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SCIENTIFIC INVESTIGATIONS

Anthropometric Measures and Prediction of Maternal Sleep-Disordered Breathing

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Study Objectives: Pregnant women are at risk for sleep-disordered breathing (SDB); however, screening methods in this dynamic population are not well studied. The aim of this study was to examine whether anthropometric measures can accurately predict SDB in pregnant women.

Methods: Pregnant women with snoring and overweight/obesity were recruited in the first trimester. Anthropometric measures were performed according to the International Standards for Anthropometric Assessment, including a seated neutral and extended neck Mallampati class. Home sleep apnea monitoring was performed using a level III device after completion of anthropometric assessment. SDB was defined as an apnea-hypopnea index ≥ 5 events/h of sleep. Pearson and Spearman tests examined correlations between various measures. Generalized linear models, sensitivity, specificity, and area under the curve as well as odds ratios were performed to test the model.

Results: A total of 129 participants were recruited, and 23 had SDB. Average gestational age was 10.6 ± 1.9 weeks. Due to concerns over multicollinearity, the final model included extended Mallampati class and upright neck circumference. Neck circumference was significantly higher in participants with Mallampati classes 2/3 and grade 4 compared to participants with Mallampati class 1 (P = .0005). Increasing neck circumference was associated with higher odds of SDB (P = .0022). In Mallampati class 1, odds ratio for SDB was 2.89 (1.19, 7.03) per unit increase in neck circumference.

Conclusions: Modeling neck circumference while allowing for differences by Mallampati class showed a nearly threefold increase in the risk of SDB with increasing neck circumference in women with Mallampati class 1. Other potential sites of airway obstruction need to be investigated in future research.

Keywords: anthropometric measures, Mallampati, neck circumference, obstructive sleep apnea, pregnancy, sleep-disordered breathing

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BRIEF SUMMARY

Current Knowledge/Study Rationale: Pregnancy is associated with physiological changes that may be transient; however, these changes may affect the pathogenesis of sleep-disordered breathing in pregnancy. This study examined the ability of clinical upper airway measurements to detect sleep-disordered breathing.

Study Impact: We found that a larger neck circumference was most predictive of sleep-disordered breathing in women with Mallampati class 1, despite this group having smaller average neck circumference compared to other Mallampati classes. Though counterintuitive, our findings suggest that physiological changes of pregnancy may affect the site of obstruction in pregnancy, begging for future studies examining measurements such as airway luminal areas and nasal resistance. A better understanding of this physiology can further the application of specific therapy of sleep-disordered breathing in this population.

INTRODUCTION

Sleep-disordered breathing (SDB) has been shown to affect almost 10% of premenopausal women based on data from the Wisconsin Sleep Cohort.[1] Prospective data from pregnancy show that 4% of all women examined with home sleep monitors have SDB in early pregnancy.[2] However, data from samples of pregnant women with obesity[3] or medical[4,5] or obstetric complications[6,7] show that the prevalence of SDB is as high as 70% in some studies. To date, screening questionnaires that have been validated in the general nonpregnant population have failed to reliably predict objectively measured SDB in pregnancy.[8,9] In addition, performance of these screening questionnaires appears to be influenced by gestational stage, with some screening tools performing better in the second and third trimester than in the first trimester.[10] Models that include body mass index (BMI), age, snoring, and hypertension have been proposed in the general and high-risk pregnant populations[9,11]; however, these remain to be validated in other studies. Hence, the ability to predict SDB in pregnant women with obesity and those at risk for pregnancy complications[12–15] remains quite limited.

