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SCIENTIFIC INVESTIGATIONS

High prevalence of obstructive sleep apnea in pregnant women with class III obesity: a prospective cohort study

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Study Objectives: To determine the prevalence of obstructive sleep apnea (OSA) in a cohort of women with class III obesity, and a comparator lean group, in the second and third trimesters of pregnancy. Secondary objectives were to compare characteristics of women with obesity with and without OSA and to assess factors that were predictive of OSA.

Methods: We performed a prospective cohort study involving 33 women with class III obesity (mean body mass index 43.5 ± 3.9 kg/m^2) and 39 lean women (body mass index 22.0 ± 1.7 kg/m^2) with singleton pregnancies. Participants completed 2 level 3 sleep studies between 12–22 weeks and 32–38 weeks gestation. OSA was defined as a respiratory event index ≥ 5 events/h (≥ 3% desaturation criteria). Levels of interleukin-6, glucose, and C-peptide were quantified in maternal blood. Logistic regression analysis was performed to determine predictors of OSA.

Results: OSA was identified in 12 (37.5%) and 14 (50.0%) women with obesity and in 1 (2.6%) and 3 (9.1%) lean women in the second and third trimesters, respectively. Women with obesity with OSA were older than those with no OSA but otherwise had similar characteristics. In unadjusted analysis of women with obesity, increased age, body mass index, homeostatic model assessment of insulin resistance, and history of nonsmoking were associated with increased odds of OSA. In multivariable analysis, only increased age remained significantly associated with OSA.

Conclusions: OSA is highly prevalent in pregnant women with class III obesity. Further research is required to establish effective management strategies for the growing number of women in this high-risk group.

Keywords: obstructive sleep apnea, pregnancy, obesity

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BRIEF SUMMARY

Current Knowledge/Study Rationale: Obstructive sleep apnea affects approximately 40% of women with obesity in the third trimester of pregnancy and is associated with an increased risk of adverse pregnancy outcomes. The prevalence of obstructive sleep apnea in pregnant women with class III obesity (body mass index ≥ 40 kg/m^2 in early pregnancy) has not been previously described in a longitudinal cohort.

Study Impact: This study highlights the high prevalence of obstructive sleep apnea in women with class III obesity and the potential challenges of identifying patients who require investigation for obstructive sleep apnea among those in this high-risk group. Further research into the optimal methods to investigate and manage obstructive sleep apnea in pregnant women with severe obesity is urgently required.

INTRODUCTION

Obstructive sleep apnea (OSA) is characterized by recurrent episodes of partial or complete upper airway collapse during sleep accompanied by oxygen desaturation and/or arousal from sleep.[1] OSA has traditionally been reported as less common among women of reproductive age compared to postmenopausal women and men.[2–5] However, the anatomical and physiological changes that accompany pregnancy can precipitate the onset of this condition or worsen the severity of pre-existing OSA.[3,6,7] Prospective studies have shown that OSA during pregnancy is associated with an increased risk of adverse maternal outcomes, in particular gestational diabetes and gestational hypertensive disorders.[8–11] The long-term impact of OSA on the offspring has yet to be established. Screening for OSA during pregnancy is challenging, and the benefits of treatment in this population are uncertain. Increasing age, higher body mass index (BMI), and frequent snoring were identified as highly predictive for OSA in the largest prospective study of OSA in pregnancy.[12] There are currently no evidence-based guidelines for the investigation and management of OSA during pregnancy.

Obesity is the most important modifiable risk factor for OSA.[1] In nonpregnant adults with obesity, the prevalence of OSA is upward of 40% in men aged ≥30 years and women aged ≥50 years.[2] Fifty-seven percent of adults with OSA had class III obesity (BMI ≥40 kg/m^2) compared to 34% of the background population in a recent population-based study of people with obesity.[13] The burden of OSA in pregnancy is therefore set

to increase due to the upsurge in the prevalence of maternal obesity.[14–16] A limited number of studies have objectively assessed the prevalence of OSA during pregnancy. In the general obstetric population, prevalence rates of 3.6%–8.4% in early pregnancy and 8.3%–19.7% in mid- to late pregnancy have been reported.[11,17] However, prevalence rates as high as 40%–43% in mid- to late pregnancy have been identified in studies of pregnant women with obesity.[17,18]

In this study, we aimed to determine the prevalence of OSA in a cohort of pregnant women with class III obesity, and in a comparator lean group, in the second and third trimesters. In secondary analyses, we compared characteristics of women with obesity who did and did not have OSA and assessed factors that were predictive of OSA. This is the first longitudinal account of OSA prevalence in pregnant women with class III obesity, a group whose prevalence is set to continue increasing rapidly.

