Risk Factors for Sleep-Disordered Breathing in Pregnancy

Grace W. Pien, M.D., M.S.C.E.[1], **Allan I. Pack, M.B.Ch.B, Ph.D.**[2,3], **Nicholas Jackson, M.P.H.**[2], **Greg Maislin, M.S., M.A.**[2], **George A. Macones, M.D., M.S.C.E.**[5], **Richard J. Schwab, M.D.**[2,3,4]

[1]Division of Pulmonary and Critical Care Medicine, Johns Hopkins University School of Medicine;

[2]Center for Sleep and Circadian Neurobiology, University of Pennsylvania School of Medicine;

[3]Sleep Medicine Division, Department of Medicine, University of Pennsylvania School of Medicine;

[4]Pulmonary and Critical Care Division, Department of Medicine, University of Pennsylvania School of Medicine;

[5]Department of Obstetrics and Gynecology, Washington University School of Medicine

Abstract

Rationale—Symptoms of sleep-disordered breathing (SDB) are common among pregnant women, and several studies link SDB symptoms with gestational hypertension and preeclampsia. However, few prospective studies objectively measuring SDB during pregnancy have been performed.

Objectives—We performed a prospective cohort study examining risk factors for third trimester SDB in pregnant women.

Measurements and Methods—105 pregnant women from the Hospital of the University of Pennsylvania obstetrics practices completed first and third trimester overnight polysomnography studies. We examined whether the number of sleep-disordered breathing events per hour of sleep increased during pregnancy. We performed unadjusted and multivariable logistic regression analyses to estimate the effects of usual and pregnancy-specific characteristics on development of third trimester OSA. In secondary analyses, we examined the relationship between objectively measured SDB, hypertensive disorders of pregnancy, and other adverse maternal-fetal outcomes.

Main Results—Mean AHI increased from 2.07 (SD 3.01) events/hour at baseline (first trimester) to 3.74 (SD 5.97) in the third trimester (p=0.009). 10.5% of women had OSA in the first trimester. By the third trimester, 26.7% of women had OSA. In multivariable analyses, first trimester BMI and maternal age were significantly associated with third trimester OSA.

Conclusions—Third trimester OSA is common. Risk factors for third trimester OSA among women without baseline SDB include higher baseline BMI and maternal age.

Keywords

Sleep Apnea Syndromes; Pregnant Women; Hypertension; Pregnancy-Induced; Pre-Eclampsia

INTRODUCTION

The prevalence of sleep-disordered breathing (SDB) is low among women of reproductive age compared to postmenopausal women and men[1]. However, during pregnancy, physiologic and hormonal changes occur that can lead to a greater propensity for apneic episodes during sleep (reviewed in [2]).

In initial case reports of obstructive sleep apnea (OSA) in pregnancy, women were uniformly obese and often developed complications such as preeclampsia[3,4]. Subsequently, studies have demonstrated that snoring and other SDB symptoms are common among pregnant women and suggest that pregnancy may accelerate development of SDB[5–7]. Nevertheless, data on whether objectively measured sleep-disordered breathing increases during pregnancy and on risk factors for incident OSA in pregnant women are limited.

A number of studies have examined the relationship between SDB and gestational hypertension or preeclampsia, since OSA clearly increases hypertension risk in the general population[8]. These studies largely suggest that SDB is a risk factor for preeclampsia [6,9–14], though in most cases, their ability to infer causality has been limited by their cross-sectional or retrospective nature, or reliance on self-reported symptoms of SDB. Few studies to date have assessed the impact of objectively measured gestational SDB on maternal-fetal health.

In this study, we performed a prospective cohort study to determine whether SDB events increased during pregnancy; and examined associations between weight, age and third trimester OSA. We hypothesized that greater baseline weight and gestational weight gain would increase the risk for OSA. In secondary analyses, we also investigated the relationship between SDB and gestational hypertension and preeclampsia; and between SDB and other adverse maternal-fetal outcomes, including preterm delivery, gestational diabetes (GDM) and low infant birthweight.

METHODS

Study Population

All women scheduled for initial obstetrics evaluation at the Hospital of the University of Pennsylvania were invited to participate. Interested women were screened for eligibility. This study was approved by the Penn Institutional Review Board. All participants provided written informed consent.

Women whose pregnancy was ≤ 14 weeks of gestation were eligible. Gestational age and estimated date of delivery (EDD) were calculated using last menstrual period (LMP) data[15]. When available (n=96), fetal ultrasonography results were used to confirm EDD[15]. Exclusion criteria were communication/cognitive/behavioral impairments

interfering with informed participation; no telephone; self-reported illicit drug use or alcoholism[16]; serious pre-existing medical conditions; sedative/hypnotic use   3x/week; or current OSA treatment.

