threatening).

Assay of Cytokines—Plasma levels of interleukin (IL)-6, IL-8, interferon (IFN)- γ and tumor necrosis factor (TNF)- α were determined by ELISA (R & D Systems) according to the manufacturer's instructions. The detection range for IL-6 was between 0.16 pg/ml – 10.0 pg/ml with a minimum detectable dose of 104 fg/ml; for IL-8 the detectable range was between 31.2 – 2000 pg/ml with a minimum detectable dose of 3.5 pg/ml; for the detectable range was IFN- γ 15.6 – 1000 pg/ml with a minimum detectable dose of <8.0 pg/ml; and for TNF- α the detectable range was between 0.5 pg/ml - 32 pg/ml with a minimum detectable dose of 0.09 pg/ml. All samples were run in duplicate and the coefficient of variation (CV) between samples was < 10%. All samples, except for TNF- α , were in detectable range. We were unable to detect TNF- α in 40 participant samples. The variance in the sample size is a reflection of available and viable plasma samples at each time point.

Statistical Analyses

Descriptive statistics are presented as means and standard deviations for continuous measures and as percentage distributions for categorical measures. Tests included t-tests for normally distributed continuous measures. Mann-Whitney U tests for non-normally distributed measures, and chi-square for categorical measures. Fisher's exact tests were calculated when chi-square test assumptions were violated. Cytokine values greater than or less than 3 standard deviations were considered severe outliers and deleted. The distribution of the sleep measures remained extremely non-normal after linear transformation. We therefore dichotomized the sleep measures into clinically meaningful categories. All cytokines were log-transformed for tests and models. Change in cytokine concentrations was calculated as the difference between cytokine concentrations at week 30 and week 20 (prior to transformation). Each set of analyses was stratified by depression status at 20 weeks depression. Models of continuous outcomes such as infant weight were fit with linear regression while models of binary outcomes such as preterm birth were fit with logistic regression. The model fit for the PES was Poisson. Analyses were conducted using SAS 9.0. Since this was an exploratory analysis, we made no statistical adjustments for multiple comparisons. Relationships were considered significant at $p < .05$ and should be interpreted accordingly.

Results

Demographic characteristics of the 168 participants are presented in Table 1. Table 2 shows the descriptive statistics for cytokine levels by weeks gestation and sleep parameter. The following analyses focus on sleep and inflammatory markers, and whether depression moderated any of these associations. Cytokine concentrations at 20 weeks gestation according to sleep category and depression status at 20 weeks are shown in Table 3, whereas cytokine concentrations at 30 weeks according to sleep category and depression status at 20 weeks are shown in Table 4. We examined the parameter estimates for the interaction between sleep parameter and depression status at 20 weeks gestation and cytokines 20 weeks gestation (see Table S1, Supplemental Digital Content 1). We further assessed the parameter estimates for the interaction between sleep parameter and depression status at 20 weeks and cytokines at 30 weeks (see Table S2, Supplemental Digital Content 1) and sleep parameter and depression status at 20 weeks and the change in cytokine levels at 30 weeks

(see Table S3, Supplemental Digital Content 1). Women with short sleep duration (< 7 hours) and depression showed a greater increase in IL-8 across time ($\beta=.506$, $p = .001$). Women with poor sleep efficiency (< 85%) and depression showed a greater increase in IL-6 over time ($\beta=.205$, $p = .006$). Lastly, women who were depressed and took daytime naps had a greater increase in TNF- α ($\beta=.105$, $p = .024$).

Cytokine levels at 30 weeks according to sleep category and depression status at 30 weeks are presented in Table S4, Supplemental Digital Content 1. The parameter estimates and the interaction between sleep parameter and depression status at 30 weeks and cytokines at 30 weeks are in Table S5, Supplemental Digital Content 1. All adjusted models were controlled for race (white vs. black and other), college education, parity, pre-pregnancy BMI, and SSRI use at 20 weeks gestation. In adjusted models, we found that among women who spent > 20 minutes awake at night, those with depression had lower levels of IL-6 at 20 weeks ($\beta=-.139$, $p = .015$). We also note that women who had < 7 hours sleep duration and who were depressed had higher TNF- α at 20 and 30 weeks ($\beta=.192$, $p = .038$; $\beta = .198$, $p = .025$), as well as higher IL-8 at 30 weeks ($\beta=.545$, $p = .008$). Women with sleep efficiency < 85% who were depressed had higher IL-8 at 20 and 30 weeks ($\beta=.354$, $p < .001$; $\beta=.455$, $p = .004$), and higher IL-6 at 30 weeks ($\beta=.272$, $p = .007$). Finally, women who took naps and were depressed at 30 weeks had higher TNF- α ($\beta = .019$, $p = .030$).

We also evaluated whether sleep at 20 and 30 weeks, as well as cytokine concentrations at 20 and 30 weeks, and the change in values from 20 to 30 weeks, were associated with pregnancy/delivery outcomes in depressed and nondepressed women (Table 5-7). We also evaluated parameter estimates and probability values for the interaction of depression status at 30 weeks gestation and cytokine level 20 weeks gestation, 30 weeks gestation, and change between 30 and 20 weeks gestation regressed on infant outcome (see Table S6, Supplemental Digital Content 1). Depressed women with a SOL > 15 at 20 weeks had higher PES scores ($\beta = 0.719$, $p = 0.037$). Depressed women with insomnia symptoms at 30 weeks delivered smaller babies ($\beta=-315.5$, $p = .047$). Similarly, depressed women who were short sleepers had smaller babies ($\beta=-251.8$, $p = .053$; $\beta = -424.3$, $p = .031$). Among women who were depressed at week 20, the change in IL-6 across pregnancy was associated with lower birth weight ($\beta = -242$, $p < .043$) but became nonsignificant after adjustment ($\beta = -133$, $p = .181$). Lastly, among women who were depressed at week 20 an increase in IL-8 across pregnancy was protective against babies weighing > 4000g, but this was diminished to a trend following covariate adjustment (OR = .72, $p = .083$). For women who were depressed at week 30, higher IFN- γ was associated with an increased risk of preterm birth (OR = 1.175, $p = .032$), while higher IFN- γ and IL-6 were modestly associated with birth weight ($\beta = -19.92$, $p = .069$; $\beta = 105.2$, $p = .085$, respectively).

