Original Research Article

A study on prevalence of obstructive sleep apnea (OSA) in patients with metabolic syndrome (MS)

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Abstract

This was a cross-sectional hospital based study conducted in metabolic syndrome patients to determine the prevalence of OSA in. Patients fulfilling IDF criteria for metabolic syndrome were the study subjects. These patients were screened for OSA by clinical history, relevant physical examinations and Epworth Sleepiness Scale. Overnight Limited Polysomnography was performed in patients with high clinical probability of OSA. Statisticalanalysis of the collected data was carried out. It was found that prevalence of OSA in patients with MS was as high as 37.2%. Sub-group analysis showed that presence of symptoms like snoring, EDS and witnessed apnea were found to be higher in OSA group in comparison withthe non OSA group. Association of different parameters like BMI, Neck circumference and waist circumference with OSA were found to be statistically significant among metabolic syndrome patients. This study reinforced the point that all the patients with MS and associated co-morbidities should be screened for undiagnosed OSA in them to stop further progression of the disease and to prevent target organ damage.

Keywords: Metabolic Syndrome, Obstructive Sleep apnea, BMI, Polysomnography.

Introduction

Metabolic syndrome has become one of the major public health challenges worldwide[1]. It was first described as a cluster of metabolic abnormalities, with insulin resistance as the central pathophysiological feature, and was labelled as 'Syndrome X'[2]. It has been defined as a constellation of inter-related risk factors of metabolic origin, including hypertension, insulin resistance, dyslipidemia and obesity / visceral obesity. The cause of the syndrome remains unknown. Insulin resistance and central obesity have been acknowledged as key driving forces for the metabolic syndrome, and they are, independently, also well known cardiovascular risk factors. The prevalence of metabolic syndrome is increasing dueto the obesity epidemic. It is associated with a three-fold and two-fold increase in type II diabetes mellitus and cardiovascular diseases respectively. It is also associated with cardiovascular mortality as it comprises established risk factors for cardio-metabolic diseases[3]. Whether the syndrome is an independent risk factor to cardiovascular disease is subject to debate. Recent data show a strong association between OSA and the metabolic syndrome, which is indicative of adverse 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]. 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 is available about the prevalence of OSA in Indian 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[8]. 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[9]. Polysomnography is considered to be the gold standard for diagnosis of OSA, estimation of its severity and measurement of treatment response.

Recently, there has been great interest in the interaction between OSA and metabolic dysfunction. In particular, OSA has been independently associated with insulin resistance, suggesting that OSA may be an important factor for the development of type 2 diabetes and the so called metabolic syndrome (MS)[10]. Obstructive sleep apnea syndrome has been associated with an increased incidence of hypertension, stroke, and cardiovascular disease[11]. Syndrome Z is defined as the co-occurrence of OSA and metabolic syndrome[12]. Although there is circumstantial evidence to implicate OSA in the development of MS, the causal relationship remains unproven. Recent community based study on prevalence of OSA ,MS and Syndrome Z in urban population in New Delhi, shows that there is a high prevalence ofOSA among the patients with MS[12].

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Aims & Objectives

Aim

The aim is to determine the prevalence of Obstructive sleep apnoea in patientsdiagnosed with metabolic syndrome.

Objectives

Objective of the study was to evaluate patients with metabolic syndrome for OSA.

- Patients meeting the criteria for metabolic syndrome were screened for symptoms of OSA.
- Epworth sleepiness scale (ESS) questionnaire was used to evaluate EDS.
- Patients with suggestive symptoms of OSA and ESS of the score more than 10 underwentlimited polysomnography with three channels which include nasal airflow measurement, chest movement and pulse oximetry. AHI > 5/Hr was considered positivefor OSA.

Materials and methods

This was a hospital-based cross-sectional study done in adult patients with MS who visited the Kurnool Medical College/General Hospital over a period of 15 months (September 2020 to November 2021)

Inclusion criteria

Patients fulfilling IDF criteria for metabolic syndrome (as mentioned below).

