ORIGINAL ARTICLE

Prevalence of Metabolic Syndrome in Obstructive Sleep Apnea Syndrome

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Abstract

Background: Obstructive sleep apnea syndrome (OSAS) and metabolic syndrome have a strong association with each other. There is also evidence, of varying strengths, from epidemiologic and clinical studies about the independent association between OSAS and individual core components of the metabolic syndrome.

Objectives: To estimate the prevalence of metabolic syndrome and its individual components in patients with OSAS.

Methods: An observational hospital-based study was conducted where 53 patients with symptoms of OSAS were included. Limited sleep study was conducted for each patient and OSAS was diagnosed if apnea–hypopnea index was 5 or more. Metabolic syndrome was diagnosed as per the definition by National Cholesterol Education Program, Adult Treatment Panel III. Analysis was then carried out to find out the prevalence of metabolic syndrome and its individual components in OSAS.

Results: Of the 53 patients recruited, 42(79%) had OSAS. Among this group of 53 patients, 38 patients (71.6%) had metabolic syndrome, 35 patients (66.03%) had systemic hypertension, 25 patients (47.2%) had diabetes mellitus or an impaired glucose tolerance, 42 patients (79.2%) had dyslipidemia, and 47 patients (88.6%) had abdominal obesity. With the exception of diabetes mellitus/impaired glucose tolerance, the prevalence of remaining conditions was found to be higher in those with moderate-to-severe OSAS than in those with mild OSAS.

Conclusion: There is a high prevalence of metabolic syndrome as well as its individual components among OSAS patients and the prevalence increases with the severity of OSA.

Keywords: OSAS, Metabolic syndrome, Prevalence.

Introduction

Obstructive sleep apnea syndrome (OSAS) is an increasingly prevalent chronic condition that is still underdiagnosed[1] and is characterized by recurrent episodes of upper airway collapse during sleep, leading to intermittent hypoxemia and sleep fragmentation.[2]It is a peculiarity of this noisy disease that it announces itself to everyone within earshot—except its victims. Various global epidemiologic studies have shown the prevalence of OSAS to vary from 0.3% to 5.1%[1,3]whereas its prevalence in adult Indian population is approximately 3.5%.[4–6]Its diagnosis requires identification of characteristic symptoms,such as snoring or excessive daytime sleepiness, and confirmation with a sleep study.[7]The metabolic syndrome (MS) represents a cluster of closely related cardiometabolic features,

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namely, visceral obesity, insulin resistance, hypertension and dyslipidemia, and is diagnosed based on the criteria laid down by the National Cholesterol Education Program, Adult Treatment Panel III (NCEP: ATP III).[8] OSAS and MS have a strong association with each other owing to their common feature of obesity.[9] This association was termed as "syndrome Z" a decade ago.[10] It has been proposed that OSAS promotes metabolic dysfunction through cycles of intermittent hypoxia, leading to oxidative stress, sympathetic activation, and inflammation.[11,12] There is intense research interest in studying the relationship between OSAS and MS due to considerable evidence from various epidemiologic and clinical studies supporting independent association between these two entities. Beyond their epidemiologic relationship, growing evidence provides support to bidirectional, feed-forward, and pernicious associations between sleep apnea, sleepiness, inflammation, and insulin resistance, all promoting atherosclerosis and cardiovascular disease. Understanding the complex interaction between these entities may lead to more effective, better tolerated treatments for sleep disordered breathing and sleepiness, thereby lowering the adverse cardiovascular and metabolic complications detrimental in these populations. We, therefore, conducted this study with an aim of estimating the prevalence of MS and each of its individual components in patients with OSAS.