METHODS

Participants

We performed a prospective cohort study involving 35 women with obesity and 40 lean pregnant women in Edinburgh, UK. Women with obesity were recruited from a metabolic antenatal clinic (Simpson Centre for Reproductive Health, Royal Infirmary of Edinburgh) that provides antenatal care for women with a booking BMI ≥40 kg/m^2. Lean women were recruited from community antenatal clinics in Edinburgh following the dating of pregnancy scan. Eligible women had a singleton pregnancy, booking BMI in the normal (18.5–24.9 kg/m^2) or class III obese (≥40 kg/m^2) range, were of White European ethnicity, and were <22 weeks gestation.[19] BMI measurements were obtained at the booking of pregnancy appointment, the initial clinic review that is completed early in the first trimester. Women of non-White European ethnicity were excluded due to differences in metabolic risk described in specific ethnic groups. In particular, lower BMI thresholds to define obesity are recommended in people of Asian ethnicity, the most common minority ethnic group represented in the clinic population. Other exclusion criteria included age < 16 or > 50 years, pregestational diabetes, chronic hypertension, gestational diabetes mellitus diagnosis in the index pregnancy, existing diagnosis of OSA, previous bariatric surgery, use of glucocorticoid treatment in the preceding 3 months, and inability or unwillingness to provide informed consent. Written informed consent was provided by participants. Ethical approval was obtained from the South East Scotland Research Ethics Committee 2.

Study protocol

Demographic details and past medical and obstetric history were obtained from participants at enrollment and confirmed using the electronic medical record. Participants completed 2 sleep studies: the first at 12 to 22 weeks gestation (second trimester) and the second at 32 to 38 weeks gestation (third trimester). Sleep study equipment was self-applied by participants following an education session on the day of the study. At each visit, body weight and neck circumference measurements were obtained, a sleep questionnaire was completed, and fasting blood samples were collected. Following delivery, clinical outcome data were collected from the maternal and offspring electronic clinical record. Gestational diabetes mellitus, gestational hypertension, and preeclampsia were defined in accordance with national guidelines.[20,21] Birthweight centiles were calculated using GROW Centile Calculator, UK v2.1.6.1 (GROW International, Perinatal Institute, Birmingham, UK). A full list of clinical outcome definitions is shown in **Table S1** in the supplemental material. Levels of interleukin-6 (IL-6; Human IL-6 High Sensitivity ELISA, Invitrogen Renfrew, UK), glucose (glucose oxidase assay, Alpha Laboratories Ltd. Eastleigh, UK) and C-peptide (Human C-Peptide Immunoassay Quantikine ELISA, R&D Systems Minneapolis, Minnesota) were quantified in maternal serum/plasma. Glucose and C-peptide values were used to calculate the homeostatic model assessment of insulin resistance (HOMA-IR), a metric of insulin resistance.[22]

Home-based level 3 sleep studies were performed using the CID-LXe device (Cidelec, Angers, France).[23] Channels recorded included nasal airflow via nasal pressure cannula, respiratory effort via respiratory inductance plethysmography bands, pulse oximetry using a transmittance pulse oximeter worn on the index finger, actimetry via a wrist-worn sensor, snoring via microphone, and body position via a 3-axis linear accelerometer. Snoring and body position signals were detected by sensors within the PneaVoX sensor, which was applied to the suprasternal area. Sleep studies were scored using Cidelec analysis software based on Version 2.4 of the American Academy of Sleep Medicine scoring recommendations for home sleep apnea testing.[24] Apnea and hypopnea events were detected manually. Apnea was defined as ≥90% reduction in airflow signal from pre-event baseline for ≥10 seconds. Hypopnea was defined as ≥30% reduction in airflow signal from pre-event baseline, lasting ≥10 seconds and associated with a ≥3% oxygen desaturation. Oxygen desaturation events, defined as a ≥3% reduction in oxygen saturation for a minimum duration of 2 seconds, were detected by the analysis software. The oxygen desaturation index was calculated by the software and indicates the number of ≥3% oxygen desaturation events per hour of monitoring time. OSA was defined as a respiratory event index (REI) ≥5 events/h, indicating the number of apneas and hypopneas (≥3% oxygen desaturation) per hour of monitoring time (referred to herein as REI 3%). OSA cases were categorized as mild (REI 3%, 5–14.9), moderate (REI 3%, 15.0–29.9) or severe (REI 3%, ≥30).[25] To assess the reliability of REI 3% scores, a random subset of studies was selected for rescoring by an experienced registered polysomnographic technologist (interobserver reliability) or by the primary scorer ≥1 year following initial scoring (intraobserver reliability).

Statistical analysis

Our sample size calculation was based on the ability to detect a difference in prevalence of OSA between the obese and lean groups in the third trimester. Based on conservative prevalence estimates of OSA in late pregnancy of 40% in women with obesity and 2% in lean women, third-trimester sleep study data were required from 22 participants in each group to detect this difference with 80% power ($\alpha = 0.05$).[11,17] To account for loss

to follow-up and potential incomplete data collection, we planned to recruit 35 to 40 participants in each group. This calculation was performed using the OpenEpi open-source calculator.[26]

Data are presented as number (%) for categorical data, mean ± standard deviation for normal continuous data, and median (interquartile range) for nonnormal continuous data. Normality of data was assessed using the Shapiro-Wilk test. Differences between groups were assessed using the independent *t* test or Mann-Whitney *U* test for normal and nonnormal distributed continuous variables, respectively, and the chi-squared test for categorical variables. OSA was used as a dichotomous outcome, defined as REI 3% ≥5. Intraclass correlation coefficient and Cohen's kappa coefficient were used to assess intraobserver and interobserver reliability of REI 3% scores. Spearman's rank correlation coefficient was used to assess the correlation between REI 3% and oxygen desaturation index. As the impact of obesity on pregnancy outcomes is well established,[27–29] we compared maternal and offspring outcomes among the women with obesity only to examine the influence of OSA.

