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Original Article

Internal Medicine Section

Assessing the Correlation between Severity of Obstructive Sleep Apnoea and Systemic Hypertension

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ABSTRACT

Introduction: Patients suffering from Obstructive Sleep Apnoea (OSA) have a strong association with acute cardiovascular events and chronic conditions such as systemic hypertension, coronary artery disease and heart failure.

Aim: To study the prevalence of hypertension in OSA patients and correlating the severity of hypertension with severity of OSA in terms of Apnoea-Hypopnoea Index (AHI).

Materials and Methods: A descriptive cross-sectional study was conducted at OPD of a tertiary care centre. The patients suffering from OSA as detected by a whole night polysomnography were included in the study. History of hypertension and number of antihypertensive medications taken for Blood Pressure (BP) control was obtained. BP measurement was done on two consecutive days and average of the readings was taken to calculate systolic and diastolic pressure. All continuous variables were summarised in terms of mean±SD, and categorical variables were expressed as percentages. Pearson's linear correlation was applied for continuous variables for comparison with AHI values and Fisher's exact test was used for nominal variables.

Results: Out of the total number of 42 patients suffering from OSA, 29 (69%) were found to be hypertensive and 4 (13.79%) of these 29 subjects were suffering from drug-resistant hypertension. Severe OSA (AHI >30) was found in 26 patients and frequency of hypertension in patients suffering from severe OSA was 23/26 (88.46%). Mild to moderate OSA (AHI <30) was seen in 16 patients and 6 (37.5%) out of these 16 patients were detected to be having hypertension. Fisher's exact test found statistically significant association between severe OSA and hypertension (p-value-0.0008). In non-obese patients, association between severe OSA and hypertension was assessed separately with p-value-0.0065. Pearson's correlation coefficient was greater for association between BP (SBP 0.643, DBP 0.653) with AHI than that of BMI.

Conclusion: Our study found the statistically significant correlation between systemic hypertension and OSA patients, independent of the confounding factor of obesity. Severity of hypertension showed linear correlation with the severity of OSA as indicated by AHI score.

Keywords: Apnoea hypopnoea index, Breathing disorder, Cardiovascular complications, Obesity

INTRODUCTION

Obstructive sleep apnoea is present when repetitive episodes of cessation of breathing or decrement in airflow occurs during sleep, associated with sleep fragmentation, arousals from sleep and fall in oxygen saturation [1]. AHI (number of apnoea and hypopnoeas per hour of sleep) is used to define as well as classify the severity of sleep apnoea. OSA syndrome is defined by AHI equal to or greater than five events/hour and persistent complains of excessive daytime somnolence or fatigue [1]. Obstructive apnoeas cause sympathetic surges conducive to development of acute cardiovascular events (i.e., stroke, myocardial infarction and nocturnal sudden death) and chronic conditions such as systemic hypertension, coronary artery disease and heart failure [2-4].

Various studies done abroad showed that about 50% of OSA patients are hypertensive and an estimated 30% of hypertensive patients also have OSA, often undiagnosed [5-9]. However, there is insufficient Indian data describing the effect of OSA on the severity of systolic and diastolic hypertension separately, independent of confounding factor of obesity in India. To fulfill this gap in knowledge, this study was carried out to determine the prevalence of hypertension associated with OSA, and to correlate the severity of hypertension with severity of OSA in terms of AHI Score.

MATERIALS AND METHODS

A cross-sectional study was conducted at Outpatient Department (OPD) of Department of Respiratory Medicine, Armed Forces Medical College, Pune, India, over a period of one year from 01 May 2016 to 30 April 2017. All cases with complaints of excessive day time sleepiness, witnessed apnoea and diagnosed as OSA based on polysomnography findings were included in the study. Haemodynamically unstable patients and patients with secondary hypertension were excluded. Patients were subjected to 32 channel polysomnography (Alice 5). It consisted of continuous polygraphic recording from surface leads for electroencephalography, electrooculography, electromyography, electrocardiogram pressure transducers for nasal airflow, thoracic and abdominal impedance belts for respiratory effort, pulse oximetry for oxyhaemoglobin level, microphone for snoring, and sensors for leg and sleep position. Patients with AHI score ≥5 were diagnosed as OSA and were taken up for further analysis [1]. OSA was further classified into mild, moderate and severe based on AHI values of 5 to 14 episodes/hour, 15 to 29 episodes/hour and more than 30 episodes/hour respectively [10]. Body weight in kg, height in cm was measured and Body Mass Index (BMI) was calculated in kg/m^2. Based on the BMI, subjects were divided into two groups, non-obese having BMI <30 kg/m^2 and obese with BMI >30 kg/m^2. This categorisation was done in order to find association between OSA and hypertension separately for obese and non-obese patients [11].

