A Study to Evaluate the Effect of Body Mass Index on the Prevalence of Sleep-Disordered Breathing in Adult Patients with Metabolic Syndrome

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Abstract

Background. Obesity is a predisposing factor for obstructive sleep apnoea (OSA). Conversely, OSA increases the risk of developing hypertension and diabetes mellitus. Whether the presence of metabolic syndrome increases the risk of sleep-disordered breathing (SDB) independent of obesity remains unclear.

Methods. Consecutive 25 non-obese and 25 obese adult patients with metabolic syndrome and Epworth Sleepiness Scale (ESS) score ≥10 underwent full night attended polysomnography. Baseline clinical and demographic parameters were recorded for all the patients. Obesity was defined as body mass index (BMI) ≥25kg/m². Occurrence of SDB (central sleep apnoea and/or OSA), sleep efficiency, and time spent in each sleep stage were noted in both the study groups.

Results. The study subjects were predominantly men (n=41, 82%) with a mean age of 47.1 years. A total of 38 (76%) subjects were diagnosed to have OSA. There was no difference in the prevalence of OSA between the study groups (non-obese versus obese, 20 [80%] versus 18 [72%]; p=0.508). Patients in both the groups had low median sleep efficiency (non-obese versus obese, 47% versus 48.7%; p=0.764), and an equal number of awakenings per hour of sleep (non-obese versus obese, median interquartile range [IQR], 21 [7.5-26.5] versus 18 [13-22.5]; p=0.763). None of the patients in either group had central sleep apnoea.

Conclusion. Obstructive sleep apnoea is highly prevalent in patients with metabolic syndrome and excessive daytime sleepiness (ESS ≥10), and the prevalence of OSA in this population is independent of BMI.

Key words: Obstructive sleep apnoea, Hypertension, Sleep disordered breathing Diabetes mellitus, Metabolic syndrome.

Introduction

Sleep-disordered breathing (SDB) is an umbrella term for a group of patho-physiologic conditions characterised by an abnormal respiratory pattern during sleep.¹ Obstructive sleep apnoea (OSA), the most common disorder in the SDB spectrum, is characterised by repeated episodes of apnoeas due to airflow obstruction in the upper airway. This leads to oxygen desaturation and arousals resulting in sleep fragmentation and its attendant consequences.² OSA clinically manifests as snoring, episodes of choking, unrefreshing sleep, excessive daytime sleepiness, memory impairment, and others.³⁻⁴ Further, repeated episodes of apnoea and hypoxia lead to sympathetic over-activity resulting in an increased risk of developing hypertension, insulin resistance, diabetes, cardiac arrhythmias and stroke.⁴

Metabolic syndrome is a condition characterised by the presence of three or more of the following: (a) waist circumference ≥90cm for men and ≥80cm for women; (b) serum triglycerides ≥150mg/dL; (c) serum high density lipoprotein (HDL) <40mg/dL in males and <50mg/dL in females; (d) systolic blood pressure ≥130mmHg and/or diastolic blood pressure ≥85mmHg; and, (e) fasting plasma glucose of ≥100 mg/dL.⁵⁻⁶ There is a strong correlation between the presence of OSA and metabolic syndrome.⁷⁻⁸ Obesity is another condition independently associated with OSA, with increasing severity of OSA with increasing body weight.⁹⁻¹¹ However, variable effect of interventions, such as weight loss for the treatment of OSA suggests that apart from anatomic narrowing of the airway in obese patients, several metabolic factors may play a role in the pathogenesis of SDB.¹²⁻¹³ A previous study¹⁴ investigating the association of OSA and metabolic

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syndrome found that the presence of OSA increased the risk of metabolic syndrome independent of BMI. However, whether the presence of metabolic syndrome increases the risk of SDB independent of obesity is not known. We hypothesised that the prevalence of SDB would be higher in obese patients with metabolic syndrome as compared to those who are non-obese. In this prospective, cross-sectional study, we investigated the effect of body mass index (BMI) on the prevalence of SDB in patients with metabolic syndrome.

**Material and Methods**

This was a prospective, observational study conducted in the Chest Clinic of the Department of Pulmonary and Critical Care Medicine, PGIMS, Rohtak (Haryana). The study protocol was approved by the Institutional Ethics Committee and a written informed consent was obtained from all patients.

Consecutive 50 adult patients (25 obese and 25 non-obese) fulfilling the criteria for metabolic syndrome and excessive daytime sleepiness were enrolled in the study. Obesity was defined as BMI ≥25 kg/m² as applicable to adult Asian Indians. Metabolic syndrome was defined as per the International Diabetes Federation (IDF) consensus worldwide definition. All patients completed the Epworth Sleepiness Scale (ESS), a self-administered questionnaire, which rates the likelihood of falling asleep (from 0 to 3) under eight different daily life situations. The maximum score is 24 and a score above 10 indicates excessive daytime sleepiness. Patients with any of the following were excluded: (i) presence of co-morbid medical conditions, such as chronic obstructive pulmonary disease, heart failure, hypothyroidism, renal failure and liver dysfunction; (ii) pregnancy; (iii) previous diagnosis of OSA; and (iv) failure to provide informed consent.

