Original Article

Evaluation of obstructive sleep apnea in metabolic syndrome

Divya Soin[1], Praveen Ashok Kumar[1], Jasmeen Chahal[1], Sumit Pal Singh Chawla[1], Sarabjot Kaur[1], Ravinder Garg[1], Rupinderjeet Kaur[1]

[1]Department of Medicine, Guru Gobind Singh Medical College and Hospital, Faridkot, Punjab, India

Abstract

Background: Metabolic syndrome has become one of the most important public health problems with a growing prevalence in both developed and developing countries. Obesity is a major risk factor for obstructive sleep apnea (OSA), which is associated with significant cardiorespiratory morbidity. **Aims:** The aims of this study were to find out the prevalence of OSA in patients with metabolic syndrome and to highlight the importance of assessment of OSA in these patients. **Methods:** This cross-sectional analytical study was conducted on 100 subjects aged 30–60 years, comprising 50 cases of metabolic syndrome and 50 controls without metabolic syndrome. Overnight polysomnography was done in all the subjects. Prevalence and severity of OSA were assessed and compared between the two groups. **Results:** Prevalence of OSA was significantly higher (66%) in patients with metabolic syndrome than in subjects without metabolic syndrome (12%). Out of 33 (66%) OSA patients with metabolic syndrome, 8 (16%) had mild OSA, 11 (22%) had moderate OSA, and 14 (28%) had severe OSA. Increasing severity of OSA was associated with higher mean levels of all the metabolic syndrome parameters except serum high density lipoprotein (HDL). **Conclusions:** OSA is highly prevalent in patients with metabolic syndrome. Also, the increasing severity of OSA is associated with poorer control of diabetes, hypertension, and dyslipidemia, which are all components of metabolic syndrome. Therefore, effective treatment of metabolic syndrome can prevent and control OSA in these patients. Similarly, reducing the severity of OSA (by early diagnosis and treatment) in patients with metabolic syndrome might help to optimize control of blood sugar, blood pressure, and serum lipids, thereby reducing the risk of cardiovascular disease. Therefore, the need for screening metabolic syndrome patients for OSA has been reinforced by this study.

Keywords: Cardiovascular disease, insulin resistance, metabolic syndrome, obesity, obstructive sleep apnea

Introduction

Obesity has become one of the most important public health problems in the world, with a growing prevalence in both developed and developing countries. This epidemic can be attributed to the modern lifestyle characterized by lack of physical activity and consumption of diets rich in fat.[1]

Since metabolic syndrome is strongly linked to obesity, the continuing rise in the prevalence of obesity is closely followed by increased rates of metabolic syndrome. Prevalence of metabolic syndrome ranges from 11% to 41% in India. While studies show a high prevalence of metabolic syndrome in Asian Indians, truly representative data from all regions of India are not available.[2]

Obstructive sleep apnea (OSA) is a clinical condition characterized by recurrent episodes of complete obstruction (apnea) or partial obstruction (hypopnea) of the upper airway, leading to increased negative intrathoracic pressure, sleep fragmentation, and intermittent hypoxia during sleep. OSA afflicts all age groups. Its severity is usually graded according to the average number of apneic and hypopneic episodes per sleep hour (apnea–hypopnea index [AHI]) in sleep studies.[3] Research on the current

Address for correspondence: Dr. Jasmeen Chahal, Department of Medicine, Guru Gobind Singh Medical College and Hospital, Faridkot, Punjab - 151 203, India.
E-mail: dr.jasmeenchahal@gmail.com

Access this article online

Quick Response Code:

Website: www.jfmpc.com

DOI: 10.4103/jfmpc.jfmpc_175_19

How to cite this article: Soin D, Kumar PA, Chahal J, Chawla SP, Kaur S, Garg R, *et al*. Evaluation of obstructive sleep apnea in metabolic syndrome. J Family Med Prim Care 2019;8:1580-6.

prevalence of OSA indicated that one-third of sleep studies showed some degree of OSA (AHI ≥ 5). Among adults aged 30 – 70 years, approximately 13% of men and 6% of women have moderate-to-severe forms of OSA (AHI ≥ 15).[4]