Data from the Sleep Heart Health Study show that the most powerful predictors of SDB in the general population are age, BMI, neck and waist circumference, snoring frequency, and loudness.[16] In addition, the change in neck circumference from the standing to the supine position is strongly predictive of obstructive sleep apnea (OSA).[17] Waist circumference appears to be more predictive of OSA and OSA severity[18] than BMI alone. Furthermore, visceral and abdominal fat appear to better correlate than BMI with indices of sleep apnea such as apnea-hypopnea index (AHI) and oxygen desaturation index.[19,20] Though data in pregnancy suggest that early weight gain, biceps and triceps skinfolds,[21] and waist circumference[22] positively correlate with metabolic abnormalities associated with OSA, there are no studies evaluating anthropometric data other than BMI and gestational weight gain in predicting OSA in pregnancy. Our previously published cross-sectional data showed a correlation between SDB in the third trimester—as determined by questionnaires—and prepregnancy BMI, as well as BMI at delivery.[13] Specific anthropometric measurements in pregnancy are not synonymous with the same measurements taken outside of pregnancy for many reasons. Weight gain and weight deposition differ by gestational age and although early weight gain may be due to fat deposition, weight gain later in pregnancy is related to an increase in amniotic fluid, plasma volume, and volume of products of conception. Furthermore, given the presence of sex hormone receptors in the upper airway, the multiple fold increase in circulating hormone levels in pregnancy may affect upper airway structure and site of obstruction.

Given the current limited ability to identify women at high risk for SDB to guide a referral for polysomnography or sleep apnea monitoring, an evaluation of the predictive ability of anthropometric measures is warranted. The aim of this study was to examine anthropometric measures that have been previously identified as predictors of SDB in a population of pregnant women with obesity in the first trimester of pregnancy. We hypothesized that these previously identified measures may perform differently in the pregnant population.

METHODS

Participants

Participants consisted of women screened in the first trimester of pregnancy. Participants were recruited from community-based practices and local hospitals that serve women in Rhode Island and southern Massachusetts. Pregnant women with overweight or obesity in their first trimester (gestational age less than 14 completed weeks) who were 18 years or older were recruited. Exclusion criteria of the parent studies included falling asleep while driving, nonsingleton pregnancies, cervical insufficiency, advanced cardiac disease or arrhythmias, chronic lung conditions, respiratory failure, severe prepregnancy hypertension, and history of treated OSA. This study was approved by the Lifespan Institutional Review Board.

Procedures

After informed consent to participate was obtained, women reported on past pregnancies and medical history. Women underwent a physical examination assessment and were instructed on the proper methods of using a home sleep apnea test.

Anthropometric Measures

Participants had anthropometric measurements performed by an experienced operator at the time of the screening visit, following guidelines by the International Standards of Anthropometric Assessment.[23] Height in meters and weight in kilograms were measured and BMI calculated. Neck circumference was measured using a disposable measuring tape at the level of the hyoid bone in the upright seated position, with the head in a neutral position. The measuring tape was kept in place and the patient was asked to assume a supine position without neck support. The measurement of neck circumference was then repeated in the supine position.

Breast circumference was measured at the widest diameter of the chest area in the seated resting position. Waist circumference was measured in the upright position as follows: a measurement at the midaxillary line is taken between the lowest point of the rib cage and the highest point of the iliac crest. Halfway of that line, waist circumference was measured horizontally at end expiration. Hip circumference was measured in the upright position at the widest diameter over the buttocks.

A modified Mallampati class was measured in a resting seated position prior to the home test by a trained research nurse. A Mallampati class estimates the size of the tongue relative to the oral cavity and is related to tongue volume. The assessment records visibility of oral cavity structures and has good interobserver agreement.[24] The patient had her neck in a neutral position, with mouth open wide at eye level of the examiner, and the tongue remaining inside the mouth.[25] A Mallampati class of 1, 2, 3, or 4 was then assigned after inspiration. Class I is identified by complete visualization of the soft palate. Class II distinguished by complete visualization of the uvula and class III by visualization of only the base of the uvula. Class IV is determined by complete lack of visibility of the soft palate. In order to mimic a sleeping position, the patient was then asked to perform a craniocervical extension. Craniocervical extension is thought to improve the specificity and the positive predictive value of the Mallampati classification system while retaining its sensitivity.[26] The upper airway was then examined similarly to Mallampati class measured in the neutral neck position. Mallampati classes of 1 through 4 were similarly recorded.

