

Screening for Comorbidities in Obstructive Sleep Apnea

SHEIKH SHOIB¹, JAVID AHMAD MALIK², SHARIQ RASHID MASOODI³, AATIF RASHID⁴

ABSTRACT

Introduction: Obstructive Sleep Apnea (OSA) is a common sleep disorder among middle-aged adults which often results in a wide range of co-morbid conditions, predominantly of the cardiovascular/respiratory, endocrine/metabolic and neuropsychiatric manifestations. These comorbidities pose a significant burden on health care and considerably influence the disease as well.

Aim: To look for any association between obstructive sleep apnea and other comorbidities and to study the prevalence of these comorbidities in patients suffering from obstructive sleep apnea.

Materials and Methods: A cross-sectional study was performed at the Modern hospital, Srinagar, Jammu and Kashmir, India, on patients that were referred from various subspecialty clinics from July 2011 to August 2012. Polysomnography studies were performed in 152 patients identified as having OSA (71 men and 81 women). Statistical analysis was performed by means of the computer program SPSS using a t-test for independent groups, a probability value of 0.05 was considered significant.

Results: A total of 152 patients were identified as having OSA (71 men and 81 women) with a mean age (\pm SD) of 54.1 years (\pm 13.6). Various comorbidities were found in 60.5% patients diagnosed with OSA. 59.2% of men and 61.7% of women with OSA had comorbidities. The individual prevalence of each comorbidity in order of decreasing prevalence was hypertension (63.2%), endocrine disorders (40.8%), coronary artery diseases (9.2%), depression (11.2%), dysthymia (5.3%), hypercholesterolemia (5.9%), asthma (7.9%), and approximately 19.7% had no comorbidities". (χ^2 : 13.2, df: 3, P: 0.004 (S).

Conclusion: This study demonstrates significant overlap between sleep apnea and multiple medical comorbidities. Understanding of various co-morbid conditions associated with OSA and their clinical consequences helps in prevention, early identification and improving the quality of life of these patients. Clinicians need more information about screening for these diseases in patients with OSA to ensure proper diagnosis and treatment of those with these conditions.

Keywords: Hypertension, Polysomnography, Type 2 diabetes

INTRODUCTION

OSA is a sleep-related disorder characterized by the collapse of the pharynx during sleep in the face of persistent ineffective breathing efforts leading to repetitive interruptions of ventilation during sleep resulting in sleep fragmentation and arterial hypoxemia [1]. OSA is common in the middle-aged population with a prevalence of about 5%. This common sleep disorder affects a plethora of organs leading to various cardiovascular diseases and neurocognitive disorders [2,3]. However, most of the cases of OSA remain unrecognized [4]. Obstructive sleep apnea is mostly unrecognized and undiagnosed. The end result is a huge financial and social burden on health care. Early assessment and intervention of OSA patients with comorbidities can go a long way in improving natural history of these diseases [2]. Various studies have implicated OSA as a contributory factor for diseases like hypertension, diabetes mellitus, and other cardiovascular diseases and this is independent of conventional risk factors such as obesity [2,3,5]. Recent work suggests that the disordered breathing during sleep exerts multi-organ pathological effects through sympathetic stimulation caused by arousal from sleep. Thus, in the link between OSA and hypertension, the emphasis is on the repeated arousals rather than the breathing abnormality [6,7]. Interestingly, hyperinsulinemia, a consequence of diabetes and obesity, also leads to increased sympathetic activity and hypertension [8]. The prevalence of OSA in patients with hypertension is very high [9]. Also, more than half of sleep apneics are hypertensive [10,11] as compared to a prevalence of 24% in the

general adult population [12].

The prevalence of obesity, diabetes and OSA in the US is alarmingly high [13]. OSA, obesity, and hypertension are all risk factors for diabetes [14-16]. Less than 10% of the subjects who met the criteria for sleep apnea had ever sought medical care or been evaluated for a sleep problem [17]. OSA is also common in patients with hypertension and congestive heart failure [18,19]. A relationship between OSA and idiopathic dilated cardiomyopathy has also been described [20]. In this setting it is associated with symptoms of sleep apnea as well as paroxysmal nocturnal dyspnoea and insomnia [21].

