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ORIGINAL ARTICLE

Sleep Science

Age-dependent influence of gender on symptoms of obstructive sleep apnea in adults

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ABSTRACT

Objective: Obstructive Sleep Apnea (OSA) is linked to classical symptoms of snoring and excessive sleepiness. However, many women with OSA may present with a diverse profile. The influence of age on the clinical differences between genders is unclear. This survey aimed to compare the clinical and polysomnographic findings of OSA between adult males and females, but considering different age groups. **Methods:** This cross-sectional study comprised a sample of 472 consecutive adult patients with OSA who underwent full-night polysomnography. Data from the medical and polysomnographic records was obtained, as well as the score on Portuguese validated version of the Epwoth Sleepiness Scale (ESS). Comparisons of main clinical aspects of OSA between genders were stratified according to three groups: young (< 30 years old), middle-aged (30 - 50 y.o.), and older patients (> 50 y.o.). **Results:** Men comprised the majority of the sample (male/female ratio of 1.6). Apnea-Hypopnea Index (AHI) was higher in men than women (median [interquartile range]: 29.7 [18.1-47.8] vs. 21.9 [11.5-36.1]; $p < 0.0001$), and body mass index alike (mean ± standard deviation: 29.0±4.9 vs. 27.6±5.2; $p = 0.004$). Snoring was more common in male than in female patients (92% vs. 84.7%; $p = 0.015$). In the subset of subjects younger than 30 years-old the differences between genders were prominent (male/female; AHI: 19.6 [13.1-28.1] vs. 11.8 [7.7-18.8], $p = 0.012$; sno ring: 89.7% vs. 55.2%, $p = 0.007$), accompanied by a trend to lower score in ESS in male patients (7.1 ± 4.3 vs. 9.2 ± 4.3; $p = 0.066$). **Discussion:** Results suggest that a classical clinical picture of snoring and severe daytime sleepiness is lacking in a considerable proportion of OSA sufferers, particularly young women, who tend to be sleepier than male patients. The awareness of OSA in young women should be based more in mild excessive daily sleepiness than in other typical OSA symptoms.

Keywords: Obstructive Sleep Apnea; Gender; Signs and Symptoms; Adults.

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INTRODUCTION

Gender differences in the expression of normal and pathological sleep have been reported in the last decades. Global data revealed that adolescent girls usually sleep half an hour more than boys on non-school days, although sleep time progressively declines with age still during adolescence[1]. On the other hand, women suffer more markedly from insomnia in general population[2,3]. A nationwide Brazilian survey showed that 76% of people older than 16 years-old had at least one complaint related to sleep, with a diverse gender profile: snoring was more common in men, whilst insomnia, light sleep, bruxism, excessive daytime sleepiness and headache upon waking up were more marked among women[3].

Snoring and excessive daytime sleepiness are classical symptoms of Obstructive Sleep Apnea (OSA)[4], a medical condition that also exhibits demographic and clinical differences regarding gender. The prevalence of OSA in adult population is reported to be about 22% in males and 17% in females[5], giving rise to a male/female ratio of about 1.3. A large Turkish survey with 2827 patients confirmed higher prevalence among men, whose OSA severity was also more prominent, accompanied by more witnessed apneas[6]. Women, instead, complained mainly of nocturnal choking, morning headache, fatigue, insomnia, impaired memory, mood disturbance, reflux, nocturia, and enuresis. Snoring and excessive daytime sleepiness were not different between males and females in that population.

Previous studies also pointed to a diverse clinical picture of OSA women[7,8], including a higher likelihood to fell unrested parallel to a lower propensity to have a score higher than 10 in the Epworth Sleepiness Scale (ESS) - a worldwide method for measuring excessive daytime sleepiness -, although feeling sleepy at similar rates[7]. Consequently, OSA tends to be more commonly underdiagnosed among women[8-11].

OSA increases in severity through life in both genders, but women have less severe syndrome in all ages[12]. Nevertheless, the effect of age/gender combination on the clinical expression and ultimately the suspicion of OSA is still an issue of research[11]. In this setting, this survey aimed to compare the clinical and polysomnographic findings of OSA between adult males and females, but considering different age groups.

