ORIGINAL ARTICLE

High Risk of Obstructive Sleep Apnea Among Hypertensive Patients at a Selected Tertiary Care Hospital

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ABSTRACT

Introduction: Obstructive sleep apnea (OSA) is a sleep-related breathing disorder characterized by partial or complete obstruction of the upper airway, which causes desaturations and arousal. Various studies have shown that OSA is a major modifiable risk factor for hypertension. Untreated OSA is increasingly associated with cardiovascular and neurocognitive sequela. Thus, our study aims to determine the high-risk of obstructive sleep apnea among hypertensive patients at a tertiary care hospital in Malaysia. **Methods:** A cross-sectional study was conducted among hypertensive patients at a tertiary hospital in Malaysia. A validated Malay version of the Berlin Questionnaire was utilized along with other questions on sociodemographic characteristics and diabetes mellitus. **Results:** A total of 161 respondents were involved in the study. The mean age was 48.35 years and among these 75% were males and 25 % were females. The majority of respondents were of Malay ethnicity (78%), followed by Chinese (11%) and Indians (10%). Of these,18 % comprised of obese patients and 29.8% had diabetes mellitus. The prevalence of high-risk OSA among hypertensive patients was 18.0% (95% CI). High risk of OSA was found to be prevalent in the elderly age group ($p<0.001$), female gender ($p<0.001$), Indian ethnicity ($p<0.001$) and among diabetes mellitus patients ($p<0.001$). **Conclusion:** The study results illustrate the high risk of OSA among hypertensive patients with advancing age and diabetes mellitus. This study finding mandates these high-risk hypertensive patients should be screened for early diagnosis and timely treatment of OSA to prevent further cardiovascular risk, morbidity and mortality.
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Keywords: Berlin Questionnaire, hypertension, Obstructive sleep apnea (OSA), polysomnography (PSG)

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INTRODUCTION

Sleep apnea is a common medical condition where there is a temporary cessation of breathing(apnea) during sleep. Obstructive sleep apnea (OSA) is characterized by normal inspiratory effort with temporary upper airway obstruction (1). Cardinal manifestations of OSA include snoring, excessive daytime sleepiness, morning headaches and short-term memory loss (2,3). OSA is associated with increased morbidity and mortality from cardiovascular causes and traumatic accidents due to excessive daytime somnolence (4-6). A study done among the adults attending primary health clinics in Malaysia revealed prevalence of high risk for OSA was 32.9% (7). Berlin questionnaire (8) is the validated and most widely used screening tool designed to identify the risk for OSA.

The gold standard for diagnosing and assessing the effects of treatment in many sleep disorders including OSA is in-laboratory polysomnography (PSG). Hypertension is defined as a persistent elevation of systolic blood pressure of 140 mmHg or greater and/or diastolic blood pressure of 90 mmHg or greater. Malaysian Community Salt Study demonstrated the prevalence of hypertension among the Malaysian population was 49.39% (9). Hypertensive patients with even severe OSA can be asymptomatic (10).

Several studies have shown OSA in hypertensive patients has a synergistic effect on the cardiovascular system (11-13). It is postulated that apneic events stimulate peripheral chemoreceptors which activate the sympathetic nervous system leading to an increase in blood pressure. Observational studies have demonstrated that the prevalence of OSA is around 30%–50% among hypertensive patients and 80% among resistant hypertensive patients (11,12,14-16).

The purpose of this study was to determine the high-risk of OSA among hypertensive patients using the Berlin questionnaire. The design of the other questions also permitted the analyses of high-risk of OSA based on age

group, gender, ethnicity, obesity, and diabetes mellitus.

MATERIALS AND METHODS

A cross-sectional study was conducted at a Malaysian tertiary hospital. The study population consisted of adult hypertensive patients receiving treatment from the medical clinic. The inclusion criteria were adult patients aged 25 years old and above. The hypertensive patients with mental /psychiatric illness, hypothyroidism and pregnancy were excluded. The sample size was calculated using Openepi.com Open Source Epidemiologic Statistics for Public Health with the average of high risk of OSA among hypertensive patients based on various studies. We estimated a 20% of non-respondent rate making the total sample size as 166. A total of 161 consented patients were included in the study and five respondents were excluded because of inadequate data.

