Original Article

Diagnosis of obstructive sleep apnea in women: Is there any difference?- Experience from a tertiary care hospital of North India

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Abstract

Context: Obstructive sleep apnea (OSA) considered classically to be a male-dominant disease, may have significant gender-based differences in clinical presentation and diagnosis. **Aims:** To evaluate gender-based differences in the clinical profile and polysomnographic features of Indian patients with OSA. **Settings and Design:** A prospective observational study was conducted over a period of 12 months involving adult ambulatory patients, referred for evaluation of OSA. **Methods and Materials:** Enrolled patients underwent detailed clinical evaluation followed by supervised polysomnography. Sleep studies were manually validated and analyzed. **Statistical Analysis Used:** Continuous variables were compared using two-tailed independent- sample *t*-test. For the univariate analysis, the Chi-square test was used. **Results:** Out of 150 enrolled patients, 94 (62.7%) were males (male-to-female: 1.7:1; age: 51.85 ± 12.60 years; BMI: 32.09 ± 5.53 kg/m^2). Most common presenting features were excessive daytime somnolence, snoring, and easy fatiguability. Women with OSA were older than men. Insomnia and anxiety were significantly higher among females. Parameters defining sleep architecture were similar in both groups. Although obstructive apneas and hypopneas were similar, mean apnea hypopnea index was significantly higher ($P < 0.05$) in males compared to females with higher titratable continuous positive airway pressure. **Conclusions:** There are gender-specific differences in the clinical presentation of OSA due to various anatomical, physiological, and psychosocial factors. Their potential influence on the clinical features, natural history, and implications on treatment need further evaluation on a larger scale.

Keywords: Apnea hypopnea index, diagnosis, gender differences, Obstructive sleep apnea, polysomnography features

Introduction

Obstructive sleep apnea (OSA), a syndrome characterized by repeated episodes of upper airway obstruction during sleep, is a common disorder with significant morbidity and mortality.[1,2] It is not only associated with disabling symptoms but also long-term health consequences requiring life-long care.[3-5] In addition to excessive daytime somnolence (EDS) and chronic fatigue, OSA is a harbinger of aggravation or onset of heart diseases, neuropsychiatric manifestations, and related mortality.[6-8]

Much of our knowledge about OSA comes from studies with largely male populations.[9-14] With most studies showing a higher prevalence of OSA in men, the gender-based discrepancy is more often evident in the clinical settings.[15,16] Young *et al.* estimated the prevalence of OSA in women, at 9% (using the data from the Wisconsin Sleep Cohort Study), while the prevalence in men was estimated at 24%.[17] Interestingly, the under-recognition

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of OSA in women was highlighted due to marked differences in disease prevalence in clinical settings (male-to-female ratio of 8-10:1) compared to an expected male-to-female ratio of 2-4:1 in the general population from epidemiological studies.[17-19] In 1997, 93% of women with moderate-to-severe OSA were thought to remain undiagnosed when comparing positive screening questionnaires against the known diagnosis of OSA.[20] Prevalence rates have continued to rise,[21,22] with recent HypnoLaus study, a population-based study estimating the prevalence of moderate-to-severe OSA in women at 23.4%.[23]

Research has documented gender-based differences in the upper airway, fat distribution, respiratory stability, and sleep physiology.[24,25] However, only a few dedicated studies have investigated the gender differences in the clinical aspects of OSA.[26,27] There is no study to our knowledge reporting the gender differences in clinical presentation and diagnosis of OSA in Indian sub-population. In our study, we aimed to specifically evaluate the gender differences in the clinical profile of patients with OSA diagnosed at our centre. The study also assessed the clinical presentation and polysomnographic data of patients suspected of having OSA.

Subjects and Methods

Study design and subjects

We conducted a prospective observational study in our department at a tertiary-care hospital in India, after approval from the Institutional Ethics Committee (The date of approval is 27-08-2019). All adult, ambulatory, and cooperative patients (age ≥18 years) referred during the study period (12 months) to our sleep clinic for evaluation of suspected OSA were assessed for suitability on the outpatient (OPD) basis. Patients with a pre-existing diagnosis of OSA or ongoing treatment with continuous positive airway pressure (CPAP) device and those having clinical features of other sleep disorders like restless leg symptoms, chronic insomnia, cataplexy, etc., were excluded. Pregnant women and patients with advanced respiratory failure requiring long-term oxygen therapy (LTOT), active infections, substance abuse, neuromuscular diseases, malignancies, and neuropsychiatric illnesses were also excluded from the study. Those fulfilling the inclusion criteria were prospectively enrolled after obtaining informed consent from all the patients.

