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The influence of gender on symptoms associated with obstructive sleep apnea

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Abstract

Background It has been reported that the clinical expression of obstructive sleep apnea (OSA) may differ in women and men.

Objective The objective of this study was to evaluate the influence of gender on reported OSA-related symptoms in a large clinical population of patients.

Methods The database from the sleep laboratory of a tertiary care center was examined. Adult patients who had undergone a diagnostic polysomnography and completed the Berlin questionnaire, a sleep questionnaire, and the Epworth sleepiness scale were selected. Multiple logistic regression analysis was performed to assess the relationship between OSA-associated symptoms and different potential explanatory variables.

Results The study sample included 1084 patients, median age was 53 years, 46.5% (504) were women, 72.7% (788) had OSA (apnea/hypopnea index ≥ 5), and 31.2% were obese. After adjusting for age, body mass index, and apnea/hypopnea index, men were more likely to report snoring (OR 4.06, $p < 0.001$), habitual or loud snoring (OR 2.34, $p < 0.001$; 2.14, $p < 0.001$, respectively) and apneas (OR 2.44, $p < 0.001$), than women. After controlling for multiple variables, female gender was an independent predictive factor for reported tiredness (OR 0.57, p 0.001), sleep onset insomnia (OR 0.59, p 0.0035), and morning headaches (OR 0.32, $p < 0.001$). Reports of excessive daytime sleepiness, nocturia, midnight insomnia, and subjective cognitive complaints were not significantly associated with gender.

Conclusion Women with OSA were more likely to report tiredness, initial insomnia, and morning headaches, and less likely to complain of typical OSA symptoms (snoring, apneas) than men.

Keywords Sleep apnea · Gender differences · Women · Sleep-disordered breathing · Clinical manifestation · Symptom presentation

Introduction

Based on available general population-based studies, the prevalence of obstructive sleep apnea (OSA) associated with accompanying daytime sleepiness is approximately 11% for adult men and 4% for adult women [1]. It has been suggested that the higher prevalence of OSA in males may result from the fact that women do not show the classic symptomatology or consult for nonspecific symptoms, and thus they may be underdiagnosed. Also, men have a longer, collapsible oropharynx, which is the pharyngeal segment involved in OSA, and a larger, fatter, posterior tongue than women and, hence, more chance of developing OSA [2].

Patients with obstructive sleep apnea usually consult for symptoms such as habitual or loud snoring, apneas, tiredness or fatigue, and excessive daytime sleepiness. Sometimes, the

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initial complaints are nonspecific symptoms such as insomnia, frequent awakenings at night, nocturia, morning headaches, or neurocognitive impairment [3]. Whereas some studies have pointed out that women complain more frequently of insomnia [4–9] and daytime tiredness [7–9] compared to men, others have shown discordant results regarding the reporting of snoring [6, 10, 11], apnea [4–6, 10], and excessive daytime sleepiness [4, 6, 7].

Several studies have conducted comparative analyses of the prevalence of symptoms between women and men with OSA, with [4, 6] or without [9, 12–14] covariate adjustment; other researchers have performed multiple regression analysis to determine whether gender independently predicted OSA symptoms [7, 8, 10, 11, 15]. In order to extend previous observations and clarify some controversies, we aimed to evaluate the influence of gender on reported OSA-related symptoms in a large population of patients referred to the sleep laboratory of our institution.

Methods

Patient selection

We examined the database from Hospital Alemán's sleep laboratory from January 2013 to January 2016 and preselected 2154 patients older than 17 years who had a polysomnography (PSG) and answered a sleep questionnaire. Since there was male predominance in the initial sample (1454), 700 males were chosen at random to equal the number of females (700). The subjects who had undergone diagnostic PSG, the Berlin questionnaire, a sleep questionnaire, and the Epworth sleepiness scale (ESS) were selected. Exclusion criteria comprised patients who did not answer questions 1 to 7 of the Berlin questionnaire or the ESS, marked more than one answer on any of the questions, had suspected narcolepsy, performed a split-night PSG, or had a PSG with less than 180 min of total sleep time. Of the 1400 patients selected, 316 were excluded for different reasons. Figure 1 shows the study flow chart.