Berlin Questionnaire (8) was chosen to assess the risk of having OSA in this study because of its highest sensitivity. A validated Malay version of the Berlin questionnaire was utilized to categorize the respondents to low or high likelihood of sleep-disordered breathing/ sleep apnea (17). The Berlin Questionnaire was divided into 3 main sections. Section 1 was concerning snoring, witnessed apneas and the frequency of such events. Section 2 addressed daytime sleepiness and drowsy driving. In Section 3, patients were to provide information on their history of hypertension, age, weight and height. Body mass index (BMI) was calculated from the weight and height of the patients in the clinic. There were also questions on gender, ethnicity, marital status and medical condition of diabetes mellitus. Risk grouping for high and low risk of sleep apnea was based on responses grouped into 3 sections. To be categorized as high risk of having sleep apnea, 2 or more sections need to obtain a positive score. A positive score for section 1 was defined as frequent symptoms of snoring and witnessed apneas. In section 2, a positive score was based on frequent symptoms in 2 or more questions about waketime sleepiness and drowsy driving. A positive score in section 3 can be obtained by having a history of high blood pressure or height and weight information giving a BMI>30kg/m^2. Those patients who denied having those symptoms were placed at low risk of having OSA.

Data analysis was done to determine the prevalence of high-risk of OSA among hypertensive patients by their age group, gender, ethnicity, obesity, and diabetes mellitus. Univariate analyses of categorical variables were performed using the Chi-square test. A Chi-Square test was performed to test for statistical significance for differences in the prevalence of high-risk of OSA by age group, gender, ethnicity, obesity and diabetes mellitus. To facilitate interpretation, some independent variables were categorized as follows: gender (male/ female), ethnicity (Malay/Chinese/Indian/Others), obesity (BMI>30kg/m^2 vs BMI<30kg/m^2) and diabetes mellitus (yes/no). The age group was divided into 4 groups, 26-40 years, 41-55years, 56-70 and 71-85years. The p-value of <0.001 was considered statistically significant for categorical values. The high-risk patients for OSA, identified during this study had been referred to the Otorhinolaryngology clinic for further clinical evaluation and management.

This study was approved by National Medical Research Registry of Malaysia (NMRR) NMRR-08-518-1673.

RESULTS

Of the 166 respondents, 161 (97%) were entered for data analysis. Socio-demographic characteristics of respondents were divided into age group, gender and ethnicity as shown in Table I. The mean age of respondents was 48.35(±13.08) and among these, the highest percentage (37.3%) belonged to the age group between 41 to 55 years. Statistical results showed age group between 56 to 70 years had a high prevalence of OSA (37.5%) while the age group of 41 to 55 had a low prevalence of obstructive sleep apnea (8.3%). The majority of respondents were male patients (75.0%) and the remaining 25.0% were female patients. Our female patients had shown a higher prevalence of high risk of OSA (39.0%) which was statistically significant (p-value <0.001), compared to that of male respondents (10.8%) as shown in the Table II.

Regarding ethnicity, the majority of the respondents were Malay race (78.0%), followed by Chinese (11.0%) and Indians (10.0%). Indian respondents had a significant prevalence (p-value <0.001) of high risk of sleep apnea (43.8%), followed by Chinese respondents (41.2%) and Malay respondents (11.1%).

Table I: Socio-demographic characteristics of respondents

Variables studied		n	%
a) Age group	26-40	50	31.1
	41-55	60	37.3
	56-70	40	24.8
	71-85	11	8.8
b) Gender	Male	120	75.0
	Female	41	25.0
c) Ethnicity	Malay	126	78.0
	Chinese	17	11.0
	Indian	16	10.0
	Others	2	1.0
d) Obesity	Non-obese (BMI<30kg/m^2)	132	82.0
	Obese (BMI>30kg/m^2)	29	18.0
e) Diabetes mellitus	With diabetes mellitus	48	30.0.
	Without diabetes mellitus	113	70.0

Table II: High risk of sleep apnea by age group, gender, ethnicity, obesity and diabetes mellitus

