Original Article

Obstructive Sleep Apnea in patients with Metabolic syndrome - A hospital Based Cross-Sectional Survey

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Objective: To determine frequency of OSA amongst patients with Metabolic Syndrome.
Methods: This was a hospital based cross-sectional study done in adult patients with MS who visited Lahore General Hospital from march 2019 to August 2019. Patients meeting the criteria for metabolic syndrome according to the new IDF definition3 (as described earlier) were screened for symptoms of OSA. Patients with end organ disease, hypothyroidism, critical illness and neoplasms were excluded from the study. Epworth sleepiness scale (ESS) questionnaire was used to evaluate EDS. Patients with symptoms indicative of OSA and ESS score of more than 10 underwent a limited sleep study with three channels recording nasal airflow measurement, chest movement and pulse oximetry. AHI > 5/Hr was considered positive for OSA. The limited PSG data was analysed and a diagnosis of OSA was made if the Apnea-Hypopnea index was >5 per hour. Further, OSA was graded as mild, moderate or severe as follows: AHI 5-15/hr: MILD OSA AHI 15-30/hr: MODERATE OSA AHI>30/hr: SEVERE OSA.
Results: Mean age of patients with OSA in our study was 55±9 years. OSA was found in 35 (37%) patients screened with ESS score>10. Twenty one out of 53 (39.6%) males and 14 out of 41 (34.1%) females had OSA. Even though the number of males was more than females in OSA group, there was no statistically significant difference between both gendes (p=0.37). Body mass index and Neck circumference were found to be significantly higher in OSA group compared with Non OSA group. Other parameters like Age, systolic and diastolic BP were not found to be significantly associated with OSA.
Conclusions: The study showed that there is a very high prevalence of OSA among patients with MS compared to that in the general population thus mandating the need for screening MS patients for undiagnosed OSA,
Keywords: obstructive sleep apnea (OSA), polysomnography, excessive daytime sleepiness (EDS), apnea-hypopnea index (AHI), metabolic syndrome (MS)

Introduction

Metabolic syndrome is becoming a matter of significant public health concern worldwide.[1] Insulin resistance plays a key role in the pathogenesis of metabolic syndrome.[2] According to the new IDF definition[3], for a person to be defined as having the metabolic syndrome they must have: (taken as it from IDF Guidelines)"Central obesity (defined as waist circumference with ethnicity specific values) plus any two of the following four factors; Recent evidence favors the notion of relation between OSA and the metabolic syndrome, which is reflective of poor cardiovascular outcomes.[4]

Obstructive sleep apnea(OSA), also known as Obstructive sleep apnea/hypopnea syndrome (OSAHS) is a sleep disorder characterized by recurrent upper airway collapse and obstruction during sleep associated with recurrent oxygen desaturation and arousals from sleep. OSA leads to symptoms such as snoring, witnessed apneas, excessive daytime sleepiness and road traffic accidents due to sleepiness. It is also associated with an increased risk of cardiovascular disease, hypertension, insulin resistance and cerebrovascular disease.[5]

Raised triglycerides:	≥150mg/dL (1.7mmol/L) or specific treatment for this lipid abnormality.
Reduced HDL cholesterol:	<40mg/dL (1.03mmol/L) in males, <50mg/dL (1.29mmol/L) in females, or specific treatment for this lipid abnormality.
Raised blood pressure:	systolic BP≥130 or diastolic BP≥85mmHg, or treatment of previously diagnosed hypertension.
Raised fasting plasma glucose:	(FPG)≥100mg/dL (5.6mmol/L), or previously diagnose type-II diabetes. If above 5.6mmol/L or 100mg/dL, OGTT is strongly recommended but is not necessary to define presence of the syndrome.