Thus, it can be concluded that obstructive sleep apnea is common sleep disorder among middle-aged adults and often results in a wide range of co-morbid conditions. These comorbidities pose a significant burden on health care and considerably influence the disease. Keeping this in view, the aim of this study was to look for the association between obstructive sleep apnea and other Comorbidities and to study the prevalence of these comorbidities in patients suffering from OSA.

MATERIALS AND METHODS

A cross-sectional study was conducted at the Modern hospital Srinagar, Jammu and Kashmir, India, which is a private Hospital that provides the primary care and specialty services. Patients from all parts of the state of Jammu And Kashmir are referred to this Hospital for sleep studies, as the Standard polysomnographic

studies within an accredited laboratory are only available in this hospital. The enrollee population in Modern Hospital is comparable to the surrounding community with respect to various demographic indices. A total of 152 patients were evaluated for sleep-related complaint between July 2011 to August 2012 and subsequently referred for polysomnography were reviewed.

The medical records provided the information related to the demographic data, general medical history, clinical information from the initial visit for sleep-related complaints as well as polysomnography results. Data obtained from medical records included age, gender, weight, height, Apnea-Hypopnea Index (AHI), and the presence or absence of medical conditions linked to OSA (including coronary artery disease, congestive heart failure, hypertension, pulmonary hypertension, stroke, depression) as well as other illnesses (asthma, chronic obstructive pulmonary disease, and diabetes mellitus). Informed consent was obtained from all OSA subjects.

All patients underwent overnight polysomnography for the assessment of sleep disordered breathing by means of a computer-based system. Polysomnographic recordings included: electroencephalogram, electrooculogram, electromyogram of the chin, nasal and oral airflow (by thermistors), abdomen and chest movement, oxygen saturation (by finger probe), snoring (by the microphone), body posture, and electrocardiogram. The data was analysed on a visual basis by an experienced investigator.

Sleep was defined according to the criteria of Rechtschaffen and Kales and apnea was defined as a cessation of airflow for at least 10s [22,23]. Hypopnea was defined as a reduction in thoracic-abdominal movements of 50% or more and a decrease in the oxygen saturation of 4% or more. The AHI was calculated as the number of apneas and hypopneas per hour of total sleep time. Obstructive sleep apnea was defined as an AHI of five or more apneas/hypopneas per hour. Daytime sleepiness was measured by the Epworth Sleepiness Scale [23]. A score of more than nine points was considered as excessive daytime sleepiness. We defined the OSAS as a combination of AHI >5 and an ESS Score >9 [24].

STATISTICAL ANALYSIS

Statistical analysis was performed by means of the computer program SPSS using a t-test for independent groups, a p-value of 0.05 was considered significant.

RESULTS

A total of 163 patients were referred from various specialties and 11 patients were excluded as per they did not consent for study. A total of 152 patients [Table/Fig-1] were identified as having OSA with mean age groups (\pm SD) of 54.1 years (\pm 13.6). Females were more in number than their male counterparts 81 (53.2%) vs. 71 (46.87%). All patients were found to be obese (BMI= 31.09 \pm 4.62). The other characteristics are summarized in [Table/Fig-1]. About 33 (21.7%) of patients were suffering from three or more comorbidities, 36 (23.7%) were suffering from two comorbidities, 53 (34.9%) of patients were suffering from only one comorbidity. 30 (19.7%) were having no having any comorbidities at all. 11.3% of males were having three or more comorbidities and 30.9% of females were having three or more Comorbidities and it was statistically significant.

Means (\pm SD) of comorbidities in women, men and total were 2.1 \pm 1.7, 1.3 \pm 1.5 and 1.7 \pm 1.7 respectively [Table/Fig-2], 60.5% of patients in our population were found to be having comorbidities. The common clinical comorbidities in our study group were: hypertension 63.2%, endocrine disorder (40.8%), and diabetes (30.3%). Female hypertensives were significantly more in number than their male counterparts 60 (74.1%) vs. 36 (50.7%). Similarly, female diabetics were more in number than their male counterparts 31 (38.3%) vs. 15 (21.1%). In our study, only 5.9% of patients had

Descriptive variables	Mean \pm Standard deviation (SD)
Age	54.1 \pm 13.6
Body mass index (BMI)	31.32 \pm 4.62
Neck circumference (NC)	40.5 \pm 3.5
AHI	26.06 \pm 12.1
ESS	14.930 \pm 3.93

[Table/Fig-1]: Basic characteristics of study population.