According to new International Diabetic Federation (**IDF) criteria[1]** for a person to be defined as having the metabolic syndrome they must have:

Central obesity – defined as waist circumference 90cm for men and 80 cm for women(Indian population).

Plus any two of the following four factors

1. Raised triglyceride (TG) level 150mg/dl or specific treatment for this lipidabnormality
2. Reduced High Density Lipid (HDL) cholesterol <40mg/dl or specific treatment for thislipid abnormality
3. Raised arterial blood pressure (B.P) systolic 130mm of Hg, diastolic 85mm of Hgor treatment for previously diagnosed hypertension.
4. Raised Fasting Blood Glucose (FBG) 100mg/dl or previously diagnosed type2diabetes.

Exclusion criteria

- Hypothyroidism
- Critically ill patients
- Patients with end stage organ disease and malignancy
- Pregnant women

Methods

The following data were compiled in all patients.

- Clinical history and demographic data.
- BMI (wt in kg/ht in meter^2)
- Blood pressure (recorded after at least 5 minutes of rest in both arms sitting/supineposition)
- Waist circumference (measured in a horizontal plane midway between the inferiormargin of the ribs and superior border of the iliac crest)
- Hip circumference
- Blood samples of 5ml will be drawn after 12 hours overnight fasting for the measurement of lipid profile, fasting plasma glucose
- Patients fulfilling the International Diabetic Federation (IDF) criteria for metabolic syndrome were screened for symptoms of OSA (snoring, witnessed apneas and excessive day time sleepiness). Epworth sleepiness scale was used to screen for Excessive Daytime Sleepiness (EDS). Physical examination was performed to look forupper airway anatomy (Mallampati grading was used). Patients with symptoms suggestive of OSA and ESS score of more than 10 underwent a limited polysomnography with three channels which included nasal airflow measurement, chest movement and pulse oximetry.

Diagnosis of 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, moderateor severe asfollows:
- AHI 5-15/hr: MILD OSA
- AHI 15-30/hr: MODERATE OSAAHI>30/hr: SEVERE OSA

Analysis of data

- All the quantitative variables in the present study were summarized in terms of descriptive statistics such as mean and standard deviation or median and range. All the qualitative variables were expressed in terms of frequencies and proportions.
- Student T test was used to compare the difference between the mean values in OSA and Non OSA groups. Chi-square test was used to find the association between the metabolic syndrome components and OSA. P value <0.05 was considered to statistically significant.

Results

Demographic Data (Table 1)

A total of 80 patients were included in this study, out of which there were 48(64.44%) male and 32 (36.66%) female patients. Majority of the patients in this study were middle aged with a mean age of 56 years. The mean BMI was 31.3kg/sq. m, mean waist circumference was103cm and 48 (51.21%) of patients were obese.

Table:1 showing distribution of age and physical examination findings.

(BMI: Body mass index, WC: waist circumference, HC: hip circumference, NC: neckcircumference.)

N= 80	Age (years)	BMI (Kg/m^2)	WC (cm)	HC (cm)	WAIST/HIP RATIO	N.C (cm)
Mean and Std deviation	51±9.11	30.22 ± 4.87	101.21±8.87	96.01± 7.01	1.011±0.037	36.87±3.2
Minimum	31	20.12	86	78	0.76	31.9
Maximum	77	56.5	136	134	1.02	53

Clinical features of OSA in patients with MS

The symptoms of OSA among subjects were intrusive snoring, excessive daytime sleepinessand witnessed apneas (Table:2). Other symptoms reported in relation to nocturnal sleep weredifficulty 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(figure: 3)

Table: 2 Symptoms of OSA

Symptoms	Number of patients (%) N= 80

Snoring	53 (88.33 %)
EDS*	16(26.66 %)
Witnessed apneas	11 (18.33 %)

*Excessive daytime sleepiness

Prevalence of OSA in patients with Metabolic syndrome (Figure: 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 80 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 Figure--. Thus, there was a high pre-test 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.

