Maternal Sleep Disordered Breathing and Neonatal Outcome

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ABSTRACT: **Background:** It has been suggested that sleep disordered breathing (SDB) during pregnancy may adversely influence maternal as well as fetal well being.

Objectives: To examine the effect of maternal SDB on neonatal neurological examination and perinatal complications.

Methods: Pregnant women of singleton uncomplicated pregnancies were prospectively recruited from a community and hospital low risk obstetric surveillance. All participants completed a sleep questionnaire in the second trimester and underwent ambulatory sleep evaluation (WatchPAT™, Itamar Medical, Caesarea, Israel). They were categorized as SDB (apnea hypopnea index › 5) and non-SDB. Maternal and newborn records were reviewed and a neonatal neurologic examination was conducted during the first 48 hours.

Results: The study group included 44 women and full-term infants; 11 of the women (25%) had SDB. Mean maternal age of the SDB and non-SDB groups was 32.3 ± 2.8 and 32.5 ± 4.7 years, respectively (P = 0.86). Mean body mass index before the pregnancy in the SDB and non-SDB groups was 25.8 ± 4.7 and 22.0 ± 2.5 kg/m2, respectively (P = 0.028). No differences were found between infants born to mothers with SDB and non-SDB in birth weight (3353.8 ± 284.8 vs. 3379.1 ± 492.4 g), gestational age (39.5 ± 0.9 vs. 39.2 ± 1.5 weeks), 5 minute Apgar scores (9.8 ± 0.6 vs. 9.9 ± 0.3), and neurologic examination scores (95.2 ± 3.9 vs. 94.6 ± 4.1). P value for all was not significant.

Conclusions: Our preliminary results suggest that maternal mild SDB during pregnancy has no adverse effect on neonatal neurologic examination or on perinatal complications.

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KEY WORDS: sleep disordered breathing (SDB), pregnancy, neurological examination, perinatal complications

Sleep disordered breathing (SDB) is common during pregnancy, and self-reported snoring has been observed in up to 46% of pregnant women [1,2]. The term SDB refers to abnormal respiration during sleep that ranges from primary (habitual) snoring to obstructive sleep apnea syndrome. SDB is characterized by episodic complete or partial obstruction of the airway during sleep, increased intra-thoracic pressure swings, disruption of normal ventilation, intermittent hypoxemia, and sleep fragmentation.

It has been suggested that similar to the general population [3], SDB during pregnancy may adversely influence the maternal as well as fetal well being. Animal models of intermittent antenatal hypoxia showed transient delay in fetal neuronal migration associated with alterations of multiple neonatal proteins [4], enhanced fetal hypothalamic pituitary adrenal activity [5], altered neonatal behavior [6], and anxiety-like behavior in adult male offspring [5]. Clinical reports have shown associations between SDB during pregnancy and fetal growth restriction, prematurity, cesarean delivery, low Apgar scores, and neonatal intensive care admission [7-10]. However, these clinical observations have thus far been inconclusive [11,12]. Furthermore, to our knowledge there are no reports on the effect of maternal SDB on neonatal neurological status.

We hypothesize that the physiologic alterations associated with maternal SDB could influence the developing fetal brain and impact neonatal outcome. The aim of the present study was to determine the short-term neonatal outcome of infants born to women with SDB.

PATIENTS AND METHODS

Women in the third trimester of a singleton uncomplicated pregnancy who attended a low risk obstetric surveillance were recruited and included in the study. Women with any pregnancy complication or chronic cardiovascular, neurologic, respiratory or inflammatory medical condition (except one case of mild asthma) were excluded from the study. The study was approved by the institutional review board. Informed consent was obtained from all participants.

During the second trimester (gestational week 25–27), all participants completed a medical history questionnaire (demographics, pregnancy, chronic illnesses) and a sleep questionnaire regarding the presence of habitual snoring before and during pregnancy, snoring loudness, presence of apneas, and daytime sleepiness using the Epworth sleepi-

ness scale [13]. Habitual snoring was defined as snoring at least three times a week [14]. Pregnancy-onset snoring was considered present when habitual snoring began during pregnancy. All participants underwent an ambulatory overnight sleep study between gestational weeks 33 and 36 using the WatchPAT 200™ device (Itamar Medical, Israel), which is a validated ambulatory sleep technology [15,16]. Apnea hypopnea index (AHI), respiratory disturbance index (RDI), oxygen desaturation index (ODI), mean SpO_2 and SpO_2 nadirs were retrieved as previously described [15,16]. Women with AHI > 5 per hour of sleep were considered to have SDB [17]. Medical records were reviewed by one of the researchers blinded to the sleep study results. Pertinent demographic information (gender, gestational age, birth weight) and clinical data (mode of delivery, Apgar scores at 1 and 5 minutes, and any perinatal complications) were collected.