Material and Methods

We conducted an observational hospital-based study in which 53 consecutive patients visiting the outpatient department of a tertiary care hospital with clinical features suggestive of OSAS were included. A questionnaire was used to assess their demographic characteristics and medical history. The medical history chiefly included inquiry about symptoms of OSAS, namely, snoring and its intensity, presence of choking or witnessed breathing pauses, recurrent awakenings from sleep, excessive daytime sleepiness (measured by using the Epworth Sleepiness Scale (ESS) score[13]), nonrefreshing sleep, increased irritability, and lapses in concentration. History regarding significant past consequences and associated conditions,for example,stroke, coronary events, chronic kidney disease, was also obtained. However, family history for diabetes, hypertension, hyperlipidemia, or OSAS could not be obtained for all patients. The physical examination included measurement of body mass index (in kilograms per meter square), neck, waist and hip circumferences (in inches), and blood pressure. Neck circumference was measured at the cricothyroid level, waist circumference midway between 12th rib and iliac crest, and hip circumference at the level of greater trochanter, using a measuring tape. Investigations conducted before sleep study included blood investigations, namely, complete blood counts, fasting blood sugar levels, lipid profile included measurement of serum total cholesterol, serum high density lipoproteins (HDL) cholesterol and serum triglycerides levels, thyroid hormones profile and arterial blood gases analyses, a two dimensional echocardiography and spirometry. The pre-test probability of OSAS was assessed using the Epworth Sleepiness Scale (ESS) and sleep apnea clinical score (SACS).[14] The patients were then subjected to a limited sleep study, which was either hospital- or home-based, depending on the preference of the patient.In 2007, the American Academy of Sleep Medicine after an exhaustive review of the literature finally approved the use of limited sleep study. It recommended that unobserved registers with type 2–3 monitors can be used as an alternative to polysomnography diagnosis in patients in conjunction with a comprehensive clinical evaluation, as was performed in our study. The limited sleep study included continuous recordings for nasal and oral airflow (thermistors and nasal pressure transducers), tracheal sounds, thoracic and abdominal efforts, limb movements, body position, and oxyhemoglobin saturation (pulse oximeter). An abnormal breathing event was defined as a complete cessation of airflow for 10 s or more (apnea) or a 50% reduction in the respiratory airflow accompanied by decrease of 4% or more oxyhemoglobin saturation (hypopnea). The apnea–hypopnea index (AHI) was defined as total number of apneas and hypopneas divided by the number of hours of sleep. OSAS was diagnosed if AHI was 5 or more. On the basis of the AHI, the severity of OSAS was graded as follows: mild, AHI of more than or equal to 5 but less than 15;moderate, AHI of more than or equal to 15 but less than 30;severe, AHI of more than or equal to 30. MS was diagnosed when the patient had at least three of the following five conditions as defined by NCEP: ATP III[8]—(1) fasting plasma glucose $\geq$100 mg/dL or previously diagnosed type 2 diabetes or specific medication;(2) hypertension: blood pressure $\geq$130 mm Hg systolic or $\geq$85 mm Hg diastolic or specific medication;(3) central obesity: waist circumference (for South Asian $\geq$ 90cms (35 inches) or $\geq$ 80 cms in women (32 inches); triglycerides $\geq$ 150mg/dL (or receiving drug therapy for hypertriglyceridemia); and(5) high-density

lipoprotein cholesterol (HDL-C) below 50 mg/dL for women or 40 mg/dL for men (or receiving drug therapy for reduced HDL-C). Analysis was then performed to find out the prevalence of MS and its individual components in OSAS. The Statistical Package for the Social Sciences, version 15, software was used for data handling and analysis. Probability (*p*) values of less than 0.05 were considered statistically significant.

Results

A total of 53 patients with clinical features suggestive of OSAS and hence either referred or came on their own to our department for evaluation of the same were enrolled in this study. Among them, 40 patients (75.5%) were males and 13 (24.5%) were females (Table 1;Figure 1). The age range of this group was 13–78 years with mean age of 49 years. There was no history of significant consequences of stroke, coronary events, or chronic kidney disease in any of the patients. There was a history of recent weight gain (over 1–3 years before presentation) in 50 out of 74 obese patients (67%). OSAS pretest probability scores were calculated in all patients. On the basis of ESS, 10 patients (18.86%) were found to have low risk and 43 patients (81.86%) were found to have high risk of OSAS(Table2;Figure2).On the basis of the Sleep Apnea Clinical Scoring system, 8 patients (15.3%) were found to have mild risk, 24 patients (46.1%) were found to have moderate risk, and 21 patients (40.4%) were found to have high risk of OSAS(Table 3; Figure 3).