Obesity is a major risk factor for OSA because it promotes enlargement of soft tissue structures within and surrounding the airway, thereby contributing significantly to pharyngeal airway narrowing.[5,6] In 1998, Wilcox *et al.* proposed the name "syndrome Z" for the combination of metabolic syndrome (syndrome X) and OSA to reflect the close association of components of metabolic syndrome with OSA.[7]

OSA also promotes metabolic dysfunction and increases the incidence of metabolic syndrome overall, as well as its individual components. Therefore, OSA seems to be more than an epiphenomenon in the metabolic syndrome. Early treatment of OSA in patients with metabolic syndrome has produced some beneficial effects on individual components of metabolic syndrome; hence, early identification and treatment of OSA in patients with metabolic syndrome is essential.

Although the incidence of metabolic syndrome in India is on the rise, there is a paucity of Indian data on its correlation with OSA. This study was undertaken to find out the prevalence of OSA in patients with metabolic syndrome and to highlight the importance of evaluating metabolic syndrome patients for OSA. The vicious nature of the combination of metabolic syndrome and OSA calls for urgent participation of physicians at all levels, especially primary care physicians to promote healthy lifestyle so as to curb the epidemic of obesity and thereby reduce the incidence of OSA. Primary care physicians also have a role in identifying OSA early in the patients of metabolic syndrome as early identification and treatment of OSA may produce beneficial effects on individual components of metabolic syndrome and may have significant cardiovascular benefit.

Methods

This cross-sectional analytical study, conducted in the department of Medicine of a tertiary care teaching hospital, enrolled 100 patients. Fifty patients with metabolic syndrome were taken as cases and 50 patients without metabolic syndrome formed the control group.

Inclusion criteria

1. For Cases

Patients of any gender above 30 and below 60 years of age, who gave informed consent, and who fulfilled the 2005 International Diabetes Federation (IDF) criteria[8] for metabolic syndrome, were included in this study.

According to the 2005 IDF criteria, metabolic syndrome is diagnosed in a patient having:

(1) central obesity (waist circumference [WC] ≥ 90 cm in males and ≥ 80 cm in females)

(2) with any two of the following:

- Serum triglycerides (TG) ≥ 150 mg/dL (1.7 mmol/L), or specific treatment for lipid abnormality.
- Serum HDL cholesterol (HDL-c) < 40 mg/dL (1 mmol/L) in males and < 50 mg/dL (1.3 mmol/L) in females, or specific treatment for lipid abnormality.
- Blood pressure (BP) in supine position (after 10 min rest): systolic BP ≥ 130 mmHg or diastolic BP ≥ 85 mmHg, or on the treatment of previously diagnosed hypertension.
- Fasting blood sugar (FBS) ≥ 100 mg/dL (5.6 mmol/L), or previously diagnosed type 2 diabetes mellitus.

2. For Controls

Patients of any gender above 30 and below 60 years of age, who gave informed consent, and who did not have metabolic syndrome, were included as controls.

Exclusion criteria

Patients below 30 and above 60 years of age, those with chronic respiratory problems, congestive heart failure, cognitive impairment, history of cerebrovascular accident within the preceding 30 days, and those on sedatives, antipsychotics, or antiobesity drugs were excluded.

Data collection procedure: The study conformed to the Helsinki Declaration. Approval was sought from the institutional ethics committee. All the participants were explained about the purpose of the study and were ensured strict confidentiality. Then, written informed consent was taken from each of them before their enrolment for the study. After a detailed history and thorough clinical examination, all subjects (50 cases and 50 controls) underwent overnight polysomnography (sleep study). The sleep study was carried out using the machine "SleepCare" which works with the software "SleepCare 1.0.3." In a sleep study, the following parameters were used to assess the sleep stages:

- Electroencephalography
- Electrooculography
- Surface electromyography of limb muscles (to detect limb movements, periodic or other)

In addition, other parameters, including nasal airflow (for evaluation of apneas and hypopneas), electrocardiography, pulse oximetry, respiratory effort (thoracic and abdominal), and sound recordings to measure snoring, were also monitored.