MATERIAL AND METHODS

Study Population

This cross-sectional study comprised a sample of 472 consecutive adult patients with an apnea-hypopnea index (AHI) ≥ 5 obstructive events per hour during a full-night exam, defined by the American Academy of Sleep Medicine (AASM) as the polysomnographic requirement for the diagnosis of OSA[13]. We retrospectively evaluated the polysomnographic and medical records of the subjects who underwent diagnostic in-laboratory study due to sleep complaints in the Instituto de Neurologia e Neurocirurgia (INN), an outpatient clinic of Passo Fundo, RS, Brazil, from November 2014 to January 2018. The clinic serves the public and private health care system of Passo Fundo and surrounding cities. Patients who presented sleep disturbances other than OSA in the polysomnographic and clinical analysis were excluded (Figure 1). Those under benzodiazepine use were routinely oriented to taper the medication before the exam in order to provide polysomnographic records without the effect of such drugs in terms of enhancing AHI.

Clinical data

Demographic and clinical informations obtained from the medical records included gender, age, race, body mass index (BMI), as well as specific sleep complains, namely: sleep fragmentation, morning fatigue / non-restorative sleep, gasping during sleep and observed sleep apneas. The patients' report of present depression or hypothyroidism, treated or not, was also assessed. The Portuguese validated version of the ESS[14] - a 8-item scale for measuring excessive daytime sleepiness that renders a score from 0 to 24 (the higher, the sleepier) - was applied to all patients before polysomnography by a trained person.

Comparisons of the two main clinical symptoms of OSA (sleepiness and snoring) between genders, as well as the AHI, were stratified according to three groups: young (< 30 years old), middle-aged (from 30 to 50 y. o.), and older patients (> 50 y. o.).

Polysomnographic data

Polysomnographies (iBlue 64 system, iCelera Medical Diagnostics, São Paulo, Brazil) were evaluated by only one experienced rater according to the standard method[15] obtained by classical parameters (international 10-20 system electroencephalography; chin and limb electromyography; electrooculography; oronasal temperature thermistor; nasal-cannula-pressure transducer; thoracoabdominal plethysmograph; electrocardiography; transcutaneal finger pulse oximeter). Polysomnographic data furnished the following variables: sleep efficiency and latency; REM latency; proportions of N1, N2, N3, and REM stages; number of arousals per hour; total sleep time; AHI (the sum of obstructive hypopneas and apneas per hour of sleep). The presence of snoring was also assessed objectively during the full-night study.

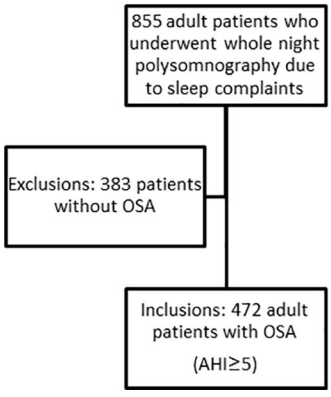

Figure 1. Study design flow chart (OSA: obstructive sleep apnea; AHI: apnea-hypopnea index).

This study was not funded

Statistical Analyses

Quantitative variables were presented as mean and standard deviation or median and 25%-75% interquartile range (IQR), the latter in case of asymmetrical distribution. Categorical data was described as percentage and was analysed with Fisher's exact test. The Student T test or, when necessary, Mann-Whitney U test was used to compare quantitative variables. The analyses were performed with commercially available *Statistical Package for the Social Sciences* (SPSS) version 16.0 (SPSS Inc, Chicago, IL, USA) and *GraphPad Prism* version 5.00 (GraphPad Software Inc, San Diego, CA, USA). Statistical significance was assumed when a two-tailed p-value ≤ 0.05.

Ethics

This research was conducted in accordance with the Declaration of Helsinki and was approved by the Ethical Committee of Universidade de Passo Fundo (UPF) (Report Number 1.710.269).

