Obstructive sleep apnea in pregnancy is associated with adverse maternal outcomes: a national cohort

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Abstract

Objective—Pregnancy and the obesity epidemic impacting women of reproductive age appear to predispose women to obstructive sleep apnea (OSA) in pregnancy. The aim of this study is to examine the association between OSA and adverse maternal outcomes in a national cohort.

Methods—The National Perinatal Information Center in the US was used to identify women with a delivery discharge diagnosis of OSA from 2010 to 2014. We used the International Classification of Diseases, 9th Revision to classify OSA diagnosis and maternal outcomes.

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Results—The sample consisted of 1,577,632 gravidas with a rate of OSA of 0.12% (N=1963). There was a significant association between OSA and preeclampsia (adjusted odds ratio (aOR) 2.22, 95% confidence interval (CI) 1.94–2.54), eclampsia (aOR 2.95, 1.08–8.02) and gestational diabetes (aOR 1.51, 1.34–1.72) after adjusting for a comprehensive list of covariates which includes maternal obesity. OSA status was also associated with a 2.5- to 3.5-fold increase in risk of severe complications such as cardiomyopathy, congestive heart failure and hysterectomy. Length of hospital stay was significantly longer (5.1 ± 5.6 vs 3.0 ± 3.0 days, p<0.001) and odds of an admission to an intensive care unit higher (aOR 2.74, 2.36–3.18) in women with OSA.

Conclusions—Compared to pregnant women without OSA, pregnant women with OSA have a significantly higher risk of pregnancy-specific complications such as gestational hypertensive conditions and gestational diabetes, and rare medical and surgical complications such as cardiomyopathy, pulmonary edema, congestive heart failure and hysterectomy. OSA diagnosis was also associated with a longer hospital stay and significantly increased odds for admission to the intensive care unit.

INTRODUCTION

Pregnancy appears to predispose women to the development of obstructive sleep apnea (OSA) due to dynamic physiological changes [1]. Furthermore, the obesity epidemic now affects women of childbearing age [2] and is likely a major contributor to OSA in this young population. Wisconsin Sleep Cohort data show that the prevalence of OSA exceeds 10% in pre-menopausal women [3], suggesting that a good proportion of women are entering pregnancy with this condition, though it likely remains under-recognized [4].

Recent studies have shown a significant association between OSA and adverse pregnancy-related outcomes. Associations between OSA and hypertensive disorders were demonstrated in prospective [5,6] and population studies [7–9] in Asia, North America and Australia. Sleep-disordered breathing and OSA are also associated with gestational diabetes [10–12]. Preeclampsia and gestational diabetes impact immediate maternal [13], fetal [14], and neonatal [15,16] health, as well as long-term metabolic [17,18] and cardiovascular health in women [19,20] and children [21], representing a substantial public health and financial burden. Hence, identifying the impact of OSA on the health of the mother and her offspring can help set the stage for future research assessing targeted screening and interventions in at-risk populations in an effort to modify the immediate and long-term health of the mother.

Data from the general population have linked OSA with cardiovascular complications [22,23]. Such complications are rare in the young pregnant population and associations with OSA would be difficult to ascertain in prospective studies. As such, national cohorts with large datasets would be ideal for examining these complications.

The goal of this study was to examine the association of a diagnosis of OSA with adverse pregnancy outcomes such as gestational hypertensive disorders and gestational diabetes, and less common medical complications. We postulated that, compared to gravidas without the diagnosis, those with OSA would be at an increased risk of these adverse outcomes.

MATERIALS AND METHODS

Study population and setting

The National Perinatal Information Center (NPIC) data is a membership organization comprised of perinatal centers across the United States (US) that submit quarterly clinical data to the Perinatal Center Data Base (PCDB). The PCDB dataset was used to identify women who had a delivery discharge from 2010 to 2014 at 95 different US hospitals. The dataset consisted of maternal characteristics, diagnosis codes based on the International Classification of Diseases, 9th Revision (ICD-9) and procedure codes. PCDB data are imported and processed quarterly and a detailed validation report generated. This validation report is communicated back to hospitals to address inconsistencies. Hospitals then examine their metrics, address potential issues with provider documentation, coding or quality, and can correct their data before they are included in the dataset.