The following respiratory events were noted: hypopnea, obstructive apnea, mixed apnea, and central apnea. The definitions of these events are incorporated in the "SleepCare" software. The number of respiratory events (obstructive apnea and hypopnea) per hour of sleep, called the AHI or respiratory disturbance index, was calculated. This index was used to grade the severity of OSA, as follows: no OSA (AHI <5 events/h), mild OSA (AHI ≥ 5 but < 15 events/h), moderate OSA (AHI ≥ 15 but < 30 events/h), and severe OSA (AHI ≥30 events/h).

The proportion of OSA in the two study groups was determined and the significance of the difference in the proportion of OSA between these two groups was assessed using the Chi-square test. The mean AHIs in the two study groups were compared using the Student *t*-test.

The subjects were also divided into subgroups according to the severity of OSA ("no OSA," mild OSA, moderate OSA, and severe OSA). The mean level of each of the metabolic syndrome parameters (FBS, systolic BP, diastolic BP, serum TG, serum HDL) was determined in each of these subgroups; comparisons between these subgroups were then made using the ANOVA *F*-test.

Results

In this study, 100 subjects were included; of these, 69 were males and 31 were females. Out of 50 cases with metabolic syndrome, 35 (70%) were males and 15 (30%) were females. Among 50 controls without metabolic syndrome, 34 (68%) were males and 16 (32%) were females. Therefore, gender-wise distribution in metabolic syndrome and nonmetabolic syndrome subject groups were comparable.

Among cases, 15 (30%) belonged to the age group 30 – 40 years, 18 (36%) were in the age group 40 – 50 years, and 17 (34%) were aged between 50 and 60 years. Among controls, 14 (28%) were in the age group 30 – 40 years, 20 (40%) belonged to the age group 40 – 50 years, and 16 (32%) were aged between 50 and 60 years. The mean age of the case group was 45.56 (±7.048) years, while that of the control group was 45.00 (±6.839) years. Therefore, both groups were age-matched.

The mean WC values in the case and control groups were 102.94 cm (±8.110) and 81.64 cm (±5.424), respectively. The mean systolic and diastolic BPs in the case group were 146.36 mmHg (±16.614) and 91.12 mmHg (±7.742), respectively, while in the control group, these were 137.68 mmHg (±8.460) and 82.88 mmHg (±7.386), respectively. The mean FBS levels in the case and control groups were 127 mg/dL (±34.118) and 95.52 mg/dL (±18.339), respectively. The mean serum TG and HDL levels in the case group were 166.36 mg/dL (±19.940) and 47.54 mg/dL (±6.538), respectively and in the control group were 142.30 mg/dL (±20.629) and 49.64 mg/dL (±5.005), respectively.

Out of the 50 cases, 33 (66%) were found to have OSA, while among the 50 controls, only 6 (12%) had OSA [Figure 1]. This difference was statistically significant ($P < 0.001$).

Overall, 61 (61%) subjects did not have OSA ("no OSA"), 10 (10%) had mild OSA, 14 (14%) had moderate OSA, and 15 (15%) had severe OSA. Among cases, 17 (34%) were found to have "no OSA," 8 (16%) had mild OSA, 11 (22%) had moderate OSA, and 14 (28%) had severe OSA. Out of the 50 controls, 44 (88%) had "no OSA," 2 (4%) had mild OSA, 3 (6%) had moderate OSA, and only 1 (2%) was found to have severe OSA. These differences were statistically significant ($P < 0.001$) [Figure 2].

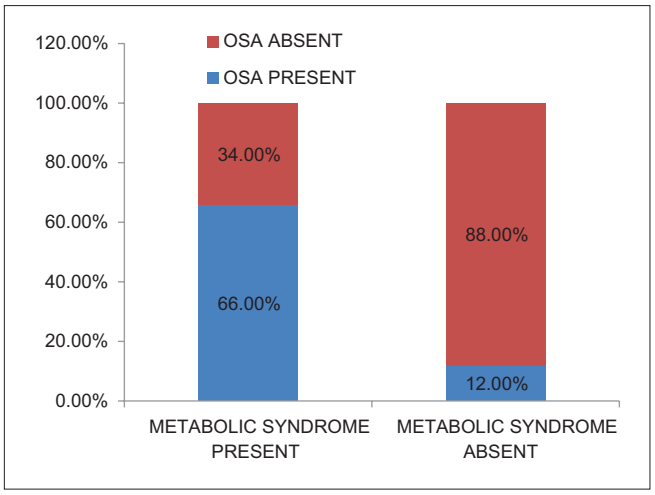

Figure 1: Proportion of OSA in metabolic syndrome (case) and nonmetabolic syndrome (control) groups

The mean AHI on polysomnography in cases was 18.394 (±14.7957) events/h, whereas in controls, it was 4.970 (±5.7826) events/h; the difference was statistically significant ($P < 0.001$).

