OBSTETRICS

Pregnancy-onset habitual snoring, gestational hypertension, and preeclampsia: prospective cohort study

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OBJECTIVE: This study aimed to prospectively examine the impact of chronic vs pregnancy-onset habitual snoring on gestational hypertension, preeclampsia, and gestational diabetes.

STUDY DESIGN: Third-trimester pregnant women were recruited from a large, tertiary medical center from March 2007 through December 2010 and screened for the presence and duration of habitual snoring, as a known marker for sleep-disordered breathing. Clinical diagnoses of gestational hypertension, preeclampsia, and gestational diabetes were obtained.

RESULTS: Of 1719 pregnant women, 34% reported snoring, with 25% reporting pregnancy-onset snoring. After adjusting for confounders, pregnancy-onset, but not chronic, snoring was independently associated with gestational hypertension (odds ratio, 2.36; 95% confidence interval, 1.48–3.77; $P < .001$) and preeclampsia (odds ratio, 1.59; 95% confidence interval, 1.06–2.37; $P = .024$) but not gestational diabetes.

CONCLUSION: New-onset snoring during pregnancy is a strong risk factor for gestational hypertension and preeclampsia. In view of the significant morbidity and health care costs associated with hypertensive diseases of pregnancy, simple screening of pregnant women may have clinical utility.

Key words: gestational diabetes, gestational hypertension, preeclampsia, pregnancy, snoring

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Sleep-disordered breathing (SDB), a spectrum of respiratory abnormalities during sleep ranging from habitual snoring to obstructive sleep apnea, is common yet often undiagnosed, especially in women.[1] Increased weight promotes SDB and, strikingly, a weight gain of only 10% has been associated with a 6-fold increase in the development of significant SDB.[2] This observation is particularly relevant to pregnancy as weight gain >10% occurs in most women. Habitual snoring, the hallmark symptom of SDB, increases during pregnancy[3-5] and is particularly common in preeclampsia.[6]

The cardiovascular implications of untreated SDB are substantial and complex. Several large, population-based studies such as the Sleep Heart Health Study and the Wisconsin Sleep Cohort Study have provided clear evidence for an independent association between SDB and cardiovascular disease, particularly hypertension and metabolic dysfunction.[7-11] The Nurses Health Study found that snoring increased the risk of incident hypertension independent of age or body mass index (BMI).[12] The mechanisms linking SDB and cardiovascular disease are likely multifactorial, involving sympathetic overactivity, inflammation, and endothelial dysfunction.

Hypertensive disorders of pregnancy are a leading cause of maternal and infant morbidity[13] and cost billions of dollars annually to treat. An emerging literature of cross-sectional studies support an association between SDB and hypertension during pregnancy.[5,14-17] The association between SDB and hypertension is particularly relevant during pregnancy as such morbidities jeopardize the health of mother and fetus, with major public health impact. Furthermore, new-onset SDB during pregnancy conceivably could have health ramifications that exceed those of chronic SDB, to which cardiovascular systems might have time to