Discussion

This exploratory study concurrently examined several variables previously associated with adverse pregnancy outcomes. First, they provide additional support to the current understanding that disturbed sleep in the context of depression is associated with alterations in cytokine concentrations (35, 50). We noted several modest associations among aspects of poor sleep and increased levels of inflammatory cytokines. The findings also provide support that disturbed sleep may be a risk factor for adverse pregnancy outcomes. Specifically insomnia symptoms (difficulty initiating or maintain sleep, or unrefreshing sleep) and short sleep duration were associated with giving birth to smaller infants among depressed pregnant women. Finally, we observed a handful of very modest associations among cytokine levels and change in levels across time with pregnancy outcomes. These results suggest that disturbed sleep and depression status may interact to increase risk for adverse pregnancy outcomes; and that one pathway may be through the promotion of an

exaggerated inflammatory profile (30). However, we acknowledge that the interpretation of these findings must be made with caution as the number of models calculated was quite large. Nonetheless, we propose that these relationships warrant further empirical evaluation given our current findings, as well as other lines of evidence which implicate persistent sleep disruption and depression as contributors to chronic low-grade inflammation (6, 39, 51-57). Low-grade chronic inflammation is a risk factor for various adverse health outcomes including cardiovascular disease, metabolic syndrome (51, 58-63) depression(64), sleep apnea (65-68), polycystic ovarian syndrome (PCOS) (69, 70), and obesity (69, 71, 72). The cytokine levels we observed were similar to these other studies that have reported on chronic low-grade inflammation. Given that these relationships are bidirectional and likely additive, it is plausible that a woman who experiences both sleep disruption and depression may substantially increase her risk for adverse outcomes as a function of an exaggerated inflammatory response.

Our findings agree with a series of investigations that link aspects of disturbed sleep in depressed individuals with higher circulating concentrations of inflammatory cytokines (73-78). Depressed women in this study with poor sleep efficiency and short sleep duration had significantly higher concentrations of IL-6, IL-8 and TNF- α at 30 weeks gestation compared to women with better sleep. Given the bi-directional nature of these associations, one could argue that poor sleep intensifies the exaggerated inflammatory state observed in depressed individuals, equally as depression intensifies the exaggerated inflammatory state observed in sleep disturbed individuals. In the current study we sought to evaluate the role of depression on disrupted sleep. We contend that it is conceivable that depressed women not only have more disrupted sleep, but that they are also more vulnerable to the physiological and psychological effects of disturbed sleep (79-81). Women who are chronically sleep deprived may report short latency to sleep and few minutes spent awake while they psychologically perceive their sleep as poor. This is a recognized correlate of inflammation (4, 54, 56, 82) and disease (83-85).

Our data partially support the findings reported by Christian and colleagues (39, 40) that depressed pregnant women have higher inflammatory cytokine concentrations. They further add to the extant literature by suggesting that the interaction of poor sleep and depression is a stronger risk factor than poor sleep or depression alone.. Currently no study has prospectively evaluated whether sleep, as measured by duration or quality, independently or dynamically affects immune function in depressed pregnant women. There are however, data to suggest that this may be the case. Christian and colleagues found that depressed pregnant women had an exaggerated inflammatory response to an in vivo immune challenge which could make them more susceptible to infection during pregnancy (40). Work done by Spiegel and colleagues indicates that sleep curtailment (short sleep) is associated with a dampened or poor immune response to a viral challenge indicative of increased susceptibility to infection (86). Studies designed to evaluate whether disturbed sleep in pregnant women augments the depression-cytokine relationship previously reported, as well as the depression-hormone relationship, is warranted given that infection and stress are leading causes of adverse pregnancy outcomes, such as preterm birth (87, 88).

Cytokines vary across pregnancy, yet it is unclear as to what constitutes “normative” increases across pregnancy (17, 89-91). An imbalance in cytokines in early pregnancy (too little or too much) is associated with miscarriage (92), whereas an elevated amount in later pregnancy is associated with preterm birth (24, 26) and preeclampsia (21, 93). Since cross-sectional assessments of cytokines do not necessarily provide an indication of the efficiency of the immune system during pregnancy, we assessed whether a change in cytokines was associated with increased risk of certain delivery/pregnancy outcomes. We noted only modest associations between changes in cytokines and outcomes which varied between

depressed and nondepressed women. An increase in IL-6, a potent stimulator of the immune response, was associated with smaller birth weights in depressed women (the effect was lost, however, in the adjusted model). An increase in IL-8, an important mediator of the immune reaction in the innate immune system response, showed an association with larger weighing infants in depressed women (this effect, too, was lost in the adjusted model). Other methods to test the efficacy of the immune system, such as stimulation assays, may provide useful information regarding the role of sleep in immune processes and subsequent risk.