Measurements

All the patients enrolled in this study underwent a diagnostic PSG which included EEG (F4/A1, C4/A1, O2/A1), EOG (two channels), chin EMG, leg EMG (two channels), ECG, airflow by nasal pressure, and an oral thermistor, thoracic and abdominal movements (two channels with piezoelectric sensors), snoring, oxygen saturation (SO_2), and body position. The PSGs were registered from 10:30–11:30 p.m. to 5:00–6:00 a.m. Prior to PSG, the patients were given the following instructions: (1) to avoid napping and alcoholic or caffeinated beverages, (2) to continue taking the usual medication, (3) to eat supper between 8 and 9 p.m., and (4) to report to the sleep laboratory between 9 and 10:30 p.m. The PSG analysis was performed manually by four trained physicians following international criteria [16]. OSA was defined as an apnea/hypopnea index (AHI) ≥ 5. On arrival at the sleep lab, the patients completed a Spanish version of the ESS [17] and the Berlin questionnaire [18], and a sleep medical record (see appendix). Body weight and height were recorded in all subjects wearing only light clothes and no shoes. The Spanish version of the Berlin questionnaire was validated against PSG, and it showed to have similar sensitivity and specificity to reports in the original literature [19, 20]. Comorbidities were detected either by self-reporting and/or the medication that the patient was taking. Restless leg syndrome was assumed when patients complained of uncomfortable sensations in their legs before sleeping and reported behaviors to relieve this discomfort. Menopause was considered when it was reported on the sleep questionnaire or when women were older than 50 years [21]. Definitions used for nocturnal and diurnal symptoms associated with OSA are shown in Table 1.

Statistical analysis

A frequency histogram and the Kolmogorov–Smirnov test were used to assess if the study variables had a normal distribution. The Mann–Whitney or the chi-square tests were used to compare differences between women and men.

Multiple logistic regression analysis was performed to assess the relationship between symptoms associated with OSA (present = 1, absent = 0) and various potential explanatory variables. Typical symptoms of OSA (snoring, apnea) were adjusted for age, gender (male = 1, female = 0), BMI, and AHI. In order to predict other less-specific symptoms of OSA (tiredness, excessive diurnal somnolence, insomnia, nocturia, morning headaches, subjective cognitive complaints), logistic regression models included other factors that could potentially explain their presence or absence (mean SO_2; minimal SO_2; T90; use of sedatives, antidepressants, or analgesics; cardiovascular comorbidities; diabetes; hypothyroidism; rhinitis; pulmonary pathology' restless leg syndrome; and gastroesophageal reflux symptoms). For the purpose of this investigation, the term comorbidities, used as predictor in logistic regression models, referred to any of the following conditions: hypertension, coronary disease, stroke, heart failure, diabetes, hypothyroidism, rhinitis, asthma, COPD, gastroesophageal reflux, nocturia, and chronic use of analgesics.

The statistical analysis was carried out with a commercial computer program, MedCalc Statistical Software version 16.8

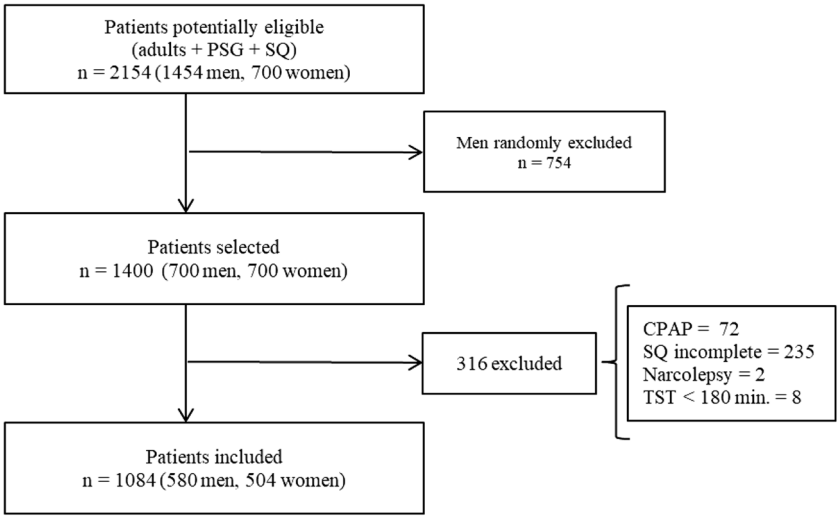

Fig. 1 Study flow chart (PSG, polysomnography; SQ, sleep questionnaires; TST, total sleep time)

(MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2016).