We performed unadjusted and multivariable logistic regression to assess the association of variables with OSA. Covariates with $P \leq .20$ in unadjusted analyses were included in the multivariable model. Unadjusted and adjusted odds ratios and 95% confidence intervals were calculated from unadjusted and multivariable tests, respectively. Levels of inflammatory and metabolic markers in maternal blood were compared using the Kruskal-Wallis *H* test and Dunn's multiple comparisons test. Statistical significance was considered at $P < .05$. Analysis was performed using SPSS v24 (IBM, Armonk, NY) and figures were prepared using GraphPad Prism v9.0.0 (GraphPad Software, San Diego, CA).

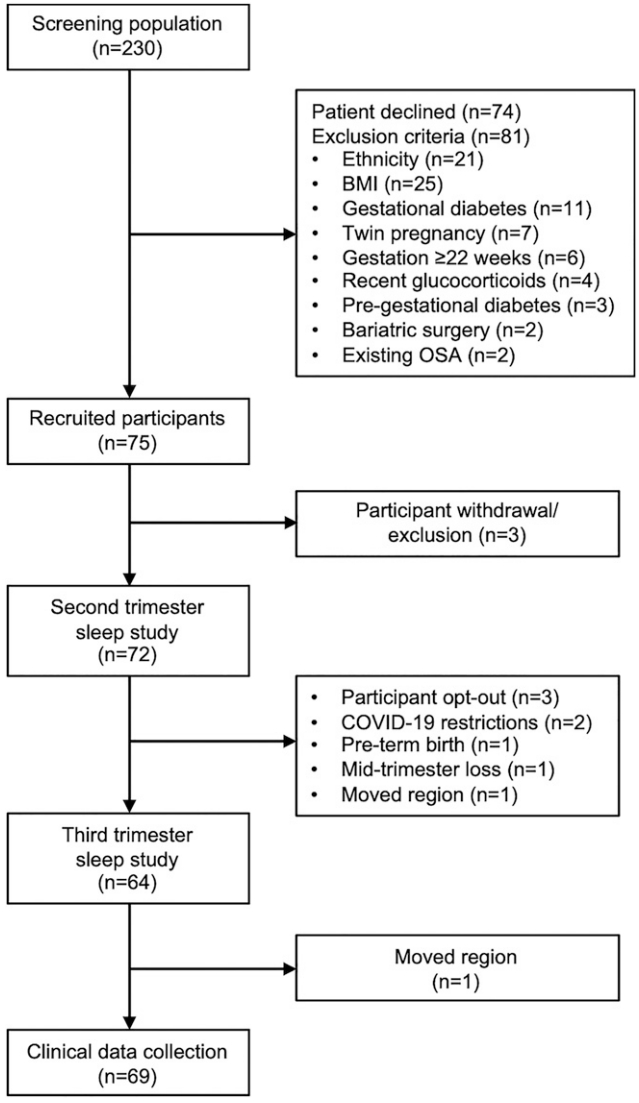
RESULTS

From a screening population of 230 women, 35 women with obesity and 40 lean women were enrolled between July 2018 and December 2019 (**Figure 1**). Three participants were withdrawn from the study prior to completion of the first sleep study due to previously unrecognized exclusion criteria (n = 2) and participant opt-out (n = 1). The baseline characteristics of the remaining 33 obese and 39 lean participants are shown in **Table 1**. Compared to lean women, women with obesity had higher systolic and diastolic blood pressure at the booking of pregnancy appointment, lived in more deprived areas as defined by the Scottish Index of Multiple Deprivation (SIMD), and were less likely to have never smoked ($P < .05$).[30] There was a small but significant difference between groups in gestation at the first sleep study.

Seventy-two second-trimester sleep studies were completed at mean 16.7 ± 2.0 weeks gestation. REI 3% results were generated for 71 participants (32 obese and 39 lean). In the third trimester, 64 sleep studies were performed at a mean of 34.8 ± 1.3 weeks gestation. REI 3% results were generated for 61 participants (28 obese and 33 lean). Of the 4 invalid studies conducted across both time points, 3 did not record any pulse oximetry signal and, in 1 case, the participant reported no sleep while wearing the recording equipment. Eight participants did not complete a third-trimester sleep study (detailed in **Figure 1**). There were no significant differences in the baseline characteristics of women who did and did not complete the third-trimester sleep study. Analysis of 15 sleep studies showed excellent interscorer and intrascorer reliability, respectively (with the exception of central hypopneas relating to the very small number of these events) (**Table S2** in the supplemental material). There was categorical agreement for the diagnosis of OSA in all studies examined for interobserver and intraobserver reliability (Cohen's $\kappa = 1.0$, $P < .001$ in both instances).

