Snoring and Risk of Obstructive Sleep Apnoea in Malaysian Pregnant Women

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Abstract: Chronic hypoxia induced by periods of hypo-oxygenation in obstructive sleep apnoea (OSA) can be associated with reduced foetal growth in pregnancy. Obesity, hormonal and physiological changes during pregnancy plus variations in the craniofacial anatomy could increase the incidence of snoring and possibly OSA. In spite of the high incidence of obesity noted in Malaysia, especially in females, there have been no studies so far conducted to study the prevalence of OSA during pregnancy in this population. Thus, we sought to determine the prevalence of snoring and those who are at high risk for OSA among pregnant women in Malaysia.

INTRODUCTION

Obstructive sleep apnoea is a form of sleep-disordered breathing involving a decrease or complete cessation in airflow that lasts for more than 10 seconds, despite a continuous effort to breathe. It can occur due to recurrent collapse or blockage of the upper airway during sleep caused by the relaxation of dilating muscles that leads to a hallmark snoring-gasping pattern [1]. This interruption in the breathing causes a reduction of blood oxygen levels that leads to occasional hypoxemia, causing an individual to arouse from sleep a few times and hence ending up with poor sleep quality. Obesity, age, male gender, smoking, alcohol intake and patients with craniofacial anomalies are some of the risk factors predisposing to OSA. The respiratory effort, respiratory centre drive and diaphragmatic contraction is preserved in OSA, making it different from central sleep apnoea [2]. The common symptoms experienced by individuals with OSA include fatigue, excessive daytime sleepiness (EDS), insomnia, nocturia and morning headaches. The prevalence of OSA among women of reproductive age is approximately 0.7 to 5% but remains under diagnosed and understudied [3]. Studies have shown that the incidence of snoring range from 11.9% to 49% in the 3rd trimester of pregnancy [4].

Malaysia has the highest prevalence of obesity at 14% among other South East Asian countries [5]. A great proportion of Malaysians are known to be habitual snorers. With an increase in obesity over the years and its relationship with OSA, there has been an alarming concern with concordance of a 22.9% obesity rate among Malaysian women [6]. Obesity is known to be one of the major risk factors for OSA [7]. Obesity alters the underlying anatomical structures, demonstrated by pharyngeal soft tissues and also pushing of the diaphragm, changing the lung volume [7, 8]. Pregnant women resemble patients with central obesity. They have anatomical changes, that is, raising of the diaphragm due to enlarging uterus, which is much the same seen in obesity, causing reduction in functional residual capacity [9]. N Edwards *et al.* [10] has postulated that there is a greater tendency of the upper airway to collapse during sleep due to the upward displacement of the diaphragm to accommodate the growing uterus; causing a 20% reduction in functional residual capacity and residual volume, thus leading to greater negative inspiratory pressures at the level of the upper airway as a result of an increased diaphragmatic effort and caudal traction on the trachea and pharynx. A marked increase in the level of circulating oestrogen and progesterone during the course of pregnancy may also play a role in the sleep architecture [11]. The hormonal changes in pregnancy cause changes in the mucous membrane of the upper airway. This can result in hypersecretion leading to nasal congestion and also mucosal oedema reducing the oropharyngeal diameter, hence predisposing pregnant women to snoring and OSA [9, 12]. OSA during pregnancy is notably significant, for it may be associated with adverse pregnancy outcomes. Low maternal oxygen saturation secondary to maternal

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apnoeic episodes during sleep can compromise foetal oxygenation, leading to chronic hypoxia and diminished foetal growth [12].

Besides this, a variant in craniofacial anatomy amongst Asian population may be a contributing risk factor for obstructive sleep apnoea. For instance, Far East Asians (Japanese, Chinese, Korean) have an increased maxillomandibular protrusion compared to the Caucasians, causing them to have more severe OSA, as proved by a case-control study that was done amongst 105 Asian living in United States [13, 14]. Banabilh *et al.* [15] has also revealed that Malay patients in Malaysia with OSA had a significantly more acute base flexure angle when compared to the control group. This may be responsible for a decrease in pharyngeal airway dimension in patients with OSA by reducing the distance between the anterior and posterior pharyngeal walls [15].

Although the 'gold standard' in diagnosing OSA is an overnight polysomnography, several screening questionnaires and clinical screening modalities have been developed to assess the risk of having OSA. The most notable are the Epworth Sleepiness Scale (ESS), STOP-Bang and The Berlin Questionnaire [16-18].

