

Original Research Article

Prevalence of obstructive sleep apnoea in metabolic syndrome

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ABSTRACT

Background: The prevalence of both OSA and metabolic syndrome is increasing worldwide, in part linked to the epidemic of obesity. Beyond their epidemiologic relationship, growing evidence suggests that OSA may be causally related to metabolic syndrome. We are only beginning to understand the potential mechanisms underlying the OSA-metabolic syndrome interaction. Objectives were to study the clinical prevalence of obstructive sleep apnoea in metabolic syndrome; and to find risk factors associated with obstructive sleep apnoea (OSA).

Methods: 50 patients attending various OPDs of a tertiary care research and referral hospital and found to have metabolic syndrome on the basis of NCEP criteria were selected. These patients were subjected to overnight polysomnography. Parameters such as apnea-hypopnoea index (AHI), respiratory efforts related arousals (RERA), minimum SpO₂, pulse rate, blood pressure, and ECG were monitored throughout the study.

Results: Central obesity was found in 34 patients, xanthelasmas in 12 patients and xanthomas in 08 patients. Pitting type of pedal oedema was noted in 14 patients. Epworth sleepiness score (ESS) was calculated in all the patients by interviewing them before the polysomnography. Most of the patients have ESS Score more than 11.03 out of 50 patients were found to have AHI<5.20 patients were found to have moderate AHI (AHI 15-30) whereas 22 were found to have severe AHI.

Conclusions: Polysomnography provides a valuable tool to access non symptomatic sleep disordered breathing at an early stage in patients with metabolic syndrome.

Keywords: AHI, Metabolic syndrome, Obstructive sleep apnoea, Polysomnography

INTRODUCTION

Sleep disorders are common among the general population.^{1,2} Sleep related breathing disorders (SRBD) can impair academic and occupational performance, cause work-related and road accidents, and disturb mood and social adjustment. Private life and relationships may be adversely affected by the patient's SRBD. In addition, sleep-related breathing disorders may lead to or

exacerbate serious medical, neurological and psychiatric problems.³ Apnea is defined as reduction in airflow greater than or equal to 90% of baseline, recorded by oronasal thermistors or nasal pressure cannulas; duration ≥ 10 sec; and aforementioned reduction in airflow at least 90% of the event. The apnea-hypopnea index (AHI) refers to the average number of apneas and hypopneas per hour of sleep. AHI is used to describe the number of complete and partial obstructive events per hour of sleep.

Obstructive sleep apnea (OSA) or obstructive sleep apnea syndrome is the most common type of sleep apnea and is caused by obstruction of the upper airway. It is characterized by repetitive episodes of partial or complete obstruction of the upper airway during sleep, ultimately leading to increased respiratory effort, oxyhemoglobin desaturation, sleep fragmentation, and excessive daytime sleepiness. These pauses in breathing, called apneas (literally, "without breath"), typically last 20 to 40 seconds.^{4,5}

The primary cause of OSA is inspiratory collapse of the pharyngeal airway. This portion of the airway has little rigid support and is largely dependent on neuromuscular control to maintain patency.⁶ Patients with OSA have an anatomically small pharyngeal airway, which in adults is primarily due to obesity and is improved by weight loss and in children is most commonly due to enlarged tonsils and adenoids.⁷ While awake, this leads to greater airway resistance that activates mechanoreceptors to trigger reflex pharyngeal dilator muscle activity, thus maintaining airway patency.⁸ During sleep, dilator muscle activity is diminished, leading to pharyngeal narrowing and intermittent collapse of the upper airway. This can lead to a combination of hypopneas, or reduction in airflow associated with a fall in oxygen saturation, or apneas, or complete cessation of airflow.⁹ OSA severity is usually determined as follows: AHI 5-15 indicates mild, 15-30 moderate and over 30 severe OSAS. The oxygen saturation index (ODI 4%) describes the number of at least 4% drops in blood oxygen levels per hour of sleep. Obstructive sleep apnoea (OSA) is widely prevalent disorder particularly amongst middle-aged, obese men, although its existence in women as well as in lean individuals is increasingly recognized. Obstructive sleep apnea is a highly prevalent but underrecognized clinical problem. In an urban setting in northern India, the prevalence of obstructive sleep apnea and the obstructive sleep apnea syndrome is reported to be 13.7% and 3.8%, respectively.¹⁰

