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ORIGINAL ARTICLE

Obstructive Sleep Apnoea: A Shrouded High-Risk Association for Development of Hypertensive Disorders of Pregnancy

Vinita Sarbhai[1] · Pooja Paswan[2] · Vikram Sarbhai[3]

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Abstract

Background This objective of this study was to diagnose Obstructive Sleep Apnoea (OSA) in pregnant women using Questionnaire-based methods and to determine any association of Sleep-Disordered Breathing (SDB) with Hypertensive Disorder of Pregnancy (HDP). Additionally, the study aimed to identify factors associated with OSA.

Methods This case–control study was conducted in department of Obstetrics in tertiary care hospital in Delhi. We Identified SDB using Berlin Questionnaire and Modified Stop-Bang Questionnaire in 100 pregnant women with Hypertension and 100 normotensive controls. We compared the groups using appropriate statistical analysis.

Results The mean age of women with HDP (25.46 ± 4.38) was found to be slightly higher than controls (24.13 ± 3.89) (p value-0.02). Sleep apnoea as depicted by the presence of either high-risk STOP Bang or Berlin score was seen more often in hypertensive women in 45% as compared to controls in 8% (p value < 0.001). Higher pre-pregnancy weight (58.58 ± 9.77 vs. 53.0 ± 6.59), higher BMI (24.03 ± 5.89 vs. 20.68 ± 1.49), higher mean neck circumference (14.97 vs. 14.27 inches) weight gain more than 11 kg during pregnancy (55.6% vs. 38.2%) were the high-risk factors more commonly associated with SDB as seen in women with OSA in hypertensive women. On logistic regression analysis, the presence of OSA was singularly responsible for development of Hypertension (Odds Ratio–13.014, 95% CI 5.237–32.337) (p value < 0.001).

Conclusion Gestational hypertension appears to be strongly associated with the presence of obstructive sleep apnoea. The recognition and treatment of OSA during pregnancy may lead to improved outcomes.

Keywords Hypertensive disorders of pregnancy (HDP) · Preeclampsia · Sleep-disordered breathing (SDB) · Obstructive sleep Apnoea (OSA) · Stop-Bang Questionnaire · Berlin Questionnaire

Introduction

Hypertensive Disorders of Pregnancy (HDP) are a leading cause of maternal and perinatal morbidity and mortality. These are common medical disorders which can result in serious foeto-maternal consequences, affecting 7–10% of pregnant women [1]. According to worldwide estimates, they are responsible for > 500,000 foetal and neo-natal deaths and > 70,000 maternal deaths every year [2]. Despite years of research, the underlying cause and pathogenesis of preeclampsia remains elusive. Recent studies suggest that

Vinita Sarbhai (MD, DNB) is a Senior Specialist, Department of Gynecology and Obstetrics, Kasturba Hospital, Delhi, India; Pooja Paswan (MBBS) is a Junior (Post Graduate) Resident, Department of Obstetrics and Gynecology, Kasturba Hospital, Daryaganj, Delhi, India; Vikram Sarbhai (MD, DNB, FCCP, FACP) is a Senior Consultant, Pulmonology, Critical Care & Sleep Medicine, President - Indian sleep disorders Association, National Heart Institute, East of Kailash, New Delhi, India.

✉ Vinita Sarbhai
vinitasarbhai@gmail.com

Pooja Paswan
pooja1477820@gmail.com

Vikram Sarbhai
vksarbhai@gmail.com

[1] Department of Gynecology and Obstetrics, Kasturba Hospital, C-36, First Floor, Pamposh Enclave, New Delhi, Delhi 110048, India

[2] Department of Obstetrics and Gynecology, Kasturba Hospital, Daryaganj, Delhi, India

[3] East of Kailash, National Heart Institute, New Delhi, India

Sleep-Disordered Breathing (SDB) such as Obstructive Sleep Apnoea (OSA) is more prevalent in pregnant women with Preeclampsia [3]. The increased prevalence of SDB during pregnancy has been attributed to weight gain, narrowing of the upper airway due to pharyngeal oedema and increased upper airway resistance [4]. The HDP and sleep disorders share many risk factors, including obesity/overweight, hypertension, and advanced age. SDB is thought to cause sympathetic activation, oxidative stress, endothelial dysfunction due to persistent and repeated episodes of hypoxia and arousal during sleep, potentially leading to development of hypertension and other cardiovascular morbidities [5, 6]. However, more research is needed to fully understand the epidemiology of SDB in pregnancy, its relation to development of hypertensive disorders of pregnancy, and its effect on maternal and foetal health remains to be explored.