Blood Pressure Recording

Two supine BP readings were taken manually by sphygmomanometer on two consecutive days and average of readings was taken to calculate Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP). Readings were taken in right arm after the patient has been resting comfortably in the supine position for at least five minutes and at least 30 minutes after smoking or coffee ingestion. BP was classified as per Joint National Committee (JNC) 8 [12]. History of hypertension from subjects was taken and number of antihypertensive medications used to control BP was obtained. The

subjects were considered to be hypertensive if they were currently receiving antihypertensive medication or not a previously diagnosed case of hypertension but detected to be hypertensive during evaluation. Patients whose BP remains uncontrolled (BP >140/90 mmHg), despite concurrent use of three or more antihypertensive agents titrated to maximally recommended doses were considered to be suffering from resistant hypertension [13].

STATISTICAL ANALYSIS

Statistical analysis was performed using a statistical software package (SPSS Statistics 20.0). All continuous variables were summarised in terms of mean±SD and categorical variables were expressed as percentages. Pearson's linear correlation was applied for continuous variables for comparison with AHI values and Fisher's-exact test was used for nominal variables. All significance tests were two-sided and p-value of ≤0.05 was considered to be statistically significant.

RESULTS

Baseline Characteristics

Total number of 75 patients underwent polysomnography and 47 patients were diagnosed to be having OSA as defined by AHI ≥5. However out of 47 patients, five patients were excluded from study as four were haemodynamically unstable and one was suffering from secondary hypertension related to renovascular disease. Rest of the 42 patients was taken up for final analysis. Neck circumference was measured with the subject in the upright position. Baseline characteristics are mentioned in [Table/Fig-1]. Age range was from 31-75 years. Mean BMI was 28.43±5.295 kg/m^2, ranging from 22 to 50.68 kg/m^2. Out of 42 patients taken up for study 15 (36%) were obese having BMI >30 Kg/m^2 and 27 (64%) were non-obese having BMI <30 kg/m^2. Out of 42 subjects 6 (14.3%), 10 (23.8%) and 26 (61.9%) respectively were suffering from mild, moderate and severe OSA respectively.

Variable	Subjects (n=42)
Age (years) mean±SD	49.66±9.51 years
Sex (M/F)	35/7
Neck circumference (mean±SD)	41.55±2.80 cm
Hypothyroidism	4/42 (9.53%)
BMI (mean±SD)	28.43±5.295 Kg/m^2
AHI (mean±SD)	47.87±30.71/hour

[Table/Fig-1]: Baseline clinical characteristics and polysomnographic data.
Data is presented as mean±SD, M-Male, F-Female, BMI-Body Mass Index, AHI-Apnoea-hypopnoea Index, SD-Standard deviation

Apnoea-hypopnoea Index and Hypertension

Out of total number of 42 patients suffering from OSA, 29 (69%) were detected to be suffering from hypertension and 13 (31%) were normotensives i.e., they were neither on antihypertensives nor detected to be hypertensive during BP recordings. Amongst the study population of 42 subjects, nine were previously diagnosed cases of systemic hypertension and four out of these nine patients were suffering from drug resistant hypertension. Rest of 33 (78.6%) out of 42 subjects were not having previous history of hypertension. Frequency of hypertension as per various categories is tabulated in [Table/Fig-2].

Association between AHI score and hypertension is tabulated in [Table/Fig-3]. Cross tabulation showed that out of 26 patients with AHI ≥30/hour, 23 were suffering from hypertension i.e., frequency of hypertension in severe OSA is 23 (88.46%) out of 26. However, in case of subjects with mild to moderate OSA (AHI <30) 6 (37.5%) out of 16 were detected to be having hypertension. This shows that frequency of patients suffering from hypertension is more in patients of severe OSA as compared to mild and moderate OSA. Odds ratio for this cross table was 12.77 (95% confidence interval, 2.65 to 61.55). This indicates that AHI index more than 30/hour leads to

	Group	Frequency
Previous h/o hypertension		**9 (21.4%)**
(a)	Controlled on treatment	5 (11.9%)
(b)	Drug resistant	4 (9.5%)
No previous h/o hypertension		**33 (78.6%)**
(a)	Normotensive	13 (31.0%)
(b)	Prehypertension	5 (11.9%)
(c)	Stage-1 hypertension	3 (7.1%)
(d)	Stage-2 hypertension	12 (28.6%)
Total		**42 (100%)**

[Table/Fig-2]: Frequency of hypertension as per various categories.