An institutional review board at two institutions (no. 881483 and no. 894311) approved the study.

Exposure and outcome variables

OSA status was established if a diagnosis code for OSA was present on the delivery discharge record (Appendix Table A1). Women without that diagnosis code were considered to not have OSA. This method of OSA diagnosis identification cannot differentiate timing of the diagnosis with regard to gestational age, disease severity or the use of therapy for OSA.

The main outcomes of interest were hypertensive disorders of pregnancy including preeclampsia (see Appendix Table A1), eclampsia, and gestational diabetes. We reported data on multiple gestations given their association with hypertensive disorders of pregnancy. Demographic and social characteristics were included in the analyses. Maternal characteristics and co-morbid conditions including those known to be associated with OSA, hypertensive disorders of pregnancy or gestational diabetes, such as obesity, chronic hypertension, and pre-gestational diabetes mellitus were investigated using diagnosis codes.

Another main aim was to also examine severe maternal complications: stroke (hemorrhagic and ischemic); cardiomyopathy (all causes); and congestive heart failure (systolic and diastolic, of any etiology). Maternal hospital length of stay and the risk of maternal admission to an intensive care unit (ICU) were also collected.

We also examined fetal diagnoses coded in the maternal record including intrauterine growth restriction (IUGR) and stillbirth.

Statistical analyses

All analyses were performed using SAS® [24]. Descriptive statistics of hospital and maternal characteristics were reported overall and by OSA status. Mean values and standard deviations were used to describe maternal age and hospital length of stay and compared using a *t*-test.

Hospital characteristics, demographic data, and co-morbidities predating pregnancy were reported using numbers and percentages and compared with chi-square tests. Co-variates tested included demographics, multiple births, pre-pregnancy hypertension and diabetes, obesity, substance use, geographic location, coronary heart disease, anemia, hyperlipidemia, hypothyroidism and disorders of the adrenal gland. We then examined maternal and fetal outcomes by OSA status. Univariate and multivariable logistic regression analyses were used to calculate adjusted odds ratios (aORs) and 95% confidence intervals (CI) for maternal and fetal outcomes with OSA as the main independent variable using three different types of multivariable models. The first series of models were adjusted for maternal obesity; the second adjusted for maternal obesity, pre-pregnancy hypertension and pre-pregnancy diabetes; and the third adjusted for the second model and for maternal age, race/ethnicity, multiple birth, tobacco use, alcohol use; drug use, rural/urban status, coronary heart disease, anemia, hyperlipidemia, hypothyroidism and disorders of the adrenal gland.

RESULTS

Hospital characteristics

Hospitals in the southern part of the United States contributed the highest proportion of patients to the dataset (43.3% of all patients), see Table 1. Hospitals in metropolitan areas, teaching hospitals, and hospitals with more than 5000 deliveries per year contributed the most to the dataset (97.2%, 73.6% and 45.1%, respectively).

Maternal demographics

The sample consisted of 1,577,632 deliveries, of which 1963 women (0.12%) had a diagnosis code of OSA. Coding for OSA increased from 0.10% in 2010 to 0.16% in 2014. Mothers with OSA were older, more likely to be Black, and to have multiple gestations and obesity ($p<0.001$) than those without OSA (see Table 2). Mothers with OSA were also more likely to have a smoking history and a drug use history ($p<0.001$) than those without OSA. There was no difference in alcohol use between the two groups.

Maternal comorbidities and covariates

Mothers with OSA had higher odds of having obesity (OR 24, 95% CI 21.9–26.3), prepregnancy hypertension (aOR 5.20, 95% CI 4.69–5.77) and pre-pregnancy diabetes (aOR 4.37, 95% CI 3.81–5.01). Anemia, disorders of lipid metabolism and the adrenal gland, coronary artery disease and hypothyroidism were also all significantly more common in women with OSA ($p<0.001$) and were included in the comprehensive model (Model 3).

OSA and adverse outcomes

Pregnant women with OSA had a higher prevalence of adverse events (see Fig. 1 and Table 3). Univariate and multivariate regression models showed a significant association between OSA and hypertensive disorders of pregnancy after adjusting for covariates in model types 1, 2 and 3 (see Table 3): preeclampsia (aOR 2.22; 95% CI 1.94–2.54), gestational hypertension (aOR 1.67; 1.42–1.97) and eclampsia (aOR 2.95; 1.08–8.02). The risk of gestational diabetes was also significantly elevated in women with OSA compared to those

without the diagnosis even after adjusting for obesity and in the fully adjusted model 3 (aOR 1.51, 1.34–1.72).