The Berlin Questionnaire is a validated instrument that has been used for simple screening to identify the risk of OSA. It contains 10 questions divided into three categories: severity of snoring (category 1), excessive daytime sleepiness (category2), and presence of hypertension or obesity (category 3). A high risk or "screen positive" individual is reported to have scores positive in at least two out of the three categories, while a low risk OSA individual is reported to score positive in only one or none of the categories. The Modified Berlin Questionnaire which was translated into Malay language has a sensitivity of 92% and a specificity or 17% [19] when used among the Malaysian population.

A study done by Netzer *et al*. has showed that the Berlin Questionnaire has a specificity of 86% and sensitivity of 77% in identifying patients with OSA [20]. It was also found to be acceptable to be used for the screening of pregnant women in the second trimester [16]. As pregnancy progresses, symptoms of OSA changes, hence performances of OSA screening questionnaires differs in each trimester. Tantrakul *et al.* [16] suggests that the Berlin Questionnaires has a poorer predictive value in the first trimester and showed to be more significant during the second and third trimesters. The prevalence of OSA increased from 10.5% to 26.7% in the first trimester to the third trimester respectively according to a recent longitudinal study. Also, there was an 11% increase (30% to 41%) in the prevalence of snoring from the first trimester to the second trimester in a Chinese population. In fact, a cross sectional study which was carried out among 238 subjects in Thailand using the Berlin Questionnaire showed that prevalence of snoring in pregnant women was 35.29% while the incidence of sleep apnoea was 5.95% [21].

Previous studies using the Berlin questionnaire were mostly conducted in European countries, among the Caucasian population [3, 17], but little data was obtained from Asian population and no data was available for Malaysian women, possibly due to differences in anatomical structures [21-23]. It is alluded that anatomical structure could lead to restricted airways and Asians have been shown to have different mandibular and neck structures [24].

We propose to determine the prevalence of snoring among Malaysian pregnant women and to identify those who are at high risk of obstructive sleep apnoea (OSA) using the Berlin Questionnaire, in consideration of several risk factors including age, ethnicity, BMI and health status such as gestational diabetes mellitus and pregnancy induced hypertension.

MATERIALS AND METHODS

A quantitative study with a prospective cross sectional method was used to determine the different groups of people who differ in the variable of interest but share other characteristics, such as socioeconomic status, educational background, and ethnicity. The research was conducted in three main primary care centres in Seremban, Negeri Sembilan, Malaysia. Approval from ethical committee and State Health office were obtained prior to the start of the study.

In this study, women with singleton pregnancy was recruited by the medical students from April 2016 to June 2016. Subjects were selected based on convenient sampling. Written consent was taken before recruitment by on-site investigators. Further explanation about the questionnaire was provided when necessary.

Sample Size

According to Population Statistic of Negeri Sembilan 2010 [19], the total population in Seremban (the capital city of Negeri Sembilan) is 320 000 and out of this

figure, 50% of them are female. The Malaysian Department of Statistics stated that one third of women would be at their reproductive age. The sampling size was targeted at 340 pregnant women following the Open Epi sample size calculator with 95% confidence interval and p-value < 0.05. From 340 subjects, extra 20 subjects were added to cover the 10-20% dropout rate.

Inclusion and Exclusion Criteria

Subjects were recruited if the age is ≥18 years, singleton pregnancy, 13 - 28 gestational weeks. Exclusion criteria include pregnant women with pre-existing diabetes mellitus or hypertension and diagnosis of OSA was made prior to pregnancy.

Data Collection Techniques

Questionnaire used was the modified Berlin questionnaire (BQ) in English and a validated Bahasa Malaysia questionnaire. Validation of Malay version of modified BQ has been published and has demonstrated good reliability [18]. The modified Berlin questionnaire consists of ten questions on three categories. It is designed to elicit information regarding snoring severity (category 1), daytime somnolence (category 2) and presence of BMI >30 kg/m2 and or hypertension (category 3) [21]. Risk for OSA is considered significant if two or more categories are positive. Other data that was collected includes age, ethnicity, pre pregnancy BMI and medical disorders in pregnancy like pregnancy induced hypertension and gestational diabetes mellitus.

Data Analysis

Statistical Analysis was performed using SPSS software version 19.0. Chi-square test was used to determine prevalence. A multivariate analysis was used to analyse the factors for snoring and other risk factors including age, ethnicity and BMI. A p value < 0.05 was considered as statistically significant.