	Apnoea-Hypopnoea Index (AHI)	Hypertension			p- value[a]
		Yes	No	Total	
All subjects (n=42)	AHI >30	23	3	26	0.0008***
	AHI <30	6	10	16	
	Total	29	13	42	
Non-obese Subjects (n=27)	AHI >30	13	2	15	0.0065**
	AHI <30	4	8	12	
	Total	17	10	27	

[Table/Fig-3]: Association of apnoea-hypopnoea index (AHI) with hypertension comprising all subjects and for non-obese subject (BMI <30 kg/m^2).
a) Fisher's exact test was applied to calculate p-value
**p-value ≤0.01 statistically significant
***p-value ≤0.001 statistically highly significant

12.7 times more risk for developing hypertension compared to AHI <30/hour. It detected statistically significant association with p-value-0.0008. Moreover, all the patients having resistant hypertension were suffering from severe OSA (AHI ≥30/hour).

To eliminate the confounding effect of obesity the association was assessed separately for patients with BMI <30 kg/m^2 and shown in [Table/Fig-3]. AHI >30 was detected in 15 patients and out of these 13 were detected to be hypertensive. AHI <30 was detected in 12 subjects and out of them only four were suffering from hypertension. Odds ratio was calculated to be 13 (95% confidence interval, 1.92 to 87.99) which implying that even in non obese patients, AHI index more than 30/hour leads to 13 times more risk for developing hypertension as compared to AHI <30/hour. Fisher's exact test used to find association between severe OSA and hypertension in non obese patients again detected statistically significant association (p-value-0.0065) as depicted in [Table/Fig-3].

Systolic blood pressure: Mean SBP noted was 134.67 mmHg (S.D±21.09). This is to note that mean of SBP suffering from OSA is higher than that of normal value of SBP and it falls in prehypertension category i.e., 120-139 mmHg.

Diastolic blood pressure: Mean DBP noted was 89.05 mmHg (SD±13.42). Similar to findings of SBP, mean of DBP was again more than normal value for SBP falling into prehypertension category (80-89 mmHg).

Pearson's linear regression was applied to assess the relationship of SBP with AHI and BMI. This has been tabulated as per [Table/Fig-4] which shows the Pearson's correlation coefficient and p-values of correlation of SBP with AHI and BMI. Value of Pearson's correlation was 0.643 for the correlation between AHI and SBP, however it was 0.313 for BMI and SBP. It implies that stronger correlation exists between SBP and AHI than BMI.

Further association of DBP with AHI score and BMI was assessed by Pearson's linear regression, shown in [Table/Fig-4]. Value of Pearson's correlation for association between DBP and AHI was calculated to be 0.653. However, it was 0.324 for association with that of BMI, again indicating that association of DBP is stronger with AHI score than BMI.

Blood Pressure		Apnoea-Hypo-pnoea Index (events/hour)	BMI (kg/m^2)
Systolic BP	Pearson's correlation coefficient (a)	0.643	0.313
	R-square linear (b)	0.413	0.098
	p-value	0.001***	0.044*
Diastolic BP	Pearson's correlation coefficient (a)	0.653	0.324
	R-Square linear (b)	0.426	0.105
	p-value	0.001***	0.036*

[Table/Fig-4]: Association between BP (Systolic/Diastolic BP) with apnoea-hypopnoea index (AHI) and body mass index (BMI).
a) Pearson's linear regression was applied to calculate correlation coefficient, indicating association of BP with AHI and BMI.
b) R-square linear is the coefficient of determination, applied to analyse how difference in BP was explained by AHI and BMI.
*p-value ≤0.05 denotes statistical significance.
***p-value ≤0.001 denotes statistical high significance.

Correlation coefficient was greater for association between DBP and AHI (0.653) than that of SBP (0.643) suggesting that association is more significant for DBP than SBP.