To enrich the sample for subjects likely to develop OSA, recruitment was stratified by BMI to increase the proportion of obese women: normal ($<25.0 kg/m^2$), overweight (25.0-<30.0), class I obesity (30.0-<35.0), class II-III obesity (35.0)[17]. Our recruitment goal was 25 subjects/category; subjects who withdrew were replaced until the goal was reached.

In total, 722 interested women were screened for inclusion into the cohort, of whom 352 women met eligibility criteria. By far, the most common reason for exclusion was pregnancy past 14 weeks of gestation (n=325). Others were excluded due to not being pregnant/ pregnancy loss/planned termination (n=17); chronic medical conditions (n=4); prenatal care at other institutions (n=9); or lack of English fluency (n=1). Many otherwise eligible women were not enrolled due to stratified recruitment by BMI (n=172) or because they were unable to attend first trimester polysomnography prior to 14 weeks of gestation (n=54).

Protocol

We obtained medical, obstetric and sleep histories at baseline (first trimester) evaluation. Overnight laboratory polysomnography (PSG) was scheduled between 8–14 weeks gestation, and for repeat between 33–34 weeks gestation. PSGs (Sandman, Melville Diagnostics) included electroencephalogram (central, occipital leads), electrooculogram, submental and tibialis electromyograms, single bipolar electrocardiogram, finger pulse oximetry (Nellcor), chest and abdominal excursion (Protech piezo belts), airflow by nasal pressure[18] and oral thermistor. Accepted methods were used to score sleep[19].

We defined apnea as complete cessation of airflow lasting   10 seconds, and hypopnea as a $> 50\%$ decrease in airflow without a requirement for associated oxygen desaturation or arousal; or a lesser airflow reduction in association with oxygen desaturation of $> 3\%$ or an arousal [20]. The Apnea-Hypopnea Index (AHI, apneas+hypopneas/hour of sleep) was computed using standard criteria[19,20]. Subjects with desaturations to $<70\%$ for   3% of time asleep and/or AHI>30 were notified (n=1) and withdrawn if they elected treatment (n=1).

Before each PSG, the Epworth Sleepiness Scale[21] and a seated manual blood pressure (BP) measurement were obtained. After delivery, charts were abstracted for maternal-fetal outcomes.

Outcome Variables

We examined 2 primary SDB outcomes: first, AHI was dichotomized at   5 events/hour to define OSA in the primary analyses. We also examined change in AHI as a continuous variable.

Gestational hypertension was defined clinically as systolic BP   140 mmHg and/or diastolic BP   90 in a previously normotensive woman >20 weeks gestation. Preeclampsia was defined as gestational hypertension with 24-hour urinary protein level >0.3 g. We also examined

third trimester mean arterial BP (calculated from BP obtained prior to third trimester PSG), pre-term delivery (gestational age<37.0 weeks), GDM (defined per [22]) and low infant birthweight (<2,500 grams) as secondary outcomes.

Determinant Variables

Determinant variables included first and third trimester BMI and neck circumference, gestational weight gain, age, race, baseline AHI, Epworth Sleepiness Scale scores and parity. Weight and gestational weight gain were examined using several paradigms: as categorized and continuous BMI, neck circumference and absolute weight change from baseline until delivery.

Data Analyses

Data were analyzed with SAS software (v. 9.1, SAS Institute, Cary, NC) for descriptive statistics and multivariable logistic and linear regression. Because AHI distribution was substantially non-normal, a log transformation (log(AHI+1)) was employed for comparisons of AHI and when AHI was used in linear regression as an outcome. For analyses in which AHI was dichotomized and when we examined change in AHI (which was normally distributed) as an outcome, we used untransformed AHI.

The power calculation was based on our primary outcome of absolute change in AHI. We calculated 25 subjects completing both PSGs in each BMI group (n=100) were needed to detect a standardized effect size of 0.28 with 80% power using a two sided paired t-test and 5% significance level. That is, if the mean AHI change is approximately ¼ the size of the standard deviation of changes, our study is likely to find that the mean difference is significantly different from 0.

We restricted our initial analyses to subjects who completed both overnight PSG studies (n=105). To maximize statistical power, analyses were repeated after imputing third trimester AHI for 21 women, using a regression model of baseline AHI, age, BMI, race, chronic hypertension, parity, gestational hypertension and preeclampsia[23].

Paired t-tests were performed to compare first and third trimester log-transformed AHI, and characteristics of women with and without third trimester OSA. After estimating unadjusted associations of each variable with third trimester OSA, multivariable logistic regression models were used to estimate the effects of covariates on the outcome. Covariates were considered for inclusion in the final model if the p-value was 0.20 in the unadjusted analyses. We also checked for collinearity between potentially related variables using Spearman's coefficient (e.g. baseline BMI and gestational weight gain, baseline BMI and age, BMI and neck circumference) during the model selection process. Final covariates were selected based on whether each variable remained significant at p<0.05 in the multivariable model. We also performed linear regression analyses to examine associations with change in AHI. Because AHI cut-point for OSA affects disease prevalence, we repeated our primary analyses using AHI 10 events/hr to verify our observations.