Women with OSA were at a significantly increased risk of developing pulmonary edema, cardiomyopathy and congestive heart failure. This increased risk persisted in all three adjusted models (see Table 4). The risk for stroke was also elevated in women with OSA compared to those without the diagnosis after adjusting for maternal obesity but not with other models. Postoperative wound complications and hysterectomy were more likely to occur in women with OSA even in the comprehensive model (Fig. 2). Women with OSA had a significantly longer hospital stay (5.1 ± 5.6 days versus 3.0 ± 3.0 days, p<0.001) and higher odds of an admission to an ICU (aOR 2.74, 2.36–3.18) in the comprehensive model.

Fetal complications

Fetal outcomes coded in the maternal record included stillbirth and growth restriction. There was a significant association between OSA status and growth restriction, and stillbirth that persisted after adjusting for maternal obesity but not once pre-pregnancy hypertension and pre-pregnancy diabetes were included in the models (Table 4).

DISCUSSION

In this national cohort, pregnant women with OSA were significantly more likely to develop adverse events. This study is the first to show a higher risk of ICU admissions and hysterectomy among pregnant women with OSA and confirms previous findings in another national cohort [8] that OSA is also associated with rare conditions such as cardiomyopathy, congestive heart failure and pulmonary edema. A diagnosis of OSA was found to be associated with a higher risk of developing gestational hypertensive disorders and gestational diabetes even after adjusting for potential confounders, suggesting that OSA is an independent risk factor for these conditions.

The increased risk of chronic cardiovascular and metabolic conditions that are unrelated to pregnancy in this population compared to controls is not surprising given the well-known and well-established associations of OSA with chronic hypertension [25,26] and type II diabetes [27,28] in the general, non-pregnant population. Notably, however, this population is significantly younger than the non-pregnant population in past studies. This suggests that the association of OSA with cardiovascular and metabolic outcomes is not age-dependent and occurs as early as the reproductive age, despite women developing cardiovascular complications later in life, when compared to men. In addition, these findings highlight that the pregnant population with OSA appears to be more complex than the average healthy pregnant population and that this population may present some significant clinical challenges. It is noteworthy, however, that these demonstrated associations of OSA with chronic conditions do not establish a temporal relationship and are rather 'cross-sectional', limiting our ability to infer a causal relationship.

Prospective studies have shown an elevated risk of preeclampsia in women with OSA compared to those without even after adjusting for important confounders such as body mass index [5,6]. National data have also been consistent with our current findings, with data from

Taiwan, the United States and Australia demonstrating a two-fold increase in the risk of preeclampsia in women with a diagnosis code of OSA [7–9]. The association of a diagnosis of OSA with gestational diabetes was also similar to previous findings; a recent meta-analysis has shown that women with sleep-disordered breathing including snoring and OSA were at a three-fold risk of being diagnosed with gestational diabetes [29]. Population studies were inconsistent though, with some national cohort studies [7,8] showing a 63–89% increase in the risk of gestational diabetes, while others did not [9]. These inconsistencies in population studies, despite similar designs, may be due to global differences in the definition of gestational diabetes, as well as the populations studied.

Mechanisms underlying the association of gestational hypertensive disorders and gestational diabetes with OSA have been speculated on, but mechanistic data remain scarce. It is possible that through airflow limitation, arousals and intermittent hypoxemia, OSA may result in a heightened sympathetic drive, an enhanced oxidative stress, a disturbed endothelial function or a dysfunctional hypothalamic pituitary adrenal axis that may result in disturbances that predispose to hypertension and abnormal glucose metabolism [30]. We have previously hypothesized that through the above-mentioned potential mechanisms, OSA may impact placental function [30]. Evidence of placental tissue hypoxia in women with OSA [31] and altered levels of placenta-secreted markers [32,33] support this hypothesis. The contributing role of obesity in these outcomes is difficult to ascertain in population studies, as coding rates of obesity were either not reported [8] or likely significantly under-coded [7]. In the Taiwanese cohort, obesity rates were reported at 2.1% in women with OSA and 1.5% in those without the diagnosis [7]. It is noteworthy, however, that prospective and cross-sectional studies which have collected body weight have shown that the association of snoring [10,34] or OSA·[6] with adverse obstetric events occurred independently of obesity.