Results

The study sample included 1084 patients, median age was 53 years, 46.5% (504) were women, 72.7% (788) had OSA (AHI ≥ 5), and 31.2% were obese. The characteristics of study population are shown in Table 2.

Gender differences in OSA population

Tables 2, 3, and 4 show gender differences in terms of clinical manifestations and PSG features. Women presented older age, lower AHI, and higher prevalence of morbid obesity than men. Seventy-one percent of the women with obstructive sleep apnea were menopausal. Women reported more hypothyroidism and restless legs syndrome than men and complained more often of tiredness, insomnia, morning headache, and subjective cognitive complaints. They also reported

Table 1 Definitions of symptoms associated with obstructive sleep apnea

Symptoms	Answers/definition
Nocturnal	
Snoring—question 1 BQ	a
Loud snoring—question 2 BQ	b, c, d
Habitual snoring—question 3 BQ	a, b
Apnea—question 5 BQ	a, b, c
Sleep onset insomnia—difficulty falling asleep (1)	≥ 5–15 times a month
Maintenance insomnia—waking up while sleeping and delay in returning to sleep (2)	≥ 5–15 times a month
Insomnia (1 and 2)	
Sleeping frequent awakenings—waking up several times during sleep	≥ 5–15 times a month
Nocturia—waking up more than once at night to urinate	≥ 5–15 times a month
Diaphoresis—sweating a lot while sleeping	≥ 5–15 times a month
Sleeping movements	≥ 5–15 times a month
Nightmares	≥ 5–15 times a month
Diurnal	
Daytime tiredness (after sleeping or during the day)—question 6 and 7 BQ	a
Excessive diurnal somnolence	Epworth > 10
Morning headache	≥ 1–3 times a week
Difficulty concentrating	Yes
Memory loss	Yes
Attention problem	Yes
Subjective cognitive complaints—concentrating, memory, and attention problems	Yes

BQ Berlin questionnaire

Table 2 Characteristics of the study population

	All	Non OSA (G1)	OSA (AHI ≥ 5)		
			Female (G2)	Male (G3)	*p**
Patient number	1084	296 (27.3)	304 (28)	484 (44.7)	< 0.001
Age (years)	53 (40–62)	46 (33.5–57)	57 (49–64)	52 (40–62)	< 0.001
Body mass index (BMI kg/m^2)	27.7 (24.5–31)	24.5 (22–27.6)	28.4 (24.4–33.3)	28.7 (26.3–31.6)	0.13
BMI ≥ 30	338 (31.2)	42 (14.2)	116 (38.1)	180 (37.2)	0.80
BMI ≥ 35	137 (12.6)	12 (4)	59 (50.9)	66 (36.6)	< 0.02
Prevalence of OSA (%)	72.7	–	60.3	83.4	< 0.001
Comorbidities and medication					
– Hypertension	341 (31.5)	55 (18.6)	109 (35.9)	177 (36.6)	0.84
– Coronary heart disease	53 (4.9)	6 (2)	16 (5.3)	31 (6.4)	0.53
– Ischemic or hemorrhagic stroke	23 (2.1)	4 (1.4)	7 (2.3)	12 (2.5)	0.9
– Heart failure	28 (2.6)	5 (1.7)	5 (1.6)	18 (3.7)	0.09
– Cardiovascular disease**	375 (34.6)	61 (20.6)	120 (39.5)	194 (40.1)	0.87
– Diabetes type II	140 (12.9)	17 (5.7)	41 (13.5)	82 (16.9)	0.19
– Hypothyroidism	170 (15.7)	50 (16.9)	85 (28)	35 (7.2)	< 0.001
– Bronchial asthma	98 (9)	40 (13.5)	30 (9.9)	28 (5.8)	0.032
– COPD	69 (6.4)	17 (5.7)	22 (7.2)	30 (6.2)	0.58
– Other pulmonary pathologies	26 (2.4)	4 (1.4)	12 (3.9)	10 (2.1)	0.14
– Pulmonary disease***	167 (15.4)	58 (19.6)	52 (17.1)	57 (11.8)	0.036
– Nasal obstruction/rhinitis	395 (36.4)	112 (37.8)	111 (36.5)	172 (35.5)	0.78
– Restless leg syndrome	227 (20.9)	55 (18.6)	92 (30.3)	80 (16.5)	< 0.001
– Dyslipidemia	163 (15)	38 (12.8)	42 (13.8)	83 (17.1)	0.22
– Antacid	393 (36.3)	92 (31.1)	140 (46.1)	161 (33.3)	< 0.001
– Sedative/Antidepressant	316 (29.2)	101 (34.1)	115 (37.8)	100 (20.7)	< 0.001
– Analgesic	92 (8.5)	40 (13.5)	28 (9.2)	24 (5)	0.021
Menopause	307 (28.3)	90 (30.4)	217 (71.4)	–	

