

## Keeping Mom Awake: Does Placental Location Impact Fetal Disruption of Maternal Sleep?

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### Abstract

**Objective:** The purpose of this study was to determine whether an association exists between placental location and maternal sleep.

**Methods:** A secondary analysis of a prospective observational cohort study was performed with (n=68) singleton gestations to evaluate the impact of placental location on maternal sleep disturbance. Sleep parameters were objectively recorded and evaluated using the Watch-PAT 200, a plethysmographic-based finger probe that measures arterial tone and pulse oximetry. A proprietary algorithm of this technology was used to study sleep arousals, sleep latency, sleep time, daytime fatigue, fatigue upon waking, snoring, obstructive sleep apnea, rapid eye movement sleep, intended sleep time, and respiratory event index. Secondary outcomes included weight gain during pregnancy, hypertension disorder of pregnancy, gestational diabetes, gestational age at delivery, mode of delivery, and fetal birth weight. Chi square was used to evaluate dichotomous variables with Yates correction. Two sample t-test was used to evaluate continuous variables and determine mean  $\pm$  standard deviation or median plus interquartile ranges as appropriate.

**Results:** Objective sleep parameters and sleep-related symptoms were relatively consistent between anterior and posterior placentation, although our study was not powered adequately to determine statistical significance. There was a significantly increased risk of Intrauterine Growth Restriction (IUGR) in pregnancies with an anterior placenta ( $p=0.017$ ).

**Conclusion:** Placental location and maternal perception of fetal movement does not appear to impact maternal sleep. Further studies are necessitated to study relationship between placentation and fetal growth restriction.

**Keywords:** Maternal Sleep; Placenta; Pregnancy; Sleep Disorders

### Introduction

Pregnancy can exacerbate sleep disruption for those with pre-existing sleep disorders. Sleep can also become disordered for those without preexisting sleep disorders, [1] and becomes most prominent in the third trimester [2]. Additionally, pregnancy has been identified as an independent risk factor for obstructive sleep apnea [3,4], with a risk of 11% in the first trimester and 27% in the third trimester [4]. Sleep deprivation in pregnancy is associated with adverse pregnancy outcomes and complications, such as hypertension, diabetes, premature delivery, need for operative

deliveries, and postpartum depression [2,5-7].

There are several factors thought to be associated with sleep disorders in pregnancy including discomfort with positioning during pregnancy, frequent urination, and increased fetal movements [8]. Fetal movements increase through the day, peaking during the evening at typical maternal sleep time, thereby contributing to sleep disruption [9]. Many factors are associated with maternal perception of fetal movements including amniotic fluid volume, fetal presentation, fetal gender, placental location, and maternal positioning. Perceptions of fetal movements are increased in the recumbent or supine position [10]. While some studies have not documented any effects of placental location on maternal perceptions of fetal movements others have demonstrated that

mothers with anterior placenta are more likely to report decreased fetal movement [10-12]. Given this relationship, we sought to evaluate the implications of placental location and perception of fetal movement on maternal sleep.

## Methods

After IRB approval from Wake Forest University a secondary analysis of a prospective observational cohort study was performed to evaluate the impact of placental location on maternal sleep disturbance. Women were recruited from prenatal outpatient clinics at the Wake Forest School of Medicine Department of Obstetrics and Gynecology from April 1, 2014 to April 30, 2015. Inclusion criteria included women between 32 0/7 weeks and 35 6/7 weeks' gestation with anticipated delivery at the Maya Angelou Center for Women's Health and Wellness at Forsyth Medical Center in Winston-Salem, North Carolina. Women were excluded if they had active substance abuse, current treatment for Obstructive Sleep Apnea (OSA), were younger than 18 years of age, unable to speak or read English proficiently, had a fundal placenta or placenta Previa. The institutional review board at both Wake Forest School of Medicine and Forsyth Medical Center approved the protocol and all participants provided written informed consent.

Sleep parameters were objectively recorded and evaluated using the Watch-PAT200 device (Itamar Medical Ltd., Caesarea, Israel). This device is a cost-effective option and has been validated in pregnancy against overnight polysomnography [13]. The Watch-PAT200 is worn on the wrist to provide accelerometry and utilizes a plethysmographic-based finger-mounted probe to measure the peripheral arterial tone and pulse oximetry. A proprietary algorithm is applied to identify apnea, hypopnea, and periods of sleep. The entire study period can be viewed and the automatically detected events can be revised manually [14]. The sleep study was uploaded and analyzed by the proprietary zzzPAT software program (Version 4.3.61, Itamar Medical Ltd., Caesarea, Israel). The Respiratory Event Index (REI) was calculated by the software and a REI  $\geq$  5 events/hour was considered diagnostic for OSA. Moderate to severe OSA was diagnosed if REI  $\geq$  15 events/hour. Upon enrollment, the women were instructed on use of Watch-PAT200 device. Women completed the Berlin Questionnaire, a validated survey used outside of pregnancy to assess OSA risk that evaluates symptoms such as daytime fatigue and snoring.