Pregnant women with OSA were also at increased risk of having a longer in-hospital stay for delivery than women without OSA as well as a higher risk of requiring an admission to the ICU, even after adjusting for chronic conditions. Hospital stay around delivery of longer than 5 days was observed more frequently in pregnant women with OSA in a prior national cohort study [8] compared to women without the diagnosis. However, the risk of an admission to the ICU has not been evaluated in the past to our knowledge in this population. Preliminary data in a cohort of non-pregnant patients admitted to medical and surgical ICUs at a single tertiary care institution has shown that patients with OSA are less likely to die and have a shorter length of stay in the ICU [35]. In our study, women with OSA were more likely to require an admission to the ICU independently of pre-pregnancy comorbidities. It is possible that the higher rate of admission to the ICU may relate to the development of pregnancy-related complications, rather than to exacerbations of pre-pregnancy conditions. However, future analyses evaluating specific diagnosis requiring an admission to the ICU are warranted.

Pregnant women with OSA were also at a higher risk of developing other severe cardiopulmonary complications such as congestive heart failure, cardiomyopathy and pulmonary edema. Louis et al. also reported these complications [8]; however, calculated adjusted odds ratios were somewhat higher in that study, despite using similar models. Contrary to our study, the study by Louis et al. found a significantly higher risk of stroke and

pulmonary embolism though confidence intervals in all models were quite large. Similarly to the study of Louis et al. [8], we describe a higher rate of wound complications; however we are the first to report an increased risk of requiring a hysterectomy. The increased risk of wound complications may be explained by poor tissue perfusion. However, as the risk of requiring blood transfusions was not significantly higher in women with OSA, a more thorough examination of underlying reasons for a hysterectomy may help shed some light on potential mechanisms.

There are numerous strengths to this study. Sample size and study design are the most important strengths of the study in that they are ideal for evaluating rare outcomes such as congestive heart failure, cardiomyopathy and pulmonary edema. The population studied is quite diverse from a geographical point of view as well as from an ethnic/racial standpoint; hospitals included vary in terms of teaching status, size, delivery volume, and location. The dataset is quite robust and collects many variables that are relevant to the study of OSA in pregnancy and has been validated for pregnancy outcomes. However, results need to be interpreted in the light of some limitations. This study shows that diagnosing and coding for OSA in pregnancy may have improved in recent years [7–9] but remains under-reported. As recent data show a prevalence of 3% and 10% in early and late pregnancy, respectively [6], it appears that less than 0.03% of OSA is being captured by hospital coding which may reflect under-diagnosing and under-coding. Under-diagnosing OSA in pregnancy is likely quite common as obstetricians rarely ask questions aimed at the identification of women at risk for OSA [4]. Under-coding is one of the inherent limitations of diagnosis-code-based datasets, which could introduce an ascertainment bias. It has been argued that a main limitation of large datasets in the diagnosis of OSA is the determination of prevalence given likely under-coding [36] but that such observational designs are likely to bias associations toward the null, underestimating associations with adverse outcomes [36–38]. It is likely that the same applies to our dataset in pregnancy. It is generally assumed that non-pregnancy conditions appearing on the delivery record are conditions of enough importance to the pregnancy or the woman to be noted in the record. This possibility may bias our sample towards having women with more 'significant' OSA. In addition, lack of data on therapy may impact the interpretation of our results. However, we would expect therapy for OSA to result in an underestimation of our findings and bias our findings toward the null. The dataset limits our ability to describe a temporal relationship between OSA and the described outcomes; hence, the findings described in this study consist of associations and do not establish a causal relationship between OSA and adverse outcomes.

CONCLUSIONS

Pregnant women with OSA have a significantly higher risk of having morbid pre-pregnancy conditions and pregnancy-specific complications such as gestational hypertensive conditions and gestational diabetes. Pregnant women with OSA also have a longer length of hospital stay and higher odds of an admission to the ICU and of having rare cardiovascular and surgical complications than women not diagnosed with OSA.

