Original Article

Preeclampsia and Baby Complications Correlated to High-Risk Score for Obstructive Sleep Apnea Screen by STOP-Bang Questionnaire

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Background: Obstructive sleep apnea (OSA) has been postulated as a risk factor for adverse maternal-fetal outcomes, especially preeclampsia. The physiological changes during pregnancy predispose a woman "at risk" towards developing OSA. Therefore, incidence of OSA may increase among pregnant population. STOP-Bang has been postulated as an acceptable screening tool for OSA in obstetric population.

Objective: To identify the correlation between preeclampsia and patients who were at risk of OSA, based on STOP-Bang, Berlin, and Epworth sleepiness scale.

Materials and Methods: A diagnostic prediction research was conducted using cross-sectional approach. Patients, who have STOP-Bang score of 3 or more and less than 3, were categorized as high-risk and low-risk for OSA, respectively. The relationship between high-risk OSA patients and preeclampsia were evaluated using logistic regression.

Results: Seven hundred and three patients were included, and 47 patients (6.7%) were diagnosed preeclampsia. Six hundred fifty and 53 patients were classified as low-risk and high-risk for OSA, respectively. Fifty percent of the high-risk group were complicated with preeclampsia compared with 2.8% in low-risk group. The odd ratio (OR) of having preeclampsia in high-risk group was 32.6 (95% CI 16.1 to 66.1). The pregnant women, classified as high-risk, were associated with neonatal complications by OR 3.4 (95% CI 1.4 to 8.2) but not maternal complications.

Conclusion: Among pregnant population, a STOP-Bang score of 3 or more is associated with the occurrence of preeclampsia and neonatal complications.

Keywords: STOP-Bang questionnaire; Obstructive sleep apnea; Pregnancy; Preeclampsia

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Obstructive sleep apnea (OSA) is characterized by recurrent episodes of complete or partial upper airway obstruction during sleep and is accompanied by oxygen desaturation and arousals[1]. Repeated episodes of hypoxia stimulate endothelial dysfunction, accelerated inflammation, and sympathetic hyperactivity, leading to multiple metabolic and cardiopulmonary disturbances[2]. As a result, OSA is postulated to increase maternal and perinatal morbidities. Maternal OSA was found to double the risks of developing gestational hypertension, preeclampsia, gestational diabetes, fetal growth restrictions, preterm delivery, cesarean section delivery, and admission to neonatal intensive care unit (NICU)[3].

Several physiological and hormonal changes during pregnancy such as gestational weight gain, decreased pharyngeal size from mucosal airway edema, and decreased in functional residual capacity, which may increase the risk of developing OSA or exacerbating the severity of pre-existing OSA[4]. Snoring, a cardinal symptom of OSA has been found in up to14% of healthy pregnant patients[5]. Prevalence of OSA during pregnancy varied from 12% to 35%[2,6-8] depending on study population being high or normal risk pregnancy.

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Polysomnography remains the gold standard diagnosis for OSA, but it is limited by cost and availability. Conventional OSA screening questionnaire including the STOP-Bang questionnaire, the Berlin questionnaire, and the Epworth sleepiness scale (ESS) had been studied in pregnant women. Meta-analysis had shown that the Berlin questionnaire and ESS had poor to fair performance on accuracy during the second and third trimester[9]. However, STOP-Bang questionnaire had been less studied in pregnancy. The questionnaire consists of eight items based on the patient's characteristics. It has been found to be an acceptable screening tool among pregnant women during the second trimester with sensitivity of 62.5% and specificity of 93.8%[10]. Lockhart et al found that STOP-Bang had the highest accuracy in identifying OSA among pregnant women during the third trimester when compared to other screening tools[8]. Despite the limitation of these questionnaire to accurately screen for OSA during pregnancy, studies had shown association between the Berlin questionnaire and the occurrence of preeclampsia[11,12]. Therefore, the present study aimed to identify the association between preeclampsia and patients who were at risk of OSA, based on the STOP-Bang questionnaire. The secondary aim is to compare the association of the preeclampsia occurrence, maternal and neonatal complications, and patient who were identified as high-risk for OSA based on the STOP-Bang, ESS, and Berlin questionnaire.

