ORIGINAL ARTICLE

Anthropometric Indices and Obstructive Sleep Apnea Severity in Syndrome Z

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Abstract

Background: Syndrome Z is the coexistence of two chronic diseases, obstructive sleep apnea (OSA) and metabolic syndrome. It is one of the under-recognized public health issues in the Indian subcontinent. Syndrome Z is associated with multiple risk factors and cardiometabolic abnormality, which increases its severity. In this study, we assess anthropometric indices and OSA severity in patients with syndrome Z.

Materials and methods: We evaluated 100 patients aged more than 50 years in chest outpatient department (OPD), who met the screening criteria for OSA using the Snoring, Tiredness, Observed apnea, Blood pressure, Body mass index (BMI), Age, Neck size, and Gender (STOPBANG) Questionnaire and the Epworth Sleepiness Scale (ESS). All patients underwent overnight level 1 polysomnography (PSG) using Alice 6 PDx Philips Sleep System. Parameters of metabolic syndrome and OSA were noted using National Cholesterol Education Program—Third Adult Treatment Panel (NCEP ATP III) and American Academy of Sleep Medicine (AASM) guidelines. We did a comparative study using baseline anthropometric indices, metabolic syndrome parameters, and apnea–hypopnea index (AHI) level in PSG in patients with syndrome Z and OSA using various correlations.

Results: Syndrome Z was present in 60% of patients with OSA. Among syndrome Z patients, male subjects were 60% and female subjects were 40%. OSA was severer in patients with syndrome Z, i.e., AHI levels in the PSG were higher in patients having both OSA and metabolic syndrome (p <0.001). Other parameters that were found to be associated in patients with syndrome Z were higher BMI, larger waist circumference (p <0.003), deranged lipid profile, hyperglycemia (p <0.001), and hypertension (p <0.001).

Conclusion: Anthropometric indices, obesity (BMI), parameters of metabolic syndrome, and AHI level should be a part of routine checkups in follow-ups of patients with syndrome Z, which will help in better management. Treating each factor individually can increase the quality of life and decrease the morbidity associated with syndrome Z.

Keywords: Apnea–hypopnea index, Metabolic syndrome, Obstructive sleep apnea, Syndrome Z.

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Introduction

Obstructive sleep apnea (OSA) and metabolic syndrome are among the most common chronic diseases, so a large number of patients suffer from both disorders. This coexistence and interaction of both OSA and metabolic syndrome is termed syndrome Z.[1,2]

Syndrome Z is one of the under-recognized public health issues in the Indian subcontinent. It is associated with multiple risk factors and cardio-metabolic abnormality, which increases its severity. It causes severer nocturnal hypoxemia than either disease alone. Patients with metabolic syndrome and OSA have a substantially greater risk of morbidity and mortality, compared to those with either metabolic syndrome or OSA alone.

OSA is defined by the presence of repetitive episodes of upper airway obstruction during sleep. An apnea–hypopnea index (AHI) of equal to or greater than 5 events/hour is commonly used to define OSA, with obstructive or mixed (rather than central) events comprising more than 50% of the total. OSA is usually defined by an AHI equal to or greater than 5 events/hour and persistent complaints of excessive daytime somnolence, un-refreshing sleep, or fatigue.[3]

OSA is categorized as mild if AHI is in the range of 5–15 events/hour, moderate if AHI is in the range of 16–30 events/hour, and severe if AHI is more than 30 events/hour. The consequences of undiagnosed and untreated OSA are medically serious and costly. If left untreated, it leads to excessive daytime sleepiness, cognitive dysfunction, impaired work performance, and decrements in health-related quality of life.[3]

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Continuous positive airway pressure (CPAP) is considered the gold standard of treatment for OSA. When adherence is optimal, CPAP improves sleep quality, reduces the risk of OSA-related comorbidities, and improves patients' quality of life. However, in spite of many technological advances in the CPAP apparatus and the patient–device interface, adherence remains a significant problem.[4]