Acknowledgments

Appendix

Appendix Table 1

International Classification of Diseases-9th Edition of exposure variable, main covariates and outcomes

Exposure, main covariates and outcomes	ICD-9 codes used
Obstructive Sleep apnea	780.53; 780.57; 780.51; 327.2; 327.23,
Obesity	278.0; 278.01, 278.03; 649.1; 79391; V853; V854; V855.4
Pre-gestational hypertension	401; 402; 403; 404; 405; 642.0; 642.1; 642.2; 642.7
Pre-gestational diabetes	250; 249
Hypertension of pregnancy	642.3
Preeclampsia	642.4; 642.5
Eclampsia	642.6
Gestational diabetes	648
Pulmonary embolism	415.1
Cardiomyopathy	425; 6745
Congestive heart failure	402.01; 402.11; 402.91; 428; 398.91
Acute pulmonary edema	518.4
Stroke	431, 433, 430, 432, 434
Wound complications	674.1; 674.3; 998.3; 998.5
Hysterectomy (procedure code)	683–689
Poor fetal growth (**Intrauterine Growth Restriction**)	656.5
Stillbirth	656.4

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Highlights

- OSA is associated with an increased risk of adverse pregnancy-related outcomes such as preeclampsia and gestational diabetes.

- Risk of having an admission to the intensive care unit and the risk of hysterectomy is increased, even after adjusting for multiple confounders.