Materials and Methods

Patient population

A cross-sectional study was conducted in all consecutive patients delivered and completed the questionnaire during June 2016 to January 2018. The exclusion criteria were patients younger than 18 years old, incomplete or absent questionnaire, previous diagnosis of OSA, received continuous positive airway pressure (CPAP) therapy, or delivery of fetus with anomalies. The study was approved by the Ethics Committee of Ramathibodi Hospital, Mahidol University, Bangkok, Thailand (#ID-05-59-15). Written informed consents were obtained from all participants.

STOP-Bang questionnaire and identification of high-risk patients

The patients who met the inclusion criteria were included in the present study. Thai versions self-reported questionnaire including STOP-Bang, Berlin, and ESS questionnaires were given during postpartum period. These questionnaires have been validated and demonstrated good reliability in Thai language[13-15]. The information regarding general sleep disturbance, fatigue symptoms, or daytime sleepiness were inquired to the patients to evaluate themselves during the past one month of pregnancy just before delivery. The investigators obtained rates of preeclampsia, demographic, and clinical data, and other pertinent data from the medical records using standardized abstraction form.

The STOP-Bang questionnaire consists of eight items based on the patient's characteristics. The presence of snoring, tiredness, and observed apnea were retrospectively asked during one last month of pregnancy. High blood pressure defined as patient with history of chronic hypertension or gestational hypertension. The other four items included pre-pregnancy body mass index (BMI) gretaer than 35 kg/m^2, age older than 50, neck circumference greater than 40 cm, and male gender. Patients who had a STOP-Bang score of greater than or equal to 3 were categorized as high-risk for OSA.

The ESS is an 8-item based questionnaire rated on a four-point scale (from 0 to 3). The items cover the chances of falling asleep while engaging in eight different activities. If a patient's ESS score was greater than or equal to 10, the patient was considered as screening positive for OSA.

The Berlin questionnaire consists of three categories of item designed to elicit the probability of sleep apnea. It includes questions regarding snoring (category 1), daytime somnolence (category 2), and presence of obesity (pre-pregnancy BMI greater than 30 kg/m^2) or hypertension (category 3). Patients scoring positive in two or more categories were categorized as high-risk for OSA.

Preeclampsia was defined by having a blood pressure greater than 140 over 90 mmHg on two occasions at least four hours apart after the twentieth week of pregnancy with new onset excess protein in the urine as more than 300 mg in 24 hours, or the presence of thrombocytopenia, impaired liver function, newly developed renal insufficiency, pulmonary edema, or new-onset cerebral or visual disturbances[16].

Sample size estimation

The sample size calculation was performed based on the odds ratios (ORs) of having preeclampsia among high-risk OSA patients, which was 6.1 (95% confidence interval [CI] 1.7 to 22.1)[17]. However, the authors used OR of 4 to calculate the sample size. The

Table 1. Baseline characteristics of participants according to high-risk and low-risk for OSA based on STOP-Bang questionnaire (n=703)