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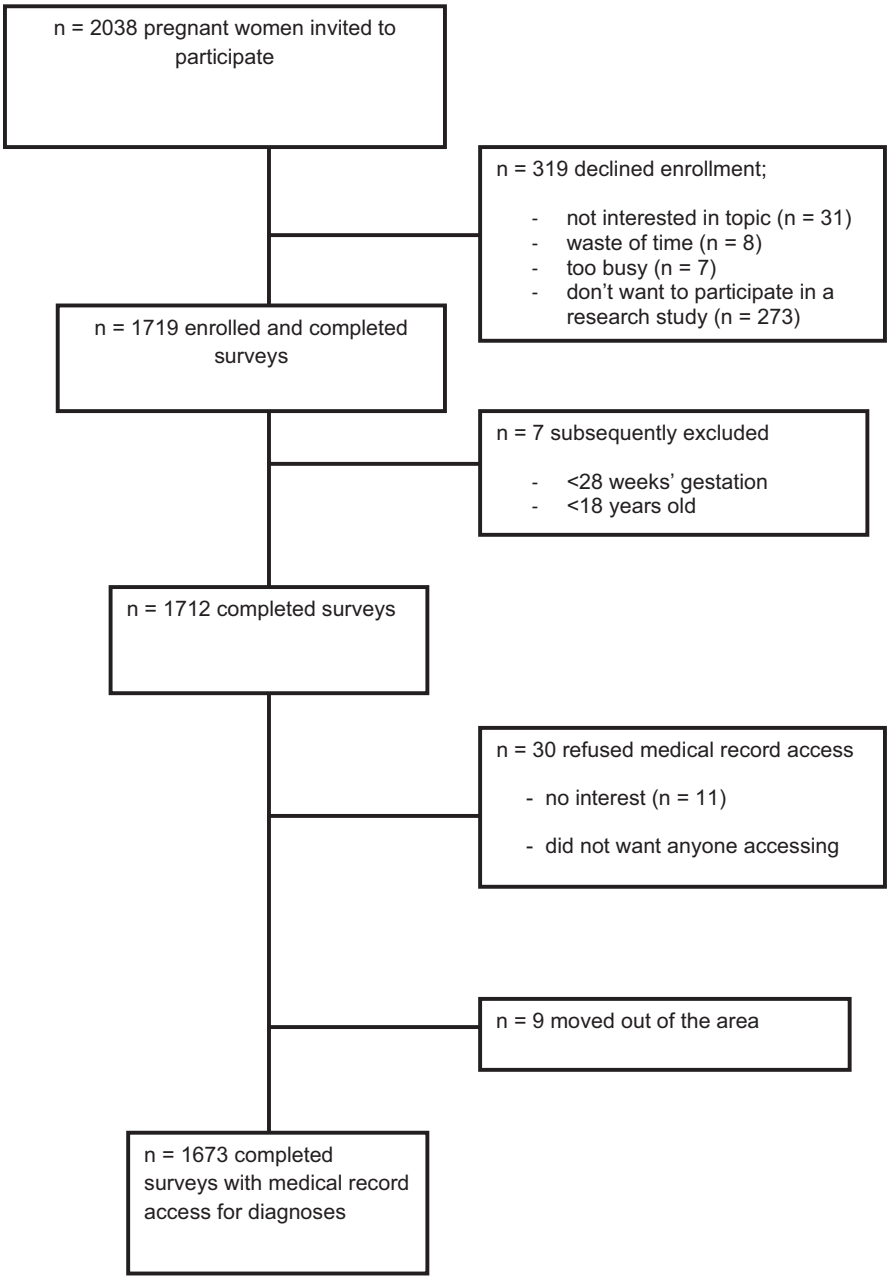
FIGURE 1
Recruitment flowchart



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adapt. An improved understanding of some vulnerabilities unique to pregnancy may offer opportunities to improve the health of both mothers and infants.

The goals of this study were to determine the prevalence and incidence of snoring during pregnancy and to examine associations with maternal health. We hypothesized that snoring, and especially pregnancy-onset rather than chronic snoring, would be associated with gestational hypertension, preeclampsia, and gestational diabetes.

Materials and Methods

In this prospective study, pregnant women were recruited from prenatal clinics within the University of Michigan from March 2007 through December 2010. Women were eligible if they were ≥18 years old and ≥28 weeks pregnant with a single fetus. There were no other exclusion criteria. Written informed consent was obtained to access medical records. A comparison group of nonpregnant control women was recruited from women aged 18-45 years attending routine gynecology visits. This study was approved by the University of Michigan Institutional Review Board.

Pregnant women completed a questionnaire about the presence of habitual snoring and whether they had "stopped breathing or gasped for air" (Appendix, Supplementary Figure). They were also asked whether a bed partner had complained. Habitual snoring was defined as snoring at least 3-4 times per week.[18,19] Similarly witnessed apneas were considered present if women "stopped breathing or gasped for air" at least 3-4 times per week. Enquiry was made about the timing of snoring to identify incident cases. Pregnancy-onset snoring was considered present when habitual snoring began during pregnancy. Chronic snoring was defined as habitual snoring both before and during pregnancy. A single question about snoring was chosen instead of a multi-item SDB questionnaire for several reasons: a single question is strongly and reliably associated with the overnight polysomnogram (PSG)-derived apnea/hypopnea index (number of apneic events per hour of sleep)[8,20]; in women a report of "often" or "usually (always or almost always)" snoring is associated with PSG-confirmed SDB with respective odds ratios (ORs) of 3.8 and 16.3[20]; its use provides an approach easily and immediately translated into clinical settings; no study has failed to associate snoring with objective measures of SDB from a PSG; validation of complex SDB screening tools in pregnancy has not been performed; most SDB scales emphasize weight, which in pregnancy will be necessarily high; and several scales rely on gender or hypertensive status, the major outcome in the current study. Nonpregnant women completed the same screening tools, with the exception of symptoms in relation to preg-

nancy. Pregnant women received a $10 gift card for participating.