RESULT

Three hundred and twenty-nine pregnant women were recruited and completed the modified Berlin Questionnaire. The response rate was 96.7%. The measured parameters were age, ethnicity, gestational week, parity, body mass index (BMI), health status, snoring and risk of obstructive sleep apnoea (OSA). The age of the participants was recorded in range; the highest number of participant aged in between 26-30

(n=119, 36.17%). Among the participants, 55.3% were Malay, 24.6% were Chinese, 19.5% were Indian and 0.6% of other races (the aborigines). The mean gestational week of pregnant mother recruited was 21 weeks, determined by the antenatal follow up record in the health clinic. 46.5% of pregnant women are nulliparous and the rest (53.5%) were multiparous up to five parity. The mean parity was 2 among the recruited pregnant women. Pre-pregnancy body mass index (BMI) recorded during first booking was at a mean of 24.52kg/m². About 8.0% of participants has gestational diabetes mellitus (GDM) while 0.61% of them has pregnancy-induced hypertension (PIH). The prevalence of snoring among pregnant women was 23.4%. Of the three hundred and twenty-nine participants, 8.2% were at high risk of obstructive sleep apnoea (OSA).

Socio-Demographic Factors

In the present study, we had analysed 2 socio-demographic factors including age factor and ethnicity shown in Table **1**. We found that the prevalence of snoring increased as the age advanced. The prevalence was the highest in 41 – 45 years old (42.9%) and lowest in 16 – 20 years old (6.7%). However, statistical analysis showed that the difference was not significant (p=0.273). In contrast, there is a significant risk of OSA as the age of the pregnant women advanced (p=0.024). In our study among the ethnicity in Malaysia, we found that ethnicity does not play a role in causing snoring (p=0.657) or is responsible for a high risk of obstructive sleep apnoea (p=0.976).

Associated Factors and Co-Morbidity

Obesity is a known associated factor in snoring and OSA in normal individuals. The BMI value for obesity was adjusted according to the Malaysian population and it was adapted from the Malaysia Clinical Practise Guidelines. BMI was found to be highly significant in our study (Table **2**). Pregnant women with high pre-pregnancy BMI snore more than those who had lower BMI with P value of 0.024. Of those who have high BMI value and snoring, they are also at higher risk of having OSA during their pregnancy (P=0.00).

We look at the two common medical disorders among Malaysian pregnant women - Pregnancy induced hypertension (PIH) and Gestational Diabetes Mellitus (GDM). Twenty six participants were found to have GDM, from which about 15.4% had a history of snoring and another 15.4% of them were unsure. About one tenth of those who snore were at high risk of

Table 1:   The Prevalence of Snoring and Obstructive Sleep Apnea in Pregnant Women of Different Demographic Factors (n,%)

	Snoring				Obstructive Sleep Apnoea		
	Snorer (n=77)	Non- Snorer (n=197)	Don't know (n=55)	P-Value	High Risk (n=27)	Low Risk (n=302)	P-Value
Age							
16-20	1 (6.7%)	12 (80.0%)	2 (13.3%)	0.273	0 (0%)	15 (100%)	0.024
21-25	9 (17.3%)	37 (71.2%)	6 (15.5%)		4 (7.7%)	48 (92.3%)	
26-30	32 (26.9%)	70 (58.8%)	17 (14.3%)		8 (6.7%)	111 (93.3%)	
31-35	21 (21%)	56 (56.0%)	23 (23.0%)		9 (9.0%)	91 (91.0%)	
36-40	11 (30.6%)	19 (52.8%)	6 (16.7%)		3 (8.3%)	33(91.67%)	
41-45	3 (42.9%)	3 (42.9%)	1 (14.3%)		3 (42.9%)	4 (57.1%)	
Ethnicity							
Malay	44 (24.2%)	104 (57.1%)	34 (18.7%)	0.657	15 (8.2%)	167 (91.8%)	0.976
Chinese	21(25.9%)	50 (61.7%)	10 (12.4%)		7 (8.6%)	74 (91.4%)	
Indian	12 (18.8%)	41 (64.1%)	11 (17.1%)		5 (7.8%)	59 (92.2%)	
Others	0 (0%)	2 (100.0%)	0 (0%)		0 (0%)	2 (100 %)	

Table 2:   The Prevalence of Snoring and Obstructive Sleep Apnea in Pregnant Women of Associated Factor and Comorbidity (n, %)