The gold standard method for diagnosing SDB or OSA is a full night polysomnography (PSG), but this technique is time consuming, highly technically complex and resource intensive, requiring skilled sleep professionals and may not be practical in all clinical settings. Nonetheless, various studies have proven that there are a few questionnaires such as the 'STOP BANG' and 'Berlin Questionnaire' that have predictive performance in diagnosing similar to polysomnography [7]. Therefore, identifying SDB or OSA can be done with fair degree of certainty using these validated, globally accepted and published questionnaires.

This study aimed to diagnose OSA in pregnant women using questionnaire-based methods and to investigate the association of Sleep-Disordered Breathing with Hypertensive Disorder of Pregnancy (HDP) (including Preeclampsia), as well as to identify factors associated with SDB during pregnancy.

Methods

This case–control study was conducted at a tertiary care hospital in Delhi, following clearance from the departmental ethics committee. The study group comprised 100 singleton pregnancies in third trimesters, including both primigravida and multigravida, with hypertension. The control group consisted of 100 gestation period and age matched normotensive pregnant women with no other medical conditions.

The identification of Sleep-disordered breathing was done using Berlin questionnaire and modified STOP-BANG questionnaire in both study and control groups, and the results were compared using appropriate statistical analysis.

The STOP BANG questionnaire consists of eight questions, related to the Snoring, Tiredness, Observed apnoea, high blood Pressure (STOP) and Body mass index (BMI), Age, Neck circumference and Gender (BANG), asked to both patient and her spouse. As Age older than 50 years and male sex are not applicable to pregnant women, the maximum STOP-BANG score in this population is six and a STOP-BANG score greater than three indicates moderate to severe OSA [8].

The Berlin Questionnaire is a validated patient survey that assesses the risk of Obstructive Sleep Apnoea (OSA) based on the presence and frequency of snoring, wake time, sleepiness or fatigue and a history of obesity and/or hypertension [9]. Patients are classified as high risk if they score positive in two or more categories and low risk if they score positive in only one or no category.

Table 1 Demographic profile of hypertensive and non-hypertensive pregnant women

	Cases	Controls	*p* value
Mean gestational age at enrolment	35.93 ± 0.78	35.79 ± 0.77	0.22
Mean pre-pregnancy BMI	21.04 ± 1.95	21.31 ± 1.37	0.26
Mean pre-pregnancy weight	54.35 ± 7.32	53.45 ± 6.23	0.35
Mean age	25.46 ± 4.38	24.13 ± 3.89	0.02

Table 2 Obstructive sleep apnoea-related parameters of hypertensive and non-hypertensive pregnant women

	Cases	Controls	*p* value
Mean neck circumference (inches)	15.15 ± 1.24	14.24 ± 1.27	**< 0.001**
Snoring	57%	22%	**< 0.001**
Day time sleepiness	55%	25%	**< 0.001**
High-risk STOP-BANG	40%	7%	**< 0.001**
High-risk Berlin Score	40%	8%	**< 0.001**
OSA	45%	8%	**< 0·001**

Results

Both study and control subjects were well matched in major confounding factors including mean gestational age (p value = 0.22), pre-pregnancy BMI (p value = 0.26), pre-pregnancy weight (p value = 0.35), parity (p value = 0.32), religion (p value = 0.44) and socioeconomic status (p value = 0.29) (Table 1). However, the mean age of women with HDP (25.46 ± 4.38) was slightly higher than controls (24.13 ± 3.89) (p value = 0.02) and the neck circumference was significantly greater in cases (15.15 ± 1.24) as compared to controls (14.24 ± 1.27) (p value < 0.001) (Table 2).