Among 35 males with metabolic syndrome, 12 (34.3%), 5 (14.3%), 8 (22.9%), and 10 (28.6%) had "no OSA," mild OSA, moderate OSA, and severe OSA, respectively. Out of 15 females with metabolic syndrome, 5 (33.3%), 3 (20%), 3 (20%), and 4 (26.7%) were found to have "no OSA," mild OSA, moderate OSA, and severe OSA, respectively. These differences were not statistically significant ($P = 0.966$). Among 34 males without metabolic syndrome, 29 (85.3%), 1 (2.9%), 3 (8.8%), and 1 (2.9%) had "no OSA," mild OSA, moderate OSA, and severe OSA, respectively. Out of 16 females without metabolic syndrome, 15 (93.8%) were found to have no OSA, 1 (6.2%) had mild OSA, and none (0%) had moderate and severe OSA. These differences were also not statistically significant ($P = 0.519$).

The mean WC values in the "no OSA," mild OSA, moderate OSA, and severe OSA groups were 85.61 cm (±9.592), 101.2 cm (±9.784), 101.86 cm (±10.369), and 104.6 cm (±9.077), respectively; these differences were statistically significant ($P < 0.001$) [Table 1].

The mean FBS levels in the "no OSA," mild OSA, moderate OSA, and severe OSA groups were 99.16 mg/dL (±20.434), 117.5 mg/dL (±29.179), 124.5 mg/dL (±33.112), and 143.93 mg/dL (±41.008), respectively; these differences were statistically significant ($P < 0.001$) [Table 2].

The mean systolic BP measurements in the "no OSA," mild OSA, moderate OSA, and severe OSA groups were 138.49 mmHg (±10.518), 142.4 mmHg (±12.322), 145.71 mmHg (±13.379),

Table 1: Mean WC in "no OSA," mild OSA, moderate OSA, and severe OSA groups

Variable	OSA severity	*n*	Mean	Std. deviation	*F*
WC	No OSA	61	85.61	9.592	25.336
	Mild	10	101.20	9.784	*P*<0.001
	Moderate	14	101.86	10.369	
	Severe	15	104.60	9.077	
	Total	100	92.29	12.715	

Table 2: Mean FBS level in "no OSA," mild OSA, moderate OSA, and severe OSA groups

Variable	OSA severity	*n*	Mean	Std. deviation	*F*
FBS	No OSA	61	99.16	20.434	12.608
	Mild	10	117.50	29.179	*P*<0.001
	Moderate	14	124.50	33.112	
	Severe	15	143.93	41.008	
	Total	100	111.26	31.510	

and 152.67 mmHg (±20.587), respectively; these differences were statistically significant ($P = 0.002$). The mean diastolic BP measurements in the "no OSA," mild OSA, moderate OSA, and severe OSA groups were 84.2 mmHg (±7.552), 88 mmHg (±6.928), 90.86 mmHg (±7.048), and 94.13 mmHg (±9.812), respectively; these differences were also statistically significant ($P < 0.001$).

The mean serum TG levels in the "no OSA," mild OSA, moderate OSA, and severe OSA groups were 146.05 mg/dL (±21.214), 157.20 mg/dL (±19.792), 165.43 mg/dL (±20.706), and 175.73 mg/dL (±20.436), respectively; these differences were statistically significant ($P < 0.001$) [Table 3].

The mean serum HDL levels in the "no OSA," mild OSA, moderate OSA, and severe OSA groups were 50.39 mg/dL (±5.336), 47.1 mg/dL (±6.350), 47.07 mg/dL (±4.565), and 43.67 mg/dL (±5.815), respectively; these differences were statistically significant ($P < 0.001$) [Table 4].