Metabolic syndrome refers to the co-occurrence of several known cardiovascular risk factors, including insulin resistance, obesity, atherogenic dyslipidemia, and hypertension. The National Cholesterol Education Program—Third Adult Treatment Panel (NCEP ATP III) definition is one of the most widely used criteria for metabolic syndrome. It accounts for the fact that

different populations, ethnicities, and nationalities have different distributions of norms for body weight and waist circumference.[5,6]

While the pathogenesis of metabolic syndrome and each of its components is complex and not well understood, central obesity and insulin resistance are acknowledged as important causative factors. Central (abdominal) obesity, easily assessed using waist circumference and independently associated with each of the other metabolic syndrome components, including insulin resistance, is a prerequisite risk factor.

Severity of syndrome Z is difficult to assess, and not many studies are present that monitor the progression, severity, and follow-up in syndrome Z patients. Anthropometric indices, body mass index (BMI), waist circumference, and AHI grading are important parameters that reflect the severity of metabolic syndrome and OSA independently. These parameters are also important tools in syndrome Z, which could tell us about its severity at a particular point of time in patients. It has been observed that OSA and metabolic syndrome act synergistically as comorbidities in syndrome Z, and detailed studies would decrease its burden in the society.

Materials and Methods

This cross-sectional study was conducted among 100 adult patients of either sex above 50 years of age between June 2019 and July 2021 at the tertiary care center in the Respiratory Medicine Department of Institute of Medical Sciences (IMS), Banaras Hindu University (BHU), Varanasi, after obtaining ethical permission from the Institutional Ethical Committee. This study included adult patients who met the screening criteria for OSA using the Snoring, Tiredness, Observed apnea, Blood pressure, Body mass index (BMI), Age, Neck size, and Gender (STOPBANG) questionnaire and the Epworth Sleepiness Scale (ESS) in the Respiratory Medicine out patient department (OPD) of IMS, BHU.

All subjects were evaluated clinically by complete history, examination, and all appropriate laboratory investigations. Anthropometric indices height, weight, BMI, waist circumference, and neck circumference were measured. Vitals, like oxygen saturation (SpO_2), blood pressure, temperature, and pulse, were recorded. Laboratory parameters, like blood glucose level, complete blood count, lipid profile, and thyroid profile, were investigated.

Subjects were evaluated and checked for metabolic syndrome and other comorbidities, like diabetes, hypertension, and hypothyroidism. Patients with known neurological and psychiatric conditions, with recent myocardial infarction, who were diagnosed as an OSA patient on CPAP treatment, and who were pregnant were excluded from the study.

All patients underwent overnight level 1 polysomnography (PSG) using Alice 6 PDx Philips Sleep System, which included multichannel electroencephalography (EEG), electromyography (EMG), and electrooculography (EOG) recording and respiratory monitoring using a nasal thermistor. Parameters of metabolic syndrome and OSA were noted using NCEP ATP III and American Academy of Sleep Medicine (AASM) guidelines and definitions.

Obstructive Sleep Apnea

OSA was considered as cessation of airflow for at least 10 seconds with persistent respiratory effort. Patients were categorized according to AHI as having mild OSA (AHI 5–15), moderate OSA (AHI 15–30), and severe OSA (AHI >30). Calculation of ESS and STOPBANG scores was done to screen the patients for OSA in the study. The higher the STOPBANG and ESS scores, the higher the probability of the person falling asleep in daytime.

Metabolic Syndrome

The NCEP ATP III definition is one of the most widely used criteria for metabolic syndrome. According to the NCEP ATP III definition, metabolic syndrome is present if three or more of the following five criteria are met:

- Waist circumference over 40 inches (102 cm) in men and 35 inches (88 cm) in women,
- Blood pressure over 130/85 mm Hg,
- Fasting triglyceride (TG) level over 150 mg/dL,
- Fasting high-density lipoprotein (HDL) cholesterol level less than 40 mg/dL in men and 50 mg/dL in women, and
- Fasting blood sugar over 100 mg/dL.