We performed logistic regression analyses using continuous and dichotomized SDB variables as independent variables to examine relationships between SDB and the

hypertensive disorders of pregnancy, preterm delivery, GDM and low birthweight individually as outcomes. We also examined the relationship between SDB and third trimester mean arterial BP using linear regression. P-values <0.05 were considered statistically significant.

RESULTS

We enrolled 126 women in the cohort. 105 women completed first and third trimester PSGs at a median of 12.1 (SD 1.9) and 33.6 (SD 2.5) weeks gestation (Table 1); 21 women completed first trimester PSGs only. 75% of participants were African-American. White women and women of other racial backgrounds were combined into a "White and Other" category. Reasons for failure to complete the third trimester PSG included delivery before the PSG (n=6), preterm labor/medically-advised bedrest (n=6) and withdrawal/loss to follow-up (n=9). Women delivered at a median of 39.1 (SD 2.0) weeks. Comparisons between women completing one and both PSGs revealed no significant differences in demographic, gynecological or baseline sleep variables (including age, race, parity, baseline AHI). Some outcomes were unavailable for 12 subjects delivered at other hospitals.

SDB Increases during Pregnancy

Mean first trimester AHI was 2.07 (Med 1.1) events/hour for subjects completing both PSGs. Third trimester AHI increased significantly to 3.74 (Med 1.5) events/hour (p=0.009). 10.5% of women in our study had first trimester OSA (AHI 5). By the third trimester, 26.7% of our participants had OSA, with 23 mild (AHI 5–14), 4 moderate (AHI 15–29) and 1 severe (AHI 30) case[24].

Women with third trimester OSA were mostly obese (BMI 30) at baseline (Table 2): 20 of 50 (40.0%) obese women at baseline assessment had third trimester OSA, v. 8 of 55 (14.5%) normal or overweight women. Third trimester OSA was characterized largely by arousal-associated hypopneas. Women with third trimester OSA were not sleepier than normal women.

As our protocol over-recruited for overweight and obese women, we utilized data from *all* women who were screened in the first trimester and provided information about BMI (n=335) to estimate OSA prevalence among the general obstetric population from which our subjects were recruited. From these data, we estimate *overall* OSA prevalence in the clinical population to be 8.4% (95% CI 5.6–11.9%) in the first trimester and 19.7% (95% CI 15.6–24.4%) in the third trimester.

Third Trimester OSA

We examined whether specific clinical characteristics were significantly associated with third trimester OSA (Table 3). Because women with AHI 5 at baseline were likely to have third trimester OSA, we restricted these analyses to women with first trimester AHI<5 (n=94). In unadjusted analyses, first or third trimester BMI, first or third trimester neck circumference, age and parity were all significant determinants of OSA (p<0.05). Additional variables examined for inclusion in multivariable models included baseline AHI and gestational weight gain (p 0.20).

We created separate multivariable models using first and third trimester weight covariates to better understand the relationship between weight and third trimester SDB. As BMI and neck circumference were highly collinear (ρ=0.80), we retained BMI since BMI is routinely measured clinically and models including BMI had greater predictive value (i.e., higher c-statistics).

Using **first trimester** characteristics, we found that first trimester BMI and maternal age were all significant determinants of third trimester OSA (Table 4). In the fully adjusted model, with every BMI increase of 5 kg/m^2, subjects were 1.93 (95% CI 1.19–3.12) times more likely to have third trimester OSA. With each 10-year increase in age, subjects were 3.24 (95% CI 1.40–7.52) times more likely to have third trimester OSA. We included baseline AHI in the model to adjust for its influence on third trimester AHI, though it was not significantly associated with OSA.

In our dataset, baseline BMI and gestational weight gain were inversely correlated but not collinear (ρ=−0.53). Including gestational weight gain in the model with baseline BMI, age and first trimester AHI suggested that heavier women who gained more weight were at greatest risk for OSA, but the interaction between BMI and gestational weight gain was not significant (p=0.274). Age and baseline BMI were not collinear.

In a multivariable model incorporating **third trimester** BMI (Table 4), third trimester BMI and age were highly significantly determinants of third trimester OSA, similar to the first trimester model.

When we repeated our analyses using imputed third trimester AHI values for those without third trimester PSGs, we observed essentially identical results (online supplement). Furthermore, in multivariable analyses using AHI 10/hour, baseline or third trimester BMI continued to predict third trimester OSA (OR 1.85–3.01, p=0.025–0.049).