	High-risk for OSA (n=58); n (%)	Low-risk for OSA (n=645); n (%)	p-value
Age (years); mean±SD	32.8±6.1	31.4 ± 5.5	0.057
Gestational age (weeks); mean±SD	36.3±3.4	38.2 ± 1.6	<0.001
BMI (kg/m^2); mean±SD	28.6±6.0	22.2 ± 8.4	<0.001
Obesity	28 (48.3)	37 (5.7)	<0.001
Weight gain (kg); mean±SD	13.0±6.7	13.0 ± 5.3	0.946
Neck circumference (cm); mean±SD	38.6±3.0	34.7 ± 2.2	<0.001
ASA physical status			<0.001
ASA 2	617 (95.7)	37 (63.8)	
ASA 3	28 (4.3)	19 (32.7)	
ASA 4	0 (0.0)	2 (3.4)	
Chronic HT	15 (28.9)	6 (0.9)	<0.001
Gestational HT	9 (15.5)	11 (1.7)	<0.001
DM	3 (5.2)	4 (0.6)	0.015
GDM	18 (31.0)	109 (16.9)	0.007
Cesarean delivery	45 (77.6)	367 (56.9)	0.002
Emergency delivery	39 (84.8)	188 (50.3)	<0.001
History of sleep abnormalities			
Snoring	52 (89.7)	114 (17.7)	<0.001
Tiredness	51 (87.9)	335 (51.9)	<0.001
Observe apnea	21 (36.2)	14 (2.2)	<0.001

ASA=American Society of Anesthesiologists; BMI=body mass index; DM=diabetes mellitus; GDM=gestational diabetes mellitus; HT=hypertension; OSA=obstructive sleep apnea; SD=standard deviation

prevalence of preeclampsia in the authors' institute was approximately 5%. The confidence level use for statistical judgment was 1–α, where α is 0.05 and power of 0.8. The authors set ratio of high-risk and low-risk OSA of eight controls per case. The required sample sizes were 686 patients.

Data analysis

Patient characteristic data were presented in the form of descriptive statistics with mean and standard deviation, frequency, or percentage. Binary unconditional logistic regression was applied to estimate OR for preeclampsia and their corresponding 95% CIs. Multivariable logistic regression was used to identify risk factors of having preeclampsia. For pairwise relationships, the two-sample t-test was used to compare the mean values of the continuous outcome measures; the chi-square test was used to compare the proportion of positive signals for binary outcomes. The p-value of less than 0.05 was defined as significant.

The predictive performance of the STOP-Bang, the Berlin questionnaire, and the ESS for sensitivity, specificity, positive predictive values (PPVs), negative predictive values (NPVs) were calculated and compared. The receiver operating characteristic curve (ROC) was performed to compare the predictive ability of the STOP-Bang, the Berlin questionnaire, and the ESS to identify preeclampsia.

Clinical trial registration

This study was registered at ClinicalTrials.gov, identifier NCT02800798.

Results

Patient characteristics and demographics

Seven hundred and three participants were included in the present study and 47 were diagnosed preeclampsia. Fifty-eight patients, who were identified as "high-risk" based on STOP-Bang questionnaire, had significantly greater neck circumference, bodyweight, rate of hypertensive disorder, rate of diabetes, gestational diabetes, and the American Society of Anesthesiologists (ASA) physical status than low-risk patient. Moreover, they delivered at a lower gestational age and had higher rate of emergency cesarean delivery. Descriptive summary statistics are given in Table 1.

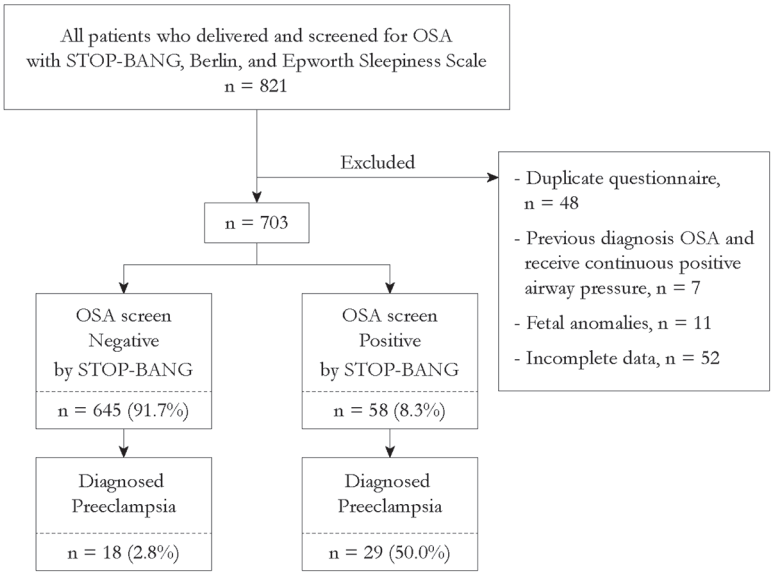

Figure 1. Diagram for patient enrolment and prediction of preeclampsia from STOP-Bang questionnaire.