Sleep parameters were also compared in both the pregnant groups (Table 2). Snoring, a surrogate marker of sleep disorders, was observed in 57% of hypertensive women,

compared to 22% of controls (p value < 0.001). Day time sleepiness (hypersomnolence), an indirect indicator of poor sleep quality, was higher in cases (55%) compared to controls (25%) (p value < 0.001). The poor sleep quality marked with sleep fragmentation and frequent arousals, likely due to breathing pauses (apnoea's), accompanying snoring in these women, may be a risk factor for development of hypertension.

High-risk STOP BANG score was seen in 40% of hypertensive women as compared to 7% of controls (p value < 0.001). Similarly, high-risk Berlin score was more commonly seen in cases (40%) as compared to controls (8%) (p value < 0.001). Sleep apnoea, as indicated by the presence of either high-risk STOP BANG or Berlin score, was observed in 45% of hypertensive women as compared to 8% of controls (p value < 0.001). These results suggest a strong association between gestational hypertension and obstructive sleep apnoea.

To identify any potential risk factors for the development of OSA amongst hypertensive pregnant women, various parameters were compared (Table 3). It was found that women with OSA had a higher pre-pregnancy weight (in Kg) (58.58 ± 9.77 vs. 53.0 ± 6.59) (p value < 0.001) and higher BMI (24.03 ± 5.89 vs. 20.68 ± 1.49) (p value < 0.001). Although the difference was not statistically significant, the weight gain (of more than 11 kg) during pregnancy was more commonly associated with OSA in women (55·6%) versus (38·2%) amongst those who did not have OSA (p value 0.08). There was a significant association between higher mean neck circumference (in inches) and the development of OSA (14.97 ± 1.75) versus (14.27 ± 1.42 inches) than those without OSA (p value = 0.02). However, there seemed to have no bearing of Obstructive Sleep Apnoea with regards to age of women or severity of hypertension in the candidates of this study group (Table 3).

In the multivariate logistic regression analysis, it was discovered that the presence of obstructive sleep apnoea was strongly linked to development of hypertension with Odds Ratio of 13.014, and 95% Confidence Interval of 5.237–32.337 (p value < 0.001) (Table 4). Furthermore, weight gain during pregnancy (> 11 kg in this group) was also identified as risk factor for development of hypertension with Odds ratio of 1.154 and 95% Confidence Interval of 1.053–1.265 (p value = 0.002). Pre-pregnancy weight, parity, maternal age, and religious ethnicity were not significant confounding factors and were not found to be associated with a high risk for development of HDP among the study participants (p value > 0.05).

These findings underscore the importance of considering sleep-disordered breathing, particularly OSA, in the evaluation and management of hypertensive disorders during pregnancy.

Discussion

The pathogenesis and development of hypertensive disorders of pregnancy has been an enigma, with multiple factors attributed to it. One of these factors is defective trophoblastic invasion of spiral arterioles, which leads to cellular ischaemia in the placenta. Consequently, an imbalance arises between anti-angiogenic and pro-angiogenic factors. Similar disturbances have also been observed in sleep disorders like obstructive sleep apnoea [10].

Table 4 Multivariate logistic regression analysis for factors affecting development of hypertension

Parameters	*P* value	Adjusted odds ratio	95% CI. for odds ratio	
			Lower	Upper
OSA	**< 0.001**	13.014	5.237	32.337
Weight gain in pregnancy	**0.002**	1.154	1.053	1.265
Pre-pregnancy BMI	0.56	1.02	0.98	1.06
Age in years	0.76	1.01	0.99	1.01
Hindu religion	0.23	1.11	0.89	1.45
Parity	0.41	0.91	0.80	1.16