Change in AHI

We examined characteristics associated with change in AHI in all subjects completing both PSGs (n=105, Table 5). In unadjusted analyses, first and third trimester BMI and third trimester neck circumference were all significant determinants of change in AHI. Larger gestational weight gains were associated with smaller AHI changes in unadjusted analyses. In the final multivariable model, first trimester BMI and first trimester AHI were all independently associated with change in AHI. Maternal age was of borderline significance (p=0.059). Each increase in baseline BMI of 5 kg/m^2 was associated with an increase in AHI of 1.43 (0.70–2.16). Higher baseline AHIs were paradoxically associated with decreases in AHI in the third trimester (p=0.022). Similar results were observed when all subjects were included using imputed third trimester AHI (online supplement).

SDB and Hypertensive Disorders of Pregnancy

Twenty women developed a hypertensive disorder of pregnancy (gestational hypertension, n=9; preeclampsia, n=10; both, n=1), including 1 with chronic hypertension and preeclampsia (online supplement). In unadjusted analyses restricted to subjects without chronic hypertension (n=100, Table 6), there were no significant associations between first

or third trimester AHI, OSA or change in AHI and gestational hypertension or preeclampsia. Likewise, associations between first or third trimester SDB variables and third trimester mean arterial BP were not significant.

SDB and Other Adverse Maternal-Fetal Outcomes

We examined the relationship between SDB variables and additional outcomes (Table 7) including pre-term delivery (n=10), GDM (n=5) and low infant birthweight (n=9). There were no significant associations between any SDB variables and these outcomes.

DISCUSSION

There are several major findings from our data. First, SDB events increase during pregnancy. Second, milder OSA is a common third trimester finding, but severe OSA is uncommon. Third, age and BMI were consistent and independent determinants of third trimester OSA. Finally, in secondary analyses, OSA, assessed early or late in pregnancy, was *not* associated with development of gestational hypertension or preeclampsia in this sample, or with preterm delivery, GDM or low birthweight.

Aside from a small case-control study (n=22)[25], our study is the first to objectively assess SDB prospectively in a large group of pregnant women. We found that AHI increased significantly during pregnancy. The overall magnitude of this increase was small, and mean AHI remained within normal. However, 10.5% of participants had OSA even in the first trimester. By the third trimester, 26.7% of women had mild OSA and 4.8% had moderate-severe OSA. As our study over-recruited obese women, these participants do not represent a general obstetrics population. However, extrapolating to the BMI distribution of all women screened for the study, we estimate nearly 1 out of 5 of women in our obstetrics practices may have third trimester OSA, with 3% developing severe OSA.

We identified several risk factors for third trimester OSA. Models using first and third trimester characteristics were ultimately very similar. Increasing first or third trimester BMI and age were strong and independent determinants of OSA. We obtained similar results when examining change in AHI, utilizing imputed data for subjects with missing third trimester AHIs and using a higher AHI cutoff for OSA. Thus, we conclude that risk factors for OSA in pregnant women are similar to those in the general population[8,26].

We were surprised to find gestational weight gain was not independently associated with third trimester OSA and that in unadjusted analyses, greater weight gain appeared protective against developing OSA. The inverse correlation between baseline BMI and gestational weight gain potentially provides an explanation, i.e. normal weight women tended to gain *more* weight than overweight and obese women (similar to large observational studies[27]). In multivariable analyses, gestational weight gain did not significantly modify OSA risk among women of different baseline BMIs. However, this may have been due to inadequate statistical power.

Although OSA is usually characterized by excessive somnolence, the Epworth Sleepiness Scale score was not significantly associated with third trimester OSA or change in AHI in

our study. This may be due to the general effects of hormonal and physical changes of pregnancy on sleep and sleepiness (e.g., high levels of progesterone; physical discomfort contributing to sleep fragmentation) [2]. In previous work, we found the prevalence of self-reported excessive daytime sleepiness (ESS score>10) to be 31.0–45.5% over the course of pregnancy in a cohort of healthy women [5]. Thus, during pregnancy, the presence of daytime somnolence may not reliably signal the presence of a clinically meaningful sleep disorder.

This is the first study to examine the relationship between objectively-measured SDB and pregnancy-induced hypertension, an area of considerable interest, in a prospective cohort study. We did not observe associations between various metrics for SDB and gestational hypertension or preeclampsia. In contrast, the prevalence of objective SDB in a recent case-control study was much higher among women with gestational hypertension compared to healthy pregnant controls[13] , though the association between SDB and gestational hypertension was not significant after adjusting for BMI. Such findings raise questions about why disparities exist between our results and other retrospective or cross-sectional studies[9,28,29]. There may be several reasons.