Home Sleep Study

The home sleep apnea test was performed using a level III recording device, Nox T3 (Carefusion, San Diego, California, United States), which uses built-in sensors to include a pressure transducer allowing recording of nasal pressure and snoring, a three-dimensional acceleration sensor for measuring body position and activity, and a microphone for true audio-recording capabilities. The external sensor options used included electrocardiography and dual abdominal/thoracic respiratory inductance plethysmography belts, the latter being the preferred noninvasive technology in the measurement of respiratory effort. The T3 device also supports wireless Bluetooth connectivity, allowing it to record signals from a Bluetooth pulse oximeter. Nox T3 autoscore has been validated against in-laboratory polysomnography and found to correctly identify 100% of individuals who do not have OSA and 88% of individuals who have OSA.[27] In addition, autoscore T3 respiratory event index (REI) strongly relates to AHI derived from polysomnography (r = .93). OSA is defined in this study as REI ≥ 5 events/h, and severity defined as 5–14.9, mild; 15–29.9, moderate; and ≥ 30, severe. Measurements of oxygen saturation parameters were also collected. Hypopnea was defined based on the recommended American Academy of Sleep Medicine rule of 3% desaturation.[28] Sleep studies were performed within 12 to 24 hours of the anthropometric assessment and scored by the same experienced polysomnography technician, and supervised by the investigative team.

Statistical Methods

Demographics of Study Sample and Anthropomorphic Measure Correlations

During preliminary analysis, Pearson and Spearman correlation coefficients were used to test the relationship between morphologic characteristics and AHI. Significant correlations among the anthropomorphic variables were found (BMI, breast circumference, and waist to hip ratio, neck circumference, Mallampati class). Upright neck circumference and supine neck circumference were tightly correlated (r = .95, P < .0001; **Table 1**). Similarly, upright and extended Mallampati classes were highly correlated (r = .98, P < .0001). Therefore, only one of the two measures was included in further analyses. Although the association of each anthropomorphic measure with SBD status was considered, given concerns over nonindependence of predictor variables (multicollinearity), the final model focused on upper airway anthropometric measures (extended Mallampati class and upright neck circumference) to predict SDB status.

Upright Neck Circumference and Extended Mallampati Class

A general linear model (*proc glimmix*) was used to test the relationship between extended Mallampati class and upright neck circumference. No difference in upright neck circumference was found between extended Mallampati classes of 2 and 3 (P = .6854). For that reason, the two classes of Mallampati were grouped as one category (2/3) for subsequent analysis. Neutral Mallampati class and supine neck circumference were also considered as possible predictors for modeling but preliminary analysis showed extended Mallampati class and upright neck circumference had marginally stronger relationships to apneic outcome and were used for the remaining analysis.

Apnea Prediction

A generalized linear model for binary outcomes (*proc glimmix*) was used to model the proportion of subjects with SDB (defined as REI ≥ 5 events/h) versus no SDB (defined as REI < 5 events/h) by their upright neck circumference and extended Mallampati class. An interaction term was included in the model to allow for differences in the relationship between neck circumference and apnea with the level of extended Mallampati class. Familywise alpha was maintained at 0.05 using the Holm adjustment for comparisons across extended Mallampati class. Odds ratios, receiver operating characteristic curves, and optimal cutoffs were also determined from the model. Sensitivity, specificity, and area under the curve (AUC or accuracy) were then reported for these cutoffs. All statistical analyses were performed using SAS version 9.4 (The SAS Institute; Cary, North Carolina, United States).

Table 1—Pearson correlation coefficients for anthropomorphic measures.

	BMI	NC Upright	NC Supine	BC
BMI	–	.724 (< .0001)	.704 (< .0001)	.858 (< .0001)
NC Upright	.724 (< .0001)	–	.949 (< .0001)	.780 (< .0001)
NC Supine	.704 (< .0001)	.949 (< .0001)	–	.794 (< .0001)
BC	.858 (< .0001)	.780 (< .0001)	.794 (< .0001)	–

Values are presented as Pearson correlation coefficients (P values). BC = breast circumference, BMI = body mass index, NC = neck circumference.

RESULTS

Demographics and Maternal Characteristics

A total of 129 pregnant participants with overweight or obesity were recruited in the first trimester of pregnancy. Average REI of the sample was 2.6 ± 6.04 events/h. Twenty-three women received a diagnosis of SDB based on an REI ≥ 5 events/h of sleep. Of those, most (87%) had mild SDB, 8.7% had moderate disease, and 4.3% had severe disease.