Prepregnancy BMI was calculated from maternal self-report of height and weight just prior to conception and cross-checked with documented BMI from the initial obstetric visit in the first trimester. Serial weights throughout the pregnancy were obtained from clinical visits and, following delivery, the total amount of weight gain was calculated. Key variables abstracted from medical records included demographics, individual or family history of gestational hypertension or preeclampsia, smoking status, and the presence of a diagnosis of chronic hypertension, gestational hypertension, preeclampsia, or gestational diabetes. The latter diagnoses were obtained from medical coding using the *International Classification of Diseases, Ninth Revision*. In reporting this study, guidelines from Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) group[21] were followed.

Statistics

Sample size was calculated based on literature available at the time of study design. We predicted the frequency of snoring as 4% in nonpregnant women and 25% in pregnant women.[5,6,22] With a sample size ≥1400 pregnant women and 200 controls there would be a power of almost 100% to detect this difference with a 2-tailed significance level of 5%. If the frequency of snoring in nonpregnant women was 16% and that in pregnant women remained at 25%, the targeted sample sizes would provide 82% power to detect a difference. We anticipated that approximately 4% of women without snoring would develop hypertension compared to 10% of women with snoring.[5] Thus a test for equal frequency of hypertension based on this study (test for equality of binomial proportions) would have power of >95%. We planned to recruit unequal group sizes because the nonpregnant controls would serve only as a comparison for frequency of snoring.

As BMI is strongly associated with SDB, and BMI changes across pregnancy, prepregnancy or early first-trimester BMI was categorized according to Institute of Medicine (IOM) recommendations.[23] Subjects were classified as underweight (BMI <18.5 kg/m^2); normal weight (BMI 18.5-24.9 kg/m^2); overweight (BMI 25.0-29.9 kg/m^2); or obese (BMI ≥30.0 kg/m^2). Absolute weight gain was determined and subjects were classified according to whether they exceeded the IOM recommendations for gestational weight gain; 28-40 lb for underweight women, 25-35 lb for normal-weight women, 15-25 lb for overweight women, and 11-20 lb for obese women.

All data obtained were double-entered into a database to ensure accuracy and analyzed with software (SPSS, version 18.0, IBM Corp, Armonk, NY). Histograms, box plots, and descriptive methods were used to examine data for errors and outliers. Between-group comparisons of continuous variables (maternal age, BMI, and gestational age) were conducted with *t* tests (snoring vs no snoring) and analysis of variance (chronic snoring, pregnancy-onset snoring, and no snoring). Dichotomized variables were compared with χ^2 tests. Logistic regression was used to determine associations between snoring and maternal outcomes after adjusting for potential covariates (maternal age, race, prepregnancy BMI, weight gain in excess of IOM recommendations, gravidity, smoking, educational level, individual or family history of gestational hypertension/preeclampsia). OR and 95% confidence intervals (CIs) were calculated. A *P* value < .05 was considered statistically significant. Population attributable risk percent (PAR%) was calculated; this represents the proportion of disease (hypertension/preeclampsia) among the total population that would not have occurred in the absence of exposure (snoring), assuming that the exposure contributes in a causal manner to the disease. The following formula was used:

$$\text{PAR\%} = \left(\text{incidence}_{\text{total\_population}} - \text{incidence}_{\text{unexposed}}\right) / \text{incidence}_{\text{total\_population}}$$

TABLE 1
Demographics of participants

Demographic	Pregnant women (n = 1712)	Controls (n = 202)
Age, y	29.7 ± 5.9	31.2 ± 7.8[a]
Baseline BMI, kg/m^2	26.5 ± 7.4	25.3 ± 6.3[a]
Third-trimester BMI, kg/m^2	31.2 ± 7.1	N/A
Racial background		
Caucasian	70.5%	75.1%
African American	14.8%	14.7%
Asian	7.4%	4.1%
Multiracial/other	7.3%	6.1%
Gestational age, wk	34.1 ± 3.7	N/A
Smoker	12.8%	15.0%
Snoring	34.1%	14.9%[b]

Data shown as mean ± SD, or proportion as appropriate.
BMI, body mass index; *N/A*, not applicable.
[a] $P < .05$. [b] $P < .001$.
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RESULTS

In total, 2038 pregnant women were invited to participate; 1719 (84%) agreed to complete the surveys, 98% of whom consented to medical record access. There were no differences in maternal age, gestational age, parity, or BMI between women who did or did not participate or who did/did not consent to medical record access (data not shown). Five women were subsequently excluded because they were <28 weeks' gestation and 2 women were excluded because they were aged <18 years. In addition, 9