RESULTS

Clinical and polysomnographic characteristics of the sample are depicted in Table 1, with a direct comparison between genders. Almost all quantitative data showed asymmetrical distribution and were presented as median and IQR. Most patients were Caucasian, reflecting the local ethnic composition in this region of South Brazil. Men comprised the majority of the population included in the study, with a male/female ratio of circa 1.6.

BMI, AIH, presence of snoring, number of arousals and the percentages of reported sleep apneas, N2 stage, and severe OSA were higher in men. Conversely, REM latency, N3 stage, REM stage, and the percentages of depression and mild OSA were higher among women.

The analyses of the main data stratified according to the three age groups are presented in Table 2. Men younger than 30 years old exhibited higher AHI and percentage of snoring, as well as a trend toward lower EES in comparison to women. AHI was also higher among men among the patients aged from 30 to 50 years-old.

DISCUSSION

The comparison of the clinical and polysomnographic profiles between men and women affected by OSA has been explored extensively[6-8]. However, the characterization of the findings of such two different populations considering diverse age groups was a new enterprise.

Table 1. Comparisons of clinical and polysomnographic characteristics of the sample (n = 472) according to the gender. Results of qualitative variables are presented as absolute number and percentage, while those related to quantitative data were depicted as median [and interquartile range] or, when otherwise stated (*), as mean ± standard deviation. Significant results highlighted in bold.

Characteristics	Male (n = 289; 61.2%)	Female (n = 183; 38.8%)	*p* value
White	n = 276; 95.5 %	n = 178; 97.5 %	0.461
Age (years)	53 [39-62]	55 [40-62]	0.797
Body mass index (kg/cm²)*	29.0 ± 4.9	27.6 ± 5.2	**0.004**
Clinical complaints			
Sleep fragmentation	n = 207; 71.4 %	n = 114; 62.0 %	0.068
Morning fatigue/non-restorative sleep	n = 203; 70.1 %	n = 141; 76.8 %	0.189
Gasping	n = 103; 35.7 %	n = 49; 26.6 %	0.085
Observed sleep apneas	n = 167; 57.6 %	n = 70; 38.2 %	**<0.001**
Comorbidities			
Depression (in treatment)	n = 59; 20.3 %	n = 61; 33.1 %	0.007
Hypothyroidism (in treatment)	n = 20; 6.9 %	n = 24; 12.8 %	0.146
ESS score	8 [5-12]	9 [5-12]	0.803
AHI	29.7 [18.1-47.8]	21.9 [11.5-36.1]	**<0.001**
Presence of snoring	n = 266; 92.0 %	n = 155; 84.7 %	**0.015**
Sleep latency (minutes)	0 [0-3.7]	0 [0-5]	0.315
REM latency (minutes)	118.5 [78-192.5]	134.5 [88.5-208.5]	**0.028**
Total sleep time (hours)*	5.5 ± 1.35	5.8 ± 1.20	0.558
Sleep efficiency (% of time in bed)	88.8 [79.4-94.9]	90 [80-96.3]	0.157
N1 stage (% of time in bed)	6.9 [4-11.4]	6.1 [3.8-10.3]	0.127
N2 stage (% of time in bed)*	56.2 ± 11.7	53.8 ± 11.5	**0.032**
N3 stage (% of time in bed)*	19.6 ± 10.3	21.9 ± 9.6	**0.016**
REM stage (% of time in bed)*	14.9 ± 6.7	16.2 ± 7.0	**0.042**
Arousals (number per hour)	35.8 [25.5-51.4]	30 [20 - 41.8]	**< 0.001**
OSA			
Mild	n = 55; 19.0 %	n = 64; 35.0 %	**< 0.001**
Moderate	n = 90; 31.1 %	n = 51; 27.9 %	0.479
Severe	n = 144; 49.8 %	n = 68; 37.2 %	**0.008**

ESS: ESS: Epworth Sleepiness Scale; AHI: apnea-hypopnea index; REM: rapid eye movements; OSA: obstructive sleep apnea.
Comparisons of qualitative data were performed with Fisher's exact test. Qualitative data was analysed with Mann-Whitney U test, except if normal distribution (*), when T test was applied.