The patients' medical records were reviewed to obtain and verify antepartum, intrapartum, and postpartum information regarding medical history and neonatal outcomes. To ensure accuracy, medical records were abstracted by only the principal investigator and co-investigators who were trained personnel with expertise in obstetric and perioperative research. All controversial categorizations were flagged and reviewed by the primary investigator.

The primary outcomes were the prevalence of sleep parameters such as number of sleep arousals, sleep latency (defined as elapsed time to transition from wakefulness to sleep), sleep time, daytime fatigue, fatigue upon waking, snoring, OSA, REM Sleep, intended sleep time (defined as the ratio of time spent sleeping to total time spent in bed), and REI. Secondary outcomes included weight gain during pregnancy, hypertensive disorder of pregnancy, gestational diabetes of pregnancy, gestational age at delivery, mode of delivery, and fetal birth weight.

We attempted to limit selection bias by recruiting from both general obstetric and maternal fetal medicine clinics.

Women who elected for continuous positive airway pressure therapy after the initial study were asked to refrain from its use the evening of subsequent studies to decrease confounding.

## Statistical Analysis

The study was powered to test the hypothesis that anterior placentation resulted in less sleep disruption, defined as increased arousals, prolonged sleep latency, decreased sleep time, increased daytime fatigue, and fatigue upon wakening, decreased intended sleep time, increased REI and presence of OSA. Based on prior studies, [1,2,4] we anticipated a sleep disruption prevalence of 25% during the third trimester [15].

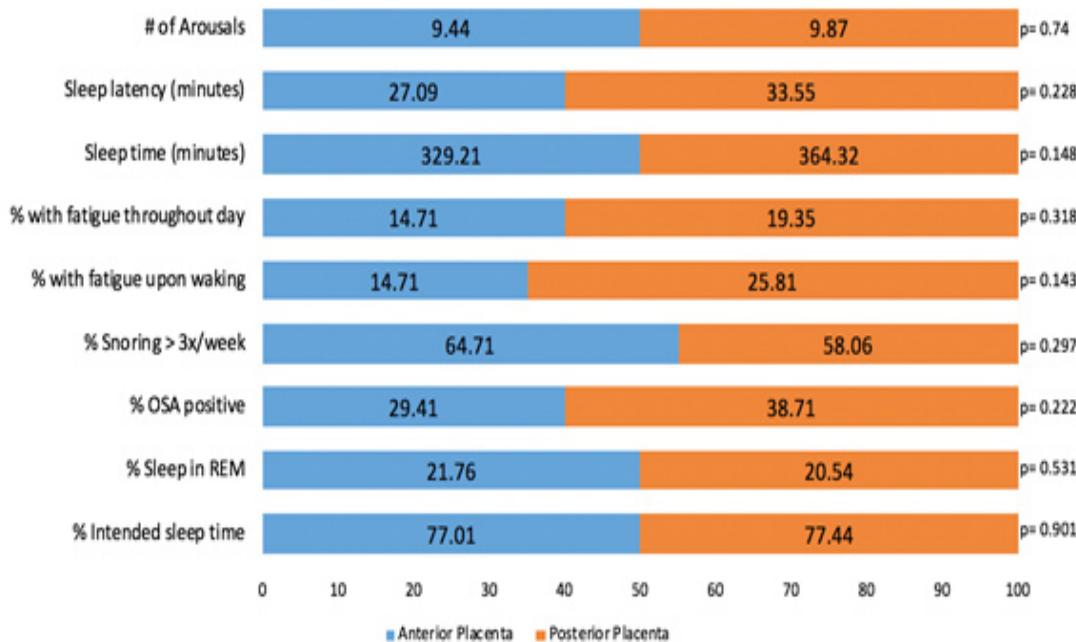
A sample size of 65 individuals was determined to provide 80% power to detect the hypothesized difference. Analyses were conducted using IBM SPSS Statistics version 22 (IBM Corp, Armonk, New York, United States). Baseline characteristics were summarized with frequencies and percentages for categorical data. Chi square was used to evaluate dichotomous variables with Yates correction when applicable. A two-sample t-test was used to evaluate continuous variables and determine mean  $\pm$  standard deviation or median plus interquartile ranges as appropriate. To account for attrition bias, only women with complete datasets were included in this analysis.