TABLE 2
Comparison between pregnant women with and without snoring

Variable	Snoring (n = 584)	Chronic snoring (n = 150)	Pregnancy-onset snoring (n = 434)	Nonsnoring (n = 1128)
Age, y	30.3 ± 5.9[a]	29.7 ± 6.2	30.6 ± 5.8[a]	29.4 ± 5.8
Women ≥35 y, %	24.6	22.4	25.4	20.2%
Baseline BMI, kg/m^2	29.3 ± 8.6[a]	31.9 ± 9.2[b]	28.5 ± 8.3[b]	25.0 ± 6.1
Obese, %	37.8[a]	52.7[b]	32.8[b,c]	19.9
Third-trimester BMI, kg/m^2	34.0 ± 6.0[a]	35.5 ± 8.5[b]	33.5 ± 7.8[b,d]	29.9 ± 6.2
Exceeded IOM weight gain, %	45.1[b]	34.5	48.9[b]	35.2
Racial background, %				
Caucasian	71.2	67.3	72.8	70.2
African American	15.7	21.6[e]	13.5[d]	13.9
Asian	6.7	5.2	7.2	7.9
Multiracial/other	6.4	5.9	6.5	8.0
Educational level, %				
<12th grade	9.1	14.9[e]	7.4[d]	8.3
≥12th grade	20.9	25.0[b]	19.7[c]	21.5
Some college	25.3[e]	28.4[e]	24.1	19.6
4-y college	35.7	27.0[a]	8.1[c]	38.9
Postgraduate	8.9	4.7[e]	10.8	11.5
Gestational age at enrollment, wk	34.4 ± 3.7[e]	33.6 ± 3.5	34.6 ± 3.8[d,e]	34.0 ± 3.7
Gravidity	2.7 ± 1.7	2.9 ± 1.9[e]	2.6 ± 1.7	2.5 ± 1.7
Parity	0.9 ± 1.1	1.0 ± 1.1	0.9 ± 1.1	0.9 ± 1.1
First pregnancy, %	28.8	23.6[e]	30.5	32.3
Smoker, %	16.7[b]	24.3[b]	13.9	10.6
Chronic hypertension, %[f]	16.4[b]	19.0[b]	15.4[b]	6.8
Gestational hypertension, %[f]	9.8[b]	7.2	10.6[b]	4.5
Preeclampsia, %[f]	12.9[a]	11.8	13.3[a]	8.2
Gestational diabetes, %[f]	19.7[e]	22.9[e]	18.7	15.0

Data shown as mean ± SD, or proportion as appropriate.
BMI, body mass index; *IOM,* Institute of Medicine.

[a] $P < .01$ for comparisons with nonsnoring controls; [b] $P < .001$ for comparisons with nonsnoring controls; [c] $P < .001$ for comparisons with chronic snoring; [d] $P < .01$ for comparisons with chronic snoring; [e] $P < .05$ for comparisons with nonsnoring controls; [f] Diagnoses obtained from medical records for 1673 women.

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women moved out of the area before delivery. Thus, the total sample was 1712 for prevalence data and 1673 for pregnancy outcomes (Figure 1). In total, 202 nonpregnant women were enrolled. Overall, 94% of women had bed partners; only 2% of partners complained about snoring when women classified themselves as nonsnorers. This did not alter the association with outcomes and thus the analyses were performed with maternal self-report only.

Table 1 shows population demographics. Pregnant women were more than twice as likely as controls to snore (34.1% vs 14.9%, $P < .0001$).

Overall, 34.1% of third-trimester women reported snoring; 66% were nonsnorers at both prepregnancy and in the third trimester, 25% started snoring during pregnancy, and 9% reported chronic snoring (Table 2). Snorers in general, as well as those with pregnancy-onset snoring specifically, were more likely to have chronic hypertension, gestational hypertension, and preeclampsia, than nonsnorers. In contrast, although snorers were more likely to have gestational diabetes compared to nonsnorers, further analysis revealed that it was the chronic, not pregnancy-onset, snorers who appeared to drive this relationship.

In unadjusted analyses, pregnancy-onset, but not chronic, snoring was independently associated with gestational hypertension (OR, 2.57; 95% CI, 1.69–

3.53; $P < .001$) and preeclampsia (OR, 1.71; 95% CI, 1.20–2.44; $P = .003$). There was no relationship with pregnancy-onset snoring and gestational diabetes (OR, 1.29; 95% CI, 0.96–1.74; $P = .09$). However, chronic snoring was associated with gestational diabetes (OR, 1.67; 95% CI, 1.10–2.52; $P = .015$).