Methodology

At the baseline study visit, details of their symptoms and comorbidities were recorded. All participants had their sleep and medical history information collected along with the use of regular medications. A thorough physical examination, including measurement of the vital signs, height, weight, body mass index (BMI), was performed. The probability of OSA was assessed using the STOP-BANG questionnaire in all the patients.[28] Epworth Sleepiness Scale (ESS) was calculated for each patient.[29] Patients also underwent the routine as well as the specific investigations to rule out various comorbidities like diabetes mellitus, hypertension, dyslipidemia, hypothyroidism, etc.

Eligible patients were assigned dates for their sleep studies as per their convenience within 2 weeks of their assessment in the sleep clinic. The study was carried out in a specially designated, quiet, and comfortable sleep laboratory with the temperature maintained around 25--28°C. Patients underwent a full-night type-I sleep study in the dedicated sleep laboratory at SGPGIMS, Lucknow, (using the Alice 6 Diagnostic Sleep System, Respironics, USA) according to the American Academy of Sleep Medicine Task Force (AASM) standard methodology.[30-32] Sixty-eight channels were used to document the following parameters: sleep stages (four-channel electroencephalogram, electrooculogram, chin-electromyogram), electrocardiogram channel, airflow at nose and mouth (thermistors, nasal flow cannula), chest and abdominal respiratory movement bands (respiratory impedance), oxygen saturation (pulse oximetry), snoring (microphone), and body position. All the polysomnographic (PSG) studies were supervised and attended by an experienced sleep technician.

The PSG data was reviewed at the laboratory by an experienced sleep specialist and results were recorded for subsequent analyses. Recordings were validated manually as well as using the software-assisted scoring method. The sleep stages were scored according to the updated AASM Manual of Scoring of Sleep and Associated Events (version 2.4).[30-32] Abnormal breathing events included apneas and hypopneas. Apnea was defined as the cessation of airflow ≥90% compared to baseline for ≥10 s. Hypopnea was defined as either a reduction in airflow ≥30% compared to baseline for ≥10 s accompanied by a ≥3% desaturation or arousal, or alternatively, a reduction in airflow ≥30% compared to baseline for ≥10 s accompanied by a ≥4% desaturation. Apnea hypopnea index (AHI) was the average number of apnea and hypopnea events per sleep hour. The events were further categorized into obstructive apneas (OAs) (cessation of airflow in the presence of respiratory effort), central apneas (CAs) (cessation of airflow with absence of respiratory effort), mixed apneas (MAs) (a respiratory event during which a central apnea is followed by an obstructive component), and hypopnea (Hs). OSA was diagnosed when a patient had AHI ≥15 or if a patient with symptoms suggesting OSA had AHI ≥5/h of total sleep time.

Statistical analysis

All statistical analyses were performed using the SPSS statistical software, version 22.0 (SPSS Inc., Chicago, IL, USA). Demographic and clinical (continuous) variables have been presented with descriptive statistics (mean ± standard deviation). Proportional data were expressed in terms of percentages. Continuous variables were compared using a two-tailed independent sample *t*-test. Categorical variables were compared using the Chi-square test when needed. For the univariate analysis, the Chi-square test was used. A P value <0.05 was taken as significant.

Results

A total of 150 patients referred to our sleep clinic for evaluation of OSA were enrolled in the study. Out of these, 94 (62.7%) were males with a male-to-female ratio of 1.7:1 and a mean age of 51.85 ± 12.60 years. Most of our patients were obese, with an average BMI of 32.09 ± 5.53 kg/m^2. Most common presenting features were EDS, snoring, and easy fatiguability. The clinical probability of OSA was high, with an average STOP-BANG score of 4.2 ± 1.9. Summary of the important clinical and PSG data of all patients is described in Table 1. The average age of the females with a diagnosis of OSA was significantly higher than that of males. EDS was the most common symptom observed in 80.6% of patients, followed by loud snoring, which was observed in 68% of patients. However, the difference in these symptoms was not statistically significant between the two groups. Insomnia and anxiety were significantly higher among females. ESS was not significantly different between the two groups. Hypertension was the most common comorbidity in our cohort as a total of 60.67% were hypertensive. Diabetes and hypothyroidism were observed in 50.6 and 33.34% patients, respectively. However, these comorbidities were similar in both groups. Univariate analysis of clinico-demographic characteristics is presented in Table 2.

Univariate analysis of PSG data of the two groups is presented in Table 3. Total recording time, total sleep time, sleep efficiency was found to be similar in both groups. Similarly, stages of sleep and sleep latency were also similar in both groups. The incidence of OAs and Hs were similar, but CAs and MAs were significantly higher in males. Time spent with saturation below 90% was statistically similar in both the groups. Mean AHI was significantly higher in males compared to females. The proportion of males having more severe OSA was also higher in males. After the diagnosis, CPAP prescription was similar in both groups. However, the highest titrable pressure was higher for males as compared to females.