Out of these 42 patients, the severity of OSAS was found to be mild in 18 (42.8%), moderate in 8 (19.04%), and severe in 16 (38.1%) patients (Table4; Figure 4).Of the eight patients with mild risk of OSAS, five (62.5%) were subsequently diagnosed as having OSAS based on sleep study whereas of 45 patients with moderate-to-high risk of OSAS, 37 patients (82.2%) were diagnosed to have OSAS based on sleep study (Table 2). The positive likelihood ratio for moderate-to-severe risk of OSAS was 1.2.

Among this group of 53 patients, 38 patients (71.6%) had MS, 35 patients (66.03%) had systemic hypertension, 25 patients (47.2%) had diabetes mellitus or an impaired glucose tolerance, 42 patients (79.2%) had dyslipidemia, and 47 patients (88.6%) had abdominal obesity (Table 5; Figure 5). There was a history of recent weight gain (over 1–3 years before presentation) in 50 patients out of total 74 obese patients (67%).

However, when the data were analyzed to find out the prevalence of MS and its individual components among patients with a positive sleep study (AHI ≥5) and hence diagnosed as OSAS, it was observed that 31 patients (73.8%) had MS, 28 patients (66.6%) had systemic hypertension, 22 patients (52.3%) had diabetes mellitus or an impaired glucose tolerance, 32 patients (76.1%) had dyslipidemia, and 39 patients (92.8%) had abdominal obesity (Table 6; Figure 6).

Further analysis was conducted to see the difference in the prevalence of MS and its components in patients with mild OSAS and in those with moderate-to-severe OSAS. In patients with mild OSAS, 10 (55.5%) had MS, 10 (55.5%) had systemic hypertension, 10 (55.5%) had diabetes mellitus or an impaired glucose tolerance, 11 (61.1%) had dyslipidemia, and 15 (83.3%) had abdominal obesity. While in patients with moderate-to-severe OSAS, 21 (87.5%) had MS, 18 (75%) had systemic hypertension, 12 (50%) had diabetes mellitus or an impaired glucose tolerance, 21 (87.5%) had dyslipidemia, and all 24(100%) had abdominal obesity (Table 7;Figures 7 and 8). The difference in the prevalence of MS between the two groups was found to be statistically significant (p=0.03).

Table 1: Gender-wise distribution of study group

Gender	No. (%)
Males	40 (75.5)
Females	13 (24.5)
Total	53

Gender-wise distribution of study group

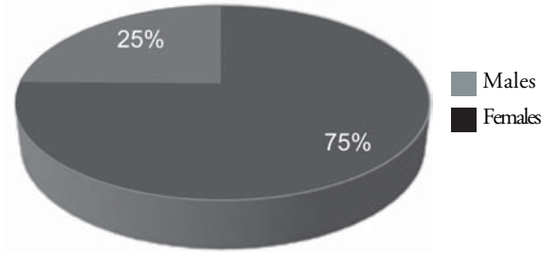

Figure 1

Table 2: Epworth Sleepiness Scale score-wise distribution of study group

ESS–Risk of OSAS	No.	Percentage
High	43	81.13
Low	10	18.86
Total	53	100.0

Epworth Sleepiness Scale (ESS) score wise distribution of study group

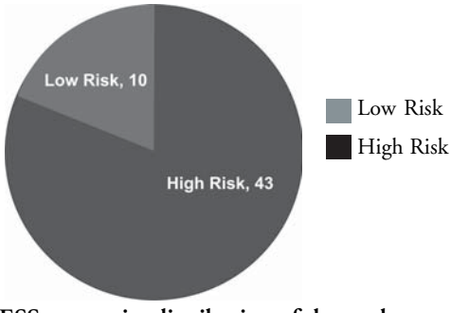

Figure 2 : ESS score-wise distribution of the study group

Table 3: Risk of OSAS based on SACS

Risk of OSAS (based on SACS)	No. of patients	Positive sleep study(AHI≥5)
Mild	8	5
Moderate	24	20
High	21	17
Total	53	42

Risk of OSAS based on SACS

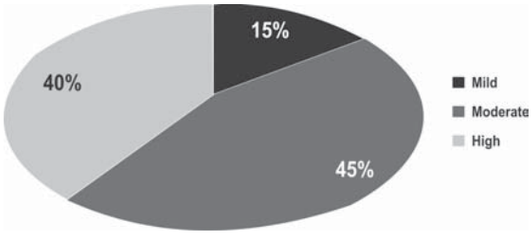

Figure 3: Risk of OSAS based on SACS

Table 4: Severity of OSAS based on sleep study

Severity of OSAS based onSleep study	No. of patients
Mild	18
Moderate	8
Severe	16
Total	42