Table 2. The association between positive screening test and preeclampsia

Risk of OSA	Unadjusted OR	95% CI	Adjusted OR[a]	95% CI
STOP-Bang questionnaire	34.83	17.37 to 69.87	32.59	16.06 to 66.13
Berlin questionnaire	10.15	5.43 to 18.97	9.48	5.04 to 17.82
Epworth Sleepiness Scale	1.10	0.59 to 2.06	1.14	0.60 to 2.14

CI=confidence interval; OR=odd ratio; OSA=obstructive sleep apnea

[a] Adjusted for diabetes and gestational diabetes

Prediction of preeclampsia from STOP-Bang and other screening tests

The prevalence of preeclampsia in the present study was 6.7%. Among the high-risk and low-risk patients, 50.0% (29/58 patients) and 2.8% (18/645 patients) were diagnosed with preeclampsia, respectively (Figure 1). On comparison of the association between preeclampsia and the other positive screening tests, the STOP-Bang questionnaire had the greatest odd ratio for identifying patients with preeclampsia (OR 34.8, 95% CI 17.4 to 69.9, p<0.001). After adjustment for confounding factors by history of gestational diabetes and diabetes, the high-risk group was associated with higher risk for preeclampsia (adjusted OR 32.6, 95% CI 16.1 to 66.1) (Table 2).

Using ROC analysis, the STOP-Bang had comparable area under the curve (AUC) to the Berlin questionnaire (p=0.86) and significantly higher than the ESS. The predictive performance of the STOP-Bang, the Berlin questionnaire and the ESS are displayed in Table 3.

Validation of risk factors associated with pre-eclampsia

Multiple risk factors were significantly associated with preeclampsia as shown in Table 4. These items were validated in a univariate regression analysis. After multiple regression analysis, the factors associated with preeclampsia were patient with history of chronic hypertension, gestational hypertension, neck circumference greater than 40 cm, and history of snoring (Table 5).

High-risk OSA and maternal and neonatal outcomes

The pregnant women classified as high-risk based on their STOP-Bang scores were associated with neonatal complications, including low birth weight, prematurity, infection, and admission to NICU. The adjusted OR of having neonatal complications was 3.42 (95% CI 1.43 to 8.19, p=0.006). However, the high-risk group was not associated with perioperative

Table 3. Validation of Screening tool against diagnosis of preeclampsia: sensitivity, specificity, likelihood ratio, and receiver operating characteristic

Screening tool	Sensitivity (95% CI)	Specificity (95% CI)	LR+ (95% CI)	LR– (95% CI)	Area under the ROC curve (95% CI)	p-value*
STOP-Bang	61.7 (46.4 to 75.5)	95.6 (93.7 to 97.0)	14.0 (9.2 to 21.3)	0.40 (0.28 to 0.58)	78.6 (71.6 to 85.7)	<0.001
Berlin	57.4 (42.2 to 71.7)	88.3 (85.5 to 90.6)	5.0 (3.5 to 6.8)	0.48 (0.35 to 0.67)	72.69 (65.6 to 80.1)	
Epworth sleepiness scale	34.0 (20.9 to 49.3)	68.1 (64.4 to 71.7)	1.1 (0.7 to 1.6)	0.97 (0.78 to 1.2)	51.1 (44.0 to 58.2)	

LR+=positive likelihood ratio; LR–=negative likelihood ratio; ROC=receiver operating characteristics curve statistics

* Statistical significant difference of area under the ROC curve

Table 4. Relation between history variables and presence of preeclampsia in 703 patients during postpartum period