Anthropometric Indices

Body measurements were taken for all the subjects in the study. Different parameters, such as altered BMI, neck circumference, waist circumference, and waist-to-hip ratio, were all considered as risk factors and were measured. BMI was graded as healthy—18.5–22.9 kg/m^2, overweight—23.0–24.9 kg/m^2, pre-obese—25.0–29.9 kg/m^2, obesity 1—30.0–34.9 kg/m^2, obesity 2—35.0–39.9 kg/m^2, and obesity 3—40.0–44.9 kg/m^2.

Waist circumference was considered high if it was more than 40 inches (102 cm) in men or 35 inches (88 cm) in women, and the cutoff for neck circumference was taken as more than 37 cm in men and 34 cm in women as the upper normal limit in overweight.

Data were collected, noted, compared, and analyzed by simple statistics using SPSS software, and mean, range, *p* value, and standard deviation were calculated.

Results

In our study, one hundred ($N = 100$) patients were included, among whom syndrome Z was present in 60%. In syndrome Z patients, 60% were male and 40% were female (Table 1).

The average age of syndrome Z patients was 65.08 ± 7.77 years, and in patients with OSA alone, it was 61.1 ± 8.64 ranging from 52 to 85 years. Syndrome Z was significantly associated with age, with a *p*-value of 0.003. Majority of patients were obese and had BMI more than the cutoff value of 30 kg/m^2. Average weight and BMI of patients with syndrome Z were 82.7 kg (range 60–102 kg) and 31.3 kg/m^2 (range 24–36.9), respectively, and in patients with

Table 1: Anthropometry and demographic data

	Syndrome Z		
Parameter	*Yes (n = 60)*	*No (n = 40)*	*p-value*
Age (years)	65.08 ± 7.77	61.10 ± 8.64	0.003
Sex			
Male	36 (60%)	22 (55%)	0.620
Female	24 (40%)	18 (45%)	
Weight (kg)	82.73 ± 15.25	79.15 ± 11.89	0.165
BMI (kg/m^2)	82.73 ± 15.25	79.15 ± 11.89	0.165
Waist circumference (cm)	99.67 ± 5.89	30.29 ± 4.33	0.304
Neck circumference (cm)	43.18 ± 2.53	42.42 ± 2.10	0.301

OSA alone, they were 79.15 kg (range 60–102 kg) and 30.2 kg/m^2 (range 22–35). Average BMI was higher in patients with syndrome Z than in those with OSA alone, i.e., syndrome Z patients were more obese than patients with OSA alone. Regarding other anthropometric measurement data, syndrome Z patients had a mean waist circumference of 99.67 ± 5.89 cm, with a range of 94–106 cm, and in patients with OSA alone, it was 95.30 ± 6.19 cm, with a range of 90–102 cm. Syndrome Z was significantly associated with waist circumference, with a *p*-value of 0.003.

Syndrome Z patients had a mean neck circumference of 43.18 ± 2.53 cm, with a range of 32–46 cm, and in patients with OSA alone, it was 42.42 ± 2.1 cm, with a range of 30–45 cm. Neck circumference was slightly higher in patients with syndrome Z than in patients with OSA alone.

In our study of 100 subjects, lipid profiles, i.e., total cholesterol, TG, low-density lipoprotein (LDL), and HDL levels, were mostly deranged in patients with syndrome Z compared with patients with OSA alone (Table 2).

Mean TG level in syndrome Z patients was 224.80 mg/dL, and in patients with OSA alone, it was 145.05 mg/dL. Mean LDL level in syndrome Z patients was 113.87 mg/dL, and in patients with OSA alone, it was 93.80 mg/dL. Mean HDL level in syndrome Z patients was 37.27 mg/dL, and in patients with OSA alone, it was 44.9 mg/dL. Mean total cholesterol level in syndrome Z patients was 189.62 mg/dL, and in patients with OSA alone, it was 185.45 mg/dL.

Another observation was that in syndrome Z patients, mean fasting blood glucose level was 135.13 ± 24.6 mg/dL, and in patients with OSA alone, it was 118.55 ± 21.56 mg/dL. In syndrome Z patients, diabetes was present in 53.3% and hypertension in 63.3%, whereas in patients with OSA alone, diabetes was present in 25% and hypertension in 30%.