Severity in Patients with OSA: (Figure:5)

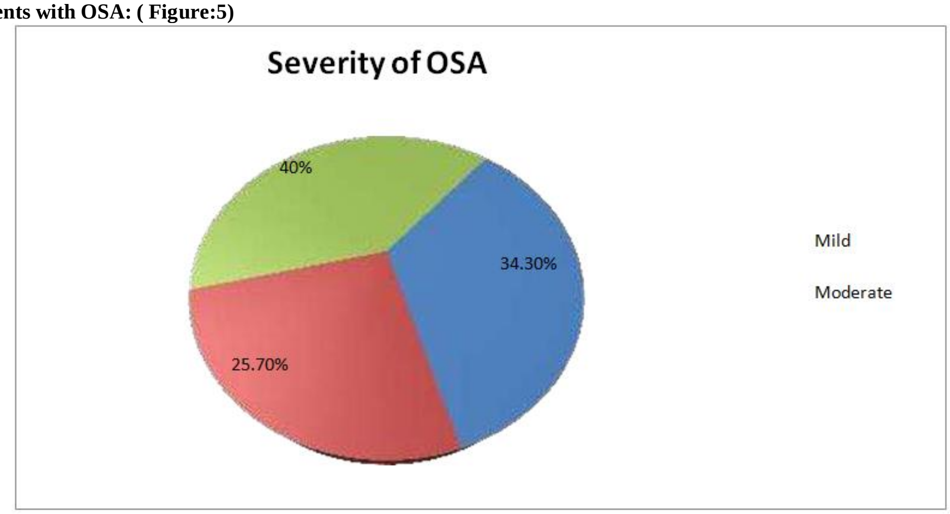

Figure: 1 Severity of OSA in Patients with MS and OSA

Comparison between ms patients with and without OSA

Age and Gender

Age group of the study population ranged from 33 years to 78 years. Mean age of patients with OSA in our study was 55 ± 8 years. Twenty one out of 12 (63.44 %) males and

13 out of 25 (32.0 %) 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). (Table: 3)

Table 3: Age distribution in OSA patients

Gender	OSA	No OSA	% with OSA
Male	12	36	25
Female	13	19	40

It was found that majority of patients with OSA belonged to age group of 50-60years.(figure)

Individual Components of MS and OSA

Further analysis was performed in order to compare various demographic parameters as well as individual criteria for MS between patients with and without OSA, the results of which are depicted below.(Table:4)

Table: 4 Comparing MS parameters between OSA and Non OSA groups

Parameters	OSA	No OSA	P value
Systolic BP (mmHg)	132.9±12.5	131.41±12.7	2.5
Diastolic BP (mmHg)	82.80±5.1	85.51± 4.6	1.02
BMI ($kg/m^{2)}$	32.5 1±7.1	26.11± 3.6	0.001
Waist circumference(cm)	102.11± 7.1	78.11 ±7.8	1.2
Neck circumference (cm)	32.1 ± 1.9	38.6 ±3.2	0.001

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.

Symptoms and OSA

As mentioned earlier, 52 (65 %) of patients in this study were snorers. Other major symptoms were excessive daytime sleepiness in 38 (47.5%) and witnessed apneasin 12 (15 %) patients. Statistical analysis was performed to determine the correlationbetweenthese symptoms and the presence of OSA.

Among patients who were snorers 28 (53.84 %) had OSA. Besides, OSA was significantly higher in patients with EDS and wittnessed apneas. (TABLE: 5)

Table: 5 Symptoms and OSA

Symptoms	Total number	OSA	NO OSA	P value
Snoring	52	28 (53.84 %)	24 (46.15 %)	<0.05
EDS	38	21 (55.26 %)	13(44.73 %)	<0.05
Witnessed apneas	12	13 (81.2%)	3 (25 %)	<0.05

Individual components of MS and OSA (Table:6)

The frequency of OSA among patients with Diabetes mellitus, hyperlipidemia and hypertension has been depicted in table below. These correlations were not found to have statistical significance.