While this study has several positive attributes, including a large community-dwelling cohort that was followed prospectively across pregnancy and the use of “gold standard” tools for clinical diagnosis of depression, there are some limitations. First, sleep data were based on retrospective recall only, although it was only recalled over the previous week. Data are considered more reliable when recalled within a shorter time period. While this is a common data acquisition method, data collected in a prospective manner, such as with sleep diaries, would assist and confirm the participant reports. Moreover, we did not have sleep history prior to pregnancy. Second, while the measurement of both sleep and circulating cytokines in pregnant women is an emerging and important area of study, time of collection is a concern in the present study. Since cytokines have an established diurnal rhythm (5, 47) it is likely that our results may have been muted by a broad time-collection window for the blood samples. Future studies need to restrict the collection window to ensure no diurnal influences. Moreover, circulating levels do not necessarily reflect the efficacy of the immune system or the maternal-fetal milieu (94, 95). Thus, other methods to determine immune function should be incorporated. Third, the study design was not *a priori* designed to answer the questions related to sleep, cytokines or adverse events. There is wide variability in sleep and cytokine measures. The available cytokine data were limited, and the number of adverse outcomes was small. Both of which could have diminished the magnitude of potential relationships. Among the women with MDD we only had cytokine data from about 25 women. There were only 17 women with a PTB and 28 with high birth weight babies. Further, it is probable that the immune alterations that occur at the onset of pregnancy may confound associations established in non-pregnant cohorts. Lastly, the issue of SSRI anti-depressant medications needs to be acknowledged. While it is clear that SSRIs affect sleep (96) and cytokine concentrations (97), the impact of specific SSRIs on these variables is less clear (96). In the current analysis we were unable to address specific medication effects given the range of SSRIs used. We previously reported that in this cohort the effect of SSRIs on sleep appears consistent with the existing literature (33). Future examinations must insure sufficient power in order to account for SSRIs effects on sleep and cytokines.

In summary, the goal of this paper was to explore associations between aspects of disturbed sleep and cytokine levels in depressed and nondepressed pregnant women, and whether we could detect a link to adverse delivery/infant outcomes. Our results support an association between disturbed sleep and inflammation in pregnant women which warrant future evaluations of these relationships. These findings may be clinically significant since adverse outcomes are augmented by various psychosocial factors. Many of which, including stress, race, education status and sleep, are modulators of inflammation (13, 39, 54, 98-100) and shown to be linked with adverse outcomes (19, 101-103). We contend that sleep is a relevant behavior to consider during pregnancy as it is a modifiable behavior that when optimized can have considerable benefits on health-related outcomes (104, 105).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Abbreviations

IL	Interleukin
TNF	Tumor necrosis factor
IFN	Interferon
CES-D	Center for Epidemiologic Studies-Depression
IUGR	Intrauterine growth restriction
SSRI	Selective serotonin reuptake inhibitor
SIGH-ADS	Structured Interview Guide for the Hamilton Depression Rating Scale with Atypical Depression Supplement
SOL	Sleep onset latency
WASO	Wake after sleep onset
SE	Sleep efficiency
PSQI	Pittsburgh Sleep Quality Index
PES	Peripartum Events Scale
MDD	Major Depressive Disorder
PTB	Preterm birth

Table 1

Demographic, clinical, and cytokine measures by depression status at 20 weeks gestation.

Measure	Depressed			Analysis		
	All (N=168)	Yes (N=32)	No (N=136)	Test statistic	df	p
Age	30.2 ± 5.7	30.4 ± 7.2	30.2 ± 5.3	t = 0.19	39	0.853
Race				P = 0.05		0.518
White	134 (80.2)	25 (78.1)	109 (80.7)			
Black	28 (16.8)	7 (21.9)	21 (15.6)			
Other	5 (3.0)	0 (0.0)	5 (3.7)			
White race	134 (80.2)	25 (78.1)	109 (80.7)	X ² = 0.11	1	0.738
Education level				P < .0001		0.004
<High school	10 (6.0)	6 (18.8)	4 (3.0)			
High school	17 (10.2)	3 (9.4)	14 (10.4)			
Some college	28 (16.8)	9 (28.1)	19 (14.1)			
College	68 (40.7)	9 (28.1)	59 (43.7)			
Graduate school	44 (26.3)	5 (15.6)	39 (28.9)			
Completed college	112 (67.1)	14 (43.8)	98 (72.6)	X ² = 9.74	1	0.002
Employed	101 (60.5)	17 (53.1)	84 (62.2)	X ² = 0.90	1	0.344
Marital status				P = 0.002		0.038
Single	36 (21.6)	11 (34.4)	25 (18.5)			
Married/cohabiting	125 (74.9)	19 (59.4)	106 (78.5)			
Divorced/separated	5 (3.0)	1 (3.1)	4 (3.0)			
Widowed	1 (0.6)	1 (3.1)	0 (0.0)			
Married/cohabiting	125 (74.9)	19 (59.4)	106 (78.5)	X ² = 5.04	1	0.025
Parity	1.9 ± 1.1	2.3 ± 1.3	1.8 ± 0.98	U = 5.50	1	0.019
Pre-pregnancy BMI	26.4 ± 7.1	28.9 ± 7.7	25.9 ± 6.9	U = 5.19	1	0.023
Smoked tobacco	17 (10.2)	6 (18.8)	11 (8.1)	P = 0.05		0.100
Drank alcohol	53 (31.7)	11 (34.4)	42 (31.1)	X ² = 0.13	1	0.721
Used illicit drugs	3 (1.8)	1 (3.1)	2 (1.5)	P = 0.38		0.474
Depressed at week 30	35 (20.8)	31 (96.9)	4 (2.9)	X ² = 138.6	1	<.0001
SSRI at week 20 or 30	34 (20.2)	13 (40.6)	21 (15.4)	X ² = 10.18	1	0.001