Mean age of participants was 29.7 ± 5.8 years (**Table 2**). Mean BMI was 34.7 ± 7.8 kg/m^2. Average neck circumference in the upright position was 36.8 ± 3.2 cm.

SDB Prediction

Given concerns over multicollinearity, the final model included only extended Mallampati class and upright neck circumference to predict SDB status. Neck circumference was significantly higher in participants with Mallampati class 2/3 (neck circumference = 37.85 ± 0.42 cm) and class 4 (neck circumference = 36.8 ± 0.43 cm) compared to participants with Mallampati class 1 (35.05 ± 0.55 cm), (P = .0005). These results are illustrated in **Figure 1**. In general, the odds of SDB increased with the Mallampati class.

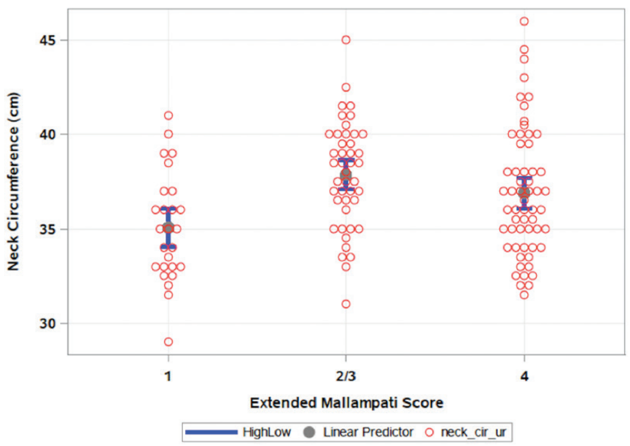
Figure 2 shows the final model and the effect of increasing neck circumference on SDB status and how the relationship changes depending on level of Mallampati class. **Table 3** shows SDB probability at various neck circumference cutoffs in different Mallampati classes. In general, increasing neck circumference was associated with higher odds of SDB (P = .0022). The risk of SDB increased significantly with increasing neck circumference in women with Mallampati class 1. Considering Mallampati class 1, the odds ratio was 2.89 (1.19, 7.03), P = .0207. For Mallampati classes 2/3, there was a trend toward statistical significance at 1.32 (0.99, 1.77), P = .0565.

Table 2—Participant demographics.

Age (years)	29.7 ± 5.8
Race, n	
Caucasian	70
African American	24
Asian	5
American Indian	2
Multiracial	22
Unreported	6
Gestational age (weeks)	10.6 ± 1.9
SDB, %	17.8
Mild	15.5
Moderate	1.5
Severe	0.8
AHI (events/h)	2.6 ± 6.0
BMI (kg/m²)	34.6 ± 8.0
Neck circumference (cm)	36.8 ± 3.2
Breast circumference (cm)	111.7 ± 13.2
Extended Mallampati class	2.25 ± 0.7

Values are presented as n, mean ± standard deviation, or %. AHI = apnea-hypopnea index, BMI = body mass index, SDB = sleep-disordered breathing.

Figure 1—Neck circumference by Mallampati class.



Gray circles represent mean neck circumference and blue bars represent 95% confidence intervals.

Though the risk was higher than 1 for Mallampati class 4, the increased risk did not reach statistical significance at 1.2 (0.95, 1.54), P = .1192. It should also be noted that the relationship between neck circumference and SDB for the Mallampati class 1 group achieved statistical significance despite this group of subjects having the smallest neck circumference (**Figure 1** and **Figure 2**).