Comorbidities	Male (n=71)	Female (n=81)	Total	
Mean \pm SD	1.3 \pm 1.5	2.1 \pm 1.7	1.7 \pm 1.7	χ^2 : 13.2, df: 3, P: 0.004 (Sig.)
3 or more	8 (11.3%)	25 (30.9%)	33 (21.7%)	
Two	17 (23.9%)	19 (23.5%)	36 (23.7%)	
One	25 (35.2%)	28 (34.6%)	53 (34.9%)	
None	21 (29.6%)	9 (11.1%)	30 (19.7%)	

[Table/Fig-2]: Number of comorbidities.

	Total	Men	Women	p-value
Co-morbidity	92 (60.5%)	42 (59.2%)	50 (61.7%)	0.746
Hypertension	96 (63.2%)	36 (50.7%)	60 (74.1%)	0.003 (S)
Endocrine	62 (40.8%)	21 (29.6%)	41 (50.6%)	0.008
Diabetes	46 (30.3%)	15 (21.1%)	31 (38.3%)	0.022 (S)
Hyperlipidemia	9 (5.9%)	3 (4.2%)	6 (7.4%)	0.407
CAD	14 (9.2%)	5 (7.0%)	9 (11.1%)	0.387
CHF	4 (2.6%)	1 (1.4%)	3 (3.7%)	0.378
AF	4 (2.6%)	2 (2.8%)	2 (2.5%)	0.894
Seizures	2 (1.3%)	1 (1.4%)	1 (1.2%)	0.925
Stroke	4 (2.6%)	1 (1.4%)	3 (3.7%)	0.378
CRF	1 (0.7%)	0 (0.0%)	1 (1.2%)	0.387
Bronchial Asthma	12 (7.9%)	6 (8.5%)	6 (7.4%)	0.812
COPD	7 (4.6%)	3 (4.2%)	4 (4.9%)	0.834
ILD	4 (2.6%)	1 (1.4%)	3 (3.7%)	0.378
RHD/PAH	3 (2.0%)	1 (1.4%)	2 (2.5%)	0.639
Increase Hemocrit	3 (2.0%)	1 (1.4%)	2 (2.5%)	0.639
Depression	17 (11.2%)	6 (8.5%)	11 (13.6%)	0.317
Dysthymia	8 (5.3%)	3 (4.2%)	5 (6.2%)	0.592
Adenoid Tonsils	3 (2.0%)	1 (1.4%)	2 (2.5%)	0.639

[Table/Fig-3]: Gender wise comorbidities in OSA population.

hyperlipidemia associated with OSA and it was significant.

Gender wise comorbidities in OSA population are given in [Table/Fig-3].

DISCUSSION

In the present study, all patients were found to be obese. Excessive body weight affects breathing in many ways and further increases the risk of developing OSA [2]. The common clinical comorbidities in our study group were: hypertension, endocrine disorders, and diabetes. The prevalence of hypertension in our study group was 63.2%. Female hypertensives were more in number than their male counterparts: 60 (74.1%) vs. 36 (50.7%). Our observation is supported by various other studies, wherein it was found that more than half of sleep apneics are hypertensive [10,11] compared to a prevalence of 24% in the general adult population [12]. Also, the prevalence of diabetes in our study group was 30.3%. Similarly, female diabetics were more in number than their male counterparts: 31 (38.3%) vs. 15 (21.1%). OSA is a clinical syndrome and is important in increasing the risk of various systemic conditions [25]. Higher prevalence of diabetes was found compared to the previous study done by Reichmuth KJ et al., [26]. Interestingly, a relationship between OSA and idiopathic dilated cardiomyopathy has also been described [20]. Two recent studies involving small numbers of patients with CHF described a 40-50% prevalence of CSA [18,19].