Factors	OR (95% CI)	p-value
Age (years)	1.05 (0.99 to 1.11)	0.091
BMI (kg/m^2)	1.03 (1.00 to 1.06)	0.098
Obesity	7.18 (3.70 to 13.94)	<0.001
Neck circumference (cm)	1.46 (1.31 to 1.63)	<0.001
Chronic HT	50.78 (18.48 to 139.58)	<0.001
Gestational HT	17.46 (6.84 to 44.56)	<0.001
DM	5.79 (1.09 to 30.66)	0.039
GDM	2.04 (1.06 to 3.93)	0.034
Snore	6.75 (3.61 to 12.60)	<0.001
Tried	2.53 (1.29 to 5.00)	0.007
Observe apnea	4.78 (2.04 to 11.21)	<0.001
Stop bang	34.83 (17.37 to 69.87)	<0.001
Berlin	10.15 (5.43 to 18.97)	<0.001
Epworth	1.10 (0.59 to 2.06)	0.757

BMI=body mass index; CI=confidence interval; DM=diabetes mellitus; GDM=gestational diabetes mellitus; HT=hypertension; OR=odd ratio

Table 5. Odd ratios for Preeclampsia on multivariate logistic regression analysis

Factors	OR (95% CI)	p-value
Chronic HT	41.25 (13.54 to 125.67)	<0.001
Gestational HT	22.93 (8.02 to 65.54)	<0.001
History of snoring	4.15 (1.52 to 11.28)	0.005
Neck circumference ≥40 cm	3.56 (1.82 to 8.16)	<0.001

CI=confidence interval; HT=hypertension; OR=odd ratio

complications including uterine atony, arrhythmia, heart failure, hypertensive crisis, postpartum hemorrhage, or tearing of adjacent organs or vessels [adjusted OR 1.56 (95% CI 0.66 to 3.69), p=0.31].

Discussion

The present study was a prospective cross-sectional study that gathered data linking results for the STOP-Bang questionnaire with preeclampsia, and adverse neonatal outcomes. When compared with the Berlin and the ESS questionnaires, STOP-Bang had the highest association with preeclampsia by OR 32.6. Although preeclampsia and OSA share common risk factors such as age, diabetes, and obesity, the authors found that history of snoring and neck circumference are the strong predictive factor for preeclampsia in pregnant women.

Maternal OSA increases the occurrence of gestational diabetes, pregnancy-related hypertension, preeclampsia, and intrauterine growth restriction[3]. The evidence linking OSA with preeclampsia has been extensively studied, as repeated episodes of hypoxia stimulate endothelial dysfunction, accelerated inflammation, and sympathetic hyperactivity, leading to adverse complications[2].

In the previous studies, the STOP-Bang had shown results consistent with those of the present study, which are positive screening on the STOP-Bang increased the OR of having preeclampsia (OR 6.1)[17] in European population, whereas positive screening on the Berlin questionnaire during the second trimester had a relative risk of 2.7[11] in Thai population. The present study results showed an OR as high as 32.6 and 9.5 in patient with positive STOP-Bang and Berlin questionnaire, respectively. The present study results are much higher than in the previous studies[11,17]. The authors hypothesized that the effect may cause by differences in population and difference period of screening test that were applied. The authors used a different BMI cutoff point, namely pre-pregnant body weight of at least 27.5 kg/m^2, which was found to be the best predictive value among the Asian population[18]. However, the calculated OR in patient with positive screening for STOP-Bang was 15.5 (95% CI 8.0 to 29.9). Therefore, further study is needed to define an exact association and screening test should be evaluated along the course of pregnancy.

Neck circumference of greater than 40 cm, obesity, history of hypertensive disorder, diabetes, observed apnea, and tiredness during the day were associated with preeclampsia. The present study results are consistent with those of previous studies[19,20].