Table 2. Comparison of daytime sleepiness, apnea-hypopnea index and presence of snoring between men and women according to the age groups. Significant results highlighted in bold.

Patients younger than 30 years old (n = 58)			
Characteristics	**Male (n = 29; 50%)**	**Female (n = 29; 50%)**	***p* value**
ESS score*	7.1 ± 4.3	9.2 ± 4.3	0.066
AHI**	19.6 [13.1 - 28.1]	11.8 [7.7 - 18.8]	**0.012**
Presence of snoring†	n = 26; 89.7 %	n = 16; 55.2 %	**0.007**
Patients from 30 to 50 years old (n = 146)			
Characteristics	**Male (n = 100; 68.4%)**	**Female (n = 46; 31.6%)**	***p* value**
ESS score**	8 [5 - 13]	9 [4.7 - 12]	0.770
AHI**	28.7 [17.2 - 45.5]	13.6 [8.9 - 26.7]	**< 0.001**
Presence of snoring†	n = 88; 88.0 %	n = 41; 89.1 %	0.540
Patients older than 50 years old (n = 268)			
Characteristics	**Male (n = 160; 59.7%)**	**Female (n = 108; 40.3%)**	***p* value**
ESS score**	8 [4-12]	8 [4.2 - 11]	0.700
AHI**	34.0 [21.7 - 51.1]	31.5 [16.7 - 46.9]	0.120
Presence of snoring†	n = 152; 95.0 %	n = 98; 90.7 %	0.132

AHI: apnea-hypopnea index; ESS: Epworth Sleepiness Scale.
* Mean ± standard deviation; comparison with T test.
** Median [and interquartile range]; analysed with Mann-Whitney U test.
† Comparison with Fisher's exact test.

As expected, our case series was composed by male majority, but the observed male/female ratio was higher (1.6) than that reported in general adult population (1.3)[5]. This may be related to the aforementioned fact that women with OSA are often underdiagnosed[8-11] in great part due to the female trend for less typical symptoms[6], therefore leading the physicians to order polysomnography less frequently to women than men.

OSA was consistently more severe (measured by AHI) in men than women, a finding also established in literature[6,16]. In fact, more women exhibited mild OSA than men; on the other hand, severe OSA was more common among male than in female patients. Men also complained more frequently on observed apneas. These findings may be related in some extent to the higher BMI observed in males in our sample, similarly to a previous Chinese study[16], although this is not uniformly seen worldwide: in the large Turkish series women had higher BMI, despite lower AHI[6]. Several sleep architecture differences were also observed in male patients (higher number of arousals and percentage of N2 stage; lower percentages of N3 and REM stages) in comparison to women and may be attributed to the increased AHI, which causes sleep fragmentation and consequently decreases the deep stages.

We attempted to give a special glance to the patients' clinical picture. Our first attention was devoted to snoring. Basoglu & Tasbakan[6] had recently reported a similar proportion of snoring in both genders, but their measurement was subjective, that is, relied on symptom reports. This may underestimate the real prevalence of snoring, because many subjects do not have a relative able to report the snoring. We in turn objectively recorded snoring in the diagnostic in-laboratory study - avoiding reference bias from the own patients or their relatives -, and found that 15% of all women with OSA do not snore, while the correspondent figure for men was only 8%.

This raises concern when one intends to identify the possibility of OSA based on the information obtained from medical history, since a considerable proportion of women with OSA actually do not snore. This is especially true for patients under 30 years-old, a group where the proportion of snorers among women was not much bigger than a half, while the correspondent figure for men was about 90%. Interestingly, middle-aged women snored as frequently as men, although the AHI was lower, and among those patients older than 50 the figures of snoring and AHI were very similar. The latter finding is expected, since it is already established that menopause leads most women to have the same OSA profile than men due to the lack of a protective effect of hormones[11]. Inflammatory markers linked to OSA also are expressed differently between genders: while men with OSA have higher blood leptin levels than controls, female patients exhibit higher TNF-α levels that decrease in postmenopause[17]. The lack of data about menopausal status in our series constitutes a limitation, especially related to the older age groups that we analysed (30-50 y.o.; more than 50 y.o.).