Variables studied		High Risk n (%)	Low Risk n (%)	χ^2	p value
Age group	26-40	6 (12.0)	44 (88.0)	15.955	p=0.001
	41-55	5 (8.3)	55 (91.7)		
	56-70	15 (37.5)	25 62.5)		
	71-85	3 (27.3)	8 (72.7)		
Gender	Male	13 (10.8)	107 (89.2)	16.445	p< 0.001
	Female	16 (39.0)	25 (61.0)		
Ethnicity	Malay	14 (11.1)	112 (88.9)	18.803	p<0.001
	Chinese	7 (41.2)	10 (58.8)		
	Indian	7 (43.8)	9 (56.2)		
	Others	1 (50.0)	1 (50.0)		
Obesity	Non-obese BMI<30kg/m^2)	21 (15.9)	111 (84.1)	2.195	p=0.138
	Obese (BMI>30kg/m^2)	8 (27.6)	21 (72.4)		
Diabetes mellitus	With diabetes mellitus	26 (54.2)	22 (45.8)	60.532	p<0.001
	Without diabetes mellitus	3 (2.7)	110 (97.3)		

Most of the respondents were non-obese (82.0%) while only 18.0% of respondents were obese. Obese respondents showed a higher prevalence of high risk of sleep apnea (27.6%) compared to those non-obese respondents (15.9%). However, there was no statistically significant difference in the prevalence of high-risk of sleep apnea by obesity as the p-value>0.05.

Concerning the association of diabetes mellitus, only 30.0% of respondents had diabetes mellitus while 70.0% of respondents were non-diabetic. Respondents with diabetes mellitus showed a higher prevalence of high risk of OSA (54.2%) than those non-diabetic respondents (3.1%) which was statistically significant with a p-value of <0.001.

In this study, the prevalence of high-risk OSA among hypertensive patients was 18.0% as shown in Fig. 1.

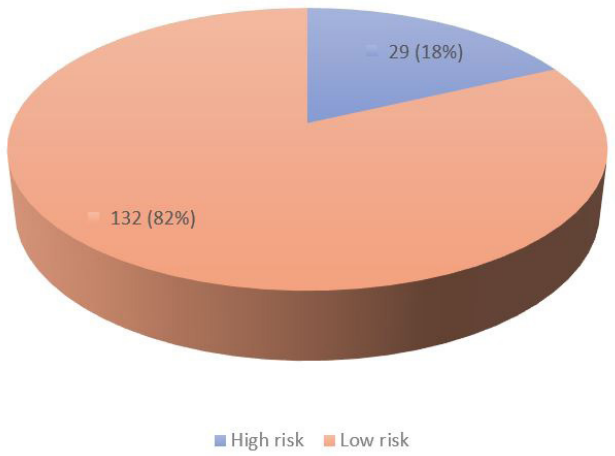

Figure 1: High risk of obstructive sleep apnea among hypertensive respondents (n=161)

DISCUSSION

Our study results demonstrated the prevalence of high risk of OSA among hypertensive patients at our institute as 18.0%. This finding was low compared to several other studies conducted even though the published results are not consistent (18-21). A literature-based analysis illustrated that globally the prevalence of OSA apnea affects around one billion people. Asian epidemiological studies demonstrated that the prevalence of OSA in patients with hypertension varies from 14 to 75% (19-21). Yeghiazarians et al mentioned in the scientific statement from the American Heart Association, OSA prevalence is as high as 40% to 80% in patients with hypertension and heart disease (22). OSA is highly prevalent in hypertensive patients, of whom 30% to 50% will have comorbid OSA. Where else study by Worsnop et al shows the wide variation of prevalence of OSA ranges from 12-83% (23). A study conducted by Pensuksan et al assessed the high risk for OSA among young adults using Berlin Questionnaire and found that the high risk for OSA among overweight and obese young adults is associated with elevated BP and hypertension, 12.9% and 4.5% respectively (20). This inconsistency and wide variation in different studies may be due to heterogeneity in the study populations, methods and monitoring devices used to assess OSA or the varying definitions of OSA and hypertension.