Even though some components of the STOP-Bang questionnaire may not be applicable to the obstetric population such as male gender or age over than 50 years old, it consists of major predictive factor including BMI at or greater than 35 kg/m², snoring, and history of hypertensive disorder[21]. Therefore, the STOP-Bang may be still useful in the absence of a standard screening test for OSA among the obstetric population. The STOP-Bang questionnaire highlighting a high-risk patient during the last month of pregnancy may give the physician more notice about potential preeclampsia since it has a specificity as high as 95.6%. Regular measurement of blood pressure or proteinuria may require more attention among high-risk patients.

Detecting OSA during pregnancy is challenging and requires a high index of suspicion, as some symptoms, such as daytime sleepiness, may be perceived as normal by the patient. It is also unclear if increased sleep fragmentation was caused by normal physiological changes, such as fetal movement, urge of urination, or leg cramps[22]. Obvious physiological changes during pregnancy predispose to the development of OSA[23]. Snoring, another sign of OSA, is common among the pregnant population, rising from 4% in the non-pregnant population to 25% with gestation[22]. Therefore, a simple and accurate screening test should be implemented during the prenatal period. Risk stratification for the probability of OSA in pregnant women will also help in prioritizing the need for further diagnostic sleep-testing. Early diagnosis and treatment of OSA, such as CPAP, should be given in pregnancy, as it offers potential benefits for pregnancy outcomes[24]. The present study may help in suggesting the use of the STOP-Bang questionnaire, rather than the Berlin or the ESS questionnaires, since it has the highest OR for predicting preeclampsia. In addition, the STOP-Bang is easy to use and shows greater consistency across different severities of apnea hypopnea index (AHI)[21,25].

The present study has some limitations. First, the results may not be applicable in all stages of pregnancy, as the question and data gathering were done during the postpartum period. However, the use of the STOP-Bang questionnaire may also be applicable for the third trimester period. As the information regarding general sleep disturbance, fatigue or daytime sleepiness was retrospectively asked during the last one month of pregnancy, recall bias may potentially occur in the present study. Further study may need to find the association during first and second trimester because the treatment such as CPAP therapy may decrease OSA associated adverse maternal and fetal outcomes. Secondly, the present study did not perform polysomnography on every patient to confirm the diagnosis of OSA. Screening positive for OSA on the STOP-Bang, the ESS, or the Berlin questionnaires is therefore not synonymous with a diagnosis of OSA. However, even in the absence of an actual OSA diagnosis, the present study result suggests that the risk of adverse maternal or neonatal outcomes arises from the combination of habitus and symptoms, indicating a far more complex relationship that will require further study.

Conclusion

In the pregnant population, a positive score on the STOP-Bang questionnaire has a strong association with preeclampsia, as well as adverse neonatal complications. History of chronic hypertension, gestational hypertension, history of snoring, and neck circumference of 40 cm or greater were a strong predictive factor of preeclampsia.

What is already known on this topic?

The physiological changes during pregnancy predispose a woman towards developing OSA. Maternal OSA was found to double the risks of developing hypertensive disorder of the pregnancy.

Gold standard diagnosis of OSA is polysomnogram, which is limited by cost and availability. The STOP-Bang questionnaire has been postulated as an acceptable screening tool for OSA.

In the previous study, the STOP-Bang showed an association with preeclampsia by ORs 6.1 (95% CI 1.7 to 22.1). To the authors' knowledge, there is no study comparing the association between the STOP-Bang, the Berlin, or the ESS questionnaires and occurrence of preeclampsia.

What this study adds?

This report describes the association between the high-risk patients based on the STOP-Bang questionnaire and the occurrence of preeclampsia. In comparing with the ESS or the Berlin questionnaire, the STOP-Bang questionnaire showed the strongest association with preeclampsia. This study may help in

suggesting the use of the STOP-Bang questionnaire, rather than the Berlin or the ESS questionnaires.

Conflicts of interest

None of the authors have any financial conflicts of interest to declare as it relates to the contents of this manuscript.

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