Table: 6 Individual components of MS and OSA

Individual components of MS	Total no N	OSA	Non OSA	P value
Diabetes mellitus	61	21 (26.25 %)	40 (50.0 %)	0.513
Hypertension	58	16(20.0 %)	42 (52.5 %)	0.218
hyperlipidemia	54	13 (16.25 %)	41 (51.25%)	0.312

Other co-morbid illnesses and OSA (Table:10)

In addition to fulfilling criteria for MS may subjects in our study had co- morbid conditions namely IHD in 24 (31.9%) and CVA in 3 (4.2%) patients. Among patients with IHD 6 (26.7%) of them had OSA and among patients with CVA 1 (25%) of them had OSA. The association was not statistically significant in both patients with IHD andCVA.

Table: 7 Co-morbid illnesses and OSA

Complication of MS	OSA (%)	No OSA (%)	P value
IHD	6 (25 %)	18 (75 %)	0.12
CVA	1 (25%)	2 (75%)	0.511

Discussion

The results of our investigation revealed that people with MS have a high prevalence of sleep apnea. This is consistent with the data that have been reported in the literature to date. A large number of studies have demonstrated a link between OSA and various components of the MS. However, there is a paucity of research associating MS as a whole with OSA. A study conducted on patients with OSA found that the prevalence of metabolic syndrome was higher in patients with OSA than in the general population or among obese non-OSA subjects[13]. It has been postulated that OSA itself may be a component of the metabolic syndrome spectrum of conditions (Syndrome Z).

Our study is unique and different from other studies since it is a hospital-based prevalence investigation of OSA in patients with metabolic syndrome, which makes it unique and different from other studies. It was discovered that 21 (26.25 percent) of the participants had OSA, which is extremely high when compared to the prevalence of OSA described in both Indian and Western literature in the general population[8].

The findings of a case-control research conducted in Japan revealed an independentconnection between OSA and metabolic dysfunction.

Men are more susceptible to the condition than women[14]. Other research has discovered connections between sleep-disordered breathing and a variety of metabolic variables associated with the metabolic syndrome that are not related to obesity. According to a study conducted by Sharma et al in 2006, obesity, rather than OSA, was the determining factor in the development of derangements in MS.15 In 2010, the same authors conducted a community-based study in South Delhi and discovered that 19.9 percent of the people investigated had MS plus OSA (syndrome Z)[12]. Because our study was conducted in a hospital setting where approximately one-third of patients had already exhibited end organ damage as a result of MS, it is possible that metabolic derangements persisted for a longer period of time. This could have resulted in the perpetuation of a vicious cycle, with the prevalence and severity of OSA among these patients potentially being higher than in the overall MS community. Given the short sample size, it was not able to differentiate individuals based on the duration of distinct MS components or to determine the likelihood of developing OSA or target organ damage. In order to answer this question, a larger study would be required.

The age range of patients with MS and OSA in our study ranged from 41 to 78 years.

Sixty-eight percent of the patients were between the ages of 40 and 60, with the remaining 32 percent being over the age of 60. According to two studies by Bixleet al[16]and the Sleep Heart Health Study[17], the majority of the age-related increase in the incidence of OSA occurs before the age of 65 and that the prevalence rate then reaches a plateau. According to our findings, the prevalence of OSA is increasing at a similar rate in individuals with multiple sclerosis (MS), supporting the concept that OSA is an underlying feature of the disease. Males outnumbered females in our group of OSA and MS patients by a three-to-one margin. Of the 48 patients with OSA, 64.44 percent were male and 32 (36.66 percent) were female. Despite the fact that there was a little male preponderance in the OSA group, this did not prove to be statistically significant.