DISCUSSION

Our study has clearly depicted the association of OSA with high risk of cardiovascular comorbidity. In our study, out of total number of 42 patients suffering from OSA, 29 (69%) were detected to be suffering from hypertension. This is in sharp contrast to prevalence of hypertension in general Indian population measured as 17-21% in all the Indian states [14]. In our study, by using linear regression method, we found that the effects of severity of OSA on systemic hypertension were independent of obesity. The present study also detected stronger influence of OSA on DBP as compared to SBP, which is not described in any of the Indian study till date. However, as our study was the hospital based study, it was anticipated to show higher prevalence of hypertension as compared to general population. A landmark population based study was conducted by Hla KM et al., comprising 147 participants of sleep apnoea, recruited from Winconsin Sleep Cohort Study, a prospective, epidemiological study of sleep disordered breathing [15]. It detected prevalence of hypertension in 53 (36.05%) patients out of 147 participants. Being a clinic population based study, the severity of the disease was expected to be higher in our study as compared to population based Hla KM et al., study [15]. In our study, mean SBP noted in the patients suffering from OSA was 134.67 mmHg (S.D±21.09) and mean DBP noted was 89.05 mmHg (SD±13.42). These values are higher than the values of mean systolic BP 131 mmHg (S.D±1.7) and mean DBP 80 mmHg (SD±1.1) observed in the study conducted by Hla KM et al., being clinic population based study [15]. Peppard PE et al., conducted a population-based study on the association between objectively measured sleep disordered breathing and hypertension [4]. It concluded that the presence of sleep disordered breathing was predictive of the presence of hypertension four years later. However, our study being cross-sectional lacks this advantage. Nieto FJ et al., has done a large cross-sectional community-based study to assess the association between Sleep Disorder Breathing (SDB) and hypertension in apparently healthy middle-aged and older persons [16]. It represented the largest cross-sectional study to date comprising 6132 subjects. Mean SBP and DBP increased with increasing levels of AHI Score. For AHI >30 mean SBP and DBP were 130.1 mmHg and 76.3 mmHg respectively. However, multiple linear regression analysis revealed that BMI partially explained these associations, however a statistically significant linear association between AHI and BP was continued to be maintained even after adjustment for BMI [16]. Similarly in our study, association between hypertension and AHI was assessed separately for non-obese patients (BMI< 30 kg/m^2) so as to eliminate the confounding effect of obesity on hypertension. Our study revealed that even in non-obese patients, there was statistically significant association between severe OSA and hypertension. Obesity is a confounding factor which can itself lead to hypertension thereby association with hypertension was assessed separately for both AHI score and BMI. Association existed for both, however it was stronger between AHI score and hypertension than with BMI. Value of Pearson correlation was 0.643 for the correlation between AHI and SBP; however it was 0.313 for BMI and SBP. It implies that stronger correlation exists between SBP and AHI than BMI. Similarly for DBP correlation with AHI and BMI were 0.653 and 0.324 respectively.

Association of SDB with isolated diastolic hypertension was stronger as compared to isolated systolic hypertension and perhaps systolic/diastolic hypertension [17]. It implies that association with AHI score exists for both SBP and DBP but association is stronger for DBP as compared to SBP.

In our study, of 42 subjects, 4 (9.5%) were suffering from drug resistant hypertension and all the patients having resistant hypertension were suffering from severe OSA (AHI >30). Similarly, another uncontrolled study, the mean AHI among patients with difficult to control hypertension was 26/hour [18]. Logan AG et al., also demonstrated high prevalence of OSA in drug resistant hypertension [19]. All these studies together signifies the important role of OSA in the causation of resistant hypertension.

LIMITATION

However, our study results had certain limitations, it was hospital based study so results of this study cannot be generalised to whole population. Our study did not include control group to detect the background prevalence of hypertension. It was study with small sample size leading to wide confidence intervals, so taking this study as reference point, future larger studies can be planned to further substantiate the association of OSA with hypertension.

CONCLUSION

Our study concluded that AHI significantly impact both systolic and DBP. Increasing AHI caused progressively higher BP levels. This linear correlation of hypertension with AHI score was more with DBP as compared to SBP. Strong statistically significant correlation of hypertension with OSA was maintained even after excluding the confounding factor of obesity. All the patients detected to be having resistant hypertension were suffering from severe OSA. The information obtained from this study reiterates the need of increasing the awareness about OSA and its outcomes among the community and the physicians. Treatment of OSA should be started early to prevent its cardiovascular consequences.

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