Measure	All (N=168)	Depressed		Analysis		
		Yes (N=32)	No (N=136)	Test statistic	df	p
20 Weeks gestation						
IFN- γ	16.7 $\pm$ 23.5	10.9 $\pm$ 5.6	18.0 $\pm$ 25.7	U = 0.75	1	0.386
IL-6	2.3 $\pm$ 1.7	2.9 $\pm$ 2.1	2.2 $\pm$ 1.6	U = 1.58	1	0.208
IL-8	6.0 $\pm$ 3.3	6.0 $\pm$ 3.7	6.0 $\pm$ 3.2	t = 0.01	154	0.992
TNF- α	1.2 $\pm$ 0.97	1.0 $\pm$ 0.87	1.3 $\pm$ 0.99	U = 1.47	1	0.225
30 Weeks gestation						
IFN- γ	12.7 $\pm$ 11.1	14.4 $\pm$ 15.3	12.3 $\pm$ 10.0	U = 0.001	1	0.973
IL-6	2.4 $\pm$ 1.5	2.3 $\pm$ 1.4	2.4 $\pm$ 1.5	U = 0.19	1	0.664
IL-8	5.7 $\pm$ 3.5	6.4 $\pm$ 4.1	5.6 $\pm$ 3.3	U = 1.07	1	0.301
TNF- α	1.4 $\pm$ 0.94	1.2 $\pm$ 0.96	1.5 $\pm$ 0.93	U = 2.39	1	0.122
Born prior to 37 weeks gestation	16 (9.5)	2 (6.3)	14 (10.3)	P = 0.23		0.739
Infant weight (g)	3473 $\pm$ 581	3352 $\pm$ 511	3500 $\pm$ 594	t = 1.27	160	0.207
High birth weight (>4 kg)	27 (16.7)	3 (10.0)	24 (18.2)	X ² = 1.18	1	0.278
PES Total	0.35 $\pm$ 0.76	0.21 $\pm$ 0.63	0.38 $\pm$ 0.78	U = 1.85	1	0.173

Data are reported as mean $\pm$ SD or n (%)

Table 2

Descriptive statistics for cytokine level by weeks gestation and sleep characteristic.