Table 3 Factors associated with OSA amongst the hypertensive cases

Parameters	With OSA (n = 45)	Without OSA (n = 55)	p value
Severity of hypertension 1. Gestational hypertension 2. Mild preeclampsia 3. Severe preeclampsia	21 (38.9%) 23 (54.8%) 1 (25%)	33 (61.1%) 19 (45.2%) 3 (75%)	0.21
Pre-pregnancy weight (Kg)	58.58 ± 9.77	53.0 ± 6.59	**0.001**
BMI	24.03 ± 5.89	20.68 ± 1.49	**0.001**
Mean age (years)	25.0 ± 4.72	25.84 ± 4.10	0.26
Weight gain > 11 kg	25(55.6%)	21(38.2%)	0.08
Mean weight gain in Preg	10 ± 4.87	11.93 ± 6.77	0.81
Mean neck circumference (inches)	14.97 ± 1.75	14.27 ± 1.42	**0.02**

The repetitive and dynamic upper airway obstruction during sleep, which can be caused by alterations in biochemical and hormonal environment, as well as inherent genetic predispositions during pregnancy, may lead to the manifestation of obstructive sleep disorders. This condition of sleep-disordered breathing is characterized by recurring episodes of apnoea/hypopnea, resulting in hypoxemia and repeated arousals from sleep. Consequently, this disrupts the normal angiogenic processes of Renin–angiotensin system, leading to endothelial dysfunction [4].

These episodes of obstructive sleep apnoea (OSA) have been hypothesized and widely accepted as high-risk factors for development of hypertension and other cardiovascular Disorders in non-pregnant individuals. Therefore, it is logical to consider that they may also play a role for development of hypertensive disorders of pregnancy [5].

The sleep parameters of 100 hypertensive pregnant women and 100 non-hypertensive pregnant women were compared in this study. Confounding factors, such as pre-pregnancy weight, socioeconomic factors, parity, pre-pregnancy BMI, period of gestation on enrolment, were found to be similar in both the groups. However, age of hypertensive women was slightly higher (p value – 0·02). Therefore, based on the findings of this study, age can be considered as a risk factor for development of hypertension during pregnancy, as the hypertensive group consisted of older women compared to non-hypertensive group. Additionally, the main high-risk factors for the development of hypertensive disorders of pregnancy were similar in both the groups and include obesity, excess weight gain during pregnancy, high BMI, and advanced maternal age among others.

In the present study, it was observed that the mean neck circumference was higher in hypertensive women (15.15 inches) compared to control group (14.24 inches). This finding suggests a potential association between neck circumference and obstructive sleep apnoea with resultant hypertension in these women, and it might be one of the causative factors for development of Obstructive sleep Apnoea.

Several studies, including the findings of John Reid, have reported a significant association between neck circumference and hypertension [11]. In this particular study, it was observed that pregnant women with pregnancy-induced hypertension had higher mean neck circumference (38.6 ± 3.4 cm), as compared to healthy pregnant women (34.2 ± 3.2 cm) (p value < 0.001) in their study. This also indicates that an increased neck circumference may serve as a potential marker or risk factor for development of OSA and resultant hypertension.

In the present study group, all the abnormal sleep characteristics such as snoring (57% vs. 22%), daytime sleepiness (55% vs. 25%), high-risk STOP BANG Score (40% vs. 7%), high-risk Berlin score (40% vs. 8%), and the presence of OSA (45% vs. 8%) were significantly associated with hypertension (p value < 0.001). These findings provide evidence supporting the likelihood of obstructive sleep apnoea being a high-risk factor for development of hypertension during pregnancy.

Our study findings are consistent with several published reports, including a study by Champagne et al. [12]. In their study, they examined 17 pregnant women with Gestational hypertension and 33 mothers with normal blood pressure for sleep-disordered breathing (SDB). The prevalence of obstructive sleep apnoea was 82% (95% CI 57–96%) among hypertensive females, compared to 45% (95% CI 26–64%) among the normotensive pregnant females. These results indicated a strong association between gestational hypertension and obstructive sleep apnoea. Furthermore, the association remained significant even after adjusting for confounding factors including maternal age, gestational age, and BMI.