Median (interquartile range) REI 3% scores in the second trimester were 0.8 (0.5–1.3) in lean women and 4.0 (2.4–8.6) in women with obesity ($P < .001$). In the third trimester, median REI 3% was 1.5 (0.5–3.0) in the lean group and 5.3 (3.2–12.1)

Figure 1—Study flow chart.



BMI = body mass index, OSA = obstructive sleep apnea.

Table 1—Baseline characteristics.

	Lean (n = 39)	Obese (n = 33)	*P* Value
Age, y	33.3 ± 4.3	32.8 ± 4.5	.62
Parity, n (%)			
0	22 (56.4)	18 (54.5)	.46
1	15 (38.5)	10 (30.3)	
≥2	2 (5.1)	5 (15.2)	
Gestation, wks	16.3 ± 1.8	17.3 ± 1.9	.02
Systolic blood pressure, mm Hg	103.2 ± 8.2	118.2 ± 11.1	<.001
Diastolic blood pressure, mm Hg	62.1 ± 4.6	75.2 ± 8.6	<.001
Booking weight, kg	61.0 ± 6.8	120.4 ± 15.0	<.001
Booking BMI, kg/m^2	22.0 ± 1.7	43.5 ± 3.9	<.001
Neck circumference, cm, median (IQR)	32.6 (31.6–33.6)	41.0 (39.5–42.7)	<.001
Smoking status, n (%)			
Never	35 (89.7)	21 (63.6)	.03
Former	4 (10.3)	11 (33.3)	
Current	0	1 (3.0)	
SIMD quintile, n (%)			
1 (most deprived)	0	2 (6.1)	.01
2	4 (10.3)	10 (30.3)	
3	2 (5.1)	4 (12.1)	
4	4 (10.3)	6 (18.2)	
5 (least deprived)	29 (74.4)	11 (33.3)	

Blood pressure measured at the booking of pregnancy appointment. Data are means ± standard deviation unless otherwise stated. Continuous variables compared using independent *t* test and Mann-Whitney *U* test for normal and nonnormally distributed data, respectively. Categorical variables compared using chi-square. Percentages may not total 100 because of rounding. BMI = body mass index, IQR = interquartile range, SIMD = Scottish Index of Multiple Deprivation.[30]

in the obese group ($P < .001$). Overall, OSA was identified at one or both time points in 3 of 39 (7.7%) lean women and 17 of 33 (51.5%) women with obesity. The prevalence and severity of OSA in both groups based on trimester is shown in **Figure 2**. All cases of OSA in the lean group and the majority of cases in the obese group were of mild severity. In the third trimester, 4 of 14 (28.6%) OSA cases in the obese group were of moderate severity. This included the 1 participant with severe OSA in the second trimester. Of the 14 women with obesity with OSA in the third trimester, 9 had evidence of OSA in the second- and third-trimester sleep studies (persistent OSA), while 5 had new-onset OSA in the third trimester only (**Figure S1** in the supplemental material). In women with obesity, oxygen desaturation index scores correlated strongly with REI 3% in the second (Spearman's $\rho = 0.95$, $P < .001$) and third (Spearman's $\rho = 0.95$, $P < .001$) trimesters. Similar results were evident in the entire study cohort (Spearman's $\rho = 0.92$ and 0.97 in the second and third trimesters, respectively).

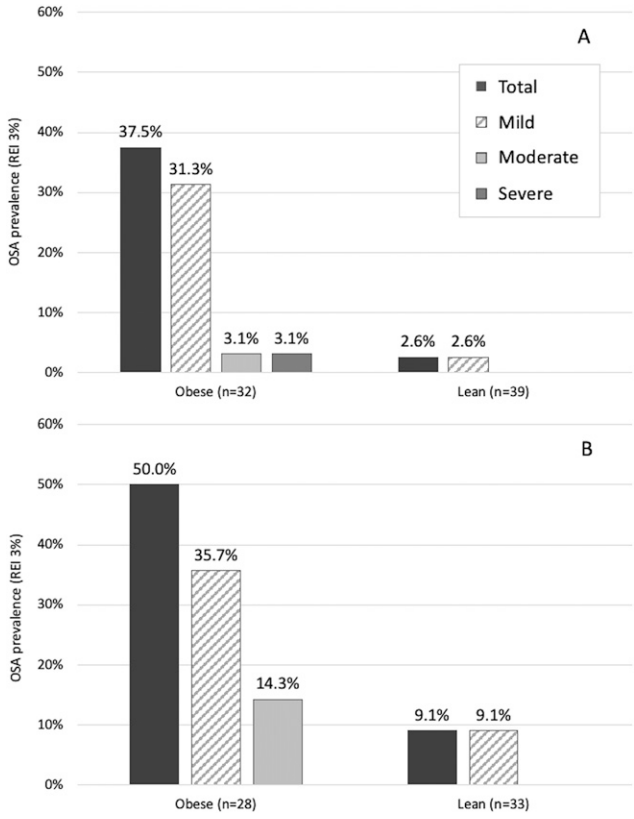
The characteristics of women with obesity who did and did not have evidence of OSA are shown in **Table 2**. Women with obesity with OSA were older than those with no OSA but otherwise had similar characteristics. In unadjusted analyses of the obese participants, increased age, BMI (booking and third trimester), HOMA-IR (second trimester), and history of nonsmoking were associated with increased odds of OSA ($P \leq .2$) (**Table 3**). As first- and third-trimester BMI were highly collinear (Spearman's $\rho = 0.66$), we retained first-trimester BMI in multivariable analysis as it is routinely measured at the booking of pregnancy appointment. In the multivariable analysis, increased age was the only variable that remained significantly associated with increased odds of OSA ($P < .05$).