Sleep characteristic	20 Weeks gestation						30 Weeks gestation						36 Weeks gestation					
	Week 20 sleep			TNF- α (N=128)			Week 20 sleep			TNF- α (N=111)			Week 30 sleep			TNF- α (N=151)		
	n (%)	M $\pm$ SD	IL-6 (N=154)	M $\pm$ SD	IL-8 (N=155)	M $\pm$ SD	n (%)	M $\pm$ SD	IL-6 (N=148)	M $\pm$ SD	IL-8 (N=148)	M $\pm$ SD	n (%)	M $\pm$ SD	IL-6 (N=131)	M $\pm$ SD	IL-8 (N=131)	M $\pm$ SD
HRSD insomnia																		
Yes	56 (35)	17.05 $\pm$ 22.65	2.34 $\pm$ 1.77	5.67 $\pm$ 3.28	1.08 $\pm$ 0.95	59 (39)	13.74 $\pm$ 12.05	2.19 $\pm$ 1.30	5.74 $\pm$ 3.82	1.31 $\pm$ 0.86	65 (42)	12.74 $\pm$ 9.04	2.17 $\pm$ 1.25	5.29 $\pm$ 2.93	1.47 $\pm$ 1.09			
No	103 (65)	17.26 $\pm$ 24.83	2.27 $\pm$ 1.67	6.06 $\pm$ 3.14	1.34 $\pm$ 0.97	93 (61)	12.21 $\pm$ 10.67	2.56 $\pm$ 1.55	5.63 $\pm$ 3.28	1.47 $\pm$ 0.96	89 (58)	12.66 $\pm$ 12.49	2.63 $\pm$ 1.57	6.00 $\pm$ 3.80	1.39 $\pm$ 0.83			
SOL >15 mins																		
Yes	68 (43)	17.67 $\pm$ 27.20	2.89 $\pm$ 2.14	5.87 $\pm$ 3.37	1.27 $\pm$ 0.93	67 (44)	14.11 $\pm$ 13.68	2.65 $\pm$ 1.77	5.90 $\pm$ 3.64	1.54 $\pm$ 0.85	56 (36)	11.85 $\pm$ 10.49	2.66 $\pm$ 1.56	5.79 $\pm$ 3.54	1.48 $\pm$ 0.87			
No	91 (57)	16.85 $\pm$ 21.58	1.90 $\pm$ 1.19	5.95 $\pm$ 3.06	1.24 $\pm$ 1.00	85 (56)	11.82 $\pm$ 8.86	2.23 $\pm$ 1.14	5.49 $\pm$ 3.35	1.29 $\pm$ 0.97	98 (64)	13.18 $\pm$ 11.51	2.30 $\pm$ 1.38	5.66 $\pm$ 3.45	1.40 $\pm$ 0.98			
WASO >20 mins																		
Yes	69 (43)	14.54 $\pm$ 21.63	2.55 $\pm$ 1.79	5.70 $\pm$ 3.24	1.12 $\pm$ 0.96	67 (44)	12.48 $\pm$ 11.85	2.48 $\pm$ 1.47	5.50 $\pm$ 3.36	1.43 $\pm$ 1.01	79 (51)	10.84 $\pm$ 10.39	2.49 $\pm$ 1.34	5.41 $\pm$ 3.55	1.48 $\pm$ 1.08			
No	90 (57)	19.17 $\pm$ 25.57	2.11 $\pm$ 1.63	6.09 $\pm$ 3.15	1.33 $\pm$ 0.97	85 (56)	13.05 $\pm$ 10.77	2.36 $\pm$ 1.45	5.80 $\pm$ 3.57	1.39 $\pm$ 0.86	75 (49)	14.57 $\pm$ 11.60	2.36 $\pm$ 1.57	6.00 $\pm$ 3.40	1.37 $\pm$ 0.79			
Takes naps																		
Yes	80 (50)	15.32 $\pm$ 13.92	2.46 $\pm$ 1.87	6.00 $\pm$ 3.29	1.34 $\pm$ 1.01	79 (52)	14.11 $\pm$ 12.33	2.41 $\pm$ 1.49	5.52 $\pm$ 3.38	1.39 $\pm$ 0.80	86 (56)	12.75 $\pm$ 12.24	2.42 $\pm$ 1.37	5.81 $\pm$ 3.78	1.38 $\pm$ 0.79			
No	79 (50)	19.05 $\pm$ 30.96	2.13 $\pm$ 1.51	5.84 $\pm$ 3.09	1.15 $\pm$ 0.92	73 (48)	11.39 $\pm$ 9.74	2.40 $\pm$ 1.44	5.83 $\pm$ 3.59	1.42 $\pm$ 1.03	68 (44)	12.62 $\pm$ 9.65	2.43 $\pm$ 1.57	5.58 $\pm$ 3.07	1.47 $\pm$ 1.08			
Time in bed <7 or >9 hrs																		
Yes	71 (45)	15.12 $\pm$ 13.98	2.29 $\pm$ 1.69	6.04 $\pm$ 3.24	1.32 $\pm$ 1.01	70 (46)	13.53 $\pm$ 12.34	2.22 $\pm$ 1.04	5.69 $\pm$ 3.52	1.41 $\pm$ 0.90	66 (43)	12.20 $\pm$ 9.72	2.55 $\pm$ 1.59	5.58 $\pm$ 3.08	1.55 $\pm$ 0.93			
No	88 (55)	18.82 $\pm$ 29.61	2.30 $\pm$ 1.72	5.82 $\pm$ 3.16	1.20 $\pm$ 0.94	82 (54)	12.21 $\pm$ 10.23	2.56 $\pm$ 1.71	5.66 $\pm$ 3.46	1.40 $\pm$ 0.94	88 (57)	13.06 $\pm$ 12.13	2.33 $\pm$ 1.34	5.80 $\pm$ 3.74	1.35 $\pm$ 0.94			
Sleeps <7 hrs																		
Yes	32 (20)	14.26 $\pm$ 10.24	2.51 $\pm$ 2.13	5.34 $\pm$ 3.13	1.24 $\pm$ 0.95	33 (22)	12.77 $\pm$ 11.48	2.27 $\pm$ 1.50	5.92 $\pm$ 4.10	1.47 $\pm$ 0.89	46 (30)	10.42 $\pm$ 8.14	2.29 $\pm$ 1.44	5.48 $\pm$ 3.35	1.23 $\pm$ 0.96			
No	127 (80)	17.90 $\pm$ 26.25	2.24 $\pm$ 1.58	6.06 $\pm$ 3.20	1.25 $\pm$ 0.98	119 (78)	12.82 $\pm$ 11.19	2.45 $\pm$ 1.45	5.60 $\pm$ 3.30	1.39 $\pm$ 0.93	108 (70)	13.64 $\pm$ 12.07	2.49 $\pm$ 1.46	5.80 $\pm$ 3.54	1.49 $\pm$ 0.93			
Sleeps >9 hrs																		
Yes	26 (16)	15.45 $\pm$ 12.36	1.91 $\pm$ 1.23	5.68 $\pm$ 3.16	1.30 $\pm$ 1.21	24 (16)	15.32 $\pm$ 11.41	2.31 $\pm$ 1.33	5.62 $\pm$ 3.90	1.57 $\pm$ 1.11	21 (14)	15.15 $\pm$ 10.84	2.77 $\pm$ 1.70	5.67 $\pm$ 3.71	1.77 $\pm$ 1.00			
No	133 (84)	17.52 $\pm$ 25.67	2.36 $\pm$ 1.77	5.97 $\pm$ 3.20	1.24 $\pm$ 0.93	128 (84)	12.34 $\pm$ 11.16	2.43 $\pm$ 1.48	5.68 $\pm$ 3.41	1.38 $\pm$ 0.89	133 (86)	12.29 $\pm$ 11.17	2.37 $\pm$ 1.41	5.71 $\pm$ 3.45	1.35 $\pm$ 0.91			
Sleep efficiency <85%																		
Yes	41 (26)	10.57 $\pm$ 6.79	2.96 $\pm$ 2.14	6.02 $\pm$ 3.12	1.26 $\pm$ 0.93	40 (26)	13.11 $\pm$ 13.62	2.54 $\pm$ 1.48	6.05 $\pm$ 3.83	1.40 $\pm$ 0.83	37 (24)	10.50 $\pm$ 8.74	2.16 $\pm$ 1.07	5.34 $\pm$ 3.20	1.41 $\pm$ 1.13			
No	118 (74)	19.43 $\pm$ 27.16	2.09 $\pm$ 1.50	5.88 $\pm$ 3.22	1.25 $\pm$ 0.99	112 (74)	12.70 $\pm$ 10.31	2.36 $\pm$ 1.45	5.54 $\pm$ 3.35	1.41 $\pm$ 0.96	117 (76)	13.36 $\pm$ 11.72	2.51 $\pm$ 1.55	5.82 $\pm$ 3.56	1.43 $\pm$ 0.90			

Abbreviations HRSD Hamilton rating scale for depression; M mean; SD standard deviation; SIGH-ADS Structured interview guide for the Hamilton rating scale for depression with atypical depression supplement; SOL sleep onset latency; WASO wake after sleep onset.

Table 3

Cytokine level at 20 weeks gestation by sleep characteristic at 20 weeks gestation and depression status at 20 weeks gestation.