Discussion

This study explored the association between metabolic syndrome and OSA. So far, various studies have focused on determining the prevalence of metabolic syndrome in OSA patients and showing that metabolic syndrome is more prevalent in such patients than in the general population. This study, on the other hand, attempted to examine the reverse association, that is, to determine the prevalence of OSA in patients with metabolic syndrome.

The present study was done on 100 subjects, 50 with and 50 without metabolic syndrome. The prevalence of OSA in patients with metabolic syndrome (66%) was much higher than in controls without metabolic syndrome (12%). Also, the mean AHI in patients with metabolic syndrome was 18.394 events/h, which was significantly higher than that in controls (4.97 events/h).

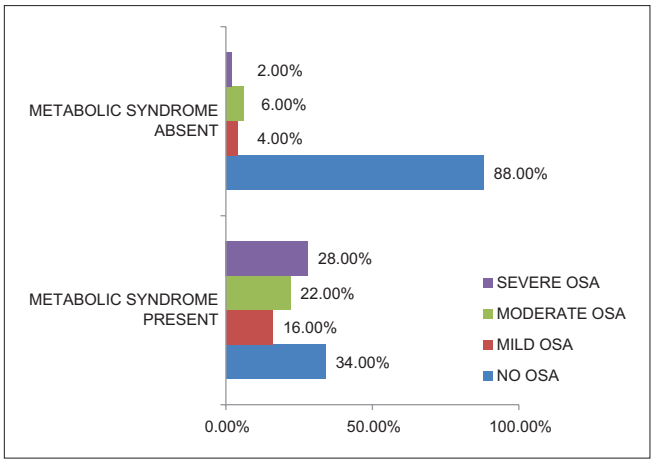

Figure 2: Proportion of "no OSA," mild OSA, moderate OSA, and severe OSA in metabolic syndrome (case) and nonmetabolic syndrome (control) groups

In a similar study conducted in 30 patients with metabolic syndrome, 22 (73.3%) were found to have OSA.[9] In another study, 24 patients with metabolic syndrome were subjected to polysomnography and the prevalence of OSA in these patients was 95.8%.[10] Perez *et al.* enrolled 83 female patients with metabolic syndrome, and they also found a high prevalence of syndrome Z (75.8%) in these patients.[11]

Metabolic syndrome is associated with obesity, which is the most important reversible risk factor for OSA. Obesity promotes enlargement of soft tissue structures within and surrounding the airway, thereby contributing significantly to pharyngeal airway narrowing. An excess of fat deposition is also observed under the mandible and in the tongue, soft palate, and uvula. Obesity also leads to a reduction of lung volumes during sleep (due to a combination of increased abdominal fat mass and recumbent posture), which reduces longitudinal tracheal traction forces and pharyngeal wall tension; this also contributes to pharyngeal airway narrowing. As compared to peripheral obesity, central obesity is associated with a higher amount of fat deposition in the neck; this leads to a more notable narrowing of the upper airway while asleep.[12,13]

In the present study, there was no significant difference in the prevalence of OSA between males and females with metabolic syndrome.

The present study showed that the mean WC in subjects with mild, moderate, and severe OSA was significantly higher than the mean WC in subjects with "no OSA." In a similar study, the mean WC in patients with OSA (110.95 cm) was also significantly higher than in subjects without OSA (98.12) ($P = 0.01$).[9] The finding of increased WC in patients with OSA supports the well-known fact that OSA is associated with central obesity.[14,15]

In this study, the mean FBS in subjects with OSA was higher than that in subjects without OSA; also, as the severity of OSA

Table 3: Mean serum TG levels in "no OSA," mild OSA, moderate OSA, and severe OSA groups

Variable	OSA severity	*n*	Mean	Std. deviation	*F*
Serum TG	No OSA	61	146.05	21.214	9.812
	Mild	10	157.20	19.792	*P*<0.001
	Moderate	14	165.43	20.706	
	Severe	15	175.73	20.436	
	Total	100	154.33	23.529	

Table 4: Mean serum HDL levels in "no OSA," mild OSA, moderate OSA, and severe OSA groups