A logistic regression model that controlled for potential covariates (maternal age, race, prepregnancy BMI, weight gain in excess of IOM recommendations, gravidity, smoking, education level, individual or family history of gestational hypertension or preeclampsia) showed that pregnancy-onset, but not chronic, snoring was independently associated with gestational hypertension (OR, 2.36; 95% CI, 1.48–3.77; $P < .001$). In this model exceeding the IOM weight gain guidelines, but not prepregnancy BMI, was also independently associated with gestational hypertension (OR, 2.68; 95% CI, 1.72–4.18; $P < .001$) (Table 3).

Similarly, in a logistic regression model controlling for the same covariates and including chronic hypertension and gestational diabetes, pregnancy-onset, but not chronic, snoring was independently associated with preeclampsia (OR, 1.59; 95% CI, 1.06–2.37; $P = .024$) (Table 4). No interactions were found between snoring and prepregnancy BMI for gestational hypertension or preeclampsia. Similarly, no interactions were found between snoring and weight gain in excess of IOM recommendations.

Blood glucose levels at the 24- to 26-week gestation 1-hour oral glucose tolerance test using a 50-g load were higher in snorers compared to nonsnorers (124.0 vs 117.2 mg/dL, $P < .001$), as was the proportion of women with abnormal glucose levels, defined as ≥140 mg/dL (30.2% vs 22.1%, $P = .003$). Glucose levels were not compared between women with and without pregnancy-onset snoring, as glucose was assessed in the second trimester. Neither pregnancy-onset nor chronic snoring was found to be associated with gestational diabetes in a multivariate model; however prepregnancy BMI and maternal age were associated (Table 5).

Figure 2 graphically depicts the OR of prepregnancy obesity (BMI ≥30) and/or snoring in separate models for gestational hypertension, preeclampsia, and gestational diabetes after adjusting for covariates that were shown in Tables 3-5 to be associated with the outcome of interest. For illustrative purposes data are shown as snorers (pregnancy-onset and chronic snoring) vs nonsnorers. Four groups are represented: lean nonsnorer (BMI < 25 kg/m^2, the reference group, n = 689); lean snorer (n = 195); obese nonsnorer (n = 189); and obese snorer (n = 217). Compared to lean nonsnorers, both lean and obese snorers had sig-

TABLE 3
Regression of gestational hypertension against snoring and other covariates

	Explanatory variables				
Variable	**Beta**	**SE**	***P* value**	**Adjusted OR**	**95% CI**
Pregnancy-onset snoring	0.859	0.238	< .001	2.36	1.48–3.77
Chronic snoring	0.542	0.393	.168	1.72	0.80–3.71
Prepregnancy BMI	0.003	0.016	.869	1.00	0.97–1.04
Excessive weight gain	0.985	0.227	< .001	2.68	1.72–4.18
Maternal age	0.000	0.000	.898	1.00	1.00–1.00
Gravida	−0.255	0.083	.002	0.78	0.66–0.91
African American	0.413	0.291	.155	1.51	0.86–267
Smoker	0.211	0.311	.498	1.24	0.67–2.27
Education level ≤high school	0.258	0.243	.289	1.29	0.80–2.08
History of GHTN/pre-E	1.135	0.369	.002	3.11	1.51–6.41
Family history of GHTN/pre-E	0.91	1.151	.607	1.81	0.19–17.23

BMI, body mass index; *CI*, confidence interval; *GHTN*, gestational hypertension; *OR*, odds ratio; *pre-E*, preeclampsia.

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TABLE 4
Regression of preeclampsia against snoring and other covariates

	Explanatory variables				
Variable	**Beta**	**SE**	***P* value**	**Adjusted OR**	**95% CI**
Pregnancy-onset snoring	0.462	0.205	.024	1.59	1.06–2.37
Chronic snoring	0.109	0.333	.745	1.12	0.58–2.14
Prepregnancy BMI	0.011	0.013	.391	1.01	0.99–1.04
Excessive weight gain	0.398	0.185	.032	1.49	1.04–2.14
Maternal age	0.000	0.000	.888	1.00	1.00–1.00
Gravida	−0.375	0.074	< .001	0.69	0.59–0.80
African American	0.578	0.242	.017	1.78	1.11–2.86
Smoker	0.541	0.251	.031	1.72	1.05–2.81
Education level ≤high school	−0.030	0.213	.890	0.97	0.64–1.48
History of GHTN/pre-E	1.524	0.304	< .001	4.59	2.53–8.34
Family history of GHTN/pre-E	−0.178	1.127	.874	0.84	0.09–7.62
Chronic hypertension	1.686	0.303	< .001	5.40	2.98–9.78
Gestational diabetes	0.549	0.219	.012	1.73	1.13–2.67

BMI, body mass index; *CI*, confidence interval; *GHTN*, gestational hypertension; *OR*, odds ratio; *pre-E*, preeclampsia.