Maternal and offspring outcomes are shown in **Table 4**. Clinical outcome data were unavailable for 3 lean participants due to midtrimester loss (n = 1) and move to a different region (n = 2). Outcomes were similar in the women with obesity who did and did not have OSA. A numerically greater number of gestational diabetes mellitus cases were diagnosed in the OSA group compared to the no-OSA group (5 vs 1); however, this did not reach statistical significance ($P = .09$). There were no differences in serum IL-6, fasting plasma glucose, or HOMA-IR among women with obesity who did and did not have OSA (**Figure S2**).

DISCUSSION

We identified OSA in 37% and 50% of women with class III obesity in the second and third trimesters, respectively. These results provide a unique account of the prevalence of OSA

Figure 2—Prevalence and severity of OSA in obese and lean participants in the second and third trimesters.



(A) Second trimester. **(B)** Third trimester. OSA categorized as mild (REI 3%, 5–14.9), moderate (REI 3%, 15–29.9), and severe (REI 3% ≥ 30). OSA = obstructive sleep apnea, REI = respiratory event index.

among pregnant women with the most severe class of obesity and add to the growing body of evidence that OSA is common among pregnant women with obesity. It is interesting to consider our results in the context of previous studies that have used the gold standard technique of in-lab polysomnography (PSG) to diagnose OSA in women with obesity. Ghesquière et al[18] evaluated 67 pregnant women with BMI ≥35 kg/m^2 between 24 to 32 weeks gestation and identified OSA in 43.4% of participants. Approximately one-fifth of participants in this study had a history of chronic hypertension or pregestational diabetes and 9% had both. Pien et al[17] identified OSA in 40% of 50 women with obesity in the third trimester (33–34 weeks gestation). Half of these participants had class I obesity, and half class II-III obesity. In this study, participants also completed in-lab PSG at 8–14 weeks gestation; however, results specific to the obese subgroup at this time point were not reported. The higher prevalence of OSA identified in our participants with obesity relative to these studies is biologically plausible relating to the more severe obesity characterized in our cohort. In contrast, Maasilta et al[31] performed in-lab PSG at 2 time points in participants with BMI > 30 kg/m^2 and identified OSA in no participants with obesity in the second trimester and 1 participant with obesity in the third trimester. However, these results are limited by a small sample size (11 and 8 participants at each respective time point).

Home-based level 3 devices have also been used previously to examine OSA prevalence during pregnancy. Dominguez et al[32] reported a prevalence of 24% between 24 and 35 weeks gestation in 80 women with BMI ≥40 kg/m^2, one-third of whom had a background of chronic hypertension. These BMI measurements were performed at the time of study enrollment (mean 30 weeks gestation); therefore, a proportion of participants can be assumed to have had a lower obesity class earlier in pregnancy. Facco et al[33] reported OSA prevalence of 30% in early to mid-pregnancy (6–20 weeks gestation) and 47% in the third trimester. This study involved 128 women with 1 or more risk factors for OSA: 62% of participants were obese and 54% had more than 1 risk factor for OSA. A recent study involving 63 mostly obese pregnant women (mean BMI = 40.4 kg/m^2) who underwent home sleep apnea testing at various gestations in pregnancy identified OSA in 60.3% of participants.[34] Chronic hypertension was present in 31.8% of the women and pregestational diabetes in 12.7%. The largest study of OSA prevalence in pregnancy included more than 700 women with obesity.[11] A prevalence of 12.9% was reported among women with obesity in early pregnancy (6–15 weeks gestation) and 23.4% in mid-pregnancy (22–31 weeks gestation).[11] While these time points are not directly comparable to this study, the lower estimates of OSA prevalence are likely to reflect the differing BMI distribution of the population with obesity, more than half of whom had class I obesity (BMI = 30–34.9 kg/m^2).[12] A considerably lower prevalence estimate of 15.4% was reported by Louis et al[35] in a study of 175 pregnant women with obesity. The cohort appeared at high risk, including a history of chronic hypertension in 37% of participants and an average BMI of 38 kg/m^2 and 46 kg/m^2 in the participants with no OSA and OSA, respectively. The reason for this discrepant result is unclear, particularly given that the level 3 device used correlated well with PSG results in a subset of participants. Studies were performed at an average of 21 weeks gestation; however, this varied widely and may contribute to the seemingly outlying result.