First, we recognize that our study likely lacked adequate statistical power to detect an association with gestational hypertension and preeclampsia, especially given the relatively few participants with moderate or severe third trimester OSA (n=5). Next, most of our subjects did not manifest OSA until the third trimester. Recently, a study utilizing a national health care database demonstrated that risks for preeclampsia were higher among women with known antepartum OSA compared to age-matched controls[14]. Thus, pre-existing OSA may represent a hazard for adverse outcomes during pregnancy, compared to incident gestational OSA. Finally, although the upper airway is smaller among preeclamptic women compared to normal pregnant women[12], objective assessments of SDB have generally been performed *after* identifying gestational hypertension or preeclampsia rather than beforehand [6,9,28,29]. Thus, whether SDB follows or precedes development of preeclampsia has not been established.

Recent data have suggested that pregnant women with SDB symptoms are at increased risk for other adverse maternal-fetal outcomes, especially GDM[30,31]. Among pregnant women with previously diagnosed OSA, GDM risk was increased even after adjusting for obesity[14]. We did not observe an increased risk for GDM among women with SDB in our study. Since few of our subjects developed GDM, however, we lacked statistical power to make this determination. Additional studies to determine whether incident OSA in pregnancy increases GDM risk are needed to better understand this relationship.

Some other strengths and limitations of our study warrant mention. Our subjects were mostly urban, African-American women, who are traditionally underrepresented in research studies but have high rates of SDB[8], gestational hypertension and preeclampsia[32]. While race was not significantly associated with OSA in our study, our results may not be generalizable to other populations.

As third trimester PSG data were not available for 21 women, we imputed missing AHIs using accepted statistical methods[23]. Baseline characteristics and results using imputed data and complete cases were similar, suggesting minimal selection bias among those completing both PSGs.

Our study provides new insights into SDB among pregnant women, demonstrating that mild third trimester OSA is common; and establishing that greater baseline BMI and maternal age increase the risk for third trimester OSA. In contrast to recent findings demonstrating increased risks of adverse maternal-fetal outcomes among women with known antepartum OSA[14], we did not observe associations between OSA and subsequent development of gestational hypertension or preeclampsia, or between OSA and preterm delivery, GDM or low birthweight in this longitudinal study. Larger, adequately powered studies that examine the impact of objectively measured sleep-disordered breathing of different severities, including incident v. pre-existing OSA, on pregnancy are needed. Of immediate clinical relevance, our findings can help obstetricians to identify women at risk for OSA during pregnancy.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGEMENTS

REFERENCE LIST

1. Bixler EO, Vgontzas AN, Lin HM, et al. Prevalence of sleep-disordered breathing in women: effects of gender. Am. J. Respir. Crit. Care Med 2001;163(3 Pt 1):608–13 [PubMed: 11254512]

2. Pien GW, Schwab RJ. Sleep disorders during pregnancy. Sleep 2004;27(7):1405–17 [PubMed: 15586794]

3. Charbonneau M, Falcone T, Cosio MG, et al. Obstructive sleep apnea during pregnancy. Therapy and implications for fetal health. Am. Rev. Respir. Dis 1991;144(2):461–3 [PubMed: 1859076]

4. Kowall J, Clark G, Nino-Murcia G, et al. Precipitation of obstructive sleep apnea during pregnancy. Obstet. Gynecol 1989;74(3 Pt 2):453–5 [PubMed: 2668822]

5. Pien GW, Fife D, Pack AI, et al. Changes in symptoms of sleep-disordered breathing during pregnancy. Sleep 2005;28(10):1299–305 [PubMed: 16295215]

6. Franklin KA, Holmgren PA, Jonsson F, et al. Snoring, pregnancy-induced hypertension, and growth retardation of the fetus. Chest 2000;117(1):137–41 [PubMed: 10631211]

7. Loube DI, Poceta JS, Morales MC, et al. Self-reported snoring in pregnancy. Association with fetal outcome. Chest 1996;109(4):885–9 [PubMed: 8635365]

8. Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: a population health perspective. Am. J. Respir. Crit. Care Med 2002;165(9):1217–39 [PubMed: 11991871]

9. Bourjeily G, Raker CA, Chalhoub M, et al. Pregnancy and fetal outcomes of symptoms of sleep-disordered breathing. Eur. Respir. J 2010;36(4):849–55 [PubMed: 20525714]

10. Connolly G, Razak AR, Hayanga A, et al. Inspiratory flow limitation during sleep in pre-eclampsia: comparison with normal pregnant and nonpregnant women. Eur. Respir. J 2001;18(4): 672–6 [PubMed: 11716173]

11. Edwards N, Blyton DM, Kirjavainen T, et al. Nasal continuous positive airway pressure reduces sleep-induced blood pressure increments in preeclampsia. Am. J. Respir. Crit. Care Med 2000;162(1):252–7 [PubMed: 10903250]