	Snoring				Obstructive Sleep Apnoea		
	Snorer (n=77)	Non- Snorer (n=197)	Don't know (n=55)	P-value	High Risk (n=27)	Low Risk (n=302)	P-Value
BMI							
<18.4	4 (16.0%)	16 (64.0%)	5 (20.0%)	0.024	0 (0%)	25 (100%)	0.00
18.5-22.9	18 (15.0%)	75 (62.5%)	27 (22.5%)		4 (3.3%)	116 (96.7%)	
23.0-27.4	26 (25.2%)	61 (59.2%)	16 (15.6%)		6 (5.8 %)	97 (94.2%)	
27.5-34.9	21 (32.3%)	37 (56.9%)	7 (10.8%)		12 (19.0 %)	53 (81.0%)	
35.0-39.9	7 (58.3%)	5 (41.7%)	0 (0%)		4 (33.3%)	8 (66.7%)	
>40	1 (25.0%)	3 (75.0%)	0 (0%)		1 (25.0%)	3 (75.0%)	
GDM							
Yes	4 (15.4%)	18 (69.2%)	4 (15.4%)	0.544	2 (7.7%)	24 (92.3 %)	0.921
No	73 (24.1%)	179 (59.1%)	51 (16.8%)		25 (8.3%)	278 (91.7%)	
PIH							
Yes	1 (50.0%)	1 (50.0%)	0 (0%)	0.613	1 (50.0%)	1 (50.0 %)	0.031
No	76 (23.3%)	196 (60.0%)	55 (16.7%)		26 (7.9%)	301 (92.1%)	

obstructive sleep apnoea. In this study, gestational diabetes mellitus was not found to be associated with snoring and higher risk of obstructive sleep apnoea. Unfortunately, we had only managed to recruit 2 patients with pregnancy induced hypertension among the 329 patients. Thus the data we obtained was insufficient to be analysed.

DISCUSSION

Of the 340 pregnant women who were approached, 329 (96.4) agreed to participate and completed the Berlin Questionnaire. The prevalence of snoring among these pregnant women was 23.4% and the prevalence of OSA among pregnant women was 8.2%. Kamil *et al.* has concluded that the prevalence of snoring among the general Malaysian population is 47.3%, while sleep apnoea is 15.2% [25]. However, it does not include pregnant women. This will be the first prevalence study of snoring and OSA among pregnant women in Malaysia. Although the prevalence of developing OSA is lower than general population and other population (elderly working in palm estate and commercial truck drivers) in Malaysia [26], but it was similar to other studies conducted among pregnant women in other Asian countries including Thailand, with prevalence of OSA of 5.9%, Hong Kong, with a prevalence of snoring of 40.5% and Korea with a 25.3% positive rates in Berlin Questionnaire [21, 23, 27].

Obstructive sleep apnea (OSA) is particularly common among Malaysians. As obesity is strongly associated with OSA, we think it is important to relook at the seriousness of the condition, now that the problem of obesity is also on the rise.

Obesity is an identified key risk factor for OSA and almost up to 50% of obese patients would be referred for some form of diagnostic sleep assessment. In our study, we had compared pregnant women who snore and non-snorers with BMI according to the Malaysian Clinical Practice Guidelines. Our data showed, more than 50% of them with BMI of 35-39.9 kg/m² are snoring, and 33.3% of women in this group have significant high risk of OSA (p - value of 0.00) and these finding correlates with a few other studies [28, 29]. In fact, one of the studies has quoted that a higher percentage of 71% of pregnant women with severe obesity has OSA [29]. The phenomenon could be explained by the possibility of increased likelihood of pharyngeal airway collapse by fat deposition around the lateral walls of pharyngeal airway in the muscles. Moreover, deposition of fat around the abdomen leads to a reduction in functional residual capacity which would eventually reduce lung volume and affects the upper airway. This is clearly expected in pregnant women with enlarged uterus [30].

The prevalence of snoring and OSA among pregnant women, however, still remains unknown [31]. Researchers think that the positive correlation between age and snoring is related to the respiratory effort in response to the upper airway occlusion as humans age [32]. As maternal age (> 25 years) advances, the prevalence of snoring increases. This can be demonstrated in our data, with the percentage of snoring increasing with age, being the peak at >40 years old. On the other hand, the risk of OSA increased as the age advances, from 0% in the youngest group, to 42.9% in the eldest group, in coherence with research done by Frederick *et al.* [32]. Furthermore with aging, daytime sleepiness would be frequent as well as waking up tired regardless of the quantity of sleep which leads to daytime impairment [22]. It is one of the contributing risk factors for OSA in older age group.