SOCIOECONOMIC STATUS

The modified, two-factor index Hollingshead scale was used for determining the family's socioeconomic status. The maternal and paternal scores were averaged [18].

NEUROLOGIC ASSESSMENT OF THE NEWBORN

A trained pediatric neurologist conducted a neonatal neurologic evaluation consisting of 66 items on the second day of life before discharge from the hospital. The items related to motor (tone, spontaneous movement, posture, tendon reflexes), occulomotor (extra-occular eye movements), neonatal reflexes, and behavioral (state change, visual orientation, consolability, response decrement, crying quantity and quality) [19]. Examiners were unaware of the clinical data and to which group the infants had been assigned (maternal SDB yes/no). Scoring of the neonatal neurologic examination was performed according to the optimality concept of Prechtl [20], whereby each test item received an "optimal" or "suboptimal" binary score. Four subscores and a total score was then calculated (maximum score 100), as previously published [19,21].

STATISTICAL ANALYSIS

The statistical analyses were performed with SPSS (version 19.0, SPSS Inc., Chicago, IL, USA). Comparisons were conducted between infants born to women with SDB (study group) and without SDB (non-SDB) using independent *t*-tests for continuous variables and the chi-square analyses for categorical variables. All reported *P* values are two-tailed with statistical significance set at $P < 0.05$.

RESULTS

We studied 44 healthy women and their infants. All women completed a sleep questionnaire and underwent ambulatory sleep evaluation. Mean maternal age was 32.5 ± 4.2 years (range 23–42 years) and mean body mass index (BMI) before pregnancy 23.1 ± 3.5 kg/m^2 (17.2–34.3). Seven women (16%) had a medical condition requiring medication (hypothyroidism in three, and asthma, anxiety, migraine, and bipolar disorder in one each). Eighteen (41%) reported habitual snoring. Of those, 3 (7%) were "chronic snorers," i.e., snored before and during pregnancy, and 15 (34%) were pregnancy-onset snorers.

Eleven women (25%) met our criteria for SDB; 33 did not (non-SDB) and they served as controls. There were no pregnancy complications such as hypertension, gestational diabetes or preeclampsia in the entire cohort. Except for one premature delivery at 36 weeks gestation in the non-SDB group, all infants were born at term. Comparisons of maternal characteristics, daytime sleepiness (the Epworth sleepiness scale) and sleep study measures between women with and without SDB are presented in Tables 1 and 2.

NEONATAL EVALUATION

Twenty-seven (61%) of the newborns were males. No adverse neonatal events were reported. Two infants from the non-SDB group were small for gestational age, i.e., birth weight < 10th percentile. Two infants (one in the non-SDB and one in the SDB group) had 1 minute Apgar score below 5. Five minute Apgar scores were above 8 in all cases. Neurologic assessment was administered during the first 48 hours of life. No significant differences were found between the two groups before and after adjustment for all confounders [Table 3].

Table 1. Comparisons of maternal characteristics between women with SDB (n=11) and without (non-SDB) (n=33) during pregnancy

	SDB (n=11)	Non-SDB (n=33)	*P* value
Age (years)	32.3 ± 2.8	32.5 ± 4.7	0.86
BMI pre-pregnancy (kg/m^2)	25.8 ± 4.7	22.0 ± 2.5	0.028
BMI third trimester (kg/m^2)	30.5 ± 6.7	27.0 ± 2.7	0.38
Weight gain (%)	22.7 ± 10.5	20.8 ± 7.3	0.69
Neck circumference (cm)	33.9 ± 2.5	30.9 ± 1.2	0.02
Delivery Normal C/S Instrumental	 9 (72%) 1 (21%) 1	 24 (82%) 7 (9%) 2 (9%)	0.65
Gravida	1.9 ± 1.2	2.4 ± 1.2	0.26
Para	1.4 ± 0.8	2.0 ± 1.0	0.06
Smoking pre-pregnancy (n, %)	3 (27%)	5 (15%)	0.37
Smoking during pregnancy (n, %)	1 (9%)	1 (3%)	0.40
Positive medical history (n, %)	2 (18%)	5 (15%)	0.81
Medication usage (n, %)	3 (27%)	6 (19%)	0.55
Socioeconomic status	50.6 ± 5.3	52.8 ± 10.6	0.67

DISCUSSION

To the best of our knowledge this is the first study to investigate the effect of maternal SDB during pregnancy on neonatal neurologic status. Our preliminary findings suggest that maternal SDB has no impact on neonatal neurologic examination or on perinatal complications.

In the current study, the frequency of maternal snoring was 41%, as previously reported [1,12]. This frequency is higher compared to non-pregnant women in this age group. In order to test our hypothesis on the effects of maternal SDB on the developing brain, we utilized a validated ambulatory sleep technology that had been used previously in pregnant women [22-24] and defined an AHI of 5 as a threshold for SDB. Since there is no distinctive threshold for SDB in pregnancy we used the standard adult criteria for SDB [17] and found that 25% of women met the criteria for maternal SDB. The maternal SDB group exhibited a higher pre-pregnancy BMI and increased neck circumference.