Our study setting is a tertiary Hospital where hypertensive patients are required to be referred since most of them are obtaining treatment from primary care health clinics. This led to a limited number of hypertensive patients attending the medical clinic. However, this was similar to a study conducted in India by Kareem et al which showed the prevalence of high risk of sleep apnea was 23.8% among hypertensive patients based on their response using the Berlin Questionnaire (19). According to population-based studies, the prevalence of high

risk of OSA in patients with uncontrolled hypertension ranges from 50% to 80% (11,12,15,19).

Our study findings revealed that among hypertensive respondents, the age group between 56-70 years old had a statistically significantly high prevalence rate of OSA. This finding was in accordance with a study done by Khamsai et al, which showed a peak prevalence rate of high risk of sleep apnea at 55 to 59 years of age in men while the corresponding figure in women the peak prevalence rate was at 60 to 64 years old (24). In contrast to this, a study conducted by Jinchai et al found a high prevalence of OSA in hypertensive patients younger than 35 years old (25).

Various previous studies demonstrated that male gender is an independent risk factor for OSA in patients with hypertension even though the reason for male predominance is unclear (18,24,26). In contrast to these findings, our study showed a statistically significant (p-value <0.001) high risk of sleep apnea among female respondents (39.0%) compared to male respondents (10.8%). O'Connor et al. also reported that female patients with moderate and severe OSA have a higher prevalence of essential hypertension than male patients (27).

Regarding the ethnic distribution of our study cohort, the prevalence of high-risk of sleep apnea was highest among the Indians (43.8%) p-value <0.001, followed by Chinese (41.2%) and Malays (11.1%). According to a Malaysian study conducted by Kamil et al, the prevalence of disordered breathing during sleep based on ethnicity was higher in Chinese (56.1%) and Indians (56.0%) than in Malays (38.3%) (28). Hou et al in their meta-analysis demonstrated that OSA and hypertension are strong among male patients and Caucasian populations (18). A study by Koo et al showed risks for OSA was positively associated with resistant hypertension in African Americans compared with Caucasians (29). Racial differences in OSA may explain the racial disparity in hypertension prevalence.

Our evaluation on the association between obesity and the high risk of prevalence of OSA revealed that obese hypertensive respondents had a high risk of sleep apnea (27.6%) compared to that of non-obese patients (15.9%). This was in line with the findings by Jehan et al and Romero et al (30,31) where a significant number of obese individuals (45%) were at high risk of sleep apnea compared to those non-obese individuals. A retrospective study by Xia et al found obesity and severe obstructive sleep apnea were independently associated with hypertension and severe OSA was associated with the presence of higher diastolic blood pressure (32). However, in our study results there was no statistically significant difference in the prevalence of high-risk of OSA by obesity as the p-value>0.05.

Among our study cohort, the prevalence of high risk of OSA in hypertensive patients with diabetes mellitus was 54.2% compared to that of non-diabetic patients. A cross-sectional study by Kawada et al observed that mild OSA was associated with a higher prevalence of impaired glucose metabolism and places patients at increased risk of the development of type 2 diabetes mellitus (33). Evaluation of epidemiological data by Kent et al also proved sleep apnea was independently associated with glucose intolerance and insulin resistance that led to type 2 diabetes mellitus (34).

There are various limitations in our study. Only consented patients were selected as respondents for the study, which means our study cohort was a convenient sample. This study was conducted in a tertiary hospital and the results might not be a representative of large general population. Another limitation is that we did not include the complete medical history of the patients which may affect the changes in blood pressure. Berlin questionnaire was utilized to evaluate the high risk of OSA even though sleep laboratory polysomnography is the gold standard test for the diagnosis of OSA in clinical settings (35). The in-lab polysomnography is expensive, time consuming and causes participant burden. We have used a validated modified Berlin questionnaire to identify the high risk for OSA before polysomnography due to limited resources. Future elaborative studies with a large cohort of hypertensive patients with various screening questionnaires to identify the high risk of OSA and further confirmation with polysomnography is recommended.

CONCLUSION

In conclusion, the findings of this study demonstrated that hypertensive patients with diabetes mellitus or within advancing age are associated with high risk of having OSA. The goal of this study was to raise public awareness of the dangers of untreated OSA in hypertensive patients as well as the potential consequences. Hypertensive patients who are at high risk for OSA should be screened early to obtain appropriate treatment and thus to reduce the associated cardiovascular risks and morbidity.

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