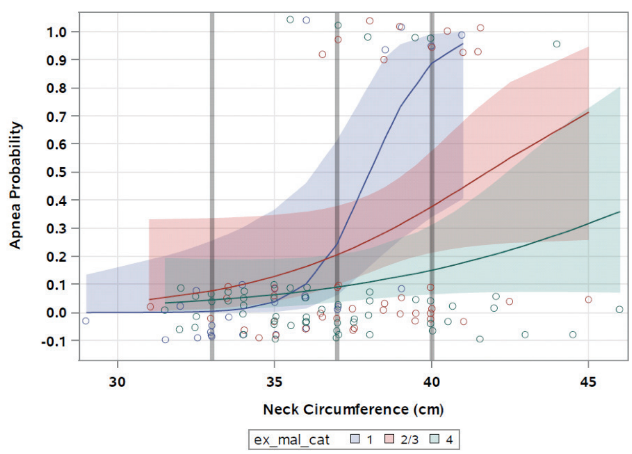
Figure 3 shows sensitivity and specificity of the model at the different levels of Mallampati classes. The cutoff with best sensitivity and specificity for neck circumference was 36.8 cm in those with Mallampati class 1 (see **Figure 3**A), 39.5 cm in those with Mallampati class 2/3 (see **Figure 3**B), and 40.7 cm in those with Mallampati class 4 (see **Figure 3**C). The AUC

Table 3—Estimated SDB probability at neck circumferences 33, 37, 40 cm for extended Mallampati classes of 1, 2/3, and 4.

Extended Mallampati Class	Neck Circumference (cm)	SDB Probability (95% CI)
1	33	0.005 (0.00, 0.26)
1	37	0.25 (0.06, 0.62)
1	40	0.89 (0.34, 0.99)
2/3	33	0.08 (0.01, 0.34)
2/3	37	0.21 (0.10, 0.38)
2/3	40	0.38 (0.21, 0.57)
4	33	0.04 (0.01, 0.19)
4	37	0.09 (0.04, 0.21)
4	40	0.15 (0.06, 0.31)

Note probabilities increase with increasing neck circumference. Magnitude of increase is greatest with an extended Mallampati class of 1. CI = confidence interval, SDB = sleep-disordered breathing.

Figure 2—Probability of obstructive sleep apnea by neck circumference in three Mallampati class categories.



Shaded red, blue, and green areas represent 95% confidence intervals. Note: Grey lines indicate where estimated probability was performed for varying neck circumference and Mallampati classes (also see **Table 2**).

or accuracy for the model was 0.815 (81.5% accuracy of the combination of neck circumference and Mallampati class to discriminate between absence of SBD and presence of SBD).