The following parameters were found to be associated in patients with syndrome Z: age ($p = 0.003$), higher BMI, larger waist circumference ($p < 0.003$), AHI category, deranged lipid profile, TG levels ($p < 0.001$), LDL levels ($p = 0.001$), HDL levels ($p < 0.001$), hyperglycemia, i.e., FBS ($p < 0.001$), diabetes ($p = 0.005$), and hypertension ($p < 0.001$).

Table 2: Laboratory investigations and metabolic syndrome parameters

	Syndrome Z		
Parameter	*Yes (n = 60)*	*No (n = 40)*	*p-value*
Total cholesterol (mg/dL)	189.62 ± 56.53	185.45 ± 48.92	0.759
LDL (mg/dL)	113.87 ± 27.54	93.80 ± 25.90	0.001
HDL (mg/dL)	37.27 ± 8.99	44.9 ± 10.64	<0.001
TG (mg/dL)	224.80 ± 67.46	145.05 ± 54.4	<0.001
Random blood glucose (mg/dL)	135.13 ± 24.6	118.55 ± 21.56	<0.001
Diabetic	32 (53.3%)	10 (25%)	0.005
Hypertensive	38 (63.3%)	12 (30%)	0.001

In our study of 100 subjects, patients suffering from syndrome Z had a mean AHI of 39.07 ± 22.4, and patients with OSA alone had a mean AHI of 35 ± 27.69. Syndrome Z is a potential risk factor for OSA severity: the severer the syndrome Z, the severer the OSA. In our study, 72% of severe OSA patients had syndrome Z, 30.8% of moderate OSA patients had syndrome Z, and 88.9% of mild OSA patients had syndrome Z. Thus, our study showed that there is a high strength of statistically significant association between OSA severity and syndrome Z ($p < 0.001$). Mean ESS in syndrome Z patients was 18.77, and in patients with OSA alone, it was 17.40. Mean STOPBANG score was 5.3 in syndrome Z patients and 4.89 in patients with OSA alone (Table 3).

Discussion

OSA and metabolic syndrome are believed to act synergistically to increase cardiovascular risk, and the co-occurrence of these conditions has been termed syndrome Z.[1] In our study, 60% of the patients had syndrome Z, whereas 40% had OSA alone ($p = 0.003$). A similar study by Coughlin et al. showed the prevalence of metabolic syndrome in patients with OSA to be 87% compared with 35% in normal controls.[7]

The burden of metabolic syndrome in patients with OSA in India is under evaluation and research. A North-Indian-population-based study found the prevalence to be 79 and 48% in patients with OSA and in normal controls, respectively.[8] Another North-Indian-population-based study by Sharma et al. showed the prevalence of syndrome Z to be 77%.[9] In a similar study in China by Lam et al., the prevalence of OSA in metabolic syndrome subjects was 62.5%.[10]

In our study, males had a higher prevalence of syndrome Z than females. Out of 60% of syndrome Z subjects among our study participants, 60% were male and 40% were female. In a similar study in urban India, the prevalence of male and female in syndrome Z was 68 and 32%, respectively.[9] Another study from the Indian capital showed the prevalence of male and female in syndrome Z to be 78 and 22%, respectively.[11]

In our study, all subjects belonged to the elderly age-group ranging from 52 to 85 years. Mean age of syndrome Z subjects was 4 years higher than the mean age of OSA alone subjects in our study. In a similar study, 42.5% of syndrome Z patients were above the age of 55 years.[2] In another study, mean age of syndrome Z subjects was 2 years higher than the mean age of OSA alone subjects.[11]

In our study, mean BMI in syndrome Z patients was 31.3 kg/m^2, which was higher than that of OSA alone patients, i.e., syndrome Z patients were more obese than patients with OSA alone. In a similar study[12] in Gujarat, mean BMI in syndrome Z patients was 29.9 kg/m^2. In another study[8] from urban India by Agrawal et al., mean BMI in syndrome Z subjects was 31.7 kg/m^2, and that in non-syndrome Z patients was 26.4 kg/m^2. Many studies in OSA and metabolic syndrome have shown that obesity increases the severity of OSA and