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TABLE 5
Regression of gestational diabetes against snoring and other covariates

	Explanatory variables				
Variable	**Beta**	**SE**	***P* value**	**Adjusted OR**	**95% CI**
Pregnancy-onset snoring	0.004	0.167	.982	1.00	0.72–1.39
Chronic snoring	−0.100	0.253	.693	0.91	0.55–1.49
Prepregnancy BMI	0.076	0.010	< .001	1.08	1.06–1.10
Excessive weight gain	−0.241	0.149	.107	0.79	0.59–1.05
Maternal age	0.000	0.000	.847	1.00	1.00–1.00
Gravida	0.019	0.041	.651	1.02	0.94–1.11
African American	−0.142	0.209	.497	0.87	0.58–1.31
Smoker	−0.067	0.230	.769	0.94	0.60–1.47
Education level ≤high school	−0.397	0.175	.023	0.67	0.48–0.95

BMI, body mass index; *CI*, confidence interval; *OR*, odds ratio.

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nificantly increased ORs for gestational hypertension (lean snorers OR, 2.82; 95% CI, 1.42–5.59; $P = .003$; and obese snorers OR, 2.39; 95% CI, 1.22–4.71; $P = .012$). Obese nonsnorers were not at increased risk of gestational hypertension (OR, 1.74; 95% CI, 0.81–3.5; $P = .15$) (Figure 2, A).

Compared to lean nonsnorers, only obese snorers had increased risk for preeclampsia (OR, 1.58; 95% CI, 1.01–2.78; $P = .05$) (Figure 2, B). Conversely, only obese women, regardless of snoring status, had increased risk for gestational diabetes (OR, 2.31; 95% CI, 1.01–5.36; $P = .05$ for obese nonsnorers; OR, 4.12; 95% CI, 1.78–9.52; $P = .001$ for obese snorers (Figure 2, C).

If snoring plays a causative role in hypertension, then the PAR% suggests that 15.0% of gestational hypertension and 14.4% of preeclampsia in this population could be ameliorated by elimination of snoring. Similarly, 18.7% of gestational hypertension and 11.6% of preeclampsia could be ameliorated by elimination of pregnancy-onset snoring.

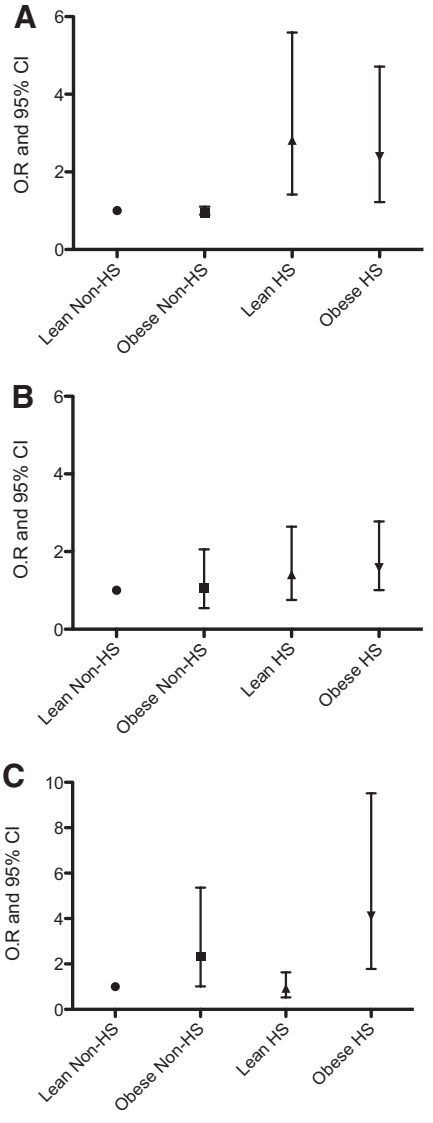
A total of 1.2% of women reported witnessed apneas. Snorers (chronic or pregnancy-onset) were more likely than nonsnorers to endorse this (3.0% vs 0.4%, respectively; $P < .001$). Women with gestational hypertension, preeclampsia, or gestational diabetes were no more likely to report apnea than women without these conditions. However, the total number of women who reported apnea was small, precluding use of regression models.