## Results

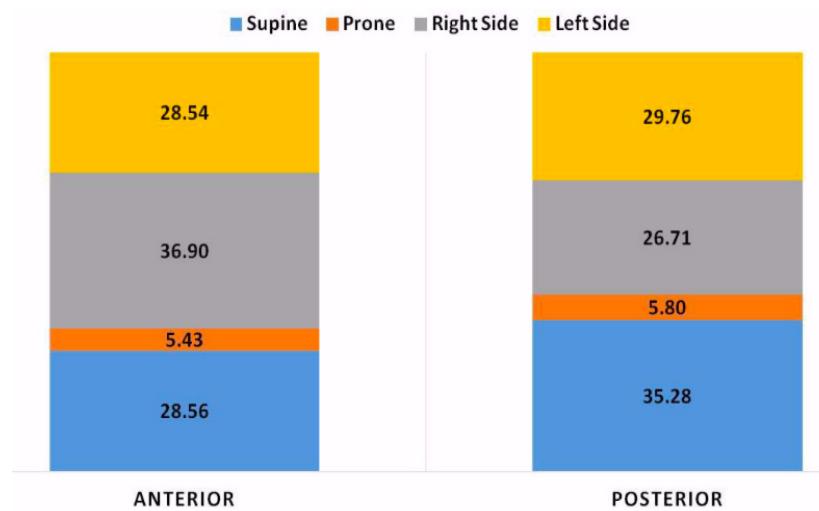
68 participants with singleton gestations, complete sleep evaluations, and ultrasound data available were enrolled within the study at Wake Forest School of Medicine Department of Obstetrics and Gynecology from April 1, 2014 to April 30, 2015. 34 participants had anterior placentas. 31 had posterior placentas, and 3 had fundal placentas and were, therefore, excluded from the study.

Objective sleep parameters and other sleep-related symptoms were relatively consistent between cohorts with few exceptions. Those with posterior placentas were noted to have increased fatigue upon awakening and increased diagnosis of OSA. Additionally, mean time per sleep position was also evaluated in relation to

placental location. There were no major differences between cohorts in mean sleep time in each position.



**Figure 1:** Sleep parameters of study cohorts.



**Figure 2:** Mean Time Per Sleep Position in Study Cohorts (p= 0.5012).

Demographically the groups were also similar (Figures 1-3). There was no difference in hypertensive disorders, gestational diabetes, postpartum hemorrhage, cesarean delivery, or infant weight. There was a significantly increased risk of Intrauterine Growth Restriction (IUGR) in pregnancies with an anterior placenta (p= 0.017).

	<b>Anterior</b>	<b>Posterior</b>	<b>P- value</b>
<b>Age years (SD)</b>	29.59 ( $\pm$ 6.8)	29.5 ( $\pm$ 4.9)	0.950
<b>Body Mass Index (BMI)</b>	33.6 ( $\pm$ 8.5)	33.3 ( $\pm$ 8.0)	0.884
<b>Maternal Weight Gain (lbs.)</b>	5.8 ( $\pm$ 12.4)	4.8 ( $\pm$ 13.3)	0.755
<b>Race</b>			0.992
<b>White</b>	19/34 (55.9%)	17/31 (54.8%)	
<b>Black</b>	12/34 (32.3%)	11/31 (35.5%)	
<b>Hispanic</b>	3/34 (8.8%)	3/31 (9.7%)	
<b>Gravity</b>	3.32 ( $\pm$ 3.5)	2.7 ( $\pm$ 2.1)	0.400
<b>Parity</b>	1.32 ( $\pm$ 1.3)	0.9 ( $\pm$ 1.3)	0.198
<b>Gestational Age (weeks)</b>	38.1 ( $\pm$ 1.5)	38.8 ( $\pm$ 1.7)	0.085
<b>Mode of Delivery</b>			0.381
<b>SVD</b>	23/34 (67.7%)	12/31 (54.8%)	
<b>C-Section</b>	11/34 (32.4%)	13/31 (41.9%)	
<b>VAVD</b>		1/31 (3.2%)	
<b>Infant weight (gms)</b>	3125 ( $\pm$ 625)	3332 ( $\pm$ 550)	0.181
<b>Fetal growth restriction</b>	5/34 (14.7%)	0/31 (0%)	0.017**
<b>Chronic Hypertension</b>	5/34 (14.7%)	7/31 (22.6%)	0.219
<b>Gestational Hypertension</b>	6/34 (17.6%)	7/31 (22.6%)	0.318
<b>Pre-eclampsia</b>	7/34 (20.6%)	3/31 (9.7%)	0.125
<b>Gestational Diabetes</b>	6/34 (17.6%)	3/31 (9.7%)	0.192
<b>Tobacco Use</b>	4/34 (11.8%)	5/31 (16.1%)	0.316