Table 3: Association between AHI category and syndrome Z ($n = 100$)

	AHI category					*Fisher's exact test*
Syndrome Z	*<5*	*5–15*	*16–30*	*>30*	*Total*	*p-value*
Yes ($n = 60$)	0 (0.0%)	16 (88.9%)	8 (30.8%)	36 (72.0%)	60 (60.0%)	<0.001
No ($n = 40$)	6 (100.0%)	2 (11.1%)	18 (69.2%)	14 (28.0%)	40 (40.0%)	
Total	6 (100.0%)	18 (100.0%)	26 (100.0%)	50 (100.0%)	100 (100.0%)	

metabolic syndrome and it is linked to each of them independently. This association acts synergistically and affects patients with syndrome Z exponentially.[13,14]

Waist and neck circumference in our study was larger in syndrome Z patients than in patients with OSA alone. Waist circumference was 4 cm larger and neck circumference was 1 cm larger approximately. With an increase in body fat percentage, the pathway for the entrance of chronic diseases opens, leading to serious atherosclerotic complications. In a similar study by Tażbirek et al. of 50 subjects with metabolic syndrome, 31 were of syndrome Z with a waist circumference larger by 3 cm and neck circumference larger by 3 cm compared with non-syndrome Z subjects.[15] Another study by Cizza et al. found that the change in neck circumference was more vital than the change in waist circumference in predicting OSA and metabolic syndrome.[16]

In our study subjects, diabetes was present in more than 53% of syndrome Z subjects and hypertension was present in more than 63% of syndrome Z subjects. It is quite clear that cardio-metabolic risk factors, like diabetes and hypertension, are equally or more severely affecting subjects of syndrome Z as they affect OSA and metabolic syndrome individually. In a study by Drager et al., the relationship of impaired hyperglycemic control with OSA and metabolic syndrome was studied, which helped in establishing its correlation with syndrome Z subjects.[17]

In another study by Robert et al., the mechanism of the relationship between OSA, obesity, and hypertension was discussed and how OSA is related to obesity-related hypertension was also discussed.[18] In another study, findings suggested that sleep-disordered breathing is likely to be a risk factor for hypertension and consequent cardiovascular morbidity in the general population.[19]

In our study, 72% of severe OSA patients, 30.8% of moderate OSA patients, and 88.9% of mild OSA patients had syndrome Z. Our study also showed that there is a high strength of association between OSA severity and syndrome Z ($p \leq 0.001$). OSA severity was observed to be high in syndrome Z patients than in patients with OSA alone or metabolic syndrome alone. A study by Perez et al. showed that the prevalence of syndrome Z increases significantly according to the AHI trend, and it also showed the association of AHI levels with the parameters of metabolic syndrome.[9]

Metabolic syndrome as a whole and its components individually are very likely to be present in patients with OSA, and this risk increases with the severity of metabolic syndrome, leading eventually to syndrome Z. Screening for metabolic syndrome components along with the workup of OSA will allow early detection of syndrome Z cases. This relationship of metabolic syndrome with OSA in syndrome Z can also explain the mechanism for increased mortality in patients with OSA and metabolic syndrome.[20,21]

Among patients with OSA, pulse wave velocity and C-reactive protein (CRP) level were higher in syndrome Z patients than in those without metabolic syndrome, and further research and studies are needed to establish specific details.[22]

Management of patients with syndrome Z needs a multidisciplinary approach, which should include detailed discussion about weight loss ideas, CPAP use guidelines, and surgical procedures, like bariatric surgery, in severe cases.[23–26]

Conclusion

Prevalence and morbidities related to syndrome Z are very high in the Indian subcontinent. Evaluation and cost-effective management guidelines to assess its severity and timely intervention could change the quality of life and mortality related to it.

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