We have compared the prevalence of snoring and obstructive sleep apnoea (OSA) among the multiracial population in Malaysia. Of this, we found that Chinese pregnant women has the highest percentage of snoring and OSA (25.9%; 8.6%) as compared to the Malay (24.4%; 8.2%) and Indian (18.8%; 7.8%). This result correlates with a study by Kamil *et al.* [25] showing the prevalence of snoring in the Chinese population (56.1%) in Malaysia is the highest among the Indian (56.0%) and Malay (38.8%) ethnic group. Our result also correlates with the research by PL Leung *et al.* [23], whereby the Chinese pregnant women snore more frequently ranges from 29.7% to 46.2% respectively in first trimester to third trimester, much higher than the prevalence in general population in Hong Kong. We found that there is no correlation between ethnicity in pregnant women and snoring as supported by a similar study previously done elsewhere [21].

Any degree of glucose intolerance with onset or first recognition during pregnancy is known as Gestational Diabetes Mellitus, typically in the second trimester. Emerging data shows that 7% of pregnant women will be affected by GDM and the prevalence rises with the increasing rate of maternal obesity. Reutrakul *et al.* have reported a strong link between sleep disturbances with glucose intolerance and gestational diabetes mellitus (GDM) independent of BMI. Their study showed that nearly 75% of women with GDM also had OSA, which is exceptionally similar to the prevalence reported in non-pregnant women and men with type II Diabetes Mellitus [33]. On the contrary, our study showed that only 15.4% out of 22 pregnant participants with GDM who snore are at a higher risk of developing OSA which is insignificant with p value of 0.921.

We also studied the relationship between OSA and pregnancy induced hypertension as elevated blood pressure in pregnancy can have detrimental effects on maternal and foetal health during the perinatal period and beyond. Haney *et al.* [34] has proposed a model of how physical and hormonal changes in pregnancy coupled with stress, result in disturbed sleep, which in turn further elevates blood pressure. Hence, pregnancy-induced hypertension is not an independent risk factor in the prevalence of OSA among pregnant women. As of current data, only one participant with pregnancy-induced-hypertension in our study was categorized as high risk based on the Berlin questionnaire in contrast with the other 26 participants.

Among the limitations identified in this study is the fact that most candidates attends antenatal follow-ups alone and were unable to verify if they snore when they are asleep unless otherwise reported by their spouses, thus affecting the scoring of the first section of the Berlin Questionnaire. Besides, it is clear that the scoring of the 2nd category of the Berlin Questionnaire depends on an evaluation of sleepiness. However, fatiguability and sleepiness are common symptoms in pregnancy, which is not indicative of an underlying sleep disorder, hence this section of the questionnaire is associated with high false referral rate.

Banabillh *et al.* [15] revealed that Malay patients had a higher risk of developing obstructive sleep apnoea due to their craniofacial anatomy. Hence, we decided to conduct this research in Malaysia as we were interested to know if ethnicity is a risk factor of obstructive sleep apnoea. However, the futility of results were caused by an unequal distribution of races in Malaysia as the department of statistics Malaysia has reported that the majority of the population are Malays, followed by the Chinese and Indians. In addition, most Malays tend to attend antenatal care in the government's primary health care clinic while the Chinese and Indians prefers to do it in a private sector. This could be the reason why majority of our candidates were Malays.

Furthermore, we also faced challenges conducting our research in the primary health care clinics as most pregnant women with maternal illnesses such as GDM and PIH will be under the care of a tertiary health care unit.

A longitudinal study on the same candidates should be conducted after she has given birth to identify if pregnancy is the main contributor to the development of obstructive sleep apnoea. This study serves as a preliminary data for our future work on whether OSA significantly increases in pregnancy and has an impact on pregnancy outcomes.

The strengths of the study include an increasing level of awareness of obstructive sleep apnoea among pregnant mothers in the general population. Most participants are now more concerned about their quality of sleep and the significance of snoring.

CONCLUSION

In Malaysia, the prevalence of snoring and OSA among general population is well established. However, there is limited data of snoring and OSA during pregnancy. Data from other Asian countries like Thailand, Hong Kong and Korea suggested high prevalence of snoring and OSA among their pregnant women. Those studies also further suggested that OSA could lead to foetal growth retardation and underweight babies. We have shown that 23.4% of pregnant women snore and 8.2% of the total respondents have high risk of OSA which are lower than what was found in the general population. The factors that are strongly and significantly associated with OSA in pregnancy are older maternal age, snoring and high BMI. Further studies are therefore required to provide a better knowledge on the impact of OSA to pregnancy outcomes in Malaysia.

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