Severity of OSAS based on sleep study

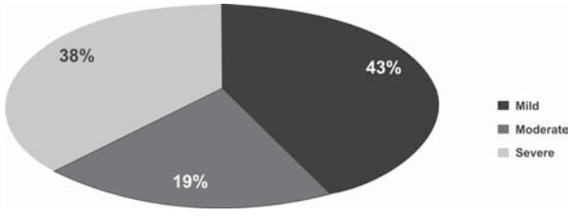

Figure 4

Table 5: Prevalence of metabolic syndrome and its individual parameters in the study group

Condition	No. of patients	%
Metabolic syndrome	38	71.6
Systemic hypertension	35	66
Diabetes mellitus or	25	47.2
Impaired glucose tolerance		
Dyslipidemia	42	79.2
Abdominal obesity	47	88.6

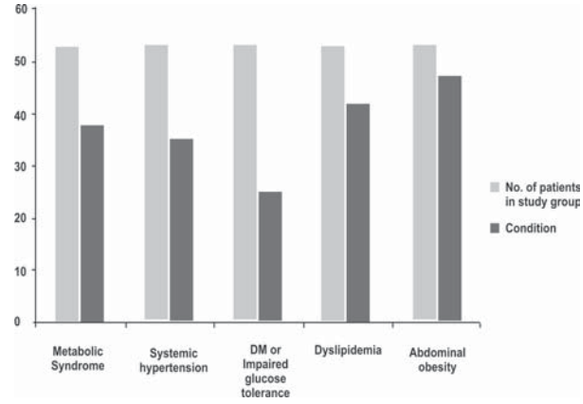

Figure 5: Prevalence of Metabolic syndrome and its individual parameters in the study group

Table 6: Prevalence of individual parameters of metabolic syndrome in patients with a positive sleep study

Condition	No. of patients with AHI≥5	%
Metabolic syndrome	31	73.8
Systemic hypertension	28	66.6
Diabetes mellitus or impaired glucose tolerance	22	52.3
Dyslipidemia	32	76.1
Abdominal obesity	39	92.8

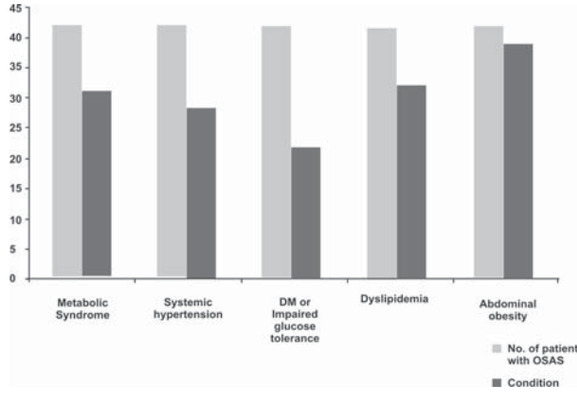

Figure 6: Prevalence of metabolic syndrome and its individual parameters in patient with a positive sleep study

Table 7: Prevalence of metabolic syndrome and its individual parameters in patients with mild and moderate-to-severe OSAS

Condition	Mild OSAS (n=18)	Moderate-Severe OSAS(n=24)	P value
Metabolic Syndrome	10 (55.5%)	21 (87.5%)	0.03
Systemic hypertension	10 (55.5%)	18 (75%)	0.03
Diabetes mellitus orimpaired glucose tolerance	10 (55.5%)	12 (50%)	0.03
Dyslipidemia	11 (61.1%)	21 (87.5%)	0.03
Abdominal obesity	15 (83.3%)	24 (100%)	0.03