In a prospective cohort study by O'Brien et al., the clinical significance of pregnancy-onset snoring was investigated among 1719 pregnant women [13]. The study found that 34% of patients had chronic snoring, while 25% experienced pregnancy-onset snoring. The results showed that new pregnancy onset snoring (but not chronic snoring) was significantly associated with gestational hypertension (OR 2.36; 95% CI 1.48–3.77; $P < 0.001$) and preeclampsia (OR 1.59; 95% CI 1.06–2.37; $P = 0{\cdot}024$) after adjustment for confounding factors. The authors estimated that snoring played a causal role in hypertensive disorders of pregnancy and when OSA is effectively treated, 18·7% of gestational hypertension cases and 11·6% of preeclampsia could be ameliorated by eliminating pregnancy-onset snoring. These findings highlight the potential impact of addressing snoring and sleep-disordered breathing in prevention and management of hypertensive disorders of pregnancy.

In a study conducted by Suri J., it was observed that there was a statistically significant higher frequency of habitual snoring in 65 mothers of gestational hypertension group compared to pregnant women without gestational hypertension. Specifically, 90% of gestational hypertension group exhibited habitual snoring, while only 12·5% of pregnant women without hypertension snored (P value $< 0{\cdot}001$) [14]. Additionally, they found an increased frequency of snoring in preeclampsia even after controlling for obesity, which is one of the major risk factors for snoring and SDB. The odds ratio for development of preeclampsia in snorers was 16.6 ($p < 0.001$), indicating a strong association between snoring and development of preeclampsia, independent of obesity. These findings emphasize the importance of considering snoring as a potential marker and risk factor for HDP.

In a study conducted by Maryam Saraei, it was found that 41.2% of individuals in the hypertensive group had two or more risk factors of sleep apnoea including snoring, tiredness and high BMI and neck circumference. In comparison, 11.9% of the control group had two or more risk factors

($p < 0.0001$) [15]. These results indicate a significantly higher prevalence of multiple risk factors for sleep apnoea in hypertensive group compared to controls.

Several factors that are known to contribute towards development of sleep-disordered breathing, particularly obstructive sleep apnoea, were observed to be more prevalent in hypertensive group. These factors include excessive pre-pregnancy weight, higher BMI, higher neck circumference, and increased weight gain during pregnancy. These factors can play a role in development of hypertension and can serve as indicators to screen and assess the likelihood of sleep-disordered breathing among pregnant women.

Moreover, there is a strong association between obstructive sleep apnoea and gestational hypertension as indicated by a very high odds ratio of 13,014 in Hypertensive pregnant ladies (95% CI 5237–32,337) (p value < 0.001). This suggests that the presence of obstructive sleep apnoea significantly increases the risk of development of hypertensive disorders during pregnancy.

Conclusion

In conclusion, sleep-disordered breathing (SDB) particularly Obstructive Sleep Apnoea (OSA) has been recognized as a significant but often overlooked risk factor for development of hypertension during pregnancy. Timely diagnosis and treatment of SDB can potentially improve both maternal and Foetal outcomes. There is growing body of research focussing on understanding the causal relationship between sleep-disordered breathing and hypertensive disorders of pregnancy, as well as developing effective interventions to manage these disorders. Further, large-scale studies are required to identify specific therapeutic targets for interventions and optimize the management of sleep-disordered breathing in pregnant mothers. By doing so, we can potentially improve the overall care and outcomes for pregnant women affected by these conditions.

Recommendation: In addition to screening, preventive measures for SDB should be considered including treatment of sleep apnoea with continuous positive airway pressure (CPAP) therapy. CPAP can help alleviate the symptoms of sleep apnoea. Life style modifications like weight reduction before pregnancy should also be encouraged to reduce the risk of development of Obstructive Sleep Apnoea (OSA) and as a result reduce the risk of development of hypertension.

By implementing these preventive measures and ensuring early diagnosis and management of sleep-disordered breathing, the adverse outcomes associated with OSA and hypertension during pregnancy can be reduced.

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Declarations

Conflict of interest This material is the authors' own original work, which has not been previously published elsewhere. The research was ethically approved by Institutional Ethics committee, Kasturba Hospital, Delhi. There is no conflict of interest.

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