- Obstructive sleep apnea is associated with severe maternal medical and surgical morbidities.
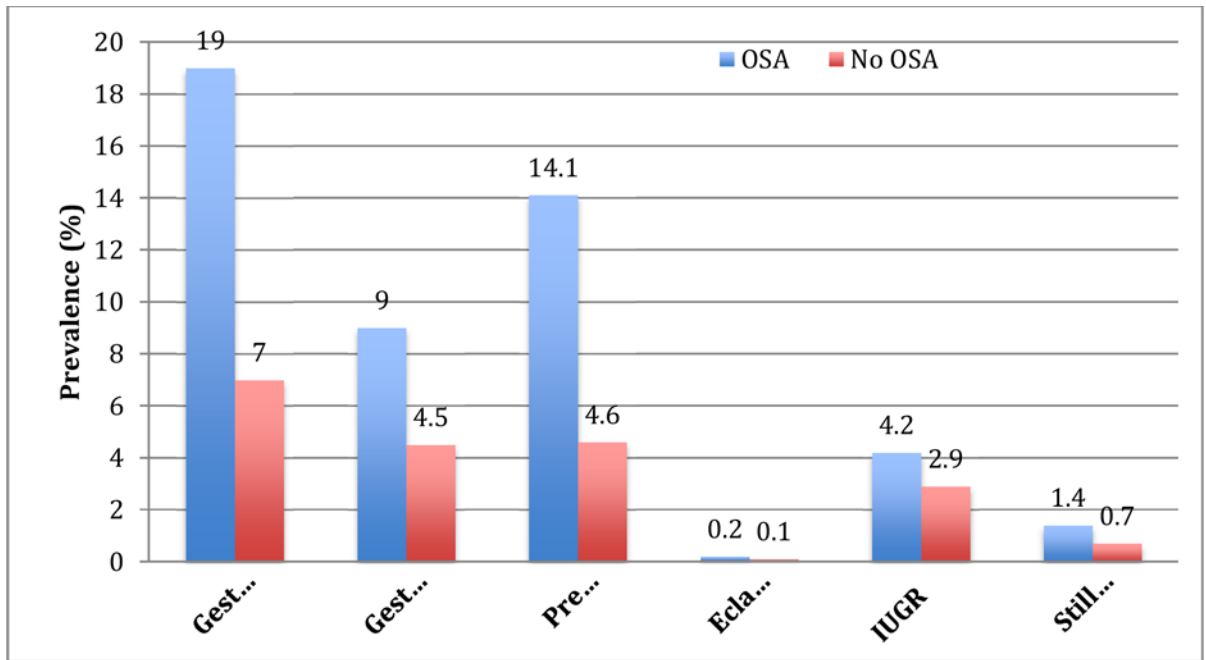
Figure 1.
Obstructive sleep apnea status and prevalence of pregnancy-specific complications
p<0.001 for all outcomes. IUGR: Intrauterine growth restriction; OSA: Obstructive sleep apnea
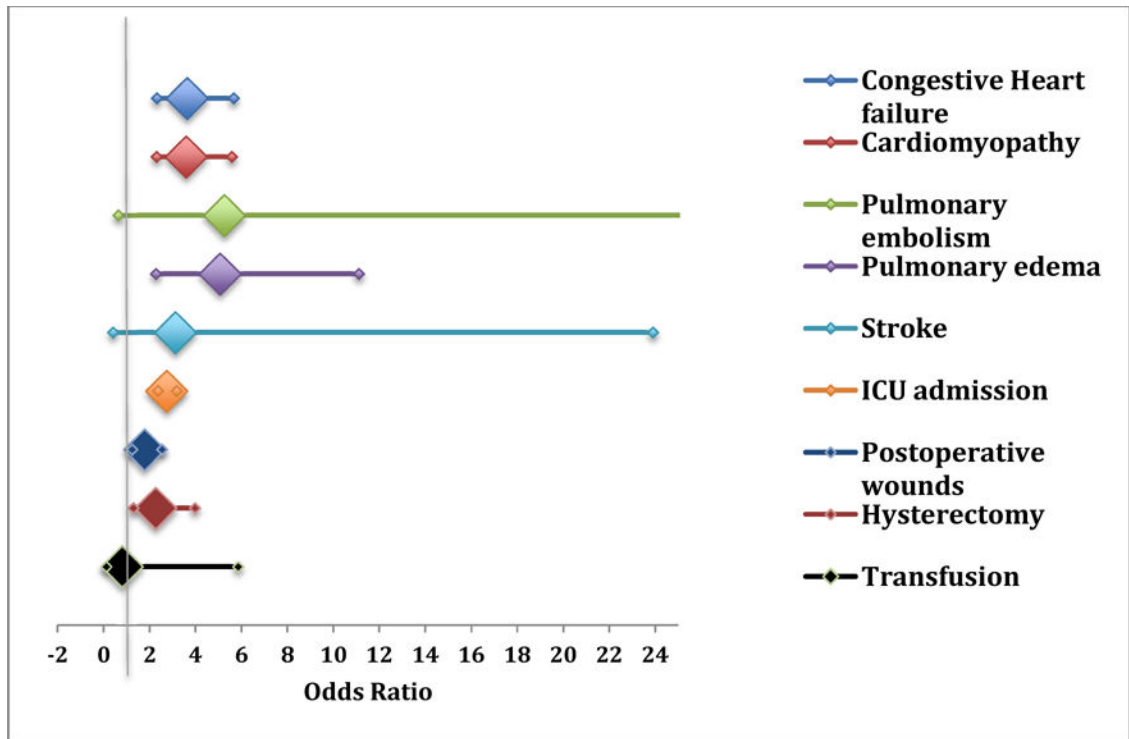
Figure 2.
Risk of maternal and surgical complications by OSA status.

Odds ratios in this figure have been adjusted using model 3. ICU: intensive care unit.

Table 1

Geographic and other characteristics of hospitals providing data.

Hospital characteristics	Total *N* (%)	OSA (%)	No OSA (%)	*p*-value for Chi-square
Hospital region (*N*=1,568,275)				<0.001
Region 1 (Northeast)	425,997 (27.2)	642 (33.3)	425,355 (27.2)	
Region 2 (Midwest)	262,227 (16.7)	401 (20.8)	261,826 (16.7)	
Region 3 (South)	679,481 (43.3)	652 (33.8)	678,829 (43.3)	
Region 4 (West)	200,570 (12.8)	235 (12.2)	200,335 (12.8)	
Hospital location (*N*=1,568,275)				0.020
METRO (Rural)	44,703 (2.9)	72 (3.7)	44,631 (2.9)	
Metro (Urban)	1,523,572 (97.2)	1,858 (96.3)	1,521,714 (97.2)	
Hospital teaching status (N=1,505,052)				<0.001
Teaching	1,092,420 (72.6)	1,576 (83.3)	1,090,844 (72.6)	
Non-teaching	412,632 (27.4)	315 (16.7)	412,317 (27.4)	
Hospital delivery volume in births per year (*N*=1,568,275)				0.149
1000	218,054 (13.9)	245 (12.7)	217,809 (13.9)	
1001–2500	98,998 (6.3)	129 (6.7)	98,869 (6.3)	
2501–5000	544,435 (34.7)	709 (36.7)	543,726 (34.7)	
>5000	706,788 (45.1)	847 (43.9)	705,941 (45.1)	
Hospital bed size				<0.001
Small (<400 beds)	574,738 (36.4)	574 (29.2)	574,164 (36.4)	
Medium (400–700 beds)	489,329 (31.0)	702 (35.8)	488,627 (31.0)	
Large (700 beds)	513,565 {32.6}	687 (35.0)	512,878 (32.6)	