Various studies have implicated OSA as a contributory factor for diseases like hypertension, diabetes mellitus, and other cardiovascular diseases and this is independent of conventional risk factors such as obesity [2,3,5]. Recent work suggests that the disordered breathing during sleep exerts multi-organ pathological effects through sympathetic stimulation caused by arousal from sleep. Thus, in the link between OSA and hypertension, the emphasis is on the repeated arousals rather than the breathing abnormality [6,7]. Interestingly hyperinsulinemia, a consequence of diabetes and obesity, also leads to increased sympathetic activity and hypertension [8].

In our study, only 5.9% of patients had hyperlipidemia associated with OSA, although it has not presented expressive values. About 7.9% were having bronchial asthma. Salles C et al., reported that OSA is prevalent in patients with asthma [27]. In the present study, 11.2% patients in our study were found suffering from depression and 5.3% from dysthymia. Depression is considered as risk factor for OSA, which can be explained by serotonergic neurotransmission. Decrease in muscle tone of the upper respiratory tract and disturbed sleep both are caused due to low serotonin levels [28].

LIMITATION

The major limitation of our study was relatively small sample size and its cross-sectional design.

CONCLUSION

The present study demonstrated the statistically significant relationship between OSA and disorders like hypertension and diabetes. This study demonstrates significant overlap between the sleep apnea and multiple medical comorbidities. Understanding of co-morbid condition and the clinical consequences helps in their prevention, early identification and in improving the quality of life of these patients. Clinicians need more information about screening patients with OSA for other comorbidities to ensure proper diagnosis and treatment of those with these medical conditions. Thus, the compounding role of OSA in complicating the management of these comorbidities is in urgent need of further assessment and current practice approaches should be modified to include systematic evaluation and treatment of OSA. Further research on this topic may provide insight about the exact association between OSA and other comorbidities.