12. Izci B, Riha RL, Martin SE, et al. The upper airway in pregnancy and pre-eclampsia. American Journal of Respiratory & Critical Care Medicine. 2003;167(2):137–40 [PubMed: 12411285]

13. Reid J, Skomro R, Cotton D, et al. Pregnant women with gestational hypertension may have a high frequency of sleep disordered breathing. Sleep 2011;34(8):1033–8 [PubMed: 21804665]

14. Chen Y-H, Kang J-H, Lin C-C, et al. Obstructive sleep apnea and the risk of adverse pregnancy outcomes. Am. J. Obstet. Gynecol 2012;206(2):136e1–5 [PubMed: 22000892]

15. Mercer BM, Goldenberg RL, Meis PJ, et al. The Preterm Prediction Study: prediction of preterm premature rupture of membranes through clinical findings and ancillary testing. The National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. American Journal of Obstetrics & Gynecology. 2000;183(3):738–45 [PubMed: 10992202]

16. Ewing JA, Ewing JA. Screening for alcoholism using CAGE. Cut down, Annoyed, Guilty, Eye opener.[Erratum appears in JAMA 1999 Feb 17;281(7):611]. JAMA 1998;280(22):1904–5 [PubMed: 9851461]

17. Flegal KM, Carroll MD, Kuczmarski RJ, et al. Overweight and obesity in the United States: prevalence and trends, 1960–1994. International Journal of Obesity & Related Metabolic Disorders: Journal of the International Association for the Study of Obesity. 1998;22(1):39–47

18. Montserrat JM, Farre R, Ballester E, et al. Evaluation of nasal prongs for estimating nasal flow. American Journal of Respiratory & Critical Care Medicine. 1997;155(1):211–5 [PubMed: 9001314]

19. Rechstaffen A, Kales A. A Manual of Standardized Terminology: Techniques of Scoring System for Sleep States of Human Subjects.: Brain Information Services/Brain Research Institute, UCLA, 1968.

20. Anonymous. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The Report of an American Academy of Sleep Medicine Task Force. Sleep. 1999;22(5):667–89 [PubMed: 10450601]

21. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep. 1991;14(6):540–5 [PubMed: 1798888]

22. Metzger BE, Coustan DR. Summary and recommendations of the Fourth International Workshop-Conference on Gestational Diabetes Mellitus. The Organizing Committee. Diabetes Care 1998;21 Suppl 2:B161–7 [PubMed: 9704245]

23. Rubin DB, Schenker N. Multiple imputation in health-care databases: an overview and some applications. Stat. Med 1991;10(4):585–98 [PubMed: 2057657]

24. AASM. The International Classification of Sleep Disorders: Diagnostic and Coding Manual. 2nd edition ed Westchester, IL: American Academy of Sleep Medicine, 2005.

25. Maasilta P, Bachour A, Teramo K, et al. Sleep-related disordered breathing during pregnancy in obese women. Chest 2001;120(5):1448–54 [PubMed: 11713118]

26. Stradling JR, Crosby JH, Stradling JR, et al. Predictors and prevalence of obstructive sleep apnoea and snoring in 1001 middle aged men. Thorax 1991;46(2):85–90 [PubMed: 2014507]

27. Chu SY, Callaghan WM, Bish CL, et al. Gestational weight gain by body mass index among US women delivering live births, 2004–2005: fueling future obesity. Am. J. Obstet. Gynecol 2009;200(3):271e1–7 [PubMed: 19136091]

28. Champagne K, Schwartzman K, Opatrny L, et al. Obstructive sleep apnoea and its association with gestational hypertension. Eur. Respir. J 2009;33(3):559–65 [PubMed: 19213789]

29. Louis JM, Auckley D, Sokol RJ, et al. Maternal and neonatal morbidities associated with obstructive sleep apnea complicating pregnancy. Am. J. Obstet. Gynecol 2010;202(3):261e1–5 [PubMed: 20005507]

30. Facco FL, Grobman WA, Kramer J, et al. Self-reported short sleep duration and frequent snoring in pregnancy: impact on glucose metabolism. Am. J. Obstet. Gynecol 2010;203(epub) [PubMed: 20451889]

31. Qiu C, Enquobahri D, Frederick IO, et al. Glucose intolerance and gestational diabetes risk in relation to sleep duration and snoring during pregnancy: a pilot study. BMC Women's Health 2010;10 [PubMed: 20350331]

32. Shen JJ, Tymkow C, MacMullen N, et al. Disparities in maternal outcomes among four ethnic populations. Ethn. Dis 2005;15(3):492–7 [PubMed: 16108310]

What is the key question?

Do objectively measured sleep-disordered breathing (SDB) events increase during pregnancy and what are risk factors for gestational obstructive sleep apnea (OSA)?

What is the bottom line?