In this study, women with obesity with OSA were on average older than women with obesity without OSA. We did not identify any other significant differences in the characteristics of these groups. Increasing age was identified as the only variable significantly associated with increased odds of OSA in multivariable regression analysis involving the obese participants. Age has consistently been shown to predict OSA during pregnancy, similar to the nonpregnant population.[12,17,18,36] We did not identify higher BMI as a predictor of OSA within the obese group. The restricted range of obese BMI based on the inclusion of women with class III obesity only is likely to contribute to this finding. Of note, BMI was significantly higher in pregnant women with OSA compared to those with no OSA in a cohort of 67 women with class II and III obesity (43.8 ± 6.2 kg/m^2 vs 41.2 ± 6.0 kg/m^2) and in a cohort of 175 women with obesity (48.3 ± 11.8 kg/m^2 vs 39.1 ± 6.2 kg/m^2).[18,35] Chronic hypertension is an established risk factor for OSA during pregnancy.[12,18,36] We chose to exclude women with chronic

Table 2—Characteristics of obese women with and without OSA.

	No OSA (n = 16)	OSA (n = 17)	*P* Value
Age, y	30.8 ± 5.0	34.7 ± 3.0	.01
Nulliparous, n (%)	9 (56.3)	9 (52.9)	.85
Smoking status, n (%)			
Never smoker	8 (50.0)	13 (76.5)	.11
Ex- or current smoker	8 (50.0)	4 (23.5)	
SIMD quintile, n (%)			
1	1 (6.3)	1 (5.9)	.83
2	5 (31.3)	5 (29.4)	
3	2 (12.5)	2 (11.8)	
4	4 (25.0)	2 (11.8)	
5	4 (25.0)	7 (41.2)	
Booking blood pressure, mm Hg*			
Systolic	114.9 ± 10.6	121.1 ± 11.0	.12
Diastolic	73.2 ± 9.3	77.0 ± 7.7	.22
BMI, kg/m^2			
Booking	42.5 ± 1.9	44.5 ± 5.0	.16
Second trimester	42.4 ± 2.0	44.2 ± 5.5	.23
Third trimester**	43.5 ± 2.6	46.2 ± 5.8	.15
Gestational weight gain, kg**	4.0 ± 6.6	3.9 ± 6.3	.97
Neck circumference, cm			
Second trimester, median (IQR)	40.8 (39.7–42.2)	42.0 (39.0–42.8)	.66
Third trimester, median (IQR)‡	40.7 (39.0–41.5)	41.0 (39.3–43.1)	.68
Frequent snoring†			
Second trimester, n (%)	8 (53.3)	10 (62.5)	.61
Third trimester, n (%)	6 (50)	11 (73.3)	.21
Serum IL-6, pg/mL			
Second trimester, median (IQR)	1.4 (1.2–1.7)	1.7 (1.1–2.2)	.36
Third trimester, median (IQR)	1.7 (1.3–2.5)	1.6 (1.1–1.8)	.25
Fasting plasma glucose, mmol/L			
Second trimester, median (IQR)	5.2 (4.8–5.3)	5.2 (4.8–5.8)	.64
Third trimester, median (IQR)	4.9 (4.6–5.3)	5.3 (4.9–5.6)	.11
HOMA-IR			
Second trimester, median (IQR)	1.5 (1.3–1.9)	1.9 (1.5–2.1)	.13
Third trimester, median (IQR)	2.5 (1.9–3.3)	2.5 (2.4–3.3)	.59

Data are means ± SD unless otherwise stated. Continuous variables compared using independent *t* test and Mann-Whitney *U* test for normal and nonnormally distributed data, respectively. Categorical variables compared using chi-square. Gestational weight gain defined as change in weight from booking to third trimester. Percentages may not total 100 because of rounding. *Blood pressure data missing from 1 participant in the obese, no OSA group. **Third-trimester weight/BMI data and gestational weight change, missing for n = 4 (no OSA) and n = 1 (OSA). †Frequent snoring data missing for n = 1 from each group in second trimester and n = 4 (no OSA) and n = 2 (OSA) in third trimester. ‡Third-trimester neck circumference data missing for n = 3 (no OSA) and n = 1 (OSA). BMI = body mass index, HOMA-IR = Homeostatic Model Assessment of Insulin Resistance, IL-6 = interleukin-6, IQR = interquartile range, OSA = obstructive sleep apnea, SD = standard deviation, SIMD = Scottish Index of Multiple Deprivation.[30]

hypertension as this allowed us to gain a greater insight into the relationship between OSA and class III obesity in the absence of this confounding factor. This feature of our study design is unique when compared to previous reports of OSA prevalence outlined above. The same rationale was applied for the exclusion of type 2 diabetes and multiple pregnancy, both of which have been implicated as possible risk factors for OSA.[33] An additional benefit of these exclusion criteria was that it allowed us to examine the frequency of gestational diabetes and hypertensive disorders in our cohort, outcomes that are associated with OSA during pregnancy.[8–11] Finally, self-reported frequent snoring has also been identified as an independent predictor of OSA in pregnant women.[12,36] Our analysis of this feature was limited by several participants indicating "don't

Table 3—Predictors of OSA in pregnant women with class III obesity.