Cytokine (M ± SD)		IFN-γ (17.19 ± 24.00)				IL-6(2.29 ± 1.70)				IL-8(5.92 ± 3.19)				TNF-α(1.25 ±0.97)			
Depression status SIGH-ADS ₉ (M ± SD)		Depressed (22.00 ± 4.95)	n	M± SD	n	Not depressed (8.76 ± 5.44)	Depressed (22.17 ± 4.76)	n	M± SD	n	Not depressed (5.9 ± 5.45)	Depressed (22.07 ± 4.88)	n	M± SD	n	Not depressed (8.60 ± 5.57)	
Sleep characteristic		n (%)	n	M± SD	n	M± SD	n	M± SD	n	M± SD	n	M± SD	n	M± SD	n	M± SD	
HRSD insomnia																	
Yes		56 (35)	18	10.97 ± 4.75	37	20.01 ± 27.04	14	2.93 ± 2.01	33	2.08 ± 1.63	19	5.72 ± 3.35	37	5.64 ± 3.28	15	0.80 ± 0.57	
No		103 (65)	11	10.69 ± 7.10	88	18.09 ± 26.12	9	2.83 ± 2.38	80	2.20 ± 1.58	11	6.40 ± 4.31	88	6.02 ± 2.99	10	1.36 ± 1.14	
SOL >15 mins																	
Yes		68 (43)	16	12.01 ± 6.37	48	19.56 ± 31.05	12	3.03 ± 2.33	42	2.85 ± 2.11	17	5.90 ± 4.20	50	5.86 ± 3.09	14	1.10 ± 1.02	
No		91 (57)	13	9.46 ± 4.42	77	18.09 ± 23.06	11	2.74 ± 1.95	71	1.77 ± 0.98	13	6.05 ± 3.02	75	5.94 ± 3.08	11	0.93 ± 0.66	
WASO >20 mins																	
Yes		69 (43)	23	11.30 ± 5.42	43	16.27 ± 26.45	17	2.37 ± 1.70	38	2.64 ± 1.84	24	6.11 ± 3.94	43	5.46 ± 2.80	19	0.85 ± 0.80	
No		90(57)	6	9.18 ± 6.66	82	19.90 ± 26.30	6	4.39 ± 2.59	75	1.93 ± 1.40	6	5.39 ± 2.50	82	6.14 ± 3.20	6	1.56 ± 0.94	
Takes naps																	
Yes		80(50)	19	10.60 ± 5.84	58	16.87 ± 15.41	14	2.51 ± 1.98	53	2.44 ± 1.86	19	5.51 ± 3.82	61	6.15 ± 3.13	15	0.85 ± 0.83	
No		79 (50)	10	11.37 ± 5.51	67	20.20 ± 33.01	9	3.50 ± 2.28	60	1.93 ± 1.27	11	6.76 ± 3.44	64	5.68 ± 3.03	10	1.28 ± 0.90	
Time in bed <7 or >9 hrs																	
Yes		71 (45)	12	8.93 ± 5.44	56	16.45 ± 14.90	8	2.55 ± 1.82	51	2.25 ± 1.68	12	6.59 ± 3.85	57	5.92 ± 3.12	10	0.92 ± 0.67	
No		88 (55)	17	12.23 ± 5.52	69	20.44 ± 32.79	15	3.08 ± 2.29	62	2.11 ± 1.51	18	5.55 ± 3.60	68	5.90 ± 3.05	15	1.09 ± 1.00	
Sleeps <7 hrs																	
Yes		32 (20)	9	12.76 ± 5.68	21	14.90 ± 11.73	8	3.89 ± 2.60	19	1.93 ± 1.65	10	6.09 ± 3.41	21	4.98 ± 3.01	8	1.61 ± 1.16	
No		127(80)	20	10.01 ± 5.54	104	19.41 ± 28.33	15	2.37 ± 1.67	94	2.22 ± 1.58	20	5.91 ± 3.88	104	6.09 ± 3.07	17	0.75 ± 0.55	
Sleeps >9 hrs																	
Yes		26(16)	5	8.39 ± 5.10	20	17.22 ± 13.08	4	1.58 ± 0.67	17	1.99 ± 1.33	5	5.88 ± 2.65	20	5.63 ± 3.33	4	0.68 ± 0.38	
No		133 (84)	24	11.38 ± 5.71	105	18.93 ± 28.16	19	3.17 ± 2.22	96	2.20 ± 1.63	25	5.99 ± 3.89	105	5.96 ± 3.04	21	1.09 ± 0.93	
Sleep efficiency <85%																	
Yes		41 (26)	15	10.59 ± 4.58	24	10.56 ± 7.96	10	3.64 ± 2.36	21	2.64 ± 2.01	16	7.41 ± 3.18	24	5.09 ± 2.77	13	1.10 ± 0.89	
No		118 (74)	14	11.17 ± 6.76	101	20.58 ± 28.70	13	2.32 ± 1.78	92	2.06 ± 1.46	14	4.32 ± 3.60	101	6.10 ± 3.12	12	0.94 ± 0.88	

Abbreviations HRSD Hamilton rating scale for depression; M mean; SD standard deviation; SIGH-ADS Structured interview guide for the Hamilton rating scale for depression with atypical depression supplement; SOL sleep onset latency; WASO wake after sleep onset.

Table 4
Cytokine level at 30 weeks gestation by sleep characteristic at 20 weeks gestation and depression status at 20 weeks gestation.