SDB events increase over the course of pregnancy and third trimester OSA is common. Age and body mass index are significant and consistent predictors of gestational OSA.

Why read on?

We report on risk factors for third trimester OSA in a cohort of pregnant women who underwent objective measurements of sleep-disordered breathing in the first and third trimesters. In secondary analyses, we examine the relationships between SDB and maternal fetal outcomes. The findings have implications for identifying women at risk for OSA during pregnancy.

Table 1.

Characteristics of Subjects Completing First and Third Trimester Polysomnography (n=105).

Characteristic	Subjects Completing Both PSGs
Age, years (SD)	26.7 (7.2)
Race, n (%)	
African-American	79 (75.2)
Caucasian	22 (21.0)
Other	4 (3.8)
Baseline BMI, kg/m^2 (SD)	33.4 (6.4)
Normal, n (%)	30 (28.6)
Overweight, n (%)	25 (23.8)
Class I obesity, n (%)	25 (23.8)
Class II-III obesity, n (%)	25 (23.8)
Gestational weight gain, kg (SD)	8.9 (5.5)
1st trimester neck circumference, cm (SD)	35.7 (3.0)
1st trimester AHI, events/hour (Median)	2.07 (1.1)
Nulliparous, n (%)	32 (30.5)
Singleton gestation, n (%)	102 (97)
Chronic hypertension, n (%)	5 (4.76)
History of hypertensive disorder of pregnancy, n (%)	9 (8.6)

Table 2.

Characteristics of Women with and without Third Trimester OSA.

	Third Trimester OSA (n=28)	No 3rd Trimester OSA (n=77)	P-value
Baseline BMI, kg/m^2 (SD)	34.1 (7.9)	28.5 (6.3)	**0.002**
Gestational weight gain, kg (SD)	7.0 (5.2)	9.6 (5.5)	**0.034**
Third trimester BMI, kg/m^2 (SD)	37.0 (7.4)	32.1 (5.5)	**0.003**
Third trimester Epworth score (SD)	10.6 (4.1)	9.2 (4.0)	0.129
First trimester AHI, events/hr (SD, Median)	4.08 (4.55, 2.6)	1.34 (1.74, 0.7)	
Third trimester AHI, events/hr (SD, Median)	10.97 (7.69, 8.3)	1.11 (1.24, 0.6)	
Apnea Index	1.79 (3.62)	0.12 (0.25)	
Hypopneas with arousal	7.30 (5.26)	0.84 (1.08)	
Hypopneas with 3% desaturation	1.89 (2.33)	0.15 (0.37)	

Table 3.

Unadjusted Associations between BMI, Age, Other Variables and Development of Third Trimester OSA (n=94).

	Odds Ratio for 3rd Trimester OSA (95% CI)	P-value
Baseline BMI, 5 kg/m^2	1.79 (1.17 – 2.74)	**0.007**
Third trimester BMI, 5 kg/m^2	1.97 (1.21 – 3.22)	**0.007**
Baseline BMI		0.070 [*]
Normal	ref	--
Overweight	2.60 (0.43 – 15.65)	*0.297*
Class I obesity	3.82 (0.66 – 22.00)	*0.133*
Class II-III obesity	8.67 (1.59 – 47.15)	***0.013***
Third trimester BMI		**0.043** [*]
Normal	ref	--
Overweight	0.08 (0.00 – 1.75)	*0.107*
Class I obesity	0.37 (0.03 – 4.90)	*0.451*
Class II-III obesity	1.16 (0.09 – 14.29)	*0.909*
Gestational weight gain, kg	0.94 (0.58 – 1.03)	0.195
First trimester neck circumference, cm	1.20 (1.00 – 1.43)	0.049
Third trimester neck circumference, cm	1.22 (1.01 – 1.47)	**0.040**
Age, 10 years	2.92 (1.38 – 6.18)	**0.005**
Baseline AHI, events/hour	1.30 (0.91 – 1.86)	0.153
First trimester Epworth score	1.03 (0.92 – 1.16)	0.554
Third trimester Epworth score	1.07 (0.94 – 1.22)	0.283
Nulliparity (ref multiparity)	0.67 (0.24 – 1.86)	0.443
Parity (total number of prior pregnancies)	1.31 (1.04 – 1.67)	**0.025**
White and other ethnicity (ref African-Am)	0.48 (0.13 – 1.83)	0.283

[*] Omnibus P-value for BMI group differences in the logistic regression model. Pairwise comparisons for subgroups are reported in italics for individual BMI groups, compared to normal BMI.

Table 4.

Multivariable Models for Development of Third Trimester OSA.