According to OSA prevalence surveys, males are 2 to 3 times more likely than women to suffer from the condition, with middle-aged obese men being the most affected[18]. In premenopausal overweight women, menopausal women who are not receiving hormone replacement treatment, and overweight women who are receiving hormone replacement therapy, this sex-protective benefit for females is lessened. When OSA and MS coexisted, we found a comparable gender ratio and susceptibility to developing OSA, which was consistent with previous research.

All of the patients in our study were obese, and it was discovered that rising grades of obesity were significantly associated with the prevalence of OSA. Comparing the OSA and non-OSA groups, it was discovered that the OSA group had a larger waist circumference. Additionally, there was a statistically significant rise in BMI in the OSAgroup compared to the Non OSA group in a similar manner. This finding was in agreement with the findings of numerous other research, which demonstrated that obesity / BMI is one of the most significant risk factors for OSA, as discussed further below.

When looking at a community-based cohort of people in their forties, Young et al[7] discovered that a one standard deviation (SD) increase in body mass index was associated with a four-fold increased risk for prevalent sleep apnea, and they discoveredthat moderately overweight men from the community who were otherwise healthy had an estimated sleep apnea prevalence of approximately 40%. The prevalence of sleep apnea in extreme obesity (BMI > 40 kg/m2) has been estimated to range between 40 and90 percent, with the severity of sleep apnea being generally greater than that reported in leaner clinical groups. More evidence has been presented by Peppard et al 41, who demonstrated that an increase in body weight of 10% was associated with an increase in the apnea–hypopnea index (AHI), which is considered to be the most important indicator of sleep apnea severity, by around 30%. In a study conducted by Vgontzas et al.[18], markers of OSA severity, such as the apnea-hypopnea index or the degree of oxygen desaturation, were found to be associated with the quantity of visceral fat.

When a patient is suspected of having sleep apnea, the neck circumference (NC) measurement is performed as part of the physical examination. During our research, we discovered that the mean neck circumference of OSA patients was significantly higher than that of the non-OSA group, and that the difference was statistically significant. It is associated with an increased risk if a woman's neck circumference is greater than 16 inches or if a man's neck circumference is greater than 17 inches. This is because a large neck circumference tends to make the retropharyngeal area shallow[82]. According to the Wisconsin Sleep Cohort, even a ten percent increase in body weight increases the risk of OSA by a factor of six times. In order to explain this increased risk, it has been postulated that excess adipose tissue surrounding the upper airway increases neck circumference and provides mechanical obstacles to the lumen of the pharynx in order for it to remain patent during sleep[19].

In our study participants, snoring was the most common symptom of OSA, followed by EDS and witnessed apneas, according to the findings. Between the OSA and non-OSA groups, there was a statistically significant difference in the occurrence of these symptoms. The prevalence of OSA among snorers was 28 percent (53.84 percent), 71.7 percent among patients with EDS, and 81.2 percent among patients who experienced witnessed apneas. According to studies, up to 63.44 percent of men and up to 36.66 percent of women in the general population are affected by habitual snoring on a consistent basis. Patients with sleep-disordered breathing may not be identified, diagnosed, or treated if medical clinicians do not recognise the impact of snoring on this population, according to the American Academy of Sleep Medicine[20]. Snoring is also an important symptom to monitor in the long-term management of OSA, because its recurrence after OSA treatment may indicate that it is necessary to re-evaluate the treatment regiment. A study conducted by Young et al[7]. (Wisconsin Sleep Cohort Study) found that habitual snoring occurs in 36 percent of individuals and more than 70 percent of those with an AHI of 5 or higher. A referral to a sleep clinic is most likely the most common problem that leads to one being referred. A study conducted by Lavieet al[21]. discovered that excessive daytime drowsiness and witnessed snoring were both good predictors of OSA.