**If BMI is >30kg/m², central obesity can be assumed and waist circumference does not need to be measured.*

OSA is a fairly common condition, but often goes unrecognized. It is estimated that about 80% of cases are not diagnosed.[6] In the western population the prevalence of OSA in the middle-aged (30 to 60 years) is 4% in men and 2% in women.[7] However, very little literature [3] is available about the prevalence of OSA in south asian population. A study done in Delhi estimated the prevalence of OSA and OSAHS in an Indian study population to be 13.7% and 3.6% respectively.[9] A recent Pakistani study by Taj et al [10] reported 24.9% of the study population snoring with males snoring twice as much as females. Although loud snoring is seen in all patients with OSA, not all snorers have OSA. Understanding the differences between patients with OSA and simple snorers is important to explain the mechanisms responsible for upper airway obstruction rather than those between OSA and normal non-snorers. Polysomnography is considered to be the gold standard for diagnosis of OSA, estimation of its severity and measurement of treatment response. Sleep Labs are scarce in the country with only very few centres offering polysomnography. This study was conducted with the principal objective of determining prevalence of OSA among patients with MS.

Methods

This was a hospital based cross-sectional study done in adult patients with MS who visited Lahore General Hospital from march 2019 to August 2019 . Patients meeting the criteria for metabolic syndrome according to the new IDF definition[3] (as described earlier) were screened for symptoms of OSA. Patients with end organ disease, hypothyroidism, critical illness and neoplasms were excluded from the study. Epworth sleepiness scale (ESS) questionnaire was used to evaluate EDS. Patients with symptoms indicative of OSA and ESS score of more than 10 underwent a limited sleep study with three channels recording nasal airflow measurement, chest movement and pulse oximetry. AHI > 5/Hr was considered positive for OSA.The limited PSG data was analysed and a diagnosis of OSA was made if the Apnea-Hypopnea index was >5 per hour. Further, OSA was graded as mild, moderate or severe as follows: AHI 5-15/hr: MILD OSA AHI 15-30/hr: MODERATE OSA AHI>30/hr: SEVERE OSA. Data was analyzed using SPSS version 21.0. T test was used to compare means and Chi-square test was used to determine the association between the metabolic syndrome components and OSA. P value of <0.05 was taken as statistically significant.

Results

The mean age of patients with OSA in our study was 55±9 years. A total of 94 patients were included in this study, out of which there were 53 (56.4%) male and 41 (43.6%) female patients. The mean BMI was 31.3kg/m^2, mean waist circumference was 101cm and 48 (51%) of patients were obese. Diabetes was positive in83 (88.6%) patients, hyperlipidemia in 67 (71.3%) and hypertension in 63 (65.1%) patients. Other major comorbidities like ischemic heart disease was present in 30 (31.9%) and cerebrovascular disease in 4 (4.3%).
The symptoms of OSA among subjects were intrusive snoring, excessive daytime sleepiness and witnessed apneas. Other symptoms reported in relation to nocturnal sleep were difficulty in falling asleep in 27(28.7%), difficulty in maintaining sleep in 24(25.5%), nightmares in 7(7.4%) and limb jerking in 5(5.3%) patients. On upper airway assessment obvious nasal deformities or nasal polyps were not present. Receding jaw was present in 6 (6.4%) , and mallampati grade: 3 (3.2%) patients had grade 1, 40 (42.6%) had grade 2, 44 (46.8%) had grade 3 and 7 (7.4%) had grade 4 All those patients with clinical features suggestive of OSA and ESS > 10 underwent an overnight sleep study (limited Polysomnography) to confirm the diagnosis. It was found that 35 (37%) out of the 94 patients screened had a history suggestive of OSA and scored >10 on ESS. Hence they were subjected to an overnight sleep study. The mean AHI in these patients was 31.7/hour and Oxygen Desaturation Index (ODI) was 32.2/hour. The severity of OSA has been depicted in **(Fig-1).** Thus, there was a high pretest clinical probability of OSA in 35(37%) of patients; however 32 (91.4%) had PSG evidence of OSA; the remaining 3(8.6%) had a normal sleep study. Since the latter sub-group of 3 patients had a strong clinical history suggestive of OSA, ESS score of>10 and reported poor quality sleep on the night of the sleep study the, they were considered as mild OSA for statistical analysis. Twenty one out of 53 (39.6%) males and 14 out of 41 (34.1%) females had OSA. Even though the number of males was more than females in OSA group, there was no statistically significant difference with respect to gender between the OSA and Non-OSA groups (p=0.37). Body mass index and Neck circumference were found to be significantly higher in OSA group compared with Non OSA group. Other parameters like Age, systolic and diastolic BP were insignificant in patients with or without OSA. **Table-1**