	Unadjusted Odds Ratio (95% CI)	*P* Value	Adjusted Odds Ratio (95% CI)	*P* Value
Age, 5 y	3.23 (1.18–8.86)	.02	4.02 (1.11–14.54)	.03
Parity				
Nulliparous	Reference	—	—	—
Parous	1.14 (0.29–4.51)	.85	—	—
SIMD quintile				
1	Reference	—	—	—
2	1.00 (0.05–20.83)	1.00	—	—
3	1.00 (0.03–29.81)	1.00	—	—
4	0.50 (0.02–12.90)	.68	—	—
5	1.75 (0.08–36.29)	.72	—	—
Smoking status				
Ex- or current smoker	Reference	—	—	—
Never smoker	3.25 (0.73–14.40)	.12	3.80 (0.57–25.35)	.17
BMI, kg/m^2				
Booking	1.18 (0.93–1.49)	.18	1.33 (0.93–1.90)	.13
Second trimester	1.13 (0.92–1.38)	.24	—	—
Third trimester	1.16 (0.94–1.44)	.17	—	—
Gestational weight gain, kg	1.00 (0.88–1.13)	.96	—	—
Neck circumference, cm				
Second trimester	0.95 (0.72–1.25)	.70	—	—
Third trimester	1.06 (0.77–1.45)	.72	—	—
Frequent snoring, second trimester				
No	Reference	—	—	—
Yes	1.46 (0.35–6.11)	.61	—	—
Frequent snoring, third trimester				
No	Reference	—	—	—
Yes	2.75 (0.55–13.75)	.22	—	—
Biomarkers, second trimester				
IL-6, pg/mL	1.76 (0.64–4.85)	.28	—	—
Glucose, mmol/L	2.55 (0.49–13.39)	.27	—	—
HOMA-IR	3.32 (0.64–17.34)	.16	2.32 (0.34–15.93)	.39
Biomarkers, third trimester				
IL-6, pg/mL	0.96 (0.73–1.26)	.78	—	—
Glucose, mmol/L	2.03 (0.60–6.82)	.25	—	—
HOMA-IR	1.01 (0.53–1.90)	.98	—	—

Odds ratios are derived from unadjusted and multivariable logistic regression analyses. Gestational weight gain was defined as change in weight from booking to third trimester. BMI = body mass index, CI = confidence interval, HOMA-IR = Homeostatic Model Assessment of Insulin Resistance, IL-6 = interleukin 6, OSA = obstructive sleep apnea, SIMD = Scottish Index of Multiple Deprivation.[30]

know" in response to a questionnaire assessment of snoring frequency, in particular in the third trimester.

The similarity in characteristics of women who did and did not have OSA highlights the potential challenges of identifying those with OSA among patients attending a specialist antenatal clinic on account of severe obesity. This is particularly the case for those in whom there is no past medical history of hypertension (> 97% of pregnant women with class III obesity in the National Health Service Lothian region).[37] In light of the considerable prevalence of OSA identified in this cohort along with the lack of characteristics that may differentiate women with OSA during screening with questionnaires or clinical risk stratification tools, it could be argued that routine assessment with an objective OSA screening test should be offered to pregnant women with class III obesity. Despite the inherent limitations of pulse oximetry, our finding of a strong correlation between

Table 4—Maternal and offspring outcomes.

	Lean (n = 36)	Obese, No OSA (n = 16)	Obese OSA (n = 17)	*P* Value
Maternal Outcomes				
Gestational diabetes	0	1 (6.3)	5 (29.4)	.09
Pregnancy-induced hypertension/pre-eclampsia*	0	1 (6.3)	4 (23.5)	.17
Mode of delivery				
Vaginal delivery	26 (72.2)	6 (37.5)	6 (35.3)	.95
Elective cesarean delivery	3 (8.3)	3 (18.8)	4 (23.5)	
Emergency cesarean delivery	7 (19.4)	7 (43.8)	7 (41.2)	
Induction of labor	9 (25.0)	4 (25.0)	7 (41.2)	.33
Delivery complication**	7 (19.4)	6 (37.5)	10 (58.8)	.22
Gestational weight gain, kg, mean ± SD‡	10.8 ± 4.2	4.0 ± 6.6	3.9 ± 6.3	.97
Offspring Outcomes				
Male	25 (69.4)	11 (68.8)	8 (47.1)	.21
Gestation at delivery, wks, median (IQR)	39.9 (39.6–40.7)	39.5 (38.4–41.0)	39.0 (38.5–39.9)	.40
Birthweight, kg, median (IQR)†	3.5 (3.3–3.8)	3.8 (2.9–3.9)	3.6 (3.4–3.9)	.68
Birthweight centile, median (IQR)	44.6 (20.0–74.9)	38.5 (21.1–61.1)	56.2 (38.0–76.8)	.10
Large for gestational age	5 (13.9)	0	2 (11.8)	.17
Small for gestational age	5 (13.9)	3 (20.0)	2 (11.8)	.52
Delivery outcome				
Live birth	35 (97.2)	16 (100)	17 (100)	—
Neonatal death	1 (2.8)	0	0	
Preterm birth	0	3 (18.8)	2 (11.8)	.58
NICU admission > 48 h	1 (2.8)	3 (18.8)	0	.06