When patients presented with symptoms suggestive of OSA, the Epworth sleepiness scale (ESS) was utilised as a screening tool, as demonstrated in our study. The ESS is a straightforward, self-administered questionnaire that examines daytime functioning, including levels of concentration, work performance, and tiredness, among other things. ESS scores were substantially higher in patients with obstructive sleep apnea syndrome than in the general population[53]. The patients in our study had an ESS score greater than 10, as well as other symptoms suggestive of OSA. They conducted an overnight sleep study, and it was determined that they were suffering from the condition. We have confirmed the efficacy of ESS as an OSA screening tool, with low false positive rates and high specificity in our study, demonstrating that it is an effective tool. A high index of clinical suspicion and related risk factors for OSA, as well as an ESS score of greater than 10, should drive additional investigation and treatment options.

Diabetes mellitus, dyslipidemia, and hypertension were the most common component disorders in our study population with metabolic syndrome, which was arranged in that order. The heart (IHD) and the brain were the most often affected target organs (stroke). A thorough statistical analysis was performed.

The study was conducted to determine whether there was a statistically significant correlation or tendency for OSA among the co-morbidities listed above, either separately or in various combinations of different components of the metabolic syndrome. It was found that the incidence of OSA was higher in MS patients when compared to the general population, according to the findings of the study. However, no specific group or co-morbidity was shown to be associated with or predisposed to OSA in particular, nor was there a statistically significant relationship between OSA and any other condition.

Patients with diabetes had a 37.3 percent prevalence of OSA, patients with hypertension had a 33.8 percent prevalence of OSA, and patients with dyslipidemia had a 38.8 percentprevalence of OSA.

Individuals with OSAS had higher levels of fasting blood glucose (95.4 mg/dl) than those without the condition (91.8 mg/dl), according to Ip et al[22]. The AHI remained a significant predictor of fasting insulin levels and insulin resistance when data were adjusted for adiposity, despite the fact that persons with OSAS were on average significantly heavier than the controls. A study conducted by Vgontzas et al[76] on obese middle-aged adults discovered that fasting blood glucose levels were nearly 20% higher in obese patients with OSAS (106.2 4.1 mg/dl) than in BMI-matched controls (85.4 4.4 mg/dl). OSA has been found to be more common in hypertensive people, according to research. According to a recent research of middle-aged individuals, overweight adults with OSAS had significantly higher TG levels than BMI-matched controls, with mean TG levels matching criteria for a MetS risk factor in the OSAS group (177.2 mg/dl) but not in the controls (141.8 mg/dl). When treating patients with refractory heart failure, resistant hypertension, nocturnal cardiac ischemia, and nocturnal arrhythmias, the diagnosis of OSA should always be evaluated. This is especially true when treating persons with risk factors for sleep apnea (e.g., central obesity, age, and male gender). It is possible that treating sleep apnea will aid in the achievement of improved clinical control in these disorders, as well as the long-term cardiovascular prognosis. Researchers from Udwadia et al discovered a statistically significant relationship between OSA and diabetes mellitus and hypertension in an urban Indian population in their research[23].

As a result, the current study has proven that the incidence of OSA among individuals with MS is significantly higher than the prevalence of OSA in the general population. Despite the fact that a larger study would have allowed for the calculation of the probabilities of acquiring OSA in patients with MS or vice versa, the current study provides compelling evidence that all patients with MS should be screened forundiagnosed sleep apnea (OSA).

Conclusion

- The incidence of OSA was significantly greater in individuals with metabolic syndrome when compared to the general population.
- There was a statistically significant link between the component disorders of MS when studied individually and when studied along with OSA.
- When OSA in MS patients is detected and treated early, it can help to prevent the development of complications in the patients as a result of the combined effects of the two disorders.
- As a result of this study, the importance of screening MS patients for undetected OSA has beenunderlined.

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