Table 1: Clinical and polysomnographic details

	Total *n*=150
Age (years)*	51.85±12.60
BMI (kg/m^2)*	32.09±5.53
ESS*	10.08±4.74
STOP-BANG*	4.2±1.9
EDS (percent)	121 (80.6%)
Loud snoring (percent)	102 (68%)
Fatigue (percent)	46 (30.6%)
Insomnia (percent)	47 (31.33%)
Anxiety (percent)	48 (32%)
Hypertension (percent)	91 (60.67%)
Diabetes (percent)	76 (50.67%)
Hypothyroidism (percent)	53 (35.34%)
AHI*	30.12±27.00
AHI <5	19
AHI 5--15	33
AHI 15--30	26
AHI >30	62
CPAP Prescribed	79
CPAP Use	67

ESS: Epworth sleepiness score, EDS: Excessive daytime somnolence, AHI: Apnea hypopnea index, CPAP: Continuous positive airway pressure. *(mean±SD). Source: Nil (Not adapted)

Table 2: Univariate analysis for clinico-demographic data

	Male *n*=94	Female *n*=56	Significance
Age (years)*	50.01±11.12	54.94±14.33	*P*<0.05
BMI (kg/m^2)*	31.51±5.16	33.05±6.02	NS
ESS*	10.34±4.60	9.64±4.98	NS
EDS	79	42	NS
Loud snoring	59	43	NS
Fatigue	26	20	NS
Insomnia	19	28	*P*<0.05
Anxiety	11	37	*P*<0.05
Hypertension	63	28	NS
Diabetes	48	28	NS
Hypothyroidism	32	21	NS

ESS: Epworth sleepiness score, EDS: Excessive daytime somnolence. *(Mean±SD). Source: Nil (Not adapted)

Discussion

OSA has emerged as a major public health problem with large community-based studies confirming prevalence as high as 15-17% in middle-aged adults, primarily obese males.[9-14] Despite the growing awareness regarding the disease, it is estimated that most patients are under-diagnosed, suggesting the inadequacy of current resources in meeting the growing demands. One of the major factors associated with under-diagnosis is the lack of awareness about this clinical entity among the primary care and family physicians in general, who are the first point of contact between patients and the healthcare facilities. Many cases are missed either due to under-reporting of symptoms by the patients or due to the ignorance of the clinicians regarding the appropriate screening for OSA in patients presenting with a multitude of symptoms. In addition, an often-neglected concern in its under-recognition remains the fact that there are significantly different gender-related aspects in the clinical presentation of OSA. The difference can be observed in all aspects of the presentation of OSA right from symptoms, PSG features, to the treatment with CPAP.

OSA seen traditionally as a disease of males can longer be ignored as significant morbidity affecting females. The latest prevalence estimates of moderate-to-severe OSA in women from various studies range from 6 to 25%,[14,23,33] resulting in male-to-female ratio from 45:1 to 2-3:1. In our study, the difference further narrowed down to a ratio of 1.7:1. As pointed out in a study on 1,166 patients,[19] it is likely that women with OSA may be under-diagnosed due to circumstances related to their families, lifestyle, and sociocultural factors, with lesser women reaching healthcare facilities and seeking medical opinion for their symptoms related to OSA.[16]

Hormones have been majorly implicated in the gender-related variations, with male hormones like testosterone tending to

Table 3: Univariate analysis for Polysomnographic data

	Male *n*=94	Female *n*=56	Significance
TRT (minutes)*	428.02±86.00	423.62±102.67	NS
TST (minutes)*	343.84±75.88	336.75±92.63	NS
SE (percent)	80.14±5.31	79.22±4.99	NS
Latency (minutes)*	21.28±4.42	21.39±4.27	NS
N1 (percent)*	12.69±4.47	12.10±4.44	NS
N2 (percent)*	43.60±10.49	43.17±10.47	NS
N3 (percent)*	26.00±10.97	27.68±9.97	NS
REM (percent)*	17.70±6.7	17.03±6.53	NS
Central apnea	23.5±51.23	9.3±15.83	*P*<0.05
Mixed apnea	19.70±32.03	7.28±12.98	*P*<0.05
Obstructive apnea	79.64±89.09	75.77±125.98	NS
Hypopnea	63.82±79.22	52.51±73.42	NS
SpO_2 time <90%(minutes)*	53.79±102.79	40.51±77.81	NS
AHI*	33.45±27.31	24.52±25.74	P<0.05
REM-AHI*	39.84±30.64	29.92±23.02	NS
AHI<5	12	7	
AHI 5--15	24	9	
AHI 15--30	16	10	
AHI>30	42	20	*P*<0.05
CPAP Prescribed	51	28	NS
CPAP Use	49	18	*P*<0.05
CPAP Highest Pressure (cm of water)	12.03	11.5	*P*=0.053