Data are n (%) unless otherwise stated. Percentages may not total 100 because of rounding. *P* values are for comparison between obese, no OSA, and obese OSA groups. Continuous variables compared using independent *t* test and Mann-Whitney *U* test for normal and nonnormally distributed data, respectively. Categorical variables compared using chi-square. *Pregnancy-induced hypertension preceded the diagnosis of pre-eclampsia in 3 of 4 cases in the obese OSA group and in the single case in the obese, no OSA group. **Delivery complication comprises postpartum hemorrhage (blood loss > 500 mL within 24 hours of vaginal delivery or > 1000 mL following cesarean delivery), suspected or confirmed intrapartum sepsis, postoperative wound infection, and retained products of conception (all based on clinician diagnosis in the electronic medical records). †Birthweight data were unavailable for 1 offspring from the obese, no OSA group. This infant could not be included in birthweight centile, large for gestational age, and small for gestational age analyses, where n = 15 for those results. ‡Gestational weight gain data missing for n = 4 (lean), n = 4 (obese, no OSA), and n = 1 (obese, OSA) group. IQR = interquartile range, NICU = neonatal intensive care unit, OSA = obstructive sleep apnea, SD = standard deviation.

REI 3% and oxygen desaturation index scores suggest that this technique offers a potential convenient and cost-effective method to screen for OSA in this population.

In exploratory analyses, we did not observe any difference in inflammatory (serum IL-6) or metabolic (fasting plasma glucose, HOMA-IR) indices comparing women with obesity who did and did not have OSA. Evidence of a proinflammatory response in maternal blood has been reported in 2 small studies involving pregnant women with OSA, although the pattern of elevation in cytokines was not consistent.[38,39] We identified that women with obesity had higher average levels of IL-6, fasting glucose, and HOMA-IR than lean women at both time points. These findings are in keeping with previous reports comparing pregnant women who were overweight and obese with lean controls.[40,41]

In this study, the obese and lean groups were well matched for age and parity. A small but significant difference in gestation was evident for the first but not the second sleep study. Differences in deprivation status and booking blood pressure are in keeping with established characteristics of obese compared to lean women.[42,43] Women with obesity were more likely than lean women to be former or current smokers, a finding consistent with the more deprived status of this group.[44]

This study is limited by the use of a level 3 sleep study device that has not been validated against PSG in pregnant women. However, we feel that the consistency of our third-trimester findings with 2 studies that used PSG in pregnant women with obesity suggests our results are robust. Furthermore, sleep study scores generated by other level 3 devices have been shown to correlate well with those generated from in-lab PSG in pregnant women with obesity, supporting the use of such devices as an effective and reliable method to diagnose OSA in this population.[35,45,46] Another limitation of our methodology is that the primary scorer was not blinded to the BMI status of study participants. However, scoring of a subset of studies by an experienced second scorer blinded to BMI status showed excellent interobserver reliability,

suggesting that the unblinded status of the primary scorer did not significantly influence scoring practices.

In conclusion, OSA was identified in 37.5% and 50% of women with class III obesity in the second and third trimesters of pregnancy, respectively. This is the first longitudinal account of OSA prevalence in women with class III obesity specifically. Women with obesity and OSA were older than those with no OSA; however, their characteristics were otherwise similar. This included exploratory analysis of inflammatory and metabolic indices in the maternal serum. In multivariable logistic regression analysis, increased age was the only variable significantly associated with an increased risk of OSA. In light of the rapid increase in the prevalence of maternal obesity and the increased risks of adverse pregnancy outcomes in women with OSA, further research is urgently required to determine effective strategies for investigation and management of OSA in this population. Women with class III obesity represent a particularly high-risk group and it can be argued that routine screening for OSA should be offered to these patients in the antenatal setting. However, robust evidence regarding the impact of OSA treatment interventions, including continuous positive airway pressure, on maternal outcomes is ultimately required before such interventions can be justified in national clinical practice guidelines.

ABBREVIATIONS

BMI, body mass index
HOMA-IR, homeostatic model assessment of insulin resistance
IL-6, interleukin-6
OSA, obstructive sleep apnea
PSG, polysomnography
REI, respiratory event index

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