**Figure 3:** Demographics and pregnancy complications of study cohorts.

## Discussion

Pregnancy has been known to be associated with sleep disturbances including insomnia, increased sleep latency, and increased arousals [8]. The few studies that have evaluated sleep in pregnancy have shown that during the third trimester, especially during the last 8 weeks of gestation, women have increased sleep fragmentation with subsequent increased daytime sleepiness and fatigue. Sleep disorders in the third trimester may also be attributed to sleep disordered breathing, restless leg syndrome, and insomnia. Sleep disruption may be related to the physiologic changes during pregnancy, but may also occur due to musculoskeletal discomfort, uterine contractions, and increased fetal movement [16]. Although the third trimester is characterized by decreased sleep time, other studies have found an increase in total sleep time and daytime sleepiness in the first trimester [16,17]. These variations in sleep are likely related to the hormonal changes that impact the different gestational ages of pregnancy. High levels of circulating estrogen and progesterone during pregnancy have been associated with decreased sleep latency [18]. Increased levels of sex steroids may also lead to sleep apnea and disordered breathing that may further impact sleep duration and quality. Although many studies on sleep comment on the importance of sleep during pregnancy, the optimal

duration of sleep is not very well studied [17].

Disrupted sleep can not only increase the risk of maternal depression and anxiety, but also has been known to be associated with adverse gestational outcomes including gestational diabetes, pregnancy-related hypertension and pre-eclampsia, preterm delivery, low birth weight and low APGAR scores [19]. In addition, research indicates that poorer sleep may be detrimental to the labor and delivery process [20]. In addition, sleep duration and sleep disturbance may also play a role intrapartum. Lee and Gay (2004) found in their prospective observational study of 131 healthy pregnant patients that duration of labor, prematurity and cesarean birth rates were increased in those women sleeping less than 6 hours a night [21]. It has been suggested that poor sleep efficiency has been associated with higher levels of pro-inflammatory cytokines, such as IL-6. These increased inflammatory cytokines may stimulate prostaglandin production that may cause cervical ripening and promote uterine contractions leading to pre-term birth [22]. Inflammation from these cytokines may also disrupt the neuromodulation of the Hypothalamic-Pituitary-Adrenal (HPA) axis and may be involved in the pathogenesis of mood disorders such as depression and anxiety [23].

Increased fetal movement, especially during times of sleep,

have been noted to contribute to sleep disruption and increased insomnia [8]. Fetal movement can be affected by amniotic fluid volume, placental location, fetal presentation, and fetal gender. Obesity and maternal smoking are other inherent maternal factors that can influence perception of fetal movement. Sasson et al (2015) found in their historic cohort study of all women that visited the maternal emergency room that anterior placenta and nulliparity were associated with reduced fetal movement. It is hypothesized that maternal perception of fetal movement relies on the stimulation of the abdominal wall structures by the direct contact of the uterus, and this stimulation may be reduced with an anterior placenta that may act as a barrier. Despite this association, there is currently no consensus on maternal sleep and how it is influenced by placental location [24]. Placental location has also been studied to understand its association with intrauterine growth restriction (IUGR), defined as a sonographic fetal weight estimate below the 10<sup>th</sup> percentile. Since the blood flow through the uterus is not uniformly distributed, placental location may play a consequential role in fetal growth and pregnancy success. Kalanithi et al (2007) found in their case-controlled study that pregnancies complicated by IUGR are more likely to have a lateral placenta in the second trimester [25].

In this secondary analysis of a prospective observational cohort study, 68 participants with singleton gestation were studied to compare placental location and subsequent maternal perception of fetal movement and its effect on sleep. Although this study found that there was no associated difference in placental location and maternal sleep, it further found that placental location may have an impact on fetal intrauterine growth restriction. Much remains to be understood about the adverse effect of sleep deprivation in the maternal and fetal outcomes of pregnancy.

## Conclusion

Placental location and subsequent maternal perception of fetal movement does not appear to impact maternal sleep parameters or perception of fatigue in the third trimester. Fetal growth restriction was increased in mothers with anterior placentas, however, the study was not powered to evaluate this relationship and further research is needed to confirm or refute this.

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