TRT: Total recording time, TST: Total sleep time, SE: Sleep efficiency, AHI: Apnea hypopnea index, REM-AHI: Apnea hypopnea index during rapid eye movement sleep, CPAP: Continuous positive airway pressure. *(Mean±SD). Source: Nil (Not adapted)

increase obesity and severity of OSA several mechanisms, while female hormones are promoting airway and ventilatory stabilization.[16,34] This difference continues up to the postmenopausal period, where female tend to catch up with their male counterparts. In consistence with the findings of previous studies,[35,36] in women from different ethnicities, our study also suggests that the differences between men and women in the prevalence of OSA decrease as age increases. However, our findings are in contrast to a large series from North America[37] in which females were much heavier and were about the same age as males. It is also noteworthy that approximately 50% of our female patients were post-menopausal with a median age of 54.9 years. Although hormonal influences in females could also affect the manifestation of comorbidities[38] (hypertension, diabetes, hypothyroidism), our study failed to demonstrate any such differences.

Another reason for the gender disparity in the diagnosis of OSA could be the possibility that healthcare providers disregard the atypical symptoms at clinical presentation in women.[15,19,36,39] One of the earlier studies[40] had shown that regardless of the severity level, women with OSA did not report their symptoms that differed significantly from men with the same level of sleep apnea. A population-based sample[27] found that up to 40% of women with AHI >15/h did not report any of the classic OSA symptoms (snoring, witnessed apneas, and daytime sleepiness). Our study has not only emphasized upon Indian women failing to acknowledge their OSA symptoms and seeking late medical help but also on reporting of atypical symptoms such as depression, anxiety, and insomnia more commonly than men. This could further manifest as non-restorative sleep, easy fatiguability, lack of energy, morning headaches, mood disturbances, and a poor quality of life.[41,42] In a recent study, waist circumference and waist-to-height ratio were better predictors for OSA in females. While in men, waist-to-height ratio and neck circumferences were associated with mild OSA and BMI was more closely associated with severe OSA.[43]

We also analyzed the gender differences in the PSG features in our group of 150 patients. As opposed to previous studies,[35-37,44] showing differences in the sleep architecture and sleep-related respiratory events, we have not found any difference in the sleep architecture (TST, sleep latency, NREM sleep, and REM sleep) of female patients as compared to males. One of the main findings in our study is that women with OSA have significantly milder disease than men. This difference was maintained even on sub-classifying the OSA based on its severity. However, the difference between REM-AHI and NREM-AHI in females could not be appreciated, unlike previous studies,[27,45,46] showing shorter apnea duration with lesser NREM-AHI in women. There may also be gender differences in the arousal response patients have to apneas.[25] In a study conducted in 3,234 Japanese patients, it was found that female sex is an important risk factor for REM-related OSA and women aged over 50 years were at a greater risk than those aged under 50 years.[47]

Interestingly, women in our study were typically as symptomatic as men, despite having less severe disease. This could be related to women, in general, having more episodes of upper airway resistance (without frank apneas) during sleep[37] and non-restorative sleep, causing uncommon clinical manifestations like insomnia and other neuropsychiatric features. Having lower AHI in females also translated into our finding of having lower CPAP titration pressures in women as compared to men. Recently, in an Italian cohort of 1,082 patients, it was shown that with CPAP therapy, males had better perceived health-related quality of life (HRQoL) at first visit.[48]

Although there are well-known gender differences, there are only a few dedicated studies investigating the effect of gender on the clinical aspects of OSA. To our knowledge, this is the first and only study in the Indian population, highlighting the gender-based differences in clinical characteristics in OSA. This study carries special importance for family physicians and physicians working at primary care level, as it not only highlights the most significant clinical features to look for in patients suspected of having OSA but also brings out the differences in clinical manifestations of OSA in males and females. This could potentially lead to more efficient screening of OSA at primary care level and reduce under-reporting of the disease burden in specific population subsets. Moreover, the gender-based differences in the PSG features of patients with OSA suggested through our study may help the physicians in providing a patient-tailored treatment and follow-up.

There are a few limitations to our study. Our sample size was relatively small for the disease burden in the community that could have affected our findings. Secondly, there is a potential weakness due to the referral bias, as the study population was selected from our sleep clinic, which may not be a representative sample for the community. Another pitfall is the lack of inclusion of a normal healthy control group of adults for comparison. Comparing females to males with OSA, rather than matched controls meant having no data on differences between female patients with OSA and the general female population, where insomnia, mood disturbances, and certain specific morbidities like hypothyroidism can be common.

In conclusion, there are significant gender-related differences in clinical presentation as well as PSG features in patients with OSA that need to be considered while screening and managing patients at healthcare facilities. Although our study manages to highlight various gender-based aspects in OSA, larger community-based studies are required to further substantiate the findings of our study.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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