Cytokine (M ± SD)	IFN- γ (12.81 ± 11.21)				IL-6 (2.41 ± 1.45)				IL-8 (5.67 ± 3.48)				TNF- α (1.41 ± 0.92)			
	Depressed (22.36 ± 4.83)	n	M ± SD	n	Not depressed (8.85 ± 5.39)	Depressed (22.32 ± 4.56)	n	M ± SD	Not depressed (9.05 ± 5.40)	Depressed (22.36 ± 4.83)	n	M ± SD	Not depressed (8.69 ± 5.36)	Depressed (21.45 ± 4.70)	n	M ± SD
Depression status SIGH-ADS ₂₀ (M ± SD)																
Sleep characteristic n (%)																
HRSD insomnia																
Yes	18	15.30 ± 15.32	39	13.02 ± 10.37	15	2.30 ± 1.21	37	2.14 ± 1.34	18	6.16 ± 3.60	37	5.53 ± 3.95	13	1.01 ± 0.41	32	1.43 ± 0.96
No	10	12.70 ± 15.81	79	12.15 ± 9.97	7	2.40 ± 1.87	69	2.58 ± 1.52	10	6.87 ± 5.08	83	5.49 ± 3.00	9	1.52 ± 1.41	57	1.46 ± 0.89
SOL >15 mins																
Yes	17	17.91 ± 18.25	46	12.71 ± 11.48	14	2.29 ± 1.62	41	2.78 ± 1.83	17	6.53 ± 4.24	49	5.68 ± 3.43	14	1.44 ± 1.12	37	1.57 ± 0.74
No	11	8.91 ± 6.41	72	12.26 ± 9.14	8	2.42 ± 1.03	65	2.20 ± 1.16	11	6.23 ± 4.09	71	5.38 ± 3.24	8	0.82 ± 0.40	52	1.37 ± 1.01
WASO >20 mins																
Yes	22	13.30 ± 12.83	41	12.05 ± 11.43	17	2.21 ± 1.18	39	2.60 ± 1.58	22	5.82 ± 3.52	41	5.32 ± 3.31	16	1.12 ± 0.89	30	1.59 ± 1.05
No	6	18.33 ± 23.25	77	12.64 ± 9.34	5	2.78 ± 2.12	67	2.32 ± 1.41	6	8.61 ± 5.65	79	5.59 ± 3.32	6	1.47 ± 1.17	59	1.38 ± 0.83
Takes naps																
Yes	18	12.78 ± 14.93	58	14.53 ± 11.53	14	2.25 ± 1.21	52	2.46 ± 1.56	18	5.47 ± 3.77	58	5.54 ± 3.29	14	1.35 ± 0.90	41	1.40 ± 0.77
No	10	17.24 ± 16.20	60	10.41 ± 8.01	8	2.49 ± 1.79	54	2.39 ± 1.40	10	8.11 ± 4.34	62	5.47 ± 3.35	8	0.98 ± 1.07	48	1.50 ± 1.02
Time in bed <7 or >9 hrs																
Yes	12	14.38 ± 17.12	54	13.34 ± 11.22	9	2.17 ± 0.77	48	2.23 ± 1.09	12	6.66 ± 3.86	55	5.47 ± 3.44	10	1.31 ± 0.91	39	1.44 ± 0.91
No	16	14.37 ± 14.27	64	11.67 ± 9.01	13	2.45 ± 1.74	58	2.58 ± 1.72	16	6.23 ± 4.40	65	5.52 ± 3.22	12	1.14 ± 1.03	50	1.46 ± 0.92
Sleeps <7 hrs																
Yes	10	13.65 ± 9.55	22	12.38 ± 12.44	8	2.94 ± 1.97	22	2.03 ± 1.26	10	8.58 ± 3.94	22	4.72 ± 3.64	6	1.91 ± 1.12	17	1.32 ± 0.77
No	18	14.78 ± 17.90	96	12.45 ± 9.52	14	1.99 ± 0.87	84	2.53 ± 1.51	18	5.21 ± 3.78	98	5.68 ± 3.22	16	0.96 ± 0.78	72	1.48 ± 0.94
Sleeps >9 hrs																
Yes	5	12.64 ± 7.63	18	16.07 ± 12.33	4	2.10 ± 0.63	15	2.37 ± 1.47	5	7.68 ± 5.48	18	5.05 ± 3.32	4	0.93 ± 0.67	12	1.78 ± 1.17
No	23	14.75 ± 16.55	100	11.78 ± 9.53	18	2.39 ± 1.54	91	2.43 ± 1.48	23	6.14 ± 3.85	102	5.58 ± 3.32	18	1.28 ± 1.02	77	1.40 ± 0.86
Sleep efficiency <85%																
Yes	14	15.44 ± 16.27	24	11.75 ± 11.98	11	3.01 ± 1.67	24	2.32 ± 1.36	14	7.93 ± 3.50	24	4.95 ± 3.64	11	1.45 ± 1.08	19	1.37 ± 0.68
No	14	13.30 ± 14.70	94	12.61 ± 9.59	11	1.66 ± 0.61	82	2.45 ± 1.51	14	4.90 ± 4.22	96	5.64 ± 3.22	11	0.98 ± 0.80	70	1.47 ± 0.97

Abbreviations HRSD Hamilton rating scale for depression; M mean; SD standard deviation; SIGH-ADS Structured interview guide for the Hamilton rating scale for depression with atypical depression supplement; SOL sleep onset latency; WASO wake after sleep onset.

Table 5

Parameter estimates and probability values for the interaction of depression status at 20 weeks gestation and sleep characteristic at 20 weeks gestation regressed on infant outcome.

Sleep characteristic	Preterm birth			Birth weight (g)			Birth weight >4 kg			PES total score		
	Unadjusted		Adjusted	Unadjusted		Adjusted	Unadjusted		Adjusted	Unadjusted		Adjusted
	OR	p	OR	p	β	p	OR	p	β	p	β	p
HRSD Insomnia	1.250	0.875	1.103	0.675	-102.7	0.934	0.273	0.512	0.343	0.413	-0.264	0.505
SOL >15 mins	2.458	0.178	1.477	0.301	-196.5	0.559	0.272	0.383	0.496	0.653	0.946	0.025
WASO >20 mins	1.050	0.982	0.823	0.874	-170.6	0.790	0.364	0.847	0.541	0.899	-0.023	0.828
Takes naps	1.920	0.465	1.170	0.649	-255.5	0.186	0.297	0.494	0.441	0.533	0.174	0.922
Time in bed <7 or >9 hrs	0.619	0.053	0.501	0.151	6.179	0.152	0.357	0.770	0.392	0.401	-0.076	0.585
Sleeps <7 hrs	1.667	0.922	1.197	0.789	-167.4	0.884	0.426	0.944	0.741	0.930	0.511	0.473
Sleeps >9 hrs	...	...	...	...	-23.64	0.614	...	...	...	...	-1.504	0.152
Sleep efficiency <85%	2.636	0.239	2.135	0.096	-344.7	0.129	0.311	0.705	0.472	0.687	0.498	0.123
												0.267
												0.102

Abbreviations HRSD Hamilton rating scale for depression; SOL sleep onset latency; WASO wake after sleep onset.