REFERENCES

- [1] American Academy of Sleep Medicine. International Classification of Sleep Disorders: Diagnostic and Coding Manual, 2nd edition. Westchester, IL: American Academy of Sleep Medicine, 2005.
- [2] Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: a population health perspective. *Am J Respir Crit Care Med.* 2002;165(9):1217-39.
- [3] Banno K, Kryger MH. Sleep apnea: clinical investigations in humans. *Sleep Med.* 2007;8(4):400-26.
- [4] Shoib S, Malik JA, Masoodi S. Depression as a manifestation of obstructive sleep apnea. *J Neurosci Rural Pract.* 2017;8(3):346-51.
- [5] Pack AI. Advances in sleep-disordered breathing. *Am J Respir Crit Care Med.* 2006;173(1):07-15.
- [6] Strohl KP, Boehm KD, Denko CW, Novak RD, Decker MJ. Biochemical Morbidity in Sleep Apnoea. *ENT Journal.* 1993;72(1):38-41.
- [7] Ziegler MG, Nelesen R, Mills P, Ancoli-Israel S, Kennedy B, Dimsdale JE. Sleep Apnoea, Norepinephrine-release Rate and Daytime Hypertension. *Sleep.* 1997;20(3):224-31.
- [8] Reaven GM, Lithell H, Landsberg L. Hypertension and associated metabolic abnormalities – the role of insulin resistance and the sympathoadrenal system. *New England Journal of Medicine.* 1996;334(6):374-81.
- [9] Silverberg DS, Oksenberg A, Iaina A. Sleep-related breathing disorders are common contributing factors to them production of essential hypertension, but are neglected, under-diagnosed and under-treated. *American Journal of Hypertension.* 1997;10(12 Pt 1):1319-25.
- [10] Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. *New England Journal of Medicine.* 1993;328:1230-35.
- [11] Burt VL, Whelton P, Roccella EJ, Brown C, Cutler JA, Higgins M, et al. Prevalence of hypertension in the us adult population: results from the third national health and nutrition examination survey, 1988-1991. *Hypertension.* 1995;25(3):305-13.
- [12] Coy TV, Dimsdale JF, Ancoli-Israel S, Clausen JL. The role of sleep-disordered breathing in essential hypertension. *Chest.* 1996;109(4):890-95.
- [13] Sajkov D, Cowie RJ, Thornton AT, Espinoza HA, McEvoy RD. Pulmonary hypertension and hypoxemia in obstructive sleep apnoea syndrome. *American Journal of Respiratory and Critical Care Medicine.* 1994;149(2 Pt 1):416-22.
- [14] Stoohs RA, Facchini F, Guilleminault C. Insulin resistance and sleep-disordered breathing in healthy humans. *American Journal of Respiratory and Critical Care Medicine.* 1996;154(1):170-74.
- [15] Javid Ahmad Malik, Bashir A. Naikoo, Sheikh Shoib. Differential Profile of OSA in Obese Kashmiri Patients of Northern India. *Journal of Medical Sciences.* 2016;19(2):e01-13.
- [16] Young T, Hutton R, Finn L, Badr S, Palta M. The gender bias in sleep apnea diagnosis: are women missed because they have different symptoms? *Arch Intern Med.* 1996;156(21):2445-51.
- [17] Naughton MT, Liu PP, Benard DC, Goldstein RS, Bradley TD. Treatment of congestive heart failure and Cheyne-Stokes respiration during sleep by continuous positive airway pressure. *Am J Respir Crit Care Med.* 1995;151(1):92-91.
- [18] Javaheri S, Parker TJ, Wexler L, Michales SE, Stanberry E, Nishiyama H, et al. Occult sleep-disordered breathing in stable congestive heart failure. *Ann Intern Med.* 1995;122(18):487-492.
- [19] Malone SPP, Holloway LR, Rutherford R, Xie A, Bradley TD. Obstructive sleep apnea in patients with dilated cardiomyopathy: effects of continuous positive airway pressure. *Lancet.* 1991;333(8781):1480-84.
- [20] Takasaki Y, Orr D, Popkin J, Rutherford R, Liu P, Bradley TD. Effect of nasal continuous positive airway pressure on sleep apnea in congestive heart failure. *Am Rev Respir Dis.* 1989;140(6):1578-84.
- [21] Rechtschaffen A, Kales A. A manual of standardized terminology, techniques, and scoring system for sleep stages of human subjects. Public Health Service, US Government Printing, 1968.
- [22] Stradling JR, Davies RJ. Sleep. Obstructive sleep apnoea/hypopnoea syndrome: definitions, epidemiology, and natural history. *Thorax.* 2004;59(1):73-78.
- [23] Johns MW. Reliability and factor analysis of the Epworth Sleepiness Scale. *Sleep.* 1992;15(4):376-81.
- [24] Malik JA, Masoodi SR, Shoib S. Obstructive sleep apnea in Type 2 diabetes and impact of continuous positive airway pressure therapy on glycemic control. *Indian J Endocr Metab.* 2017;21(1):106-12.
- [25] White DP. Pathogenesis of obstructive and central sleep apnoea. *Am J Respir Crit Care Med.* 2005;172(11):1363-70.
- [26] Reichmuth KJ, Austin D, Skatrud JB, Young T. Association of sleep apnea and type II diabetes: a population-based study. *Am J Respir Crit Care Med.* 2005;172(12):1590-95.
- [27] Salles C, Terse-Ramos R, Souza-Machado A, Cruz AA. Obstructive sleep apnea and asthma. *J Bras Pneumol.* 2013;39(5):604-12.
- [28] Veasey SC. Serotonin agonists and antagonists in obstructive sleep apnea: therapeutic potential. *Am J Respir Med.* 2003;2(1):21-29.

PARTICULARS OF CONTRIBUTORS:

1. Psychiatrist, Directorate of Health Services, Srinagar, Jammu and Kashmir, India.
2. Associate Professor, Department of Pulmonary Medicine, SKIMS Medical College, Srinagar, Jammu and Kashmir, India.
3. Professor, Department of Endocrinology, SKIMS, Srinagar, Jammu and Kashmir, India.
4. Dermatologist, Directorate of Health Services, Jammu and Kashmir, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Sheikh Shoib,
Psychiatrist, Directorate of Health Services, Srinagar-190001, Jammu and Kashmir, India.
E-mail: sheikhshoib22@yahoo.com

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