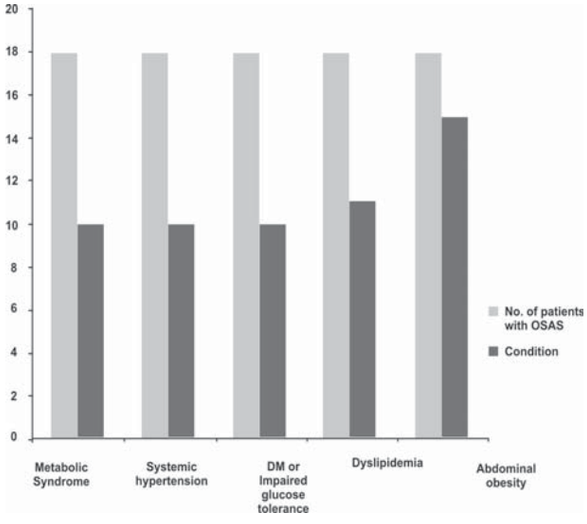

Figure 7: Prevalence of individual parameters of metabolic syndrome in patients with OSAS

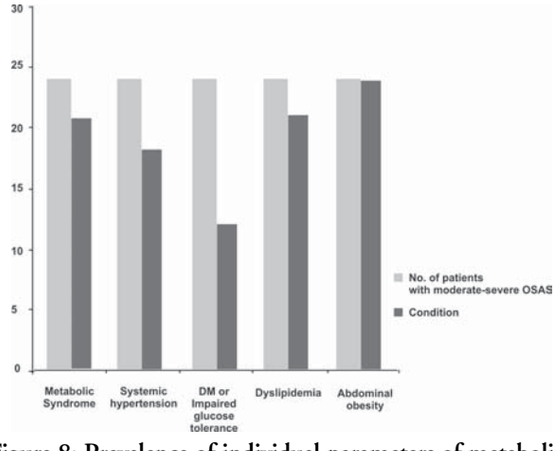

Figure 8: Prevalence of individual parameters of metabolic syndrome in patients withmoderate-to-severe OSAS

Discussion

In OSAS, there are recurrent obstructive events that cause cyclic intermittent hypoxia and sleep fragmentation, all of which lead to sympathetic activation, cellular oxidative stress, and systemic inflammation. This pathogenesis eventually leads to the development of characteristic features of MS.[11,15,16] We found 79% prevalence of MS in patients with OSAS, which is in concordance with that reported in a similar recently conducted hospital-based study among the Indian population by Agrawal *et al.*[17] Compared to another hospital-based study by Coughlin *et al.*,[9] our study showed lower values (87% vs 79%). This may be attributed to the ethnic difference in patient populations. We also found a high prevalence of systemic hypertension, diabetes/impaired glucose tolerance, dyslipidemia, and abdominal obesity among the OSA patients with a trend toward a higher prevalence in those with moderate-to-severe OSA as against those with mild form of OSA. These findings are also in concordance with those reported in previous studies, showing a higher prevalence of systemic hypertension,[17–19] diabetes/impaired glucose tolerance,[17,18] dyslipidemia,[17,18,20,21] and abdominal obesity[17,22,23] among patients with OSA. The Wisconsin Sleep Cohort study[19], a benchmark prospective study, showed a dose–response relationship between OSA at baseline and the presence of hypertension 4 years later. The findings of this study imply that there is a high prevalence of MS in patients presenting to the sleep clinics with symptoms suggestive of OSA. MS as a single entity as well as its individual components have a high likelihood of being present in patients with OSA and the risk increases with the severity of OSA. Hence, the screening of all patients with OSA for the MS component will allow an early detection of these cases. Also, an early intervention for OSA may decrease the severity of metabolic abnormalities, as shown in a study conducted by Sharma *et al.*[24] where treatment with continuous positive airway pressure therapy partially reversed the metabolic abnormalities, especially systemic hypertension.

Our study has some limitations. Being a hospital-based study, there was a referral bias with most referred patients having symptoms of OSAS as well as metabolic abnormalities. Hence, even those who were not having OSA were still more likely to have hypertension, diabetes, dyslipidemia, and obesity as compared to normal individuals.

This study shows that there is a high prevalence of MS as well as its individual components, namely, systemic hypertension, diabetes mellitus or an impaired glucose tolerance, dyslipidemia, and abdominal obesity, among patients with OSAS and the prevalence increases with the severity of OSA. Both OSAS and MS and their outcomes regardless of whether they are independent, additive, or synergistic are well established to be completely modifiable by lifestyle measures and other more specific interventional therapies. Therefore, an urgent need for the increased awareness of their strong association and thus an early detection of various cardiometabolic comorbidities cannot be overemphasized.

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