Comment

This is the first large, prospective study to demonstrate that pregnancy-onset snoring confers significant risk to maternal cardiovascular health. These novel findings strongly implicate a role not only for snoring in general but, more specifically, for pregnancy-onset snoring in both gestational hypertension and preeclampsia. Furthermore, the PAR% suggests that if snoring plays a causal role in maternal hypertension, approximately 12-19% of hypertensive disorders during pregnancy might be ameliorated through treatment of snoring and any associated SDB. In contrast, the data did not suggest any independent role for snoring in gestational diabetes.

Notably, weight gain in excess of IOM recommendations, but not prepregnancy BMI, was found to play an independent role in gestational hypertension. Both prepregnancy BMI and excessive weight gain were independent predictors of preeclampsia. Although excessive weight gain is a known risk factor for postpartum weight retention,[24] this is the first study to show its independent relationship to cardiovascular outcomes. This novel finding could have important implications for clinical care.

FIGURE 2
Adjusted OR and 95% confidence intervals of maternal morbidity by obesity and snoring status



OR for **A,** gestational hypertension; **B,** preeclampsia; and **C,** gestational diabetes by obesity and snoring status. **A,** OR adjusted for weight gain in excess of Institute of Medicine (IOM) recommendations, gravidity, and history of gestational hypertension/preeclampsia. **B,** OR adjusted for weight gain in excess of IOM recommendations, gravidity, race, history of gestational hypertension/preeclampsia, smoking, chronic hypertension, and gestational diabetes. **C,** OR adjusted for prepregnancy body mass index and education level.

CI, confidence interval; *HS*, habitual snoring; *OR*, odds ratio.

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Our findings support and extend earlier observations that the frequency of snoring increases throughout pregnancy, peaks in the third trimester,[4] and is a risk for hypertension.[14,15,22,25,26] However, none of the previous studies investigated the impact of incident habitual snoring on maternal outcomes. Previous studies suggest that 14-23% of pregnant women habitually snore, compared to 4% of nonpregnant women,[5,22] although more recent estimates suggest a considerably higher proportion[6,15] particularly in preeclampsia.[6] Potential explanations of the lower frequencies in earlier studies are that only women attending low-risk clinics who had vaginal deliveries were included[5] and obesity was relatively infrequent in some populations.[5,22]

Intriguing preliminary data suggest that new snoring during pregnancy is associated with increased erythropoiesis and consequently increased levels of nucleated red blood cells in the umbilical cord.[27] Erythropoiesis occurs during periods of hypoxia, and conditions such as uterine growth restriction and maternal hypertension are associated with elevated counts.[28] These findings in combination with our own implicate pregnancy-onset snoring as a particular concern.

Contrary to recent reports[15,29,30] we did not find that snoring is associated with gestational diabetes. This discrepancy may be explained in part by different methodologies including recruitment of postpartum women,[15] few women with the variable of interest,[29,30] and the lack of information about prepregnancy BMI.[15] Nonetheless, the role of sleep in glucose control during pregnancy merits further investigation.

Although the pathogenesis of preeclampsia is not completely understood, the biological pathways include endothelial dysfunction, oxidative stress, and inflammation, with obesity being a major risk factor. The pathogenic process likely originates in the placenta during early pregnancy with abnormal implantation and vasculature development, leading to oxidative stress and inflammation with subsequent release of antiangiogenic factors and widespread endothelial dysfunction.[31] Of note, the mechanisms of sleep disruption that affect cardiovascular morbidity in nonpregnant individuals are remarkably similar to the biological pathways for preeclampsia, with strong evidence for oxidative stress, inflammation, sympathetic nervous systemic activation, endothelial dysfunction, dyslipidemia, and obesity as major factors in the pathophysiology of cardiovascular morbidity in SDB.[32] These shared mechanistic pathways have been reviewed recently.[33]

Considering these overlapping risk factors, the finding that pregnancy-onset, but not chronic, snoring was associated with gestational hypertension and preeclampsia may be surprising. Sleep disruption and the consequent inflammatory cascade in early pregnancy may interfere with normal placental implantation,[34] although this may not completely explain our findings since the majority of women with pregnancy-onset snoring started in their second or third trimesters. The possibility remains, however, that pregnancy-onset snoring could exacerbate underlying inflammatory processes and enhance underlying cardiovascular dysfunction. Another possibility is that fluid shifts[35] or inflammation promotes the appearance of SDB. However, preliminary data show that treatment of SDB during pregnancy may improve blood pressure,[36,37] suggesting that SDB is more likely to contribute to hypertensive disease, rather than result from it or from a third process that causes both hypertension and SDB.