NOTES: Adjusted models covary for white race, college education, parity, pre-pregnancy body mass index, and selective serotonin re-uptake inhibitors use at 20 weeks gestation. All tests are two-tailed.
... Inestimable

Table 6

Parameter estimates and probability values for the interaction of depression status at 30 weeks gestation and sleep characteristic at 30 weeks gestation regressed on infant outcome.

Sleep characteristic	Preterm birth				Birth weight (g)				Birth weight >4 kg				PES total score			
	Unadjusted		Adjusted		Unadjusted		Adjusted		Unadjusted		Adjusted		Unadjusted		Adjusted	
	OR	p	OR	p	β	p	β	p	OR	p	OR	p	β	p	β	p
HRSD Insomnia	1.933	0.77	1.257	0.50	-328.4	0.086	-315.5	0.047	0.334	0.52	...	...	-0.541	0.45	-0.668	0.60
SOL >15 mins	1.194	0.90	0.711	0.88	18.021	0.37	81.61	0.12	0.778	0.82	1.420	0.23	-0.043	0.95	-0.266	0.96
WASO >20 mins	0.923	0.20	0.509	0.22	-46.04	0.43	-41.55	0.62	1.093	0.21	1.040	0.37	-0.543	0.12	-0.664	0.17
Takes naps	1.523	0.78	0.831	0.84	-70.93	0.63	-44.17	0.72	0.518	0.73	0.471	0.50	-0.487	0.24	-0.665	0.33
Time in bed <7 or >9 hrs	1.310	0.72	1.001	0.67	-276.3	0.091	-251.8	0.053	0.136	0.043	0.157	0.056	-0.518	0.26	-0.647	0.37
Sleeps <7 hrs	3.637	0.27	3.748	0.11	-318.2	0.20	-424.3	0.031	0.545	0.93	...	...	-0.912	0.25	-0.664	0.62
Sleeps >9 hrs	...	...	...	...	-85.98	0.91	103.7	0.49	...	...	...	...	-0.087	>.99	-0.045	0.79
Sleep efficiency <85%	1.647	0.95	1.259	0.65	-261.1	0.22	-230.9	0.21	0.368	0.57	...	...	-0.657	0.30	-0.648	0.56

Abbreviations HRSD Hamilton rating scale for depression; SOL sleep onset latency; WASO wake after sleep onset.

NOTES: Adjusted models covary for white race, college education, parity, pre-pregnancy body mass index, and selective serotonin re-uptake inhibitors use at 30 weeks gestation. All tests are two-tailed.
... Inestimable

Table 7

Parameter estimates and probability values for the interaction of depression status at 20 weeks gestation and cytokine level 20 weeks gestation, 30 weeks gestation, and change between 30 and 20 weeks gestation regressed on infant outcome.

Cytokine	Preterm birth				Birth weight (g)				Birth weight >4 kg				PES total score			
	Unadjusted		Adjusted		Unadjusted		Adjusted		Unadjusted		Adjusted		Unadjusted		Adjusted	
	OR	p	OR	p	OR	p	OR	p	OR	p	OR	p	OR	p	OR	p
Week 20	OR	p	OR	p	OR	p	OR	p	OR	p	OR	p	OR	p	OR	p
IFN- γ	1.106	0.48	1.110	0.51	-9.527	0.76	-5.01	0.90	0.859	0.49	0.899	0.66	-0.083	0.57	-0.096	0.50
IL-6	0.705	0.34	0.900	0.59	72.36	0.31	29.96	0.70	1.884	0.21	1.828	0.31	-3.819	0.52	-3.266	0.58
IL-8	1.044	0.66	1.170	0.34	8.286	0.98	-13.25	0.53	1.237	0.17	1.212	0.22	0.099	0.35	0.118	0.26
TNF-a	0.474	0.42	0.322	0.31	-147.5	0.29	-81.18	0.50	0.402	0.36	0.379	0.35	-0.037	0.84	-0.074	0.83
Week 30	OR	p	OR	p	OR	p	OR	p	OR	p	OR	p	OR	p	OR	p
IFN- γ	0.990	0.65	1.001	0.93	-3.201	0.68	-6.932	0.56	0.802	0.34	0.754	0.27	-0.004	0.84	-0.000	0.65
IL-6	1.517	0.54	1.689	0.35	-137.4	0.085	-109.7	0.11	0.068	0.27	0.005	0.18	-0.057	0.99	-0.093	0.98
IL-8	1.034	0.78	1.059	0.69	-5.528	0.63	-6.257	0.81	0.878	0.42	0.858	0.51	0.116	0.23	0.131	0.16
TNF-a	0.393	0.59	0.403	0.43	-49.96	0.50	-19.89	0.72	1.671	0.52	2.461	0.27	-0.887	0.47	-0.601	0.68
Change	OR	p	OR	p	OR	p	OR	p	OR	p	OR	p	OR	p	OR	p
IFN- γ	0.967	0.82	0.976	0.99	0.438	0.58	-5.026	0.20	0.949	0.26	0.918	0.16	-0.041	0.58	-0.031	0.66
IL-6	3.948	0.18	4.086	0.21	-242.2	0.043	-132.8	0.18	...	...	...	...	7.299	0.80	7.097	0.86
IL-8	1.017	0.38	0.958	0.22	-28.47	0.36	-1.997	0.94	0.739	0.047	0.717	0.083	-0.081	0.83	-0.094	0.76
TNF-a	0.847	0.84	2.164	0.62	-188.8	0.24	-190.8	0.27	0.888	0.61	0.943	0.75	-0.240	0.73	-0.366	0.82

Abbreviations PES Peri-partum events scale.

NOTES: Adjusted models covary for white race, college education, parity, pre-pregnancy body mass index, and selective serotonin re-uptake inhibitors use at 20 weeks gestation. All tests are two-tailed.
... Inestimable