Variable		Odds Ratios Using Baseline BMI (95% CI)	P-value		Odds Ratios Using Third Trimester BMI (95% CI)	P-value
Age, 10 yrs		3.24 (1.40 – 7.52)	**0.006**		4.04 (1.62 – 10.05)	**0.003**
Baseline BMI, 5 kg/m^2		1.93 (1.19 – 3.12)	**0.008**			
Third trimester BMI, 5 kg/m^2					2.36 (1.32 – 4.22)	**0.004**
Baseline AHI		1.03 (0.67 – 1.57)	0.904		1.10 (0.72 – 1.71)	0.653

Table 5.

Unadjusted and Adjusted Relationships between BMI, Age, Other Variables and Change in AHI (n=105).

Variable		Unadjusted Change in AHI, events/hr (95% CI)	P-value		Adjusted Change in AHI, events/hr (95% CI)	P-value
Baseline BMI, 5 kg/m^2		1.11 (0.43 – 1.80)	**0.002**		1.43 (0.70 – 2.16)	**0.0002**
Third trimester BMI, 5 kg/m^2		1.13 (0.34 – 1.92)	**0.016**			
Baseline BMI			0.070 [*]			
Normal		ref	--			
Overweight		1.76 (−1.00 – 4.52)	*0.211*			
Obese I		2.11 (−0.65 – 4.87)	*0.134*			
Obese II/III		3.77 (1.01 – 6.54)	***0.007***			
Gestational weight gain (kg)		−0.23 (−0.42 - −0.05)	**0.012**			
First trimester neck circumference, cm		0.33 (−0.00 – 0.67)	0.052			
Third trimester neck circumference, cm		0.44 (0.08 – 0.80)	**0.016**			
Age, 10 years		1.03 (−0.37 – 2.44)	0.149		1.32 (−0.05 – 2.68)	0.059
Baseline AHI		−0.09 (−0.43 – 0.25)	0.604		−0.42 (−0.77 - −0.06)	**0.022**
Third trimester ESS		0.19 (−0.07 – 0.45)	0.150			
Change in ESS		0.02 (−0.07 – 0.37)	0.186			
Nulliparity		−0.01 (−2.06 – 2.03)	0.990			
Total parity		0.39 (−0.12 – 0.90)	0.134			
White and other ethnicity (ref African-Am)		−1.91 (−4.25 – 0.42)	0.108			

[*] Omnibus P-value for BMI group differences in the logistic regression model. Pairwise comparisons for subgroups are reported in italics for individual BMI groups, compared to normal BMI.

Table 6.

Unadjusted Associations of SDB and Other Variables with Hypertensive Disorders of Pregnancy (n=100).

Variable	Odds Ratio for Pregnancy-Induced Hypertension (95% CI)	P-value
1st trimester AHI	1.04 (0.90 – 1.21)	0.584
3rd trimester AHI	0.96 (0.86 – 1.07)	0.485
1st trimester OSA (AHI 5 events/hr)	0.44 (0.05 – 3.74)	0.455
3rd trimester OSA (AHI 5 events/hr)	0.50 (0.13 – 1.90)	0.310
Change in AHI	0.93 (0.82 – 1.06)	0.270
Age, 10 yrs	0.52 (0.23 – 1.16)	0.109
1st trimester BMI, 5 unit	1.17 (0.84 – 1.64)	0.348
3rd trimester BMI, 5 unit	1.27 (0.87 – 1.84)	0.220
Gestational weight gain	1.05 (0.95 – 1.15)	0.347
1st trimester neck circumference	1.13 (0.96 – 1.33)	0.135
3rd trimester neck circumference	1.10 (0.94 – 1.29)	0.235
Nulliparity (ref = multi)	3.00 (1.03 – 8.67)	**0.043**
Prior history of hypertensive disorder of pregnancy	1.29 (0.24 – 6.99)	0.765
White and other ethnicity (ref African-Am)	1.09 (0.35 – 3.40)	0.883

Table 7.

Unadjusted Associations of SDB and Other Variables with Gestational Diabetes, Preterm Delivery and Low Birthweight

	Gestational Diabetes (n=5)		Preterm Delivery (n=10)		Low Birthweight (n=9)	
	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
1st TM AHI	1.05 (0.82 – 1.34)	0.710	1.02 (0.84 – 1.24)	0.851	0.95 (0.72 – 1.25)	0.715
3rd TM AHI	1.03 (0.93 – 1.15)	0.536	1.02 (0.94 – 1.12)	0.586	1.03 (0.94 – 1.13)	0.546
1st TM OSA	2.39 (0.24 – 23.74)	0.457				
3rd TM OSA	2.09 (0.33 – 13.27)	0.436	0.75 (0.15 – 3.84)	0.730	1.67 (0.38 – 7.34)	0.500
Change in AHI	1.03 (0.91 – 1.18)	0.619	1.03 (0.93 – 1.14)	0.619	1.04 (0.95 – 1.15)	0.391