Key strengths of the present study include the largest sample size to date, prospective design, high response rate, adjustment for other known risk factors for gestational hypertension/preeclampsia (particularly an individual and family history of these conditions), and a population pool representative of other major medical centers. The University of Michigan Health System is the larger of only 2 in Washtenaw County that provides maternity services. Therefore, selection bias of a tertiary referral center should be minimal.

Use of symptom-based screening not yet validated against PSG in pregnant women could be a limitation. However, the major goal was to validate the utility of snoring directly as a predictor of maternal outcomes. Self-report of snoring is strongly and reliably associated with the PSG-derived apnea/hypopnea index[8,20] and our own data confirm this in pregnancy.[38] The present large-sample focus on snoring is also a strength of the study design as queries about snoring can be readily adopted in clinical practice for little expense. However, elucidation of mechanisms that underlie any association between SDB and pregnancy outcomes require investigation in PSG studies that allow assessment of whether respiratory effort, airflow limitation, sleep fragmentation, or gas exchange abnormalities best predict adverse outcomes and treatment response.

It is possible that some recall bias occurred with regard to snoring duration. Although information was obtained prospectively, women may have been less aware of their prepregnancy snoring. A further limitation is the temporal relationship between snoring onset and time of a diagnosis of gestational hypertension, preeclampsia, or gestational diabetes. This study cannot prove the direction of this relationship but clearly suggests an independent association.

In conclusion, pregnancy-onset, rather than chronic, snoring is independently associated with gestational hypertension and preeclampsia but not gestational diabetes. Rather than a multi-item composite SDB screen, 2 simple questions about snoring and the timing of its appearance could be an effective strategy in busy clinical settings to assist in identification of pregnant women at high risk for hypertensive disorders. These findings reinforce the need for a randomized controlled trial to investigate the impact of treatment interventions on maternal hypertension. ■

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APPENDIX
Supplementary Figure Pregnancy sleep questionnaire

PREGNANCY SLEEP QUESTIONNAIRE

<u>These questions refer to a typical week just before BEFORE your pregnancy:</u>

Before you became pregnant did you snore?
O Never O Rarely *(1-2 times/month)* O Occasionally *(1-2 times/week)* O Often *(3-4 times/week)* O Almost Always *(Almost every day)*

Before you became pregnant did your partner complain about your snoring?
O Never O Rarely O Occasionally O Often O Almost Always

If you snored before you became pregnant, how loud was the snoring?
O Very Quiet O Quiet O Variable O Loud O Very Loud

Before you became pregnant did you stop breathing or gasp for air?
O Never O Rarely O Occasionally O Often O Almost Always

Before you became pregnant did your partner complain that you stopped breathing or gasped for air?
O Never O Rarely O Occasionally O Often O Almost Always

Before you became pregnant, how often did you have a problem with excessive sleepiness during the daytime?
O Never O Rarely O Occasionally O Often O Almost Always

<u>These questions refer to the past week, during your CURRENT pregnancy:</u>

Have you snored during your pregnancy?
O Never O Rarely *(1-2 times/month)* O Occasionally *(1-2 times/week)* O Often *(3-4 times/week)* O Almost Always *(Almost every day)*

Does your partner complain about your snoring?
O Never O Rarely O Occasionally O Often O Almost Always

How loud is the snoring?
O Very Quiet O Quiet O Variable O Loud O Very Loud

If you have snored during this pregnancy, when did the snoring begin?
O Already snored before pregnancy O Snoring started in 1st trimester (wks 1-12)
O Snoring started in 2nd trimester (wks 13-24) O Snoring started in 3rd trimester (wks 25+)

If you already snored before you became pregnant, is the snoring during your current pregnancy:
O Much less than before O Less than before O About the same O Worse than before
O Much worse than before

During this pregnancy have you stopped breathing or gasped for air?
O Never O Rarely O Occasionally O Often O Almost Always

During this pregnancy has your partner complained that you stopped breathing or gasped for air?
O Never O Rarely O Occasionally O Often O Almost Always

How often in the past week have you had a problem with excessive sleepiness during the daytime?
O Never O Rarely O Occasionally O Often O Almost Always

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