OSA, obstructive sleep apnea.

Table 2

Distribution of maternal sociodemographic, perinatal, behavioral, and hospital characteristics for all delivery discharges from 2010 to 2014, overall and by obstructive sleep apnea status.

Characteristic	Total *N*	OSA	No OSA	*p*-value for chi-square or *t*-test
		N (%)	*N* (%)	
Overall	1,577,632	1963 (0.1)	1,575,669 (99.9)	
Maternal age	29.6 (SD=6.0)	32.3 (SD=6.0)	29.6 (SD=6.0)	<0.001
Maternal race				
White	710,872 (45.1)	821 (41.8)	710,051 (45.1)	<0.001
Black	292,318 (18.5)	642 (32.7)	291,676 (18.5)	
Hispanic	109,842 (7.0)	84 (4.3)	109,758 (7.0)	
Asian	74,120 (4.7)	32 (1.6)	74,088 (4.7)	
American Indian/Alaska Native	5640 (0.4)	8 (0.4)	5632 (0.4)	
Native Hawaiian/Pacific Islander	8552 (0.5)	5 (0.3)	8547 (0.5)	
Other/unknown	376,288 (23.9)	371 (18.9)	375,917 (23.9)	
Tobacco use	57,435 (3.6)	176 (9.0)	57,259 (3.6)	<0.001
Alcohol use	1760 (0.1)	1 (0.1)	1759 (0.1)	**0.421**
Drug use	22,768 (1.4)	47 (2.4)	22,721 (1.4)	<0.001
Multiple gestation	39,018 (2.5)	93 (4.7)	38,925 (2.5)	<0.001
Obesity	94,513 (6.0)	1181 (60.2)	93,332 (5.9)	<0.001
Pre-pregnancy hypertension	45,757 (2.9)	572 (29.1)	45,185 (2.9)	<0.001
Pre-pregnancy diabetes	19,461 (1.2)	255 (13.0)	19,206 (1.2)	<0.001
Coronary heart disease	605 (0.04)	11 (0.6)	594 (0.04)	<0.001

Mean (standard deviation, SD) with *t*-test for continuous variables; number (%) with chi-square test for categorical variables. OSA, obstructive sleep apnea.

Table 3

Prevalence of severe maternal medical and surgical outcomes.

Outcomes	Total *N*	OSA	No OSA	*p*-value for chi-square
Maternal medical outcomes				
Pulmonary edema	329 (0.02)	7 (0.4)	322 (0.02)	<0.001
Pulmonary embolism and infarction	40 (<0.01)	1 (0.1)	39 (<0.01)	<0.001
Congestive heart failure	734 (0.1)	25 (1.3)	709 (0.04)	<0.001
Cardiomyopathy	1075 (0.1)	24 (1.2)	1051 (0.1)	<0.001
Stroke	106 (0.01)	1 (0.1)	105 (0.01)	0.017
Surgical outcomes				
Postoperative wounds	6472 (0.4)	32 (1.6)	6440 (0.4)	<0.001
Hysterectomy	2005 (0.1)	14 (0.7)	1991 (0.1)	<0.001
Transfusion	739 (0.1)	1 (0.1)	738 (0.1)	**0.933**
Disposition				
Length of stay	3.0 (3.0)	5.1 (5.6)	3.0 (3.0)	<0.001
ICU admission	29,416 (1.9)	229 (11.7)	29,187 (1.9)	<0.001
Death	79 (0.01)	0 (0.0)	79 (0.01)	**1.000**

OSA, obstructive sleep apnea.

Table 4

Obstructive sleep apnea and risk of maternal and newborn outcomes.