Variable	OSA severity	*n*	Mean	Std. deviation	*F*
Serum HDL	No OSA	61	50.39	5.336	7.006
	Mild	10	47.10	6.350	***P***<0.001
	Moderate	14	47.07	4.565	
	Severe	15	43.67	5.815	
	Total	100	48.59	5.888	

increased, the mean FBS levels also increased. In a similar study conducted by Dubey *et al.*, in which 50 patients with metabolic syndrome were evaluated for OSA, the mean FBS levels in patients with mild, moderate, and severe OSA were 115.4, 110.9, and 143.68 mg/dL, respectively. In this study, a significant correlation was found between uncontrolled blood glucose and the severity of OSA.[16] In another study, the mean FBS in patients with OSA was 135.45 mg/dL, which was significantly higher than in subjects without OSA (109.37 mg/dL).[9] Perez *et al.* in their study observed that the mean FBS in subjects without OSA was 99.8 mg/dL, while the mean FBS levels in patients with mild, moderate, and severe OSA were 117.6, 139.7, and 142.3 mg/dL, respectively; the differences were statistically significant ($P < 0.001$).[11] Aronsohn *et al.* showed that increasing severity of OSA was associated with poorer glucose control.[17] Priou *et al.* also observed that increasing OSA severity was associated with higher HbA1c.[18] In yet another study, the severity of OSA was associated with increased HbA1c level independent of body mass index in Japanese individuals, especially in those without diabetes.[19]

Thus, increasing severity of OSA is associated with poorer glycemic control. This might be due to the effect of OSA on glucose metabolism. OSA is linked with glucose intolerance and insulin resistance. Thus, reducing the severity of OSA may be an important therapeutic approach to optimize glycemic control in patients having OSA and glucose intolerance.[20-22]

In the present study, the mean systolic and diastolic BPs in patients with OSA were higher than those in subjects without OSA; also, as the severity of OSA increased, the mean systolic and diastolic BPs also increased. In the study by Dubey *et al.*, the mean systolic BPs in patients with no OSA, mild, moderate, and severe OSA were 142, 145.2, 147.81, and 153.18 mmHg, respectively; and the mean diastolic BPs in these patients were 88, 91.2, 93.9, and 97.82 mmHg, respectively, reflecting higher values in patients with OSA than in those without OSA.[16] In another study, the mean systolic BP in patients with OSA was 146.81 mmHg, which was significantly higher than in patients without OSA (125 mmHg).[9] Similar results were found in studies conducted by Perez *et al.*[11] and Walia *et al.*[23], suggesting a strong association between severe OSA and resistant elevated BP. Martinez-Garcia *et al.* also found higher uncontrolled systolic BP in severe OSA and noted that patients with severe OSA had poorer BP control than those without severe OSA.[24] The above data suggest that increasing severity of OSA is associated with higher and difficult-to-control BP. There are several potential mechanisms to explain this association. Severe OSA may cause endothelial dysfunction, which is primarily driven by OSA-associated intermittent hypoxia; and endothelial dysfunction is thought to contribute to hypertension. Aldosterone excess and increased sympathetic activity might play a role in the relation between severity of OSA and difficult-to-control BP. Therefore, reducing the severity of OSA might help to optimize BP control in patients with severe OSA and refractory hypertension.[23,24]

This study revealed that the mean serum TG levels in patients with OSA were significantly higher than in subjects without OSA; also, as the severity of OSA increased, the mean serum TG levels increased. Similarly, the mean HDL levels in patients with OSA were lower than in subjects without OSA. These levels showed a downward trend with an increase in the severity of OSA, which was statistically significant. Dubey *et al.* also noted similar findings; the mean serum TG levels in patients with mild, moderate, and severe OSA were 172.6, 180.86, and 214.91 mg/dL, respectively.[16] In another study, the mean serum TG in patients with OSA was 170.31 mg/dL, which was significantly higher than in subjects without OSA (151.12).[9] Nadeem *et al.* found that HDL-c levels correlated well with the severity of OSA; as the severity of OSA increased, the levels of HDL-c decreased. Also, the serum TG levels were significantly higher in patients with severe OSA ($P = 0.0001$).[25]