As mentioned earlier, 67 (73.4%) of patients in this study were snorers. Other major symptoms were excessive daytime sleepiness in 46 (48.9%) and witnessed apneas in 16(17%) patients. Statistical analysis was performed to determine the correlation between these symptoms and the presence of OSA. Among patients who were snorers, 35(50.7%) had OSA. Besides, OSA was significantly higher in patients with EDS and witnessed apneas.

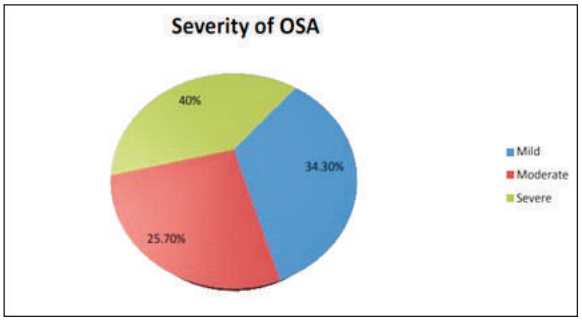

Fig-1: Severity of OSA in patients with MS and OSA.

Table-1: Comparing MS parameters between OSA and Non OSA groups.

Parameters	OSA	No OSA	P-value
Systolic BP (mmHg)	134.9±15.3	136.41±14.0	2.5
Diastolic BP (mmHg)	86.80±5.9	85.56±6.3	1.02
BMI (kg/m^2)	34.5617±6.1	29.4880±4.8	0.00
Waist circumference (cm)	1.3.37±8.5	99.93±8.9	1.4
Neck circumference (cm)	37.41±2.3	41.60±3.2	0.00

Table-2: Individual components of MS and OSA.

Individual components of MS	Total No of N	OSA	No OSA	p-value
Diabetes Mellitus	83	31 (37.3%)	52 (62.7%)	0.613
Hypertension	65	22 (33.8%)	43 (66.2%)	0.304
Hyperlipidemia	67	26 (38.8%)	41 (61.2%)	0.400

Discussion

Our study has demonstrated there is a high prevalence of OSA in patients with MS. It has been hypothesized that OSA itself may be a part of the spectrum of metabolic syndrome (Syndrome Z). Our study is unique and different from other studies for being a hospital based prevalence study of OSA in patients with metabolic syndrome. The prevalence of OSA was found to be as high as 37.2%, which is very high when compared with that reported in the general population in Pakistani as well as Western literature.[10,12-13]

Coughlin and Gruber et al reported a nine-fold and six-fold risk respectively, for independent association between OSA and metabolic syndrome.[11,14] Likewise, a study amongst Chinese subjects showed OSA subjects were at a five-fold risk of having the metabolic syndrome[15] and there was a positive correlation between AHI and the number of metabolic components present. Sharma et al conducted a community based study in South Delhi in 2010 and reported that MS and OSA (syndrome Z) in 19.9% of the population studied.[16]