The metabolic syndrome, a cluster of cardiovascular risk factors, is associated with obstructive sleep apnea.³ Its prevalence varies from 74 to 85% among patients with obstructive sleep apnea and from 37 to 41% among patients with nonobstructive sleep apnea.¹¹ Obstructive sleep apnea has been shown to be an independent risk factor for hypertension and insulin resistance.^{12,13}

Patients with OSA have abnormalities in each of the "core" components of the metabolic syndrome- high blood pressure, high fasting glucose, increased waist circumference, low HDL cholesterol, and high triglycerides as well as in many of its other features, including sympathetic activation, endothelial dysfunction, systemic inflammation, hypercoagulability, and insulin resistance. It has even been suggested that the metabolic syndrome ("Syndrome X") should encompass OSA ("Syndrome Z").¹⁴

Metabolic syndrome (MS) is a combination of medical disorders that, when occurring together, increase the risk of developing cardiovascular disease and diabetes. This syndrome includes the clustering of abdominal obesity, insulin resistance, dyslipidemia, and elevated blood pressure. Additionally, it is associated with an immense number of other comorbidities.^{8,15} As the term syndrome implies, a single specific causative etiology to MetS is not clear. Nevertheless, abdominal adiposity and insulin resistance appear to be at the core of the pathophysiology of MetS and its individual components. The most accepted and unifying hypothesis to describe the pathophysiology of metabolic syndrome is insulin resistance. Although the incidence of metabolic syndrome in India is on the rise, there is paucity of Indian data on its correlation with obstructive sleep apnoea.¹⁵ This study was primarily designed to study the clinical prevalence of in metabolic syndrome; and to find risk factors associated with obstructive sleep apnoea (OSA).

METHODS

Setting

This study was undertaken at a tertiary care, research-oriented, super-specialty Hospital of Indian army. This centre has got high volume of patients with likely metabolic syndrome and has got all the facilities for adequate work-up and management of such cases as per standard guidelines.

Study design

It was a prospective observational and interventional study. Before conduct of study, the study design was exhaustively discussed in scientific committee and ethical committee of the institute and due permissions obtained. The objectives of the study and the criteria for patient selection were well-defined. The study period ranged from May 2010 to April 2013. 50 patients attending various OPDs at Army Hospital (R and R), Delhi Cantonment, New Delhi, India and found to have metabolic syndrome on the basis of NCEP criteria were selected for the study. These patients were subjected to overnight polysomnography and parameters such as apnea index (AHI), RERA, minimum SpO₂, pulse rate, blood pressure, and ECG were monitored throughout the study.

Subjects

All patients who were found to have metabolic syndrome on the basis of NCEP criteria in the study period were included.

Study criteria

The individual must fulfil criterion A, B and D, or C and D for obstructive sleep apnea-hypopnea syndrome (OSAHS).

A. At least one of the following:

- Sleepiness, hypersomnolence, exhaustion or insomnia
- Arousals with feeling of asphyxiation/ suffocation.
- Snoring, breathing pauses witnessed by sleep partner.

B. Polysomnography findings:

- Apnea, hypopnea or RERAs ≥ 5 per hour of sleep.
- Recording of respiratory effort during part of or the whole event.

C. Polysomnographic findings:

- Apnea, hypopnea or RERAs ≥ 15 per hour of sleep.
- Recording of respiratory effort during part of or the whole event.