Hence, the increasing severity of OSA is associated with poorer control of dyslipidemia. This might be due to the effect of OSA on lipid metabolism. Chronic intermittent hypoxia induced by OSA is associated with the generation of sterol regulatory element-binding protein-1 and stearoyl-coenzyme A desaturase-1, peroxidation of lipids, HDL dysfunction, increased total cholesterol level, and sympathetic dysfunction. Altogether, these factors create a proinflammatory milieu responsible for the development of dyslipidemia and propagation of atherosclerosis in OSA.[26]

A meta-analysis performed in 2016 evaluated the relationship between metabolic syndrome parameters and OSA. Patients with OSA had higher systolic BP, lower HDL, and higher low density lipoprotein (LDL) levels than subjects without OSA. OSA was also found to be associated with increased TG levels and higher FBS. This meta-analysis found that OSA was associated with abnormal levels of multiple parameters that are markers of metabolic syndrome and suggested that OSA broadly affects this disease.[27]

Thus, the current study suggests that OSA is quite common in patients with metabolic syndrome, which is associated with an increased risk of cardiovascular disease. In addition, the severity of OSA has a strong correlation with all the components of metabolic syndrome.

Strength of the study

This study highlights the vicious relationship between OSA and metabolic syndrome. There is a high prevalence of OSA in patients with metabolic syndrome and increasing severity of OSA is associated with poorer control of diabetes, hypertension, and dyslipidemia, which are all components of metabolic syndrome. This study emphasizes the urgent need for recognition of the high prevalence of OSA in patients of metabolic syndrome and also reinforces the importance of screening of OSA in these patients.

Limitations of the study

This was a single-center study with small sample size.

Conclusions

OSA is highly prevalent in patients with metabolic syndrome, which is associated with an increased risk of cardiovascular disease. Also, the increasing severity of OSA is associated with poorer control of diabetes, hypertension, and dyslipidemia, which are all components of metabolic syndrome. Poor control of these components, in turn, further increases the risk of cardiovascular disease. Therefore, reducing the severity of OSA (by early diagnosis and treatment) in patients with metabolic syndrome might help to optimize control of blood sugar, BP, and serum lipids, thereby reducing morbidity and mortality. Therefore, the need for screening metabolic syndrome patients for OSA has been reinforced by this study.

Financial support and sponsorship

Nil

Conflicts of interest

There are no conflicts of interest.