Our study, being a hospital based study wherein nearly one third of patients had already developed end organ damage as a result of MS could have had metabolic derangements for a longer duration. This could have perpetuated a vicious cycle wherein the occurrence and severity of OSA among these patients could have been higher than that in the general population with MS. Due to the small sample size, it was not possible to sub-group patients on the basis of duration of various components of MS and assess the odds of having OSA or target organ damage. A larger study would be required to address this question. In our study, all patients were obese and it was found that increasing grades of obesity correlated well with presence of OSA. A higher waist circumference was noted in OSA when compared to the Non OSA group. Similarly, there was a statistically significant increased BMI in OSA group than in the Non OSA group. This observation was in concordance with many other studies which showed that obesity/BMI is one of strongest risk factors for OSA. Peppard et al[17] for instance showed that a 10% change in body weight was associated with a parallel change of approximately 30% in the apneahypopnea index (AHI), the major index of sleep apnea severity. Measurement of neck circumference (NC) is a part of the physical examination of patients suspected of having sleep apnea. The mean neck circumference in OSA patients in our study was higher than that of the non OSA group and the difference was statistically significant. Neck circumference > 16 inches in females and >17 inches in males amounts to an increased risk as it tends to make the retropharyngeal space shallow.[18] People with increased neck circumference have too much adipose tissue around the upper airway making it hard for the lumen of the pharynx to stay patent during sleep. In our study patients, snoring was commonest symptom of OSA followed by EDS and witnessed apneas. There was a significant difference between the OSA and Non OSA group in the incidence of these symptoms. Frequency of OSA among snorers was 50.7%, that among patients with EDS was 71.7% and it

was 81.2% in patients with witnessed apneas. Studies have shown that habitual snoring affects up to 50% of men and up to 30% of women in the general population. This goes largely unaddressed by medical providers due to decreased awareness regarding the issue. Snoring is also an important symptom for monitoring in long term management of OSA, because its recurrence after OSA treatment may signal a need to re-evaluate the therapy. According to Young et al.[7] (Wisconsin Sleep Cohort Study), habitual snoring occurs in 36% in adults and in more than 70% in subjects with an AHI of 5 or higher. Snoring is probably the most common complaint precipitating a referral to a sleep clinic. Excessive daytime sleepiness and witnessed apneas have been reported to be good predictors of OSA.[19] In our study, Epworth sleepiness scale (ESS) was used as a screening tool in patients presenting with symptoms suggestive of OSA. ESS is a simple, self-administered questionnaire which assesses daytime functioning including concentration levels, work performance and sleepiness. In patients with obstructive sleep apnea syndrome ESS scores were significantly higher.[19] In our study, 35(37.2%) patients had ESS score >10 and with other symptoms suggestive of OSA they underwent overnight sleep study and were proven to have OSA. Thus, the usefulness of ESS as a screening tool for OSA with almost no false positivity and good specificity has been reiterated in our study. Thus, symptoms, a high index of clinical suspicion and associated risk factors of OSA, along with an ESS score of >10 should guide further workup.

In our study population with metabolic syndrome most common component diseases were diabetes mellitus, dyslipidemia and hypertension in that order. The conclusions obtained from the analysis were that the incidence of OSA was higher in MS patients in comparison with general population. However, there was no particular group or co-morbidity that had a statistically significant association or predisposition to OSA in particular. Patients with diabetes had 37.3% prevalence of OSA, hypertension was associated with OSA in 33.8% and 38.8% had OSA among the patients with dyslipidemia. The diagnosis of OSA should always be considered in high risk patients with refractory heart failure, resistant hypertension, nocturnal cardiac ischemia and nocturnal arrhythmia. Treating sleep apnea can reduce the morbidity associated with these disease and help achieve better clinical outcomes. Significant association was seen between OSA and presence of diabetes mellitus and hypertension in the study by Udwadia et al[20] among urban Indian population.

Conclusion

The present study has demonstrated that there is a very high prevalence of OSA among patients with MS compared to that in the general population. Although a bigger study would have enabled derivation of the odds of developing OSA with MS or vice versa, there is convincing evidence from the present study to mandate screening for undiagnosed OSA in all patients with MS.

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