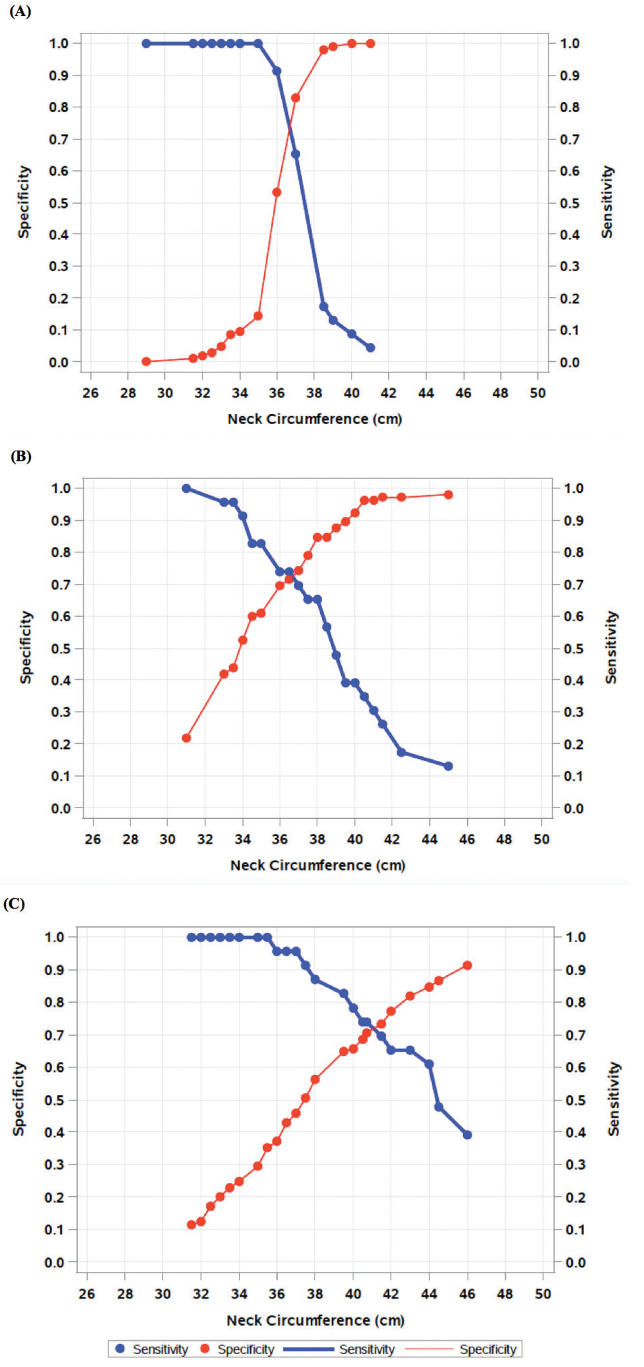
DISCUSSION

We found a relationship between higher BMI, neck circumference, breast circumference, and waist-to-hip ratio with SDB. However, because of concerns about multicollinearity with the anthropomorphic measures, our approach incorporated the measures that were physiologically most closely associated with airway obstruction. Our final model tested the specific effects of upper airway anthropometrics (Mallampati class and neck circumference) on SDB. In general, we found increased risk of SDB with increased neck circumference. However, modeling neck circumference and allowing for differences by level of Mallampati class, the risk of SDB was higher with larger neck circumference, in women with Mallampati class 1 specifically, and the probability of having SDB was mainly driven by increases in neck circumference. Women with Mallampati class 1 saw a higher risk of having SDB by more than twofold for every unit increase in neck circumference. Mallampati classification has been shown to be a good predictor of SDB in the general nonpregnant population. Numerous studies have shown an increased prevalence and risk for SDB[29–31] with higher Mallampati classes, as well as evidence of a positive correlation between AHI and more pharyngeal crowding.[30] This association was also demonstrated in samples that consisted exclusively of women.[32] However, Mallampati class only explained 1.7% of the variability in AHI in one large retrospective study (64% male),[30] and one study demonstrated an association only in subgroups of patients with nasal obstruction.[33] Neck circumference has also been demonstrated to be a valuable tool in screening for OSA[34] and has been included in various predictive models in the nonpregnant population.[35,36] Predictive ability of these measures to detect SDB in pregnancy may relate to physiologic changes that are specific to pregnancy and that may play a role in upper airway patency and the anatomic location of airflow limitation.

Airway patency depends on numerous factors including characteristics that are inherent to sex, weight, and weight distribution, as well as length of the airway, and obstruction leading to airflow limitation can occur at different levels in the airway. Mallampati class and neck circumference measure different areas of the upper airway, and despite BMI contributing to and affecting both measurements in our sample, the two measurements did not correlate with one another. The Mallampati classification system, originally described to predict difficult intubations,[37] is dependent on tongue volume, mandibular size, and pharyngeal crowding. However, neck circumference is a reproducible measure[38,39] that assesses a more distal area in the upper airway. Both Mallampati class and neck circumference are influenced by fat deposition and fluid shifts. Even though obesity is an important contributing factor to OSA because of peripharyngeal fat accumulation and an increase in neck circumference,[40] it only accounts for a small portion of the variability of the frequency of SDB.[41,42] Wasicko et al. have shown that systemic vasodilation in anesthetized cats reduces pharyngeal cross-sectional area and increases pharyngeal collapsibility, whereas systemic vasoconstriction has the opposite effect.[43] Human studies have suggested that rostral redistribution of fluids from the lower extremities to the upper airway influences neck circumference and pharyngeal resistance,[44] pharyngeal cross-sectional area,[45] and airway collapsibility.[46]

Pathobiology of SDB in pregnancy may also be different because of sex and pregnancy-specific factors that may affect airway patency. Though men and women have similar amounts of fluid movement from the legs, more fluid accumulates in the thorax and the neck area in men.[47,48] Sex hormones have been implicated in the pathogenesis of SDB and may play either a predisposing role or a protective role, possibly depending on the anatomical level in question. It has been proposed that progesterone, acting as a respiratory stimulant, may lead to a vacuum effect on the upper airway, predisposing to airway

Figure 3—Sensitivity and specificity versus increasing neck circumference by Mallampati class.