The major issue to be discussed is about daytime somnolence indeed. A score higher than 10 in the ESS is traditionally employed as a watershed between normal and excessive daytime somnolence, but we think such a cut-off point may not serve as a sensitive tool in order to screening for OSA, because of most of our patients exhibited ESS lower than 10. Besides, the traditional value may not be representative of real biological differences of daytime somnolence between genders. Taking strictly this into account, literature brought that women were considered with the same[6,18] or with a lower[7,16] propensity than men to have a score higher than 10 in the ESS, along with AHI less prominent in two case series[6,16]. By the way, a consistent finding in several studies is the positive relation of ESS with AHI[15,18].

This study was not funded

However, data about our subset of patients under 30 year-old suggests a different scenario: despite lower AHI, women exhibited a trend to higher ESS, besides the aforementioned less common snoring. This contrasts with the results of the middle-aged and older women, where ESS was the same in female and male patients and the proportion of snorers was similar. Altogether, these findings suggest that age interferes markedly with the role of gender in the clinical expression of OSA, pointing to a more similar picture in subjects older than 30 years-old, but not in younger adults, whose daytime sleepiness (although still up to 10 in most cases) and absence of snoring may be more characteristic of female than male patients.

This may find some explanation in studies that outweigh the field of respiratory sleep disturbances. Indeed, a recent survey that included general population found that female subjects tended to be sleepier in their 3rd and 4th lifetime decade, whilst male subjects scored significantly higher in their 7th decade[19]. Noteworthy is also the aforementioned reference to a more conspicuous need for total daily sleep time in female adolescents and[1], consequently, the potential for higher ESS than counterpart males in a setting of sleep deprivation commonly seen in adolescents and young adults. Sleep of young women is more resistant to external stressors than that of coetaneous men, another possible influence of gonadal hormones[20].

Sleep privation was not assessed in our sample, a fact limits a deeper analysis of its weigh in the expression of sleepiness in OSA. Another variable that could be related to higher somnolence in female OSA patients is the higher prevalence of reported depression in our series and, consequently, antidepressant use. Due to the retrospective design of the study, we cannot adequately ascertain if this reported diagnosis is actually correct, if the symptoms are still present and the details on medication use (dose, time of intake during the day, drug interactions).

Our study has other limitations that must be stressed. First, our sample is not population-based and most other OSA case series worldwide alike. There are considerable logistic and financial obstacles for performing a population study about OSA because of the need of confirming the diagnosis with the aid of polysomnography. Our sample was obtained from both public and private health care systems in an attempt to avoiding an economic bias regarding the study population. Nevertheless, our results enables the suspicion of the existence of an even larger group of undiagnosed female OSA patients in general community.

Second, our sample size of OSA patients aged less than 30 was small, a fact that could eclipse more significant results. Despite this limitation, we demonstrated a trend toward significance in terms of higher daytime sleepiness in young women with OSA, even with a lower AHI, and a striking difference in snoring prevalence. A lager sample could probably confirm such a trend regarding sleepiness.

Even though some limitations exist, results here presented are in accordance with other published literature that suggests the ineffectiveness of assessment for OSA in primary care[8-11,21]. This derives in part from to the lack of a classical clinical picture of snoring or severe daytime sleepiness in a considerable proportion of OSA sufferers, particularly young female patients. Despite recent cluster analysis have pointed to several clinical profiles in terms of OSA presentation[22,23], our study was the first one suggesting the non-snoring but sleepier type related to young women with OSA.

We conclude that the awareness of OSA in young women should be based more in mild excessive daily sleepiness, even with ESS scores lower than the classical "10" edge, than in other typical OSA-related symptoms, as snoring.

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