Repetitive episodes of maternal airway obstruction during sleep may lead to intermittent gestational hypoxemia and increased intra-thoracic pressure swings, which could potentially result in disturbed uteroplacental blood flow and subsequent altered fetal brain developmental processes.

Notwithstanding such considerations, the findings from the current study show that neonatal neurological examination was not affected by maternal SDB. However, in the present study, most of the SDB cases were mild with no significant desaturations and, therefore, the findings should be viewed accordingly.

Our findings are consistent with a previous observation that showed no effect of maternal SDB during pregnancy on neonatal and infant spontaneous general movements, according to Pechtl's assessment [25]. Since both assessments are primarily based on neuromotor functions, one could speculate that neuromotor assessment may not be sufficiently sensitive to detect the impact of SDB on the neonatal status. Future studies should use behaviorally oriented evaluations to further test this hypothesis.

On the other hand, one may postulate that despite transient nocturnal gestational hypoxemia, the high fetal hemoglobin concentration and its oxygen-carrying capacity and the enhanced fetal tissue oxygen uptake could serve as protective factors that prevent fetal brain alterations. Further investigation of this point is warranted since our study cohort consisted mainly of mild cases of SDB.

Moreover, we did not find an association between maternal SDB and mode of delivery, birth weight, gestational age, Apgar scores, or neonatal complications. The perinatal outcome data of this study are in agreement with prior studies [11,12] and disagree with studies reporting such associations [7-10]. An explanation for this discrepancy may be that other maternal confounders and pregnancy complications – such as hypertension, diabetes, smoking or obesity – contribute to the occurrence of both maternal SDB and perinatal outcome. In this study, conducted on a healthy "low risk" cohort of pregnant women, we tried to isolate the effect of maternal SDB on neonatal outcome and found no impact of maternal SDB on perinatal complications.

The cohort of this prospective study was relatively small and consisted of a small number of mothers with SDB. Therefore, our results should be viewed as preliminary and await future confirmation.

In conclusion, this is the first study examining the effect of gestational maternal SDB on the neonatal neurologic examination. Our preliminary results suggest that maternal mild SDB during pregnancy has no adverse effect on neonatal outcome. Further studies using comprehensive neurobehavioral tools, larger sample size, and long-term developmental follow-up are warranted.

Table 2. Comparisons of sleep measures between women with SDB (n=11) and without non-SDB (n=33) during pregnancy

	SDB (n=11) No. (%) or mean ± SD	Non-SDB (n=33) No. (%) or mean ± SD	*P* value
Epworth sleepiness scale score	7.4 ± 3.7	8.1 ± 3.9	0.60
Abnormal ESS score (n, %)	3 (27%)	8 (25%)	0.88
Total sleep time (min)	348.5 ± 61.5	348.5 ± 78.4	0.97
Respiratory disturbance index	14.1 ± 5.5	6.4 ± 3.2	0.001
Apnea hypopnea index	11.6 ± 5.2	1.5 ± 1.3	‹ 0.0001
Oxygen desaturation index	2.9 ± 1.9	0.3 ± 0.4	0.001
Mean SpO_2	94.8 ± 0.6	96.1 ± 0.8	‹ 0.0001
SpO_2 nadir	89.8 ± 2.2	92.9 ± 2.6	0.001

ESS = Epworth sleepiness scale

Table 3. Comparison of neonatal characteristics and neurological outcome of study group (SDB) and control group (non-SDB)

	SDB (n=11) No. (%) or mean ± SD	Non-SDB (n=33) No. (%) or mean ± SD	*P* value
Newborn characteristics			
Gender (male)	5 (45.5%)	22 (66.7%)	0.19
Gestational age (weeks)	39.5 ± 0.9	39.2 ± 1.5	0.6
Birth weight (g)	3353.8 ± 284.8	3379.1 ± 492.4	0.9
Birth percentile	62 ± 23.3	63.4 ± 27.7	0.9
Apgar 1	8.8 ± 1	8.6 ± 1.6	0.5
Apgar 5	9.8 ± 0.6	9.9 ± 0.3	0.5
Cord PH (vein)	7.3 ± 0.8 (n=7)	7.3 ± 0.9 (n=20)	0.5
Neonatal neurologic examination			
Motor	92.4 ± 6.1	91.9 ± 7.2	0.8
Reflex	95.8 ± 5.3	96.5 ± 6.4	0.7
Occulomotor	100	98.8 ± 4.9	0.4
Behavioral	94.1 ± 11.7	92.3 ± 10.6	0.6
Total	95.2 ± 3.9	94.6 ± 4.1	0.7

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