Sensitivity and specificity versus increasing neck circumference for **(A)** Mallampati class 1, **(B)** Mallampati class 2/3, and **(C)** Mallampati class 4.

collapsibility.[49] Both estrogens and progesterone have been implicated in fluid retention and regulation.[50,51] As levels of these hormones are significantly increased compared to pre-pregnancy levels, a hormonal contribution to airway patency would be extremely relevant in the pregnant population. As measurements in our study occurred in early pregnancy at an average of 10.3 weeks of gestation, changes related to plasma volume and fluid retention would likely have played some role, though plasma volume does not peak until the second half of pregnancy.

Estrogens may also act to predispose to nasal obstruction—which has been linked to reduced upper airway patency and SDB[52,53]—via histamine receptors in the nasal epithelium and microvascular endothelial cells.[54] Nasal obstruction may occur due to direct hormonal changes such as nasal vascular smooth muscle relaxation by progesterone, or may be mediated via changes in systemic blood volume and increased concentration of neurotransmitter substance P, altered by both estrogen and progesterone.[55]

Nonvascular effects of sex steroid hormones on upper airway patency cannot be discounted and may also affect the location of upper airway obstruction. As previously noted, progesterone is a respiratory stimulant, and stimulates upper airway dilator muscles.[56] Similarly, estrogens such as 17-beta estradiol accentuate contractility of the rat genioglossus muscle,[57] reverse the effect of chronic intermittent hypoxia in ovariectomized rats,[58] and can directly modulate the output of respiratory motor neurons.[59] Furthermore, estrogen has been reported to inhibit hypoxia-inducible factor 1-alpha expression, thereby exerting protective effects on the genioglossus muscle in chronic intermittent hypoxia.[60]

Our findings are somewhat counterintuitive in showing that changes in neck circumference have the greatest effect in patients with Mallampati class 1, among whom average neck circumference was smallest, compared to other Mallampati classes. Hence, previously cited literature examining the contribution of sex hormones to upper airway patency and our current findings suggest that the location of upper airway narrowing and airflow limitation may be different in pregnancy due to pregnancy physiology. This understanding of the effect of female sex hormones suggests that pregnant women may be protected by increased contractility of the genioglossus muscle but may be more prone to fluid retention and to having higher anatomical levels of obstruction in the nasal passages. Future studies examining physiological data regarding airway collapsibility and impedance, including nasal obstruction and resistance as they relate to SDB and female sex hormones, are sorely needed, as a better understanding of these pathophysiologic mechanisms can affect the application of specific therapy.

Strengths of this prospective study include the objective identification of SDB and the performance of anthropometric measures by a trained operator. Measurements of all anthropometric measures were blinded to SDB status. A limitation of this study is the use of a home sleep apnea study rather than in-laboratory polysomnography. The lack of recording of electroencephalogram to measure sleep and arousals may lead to an underestimation of hypopneas. Hypopneas associated with arousals and without significant desaturations could have been missed. However, level III devices have been validated in the evaluation of SDB in pregnant women.[61] Additionally, because our population consisted of women with obesity and overweight, our results may not be generalizable to the normal weight population suspected of OSA, although excess body weight is a major driver of SDB in pregnancy.[11] Furthermore, our study was designed to examine these markers in the first trimester to standardize the effect of pregnancy; however, because pregnancy is a dynamic state, our current findings may not apply to later stages of gestation and future studies should examine the predictive ability of these measures in late gestation. Similarly, as lung volumes and their associated changes across pregnancy may be a confounding factor, future research should examine the effect of lung volume and its changes on SDB prediction. Last, for logistical reasons, neck circumference measures could not be performed at the same time of day in all participants; hence, variability across patients could have occurred depending on time of day of measurement and may change based on day-to- day variability.

ABBREVIATIONS

AHI, apnea-hypopnea index
AUC, area under the curve
BMI, body mass index
OSA, obstructive sleep apnea
REI, respiratory event index
SDB, sleep-disordered breathing

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