D. The disorder cannot be attributed to other conditions, use of medicines or other substances.

RESULTS

Study was carried on 50 patients of metabolic syndrome as per National Cholesterol Education Programme Adult Treatment Panel (NCEP ATP III) who were subjected to overnight polysomnography. There were 42 males and 08 females.

The age of the patients in the study ranged from 29 to 74 years with a mean age of 54.8 ± 11.7 years. Age of male patients ranged from 38 to 74 years with mean age of

55.86 ± 11.60 years, whereas age of female patients ranged from 29 to 65 years with mean age of 49.25 ± 11.71 years. Mean body mass index of the study group was $30.23 \pm 1.9 \text{ kg/m}^2$. In males BMI ranged from 26.5 to 35.3 kg/m^2 with a mean of $30.36 \pm 1.85 \text{ kg/m}^2$. In females mean BMI was $29.55 \pm 1.85 \text{ kg/m}^2$.

Table 1: Correlation of BMI with AHI.

BMI_g	AHI_g				Total
	Normal	Mild	Moderate	Severe	
BMI 25 to 29.9	0	3	8	4	15
BMI ≥ 30	2	2	13	18	35
Total	2	5	21	22	50
Pearson Chi-square	5.119 p-value 0.163				

General physical examination revealed central obesity in 34 patients. Xanthelasmas were found in 12 patients, while 8 patients were having Xanthomas. Pitting type of pedal oedema was noted in 14 patients. Epworth sleepiness score (ESS) was calculated in all the patients by interviewing them before the Polysomnography. It was found that most of the patients have ESS score more than 11.

Out of 50 patients three (6%) had normal AHI (AHI<5). Five (10%) had mild OSA with AHI between 5 and 15. Twenty (40%) patients had moderate OSA (AHI 15 to 30). Twenty-two (44%) people had severe OSA (AHI>30). The majority of severe OSA patients (64%) were in the middle-aged group.

Table 2: Mean values of different variables according to AHI group.

AHI_g	Normal	Mild	Moderate	Severe	Total
BMI (kg/m ²)	31.12	29.45	29.81	30.73	30.23
Waist Circumference(cm)	104.5	102.75	98.81	101.8	100.75
Hip circumference (cm)	112	106.4	102.62	103.77	103.88
WHR	0.93278	0.96639	0.96327	0.98199	0.9706
Systolic	142	145.2	147.81	153.18	149.68
Diastolic	88	91.2	93.9	97.82	95.12
Fasting plasma glucose(mg/dl)	135	115.4	110.9	143.68	126.74
TG	177.5	172.6	180.86	214.91	194.88
CHOL	170	194.6	184.52	214.45	198.12
HDL	65	55.2	56.67	57.86	57.38

The mean BMI of the series of 30.23 kg/m^2 . Sixty eight percent (68%) of patients were obese whereas 32% patients were pre-obese (overweight) and non-obese. OSA was found in pre-obese and even non-obese but

severity of OSA was more in obese patients. The correlation of BMI with AHI is shown in Table 1. The Mean values of different variables according to AHI group is shown in Table 2.

Thirty-three (66%) patients were having fasting plasma glucose in diabetic range. Out of 33 patients, 21 (64%) had severe OSA. Significant correlation was found between uncontrolled plasma glucose and severity of OSA. Mean systolic blood pressure (SBP) of the series was 149.7 mm of Hg. Out of 50 patients, 32 (64%) patients were hypertensives. None of the hypertensives had normal AHI whereas 64% of hypertensives had severe OSA. Forty-nine (98%) patients were dyslipidemics. Only 4 % of them had normal AHI. Thirty eight percent (38%) had moderate OSA whereas 46% had severe OSA.

DISCUSSION

This work explores the association between MS and OSA in otherwise-healthy Caucasian male. So far, various studies have focused on detecting MS in OSA patients and showing that MS is more frequent in such patients than in the general population. The new aspect of this study is attempting to examine the reverse association.