Outcomes	Crude OR	Model 1	Model 2	Model 3
Maternal				
Gestational diabetes[a]	3.64 (3.25–4.09)	2.08 (1.85–2.34) $p<0.001$	1.75 (1.55–1.97) $p<0.001$	1.52 (1.34–1.72) $p<0.001$
Gestational hypertension[b]	3.02 (2.58–3.54)	1.77 (1.51–2.08) $p<0.001$	1.72 (1.47–2.02) $p<0.001$	1.67 (1.42–1.97) $p<0.001$
Preeclampsia	3.42 (3.01–3.89)	2.07 (1.82–2.36) $p<0.001$	2.24 (1.96–2.56) $p<0.001$	2.22 (1.94–2.54) $p<0.001$
Eclampsia	3.49 (1.31–9.32)	2.70 (1.00–7.29) $p=0.050$	2.68 (0.99–7.26) $p=0.053$	2.95 (1.08–8.02) $p=0.034$
Pulmonary edema	17.5 (8.27–37.1)	9.92 (4.56–21.6) $p<0.001$	5.63 (2.55–12.4) $p<0.001$	5.06 (2.29–11.1) $p<0.001$
Congestive heart failure	28.7 (19.2–42.8)	10.6 (6.98–16.1) $p<0.001$	4.14 (2.71–6.34) $p<0.001$	3.63 (2.33–5.66) $p<0.001$
Cardiomyopathy	18.5 (12.3–27.9)	8.85 (5.81–13.5) $p<0.001$	4.05 (2.64–6.21) $p<0.001$	3.59 (2.31–5.58) $p<0.001$
Pulmonary embolism and infarction	20.6 (2.83–150.0)	8.39 (1.08–65.0) $p=0.042$	4.92 (0.61–39.9) $p=0.135$	5.25 (0.64–42.9) $p=0.122$
Postoperative wounds	4.05 (2.85–5.74)	2.50 (1.75–3.56) $p<0.001$	2.00 (1.40–2.85) $p<0.001$	1.77 (1.24–2.54) $p=0.002$
Hysterectomy	5.69 (3.36–9.64)	4.15 (2.43–7.10) $p<0.001$	3.32 (1.94–5.71) $p<0.001$	2.26 (1.29–3.98) $p=0.005$
Transfusion	1.09 (0.15–7.74)	1.19 (0.17–8.49) $p=0.865$	0.93 (0.13–6.67) $p=0.941$	0.81 (0.11–5.85) $p=0.833$
Stroke	7.65 (1.07–54.8)	8.25 (1.10–62.0) $p=0.040$	3.93 (0.51–30.2) $p=0.188$	3.12 (0.41–23.9) $p=0.274$
Length of stay*	2.13 (2.00–2.26)	1.74 (1.61–1.88) $p<0.001$	1.28 (1.14–1.41) $p<0.001$	1.18 (1.05–1.32) $p<0.001$
ICU admission	7.00 (6.09–8.04)	4.64 (4.03–5.35) $p<0.001$	2.87 (2.48–3.33) $p<0.001$	2.74 (2.36–3.18) $p<0.001$
Fetal				
Poor fetal growth	1.48 (1.19–1.84)	1.43 (1.15–1.79) $p=0.001$	1.08 (0.86–1.35) $p=0.505$	1.05 (0.84–1.31) $p=0.681$
Stillbirth	2.10 (1.43–3.07)	1.89 (1.29–2.77) $p=0.001$	1.25 (0.85–1.84) $p=0.254$	1.17 (0.79–1.73) $p=0.427$

Outcomes are presented as adjusted odds ratios (ORs) with 95% confidence intervals.

Model 1: Adjusted for maternal obesity. Model 2: Adjusted for maternal obesity, pre-pregnancy hypertension, pre-pregnancy diabetes. Model 3: adjusted for maternal obesity, pre-pregnancy hypertension, pre-pregnancy diabetes, maternal age, race/ethnicity, multiple birth, tobacco use, alcohol use; drug use, rural/urban status, coronary heart disease, anemia, hyperlipidemia, hypothyroidism, disorders of the adrenal gland. ICU, intensive care unit.

[a] All models excluded women with pre-gestational diabetes

[b] All models excluded women with pre-gestational hypertension