References

1. Poirier P, Giles TD, Bray GA, Hong Y, Stern JS, Pi-Sunyer FX, *et al.* Obesity and cardiovascular disease: Pathophysiology, evaluation, and effect of weight loss. Circulation 2005;113:898-918.
2. Misra A. Metabolic syndrome. In: Munjal YP, editor. API Textbook of Medicine. 9th ed. New Delhi: Jaypee Brothers Medical Publishers (P) Ltd; 2012. p. 1279-80.
3. Sleep-Related Breathing Disorders in Adults: Recommendations for syndrome definition and measurement techniques in clinical research. The report of an American Academy of Sleep Medicine Task Force. Sleep 1999;22:667-89.
4. Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, Hla KM. Increased prevalence of sleep-disordered breathing in adults. Am J Epidemiol 2013;177:1006-14.
5. Horner RL, Shea SA, McIvor J, Guz A. Pharyngeal size and shape during wakefulness and sleep in patients with obstructive sleep apnoea. Q J Med 1989;72:719-35.
6. Shelton KE, Woodson H, Gay S, Suratt PM. Pharyngeal fat in obstructive sleep apnea. Am Rev Respir Dis 1993;148:462-6.
7. Wilcox I, McNamara SG, Collins FL, Grunstein RR, Sullivan CE. "Syndrome Z": The interaction of sleep apnea, vascular risk factors and heart disease. Thorax 1998;53:25-8.
8. Alberti KG, Zimmet P, Shaw J. The metabolic syndrome-A new worldwide definition. Lancet 2005;366:1059-62.
9. Suryakumari V, Vulli V, Rao GS, Anusha A, Kumar VS. Study of prevalence of obstructive sleep apnea in patients with metabolic syndrome. IOSR J Dent Med Sci 2018;17:51-5.
10. Venkateswaran S, Shankar P. The prevalence of syndrome Z (the interaction of obstructive sleep apnea with the metabolic syndrome) in a teaching hospital in Singapore. Postgrad Med J 2007;83:329-31.
11. Perez EA, Oliveira LVF, Freitas WR, Malheiros CA, Ilias EJ, Silva AS, *et al.* Prevalence and severity of syndrome Z in women with metabolic syndrome on waiting list for bariatric surgery: A cross-sectional study. Diabetol Metab Syndr 2017;9:72.
12. Grundy SM, Brewer HB Jr, Cleeman JI, Smith SC Jr, Lenfant C. Defnition of metabolic syndrome: Report of the national heart, lung, and blood institute/American heart association conference on scientific issues related to definition. Circulation 2004;109:433-8.
13. Lorenzo C, Okoloise M, Williams K, Stern MP, Haffner SM. The metabolic syndrome as predictor of type 2 diabetes: The San Antonio heart study. Diabetes Care 2003;26:3153-9.
14. Castenada A, Jauregui-Maldonado E, Ratnani I, Varon J, Surani S. Correlation between metabolic syndrome and sleep apnea. World J Diabetes 2018;9:66-71.
15. Drager LF, Togeiro SM, Polotsky VY, Lorenzi-Filho G. Obstructive sleep apnea: A cardiometabolic risk in obesity and the metabolic syndrome. J Am Coll Cardiol 2013;62:569-76.
16. Dubey AP, Rajput AK, Suhag V, Sharma D, Kandpal A, Keisham R. Prevalence of obstructive sleep apnea in metabolic syndrome. Int J Adv Med 2017;4:722-7.
17. Aronsohn RS, Whitmore H, Van Cauter E, Tasali E. Impact of untreated obstructive sleep apnea on glucose control in type 2 diabetes. Am J Respir Critical Care Med 2010;181:507-13.
18. Priou P, Vaillant ML, Meslier N, Chollet S, Pigeanne T, Masson P, *et al.* Association between obstructive sleep apnea severity and glucose control in patients with untreated versus treated diabetes. J Sleep Res 2015;24:425-31.
19. Kurosawa H, Saisho Y, Fukunaga K, Haraguchi M, Yamasawa W, Kurihara I, *et al.* Association between severity of obstructive sleep apnea and glycated hemoglobin level in Japanese individuals with and without diabetes. Endocr J 2018;65:121-7.
20. Pamidi S, Aronsohn RS, Tasali E. Obstructive sleep apnea: Role in the risk and severity of diabetes. Best Pract Res Clin Endocrinol Metab 2010;24:703-15.
21. Kim NH. Obstructive sleep apnea and abnormal glucose metabolism. Diabetes Metab J 2012;36:268-72.
22. Tasali E, Mokhlesi B, Cauter EV. Obstructive sleep apnea and type 2 diabetes: Interacting epidemics. Chest 2008;133:496-506.
23. Walia HK, Li H, Rueschman M, Bhatt DL, Patel SR, Quan SF,

et al. Association of severe obstructive sleep apnea and elevated blood pressure despite antihypertensive medication use. J Clin Sleep Med 2014;10:835-43.

24. Martinez-Garcia MA, Gomez-Aldaravi R, Gil-Martinez T, Soler-Cataluna JJ, Bernacer-Alpera B, Roman-Sanchez P. Sleep-disordered breathing in patients with difficult-to-control hypertension. Arch Bronconeumol 2006;42:14-20.
25. Nadeem R, Pahomov E, Ahmed S, Sharieff A, Tanna S, Sidhu H, *et al*. Association of severity of dyslipidemia with severity of obstructive sleep apnea. Am J Respir Crit Care Med 2014;189:2152.
26. Adedayo AM, Olafiranye O, Smith D, Hill A, Zizi F, Brown C, *et al*. Obstructive sleep apnea and dyslipidemia: Evidence and underlying mechanism. Sleep Breath 2014;18:13-8.
27. Kong DL, Qin Z, Wang W, Pan Y, Kang J, Pang J. Association between obstructive sleep apnea and metabolic syndrome: A meta-analysis. Clin Invest Med 2016;38:161-72.