All the patients underwent overnight polysomnography (Somnologica studio 3.3.2 Embla N7000 sleep unit system). The sleep study was attended throughout the night by a sleep technician. The sleep data recorded were manually scored for sleep stages and respiratory events (hypopnoeas, desaturation, respiratory awakenings and others) as per the American Academy of Sleep Medicine (AASM) guidelines. Sleep efficiency was considered abnormal when total sleep time was less than 85% of the total recording time. A value less than 85% was considered abnormal.

**Insulin Resistance**: Plasma insulin was measured after an overnight fast by chemiluminescence enzyme immunoassay technique using Abnova chemiluminescent immunoassay (CLIA) kit. Insulin resistance was assessed from fasting plasma glucose and insulin values using homeostasis model assessment (HOMA-IR) calculations as previously described (fasting plasma glucose x fasting plasma insulin/405).

**Statistical Analysis**

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS version 22, for Windows; IBM Inc., Armonk, NY). Data are presented in a descriptive fashion as either mean (standard deviation [SD]), median (interquartile range [IQR]) or number (percentage). Continuous variables were compared using Mann-Whitney U test if not normally distributed and student’s ‘t’ test if normally distributed. Chi-square test was used to analyse the differences between categorical variables. Pearson’s coefficient was calculated for analysing the correlation between HOMA-IR and apnoea-hypopnoea index (AHI). P values less than 0.05 were considered as statistically significant. Univariate logistic regression analysis was performed to study the effect of each component of metabolic syndrome on SDB.

**Results**

The study population comprised predominantly of men (n=41, 82%) with a mean (standard deviation [SD]) age of 47.1 (6.6) years (Table 1). The body weight, waist circumference, and BMI were significantly higher in the obese group. The median IQR plasma insulin level (7.05 [6.2-7.8] µIU/L versus 5.5 [4-6] µIU/L, p<0.001) and the HOMA-IR (1.9 [1.6-2.2] versus 1.7 [1.1-1.9], p=0.045) were significantly higher in the obese compared to the non-obese group.

Overall 38 (76%) patients (33 men, 5 women) had OSA. The prevalence of OSA was similar in the two groups (non-obese group, n=20 [80%], obese group, n=18 [72%]; p=0.508). Twelve patients in non-obese group and 11 in obese group suffered from severe OSA (AHI≥30/hour) while eight non-obese and seven obese subjects had mild to moderate OSA. There was no difference in the median AHI (25 versus 16.4, p=0.535) between the non-obese and obese individuals. None of the patients had central or mixed apnoeas. Majority of the study patients had poor sleep efficiency (n=44, 88%); the median sleep efficiency was similar in both the two groups (non-obese versus obese, 47% versus 48.7%; p=0.764). There was no difference in the number of arousals and time spent in each stage of sleep across the two groups (Table 2). Overall, patients spent more time in sleep stage N2 and stage N3 and lesser time in stage N1 and rapid eye movement (REM) sleep stage. Patients in both the groups had more apnoeas during non-rapid eye movement (NREM) sleep when compared
with the REM sleep. There was no difference in the HOMA-IR between subjects with or without OSA (mean [SD] 1.7 [0.6] versus 1.8 [0.4], p=0.62). Further, there was no correlation of HOMA-IR with the AHI (Pearson correlation 0.05, p=0.72). On univariate logistic regression analysis, presence of diabetes mellitus was associated with higher odds of OSA (Table 3).

Discussion

The results of this study highlight a high prevalence (76% in this study) of OSA in adult North Indian patients with metabolic syndrome and excessive daytime sleepiness, with the prevalence being similar in non-obese and obese individuals. The prevalence of OSA in metabolic syndrome seen in our study is not representative of the general population as our study included a high-risk population with ESS ≥10, where the prevalence of OSA has been reported to range from 39% to 68.3%..

Obstructive sleep apnoea has been linked with several components of metabolic syndrome. A high waist circumference and the presence of insulin resistance increased the risk of developing OSA, in the Sleep Heart Health Study comprising of 6600 adults, increasing waist-hip ratio, hypertension, hypercholesterolemia were all associated with a higher risk of SDB. The presence of insulin resistance and diabetes mellitus leads to soft tissue oedema of the neck, thereby increasing the risk of developing SDB. Also, diabetes mellitus is associated with depression of central ventilatory control and exposes an individual to a higher risk of SDB. In our study, the presence of diabetes mellitus was associated with higher odds of OSA on univariate analysis.

Although obesity is known to predispose to OSA due to the increased subcutaneous neck fat resulting in reduced caliber of the upper airway, the relationship of metabolic syndrome with OSA is more complex. In the current study, the prevalence of OSA was independent of obesity in patients with metabolic syndrome and ESS ≥10 suggesting that OSA has a complex two-way cause-and-effect relationship with metabolic syndrome. This observation can be attributed to the combined effect of diabetes mellitus and inflammatory cytokines, such as TNF-α, and IL-6, which are all components of the metabolic syndrome.
on the central neural pathways. However, we did not measure the levels of various cytokines, and further studies are required to investigate this aspect.

Finally, our study is not without limitations. We did not measure the neck circumference and have not assessed the upper airway anatomy radiologically. We have also not measured the cytokine levels that could have helped in elucidating the possible reasons for a higher incidence of OSA in non-obese patients with metabolic syndrome. Due to a small study sample the results of this study may be under-powered and cannot be generalised and the results of this study need to be confirmed in a larger multicentric study.

In conclusion, there is a high prevalence of OSA in patients with metabolic syndrome and excessive daytime sleepiness, however it is independent of the presence of obesity.

References