There is adequate scientific evidence to suggest that obstructive sleep apnoea is a very prevalent disorder amongst middle aged, obese men, though its existence in women is also increasingly recognized.¹⁶ 4% of men and 2% of women in general population meet the clinical and polysomnographic criteria for the diagnosis of sleep apnoea, warranting immediate therapeutic intervention. A much larger group, 17-24% of men and 5-9% of women demonstrate Apnoea-hypopnoea index of more than 5 events per hour of sleep which was originally proposed criteria for sleep apnoea.¹⁷

In present study conducted on 50 diagnosed patients, who fulfilled the criteria for metabolic syndrome, a very high prevalence of sleep disordered breathing was observed. Despite the extensive literature on the role of anatomical abnormalities in pathogenesis of sleep apnoea, the large majority of sleep apnoeics do not demonstrate structural abnormalities and vice versa.^{18,19}

Although studies have proven OSA as an independent risk for hypertension, present study demonstrates that severity of OSA correlates with severity of hypertension.^{20,21} Severe hypertension was associated with higher AHI as compared to mild and moderate hypertension. Presently there are a couple of sets of defining criteria for metabolic syndrome set out by two different sources- the International Diabetes Federation and the revised National Cholesterol Education Program (NCEP).^{9,22-25} These are very similar and they identify individuals with a given set of symptoms as having metabolic syndrome. In the study conducted NCEP criteria has been used to ascertain metabolic syndrome among the subjects.

The US National Cholesterol Education Program Adult Treatment Panel III (2001) requires at least three of the following: central obesity: waist circumference ≥ 102 cm

or 40 inches (male), ≥ 88 cm or 36 inches (female); dyslipidemia: TG ≥ 1.7 mmol/L (150 mg/dl); dyslipidemia: HDL-C < 40 mg/dL (male), < 50 mg/dL (female); blood pressure $\geq 130/85$ mmHg; and fasting plasma glucose ≥ 6.1 mmol/L (110 mg/dl).

The present reference or “gold” standard for evaluation of sleep and sleep-related breathing is the in-laboratory polysomnogram (PSG), which was established through evidence-based reviews conducted by the American Academy of Sleep Medicine (AASM).²⁶ This method has been proven to be accurate with a low failure rate because the study is attended by technical staff.²⁷

In present study, 33 patients (66%) were having fasting plasma glucose in diabetic range, out of which 64% had severe OSA; while 32 (64%) patients were hypertensives, out of which 64% of hypertensives had severe OSA. Obstructive sleep apnoea (OSA) is associated with increased cardiovascular morbidity and mortality.

Although it was previously assumed that this was due to its relationship with obesity, recent data suggest that OSA is independently associated with the cardiovascular risk factors that comprise metabolic syndrome, including hypertension, insulin resistance, impaired glucose tolerance, and dyslipidaemia. Coughlin SR and colleagues demonstrated that OSA was independently associated with increased systolic and diastolic blood pressure, higher fasting insulin and triglyceride concentrations, decreased HDL cholesterol, increased cholesterol: HDL ratio, and a trend towards higher HOMA values.²⁸ In this study, metabolic syndrome was 9.1 times more likely to be present in subjects with OSA.

Gruber A and colleagues demonstrated that OSA is associated with MS independent of obesity predominantly due to increased triglyceride, glucose and Epworth score values but not insulin resistance (IR) or microalbuminuria status.²⁹ This observation suggests an alternative pathogenic factor mediating the increased cardiovascular risk in patients with OSA and MS, other than that due to IR.

CONCLUSION

Polysomnography provides a valuable tool to access non-symptomatic sleep disordered breathing at an early stage in patients with metabolic syndrome. In view of rising incidence of metabolic syndrome worldwide, the various diagnostic tools to establish and manage OSA must be exhaustively used. More studies need to be undertaken in Indian setup to establish guidelines for management of such cases.

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Ethical approval: The study was approved by the institutional ethics committee

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