Data are presented as median (25–75% percentiles), or *n* (%)

*Differences between G2 and G3

**Cardiovascular disease: hypertension or coronary heart disease or stroke or heart failure

***Pulmonary disease: bronchial asthma or COPD or other pulmonary pathologies

taking more sedatives/antidepressants, analgesics, and antacids.

Factors associated with OSA symptoms

Table 5 shows the results of the different logistic regression models used to identify the explanatory variables of OSA-related symptoms.

Specific OSA symptoms

Snoring (S) and habitual snoring (HS) were significantly associated with male gender (S: coefficient 1.40, OR 4.06, $p < 0.001$; HS: coefficient 0.85, OR 2.34, $p < 0.001$), BMI (S: coefficient 0.038, OR 1.04, p 0.039; HS: coefficient 0.076, OR 1.08, $p < 0.001$), and AHI (S: coefficient 0.067, OR 1.07, $p < 0.001$; HS: coefficient 0.026, OR 1.03, $p < 0.001$). Loud snoring had a significant relationship with age (coefficient − 0.0095, OR 0.99, p 0.041), male gender (coefficient 0.76, OR 2.14, $p < 0.001$), BMI (coefficient 0.031, OR 1.03, p 0.015), and AHI (coefficient 0.025, OR 1.03, $p < 0.001$). Apnea also showed a significant association with age (coefficient − 0.015, OR 0.98, p 0.004), male gender (coefficient 0.89, OR 2.44, $p < 0.001$), and AHI (coefficient 0.035, OR 1.03, $p < 0.001$).

Nonspecific OSA symptoms

Tiredness showed a marked relationship with age (coefficient − 0.014, OR 0.98, p 0.02), female gender (coefficient − 0.55, OR 0.57, p 0.001), insomnia (coefficient 0.83, OR 2.29,

Table 3 Polysomnography

	All	Non OSA (G1)	OSA (AHI ≥ 5)		
			Female (G2)	Male (G3)	*p**
– TRT (total recording time, min)	396.5 (380–421.2)	396.5 (377.8–420)	394.2 (368–418.7)	400 (390.2–421.3)	< 0.01
– TST (total sleep time, min)	333 (298.7–361.8)	320.3 (284.3–348)	321.1 (291.3–352)	346.1 (309.9–368)	< 0.001
– SE (sleep efficiency)	84.6 (77.2–89.7)	81.3 (72.8–86.6)	84.2 (76.2–89)	86.4 (80.1–91.1)	< 0.01
– TNREM (min)	277.3 (248–301.5)	270.2 (236–291.2)	272.9 (243–299)	284.5 (257.4–306.8)	< 0.01
– TREM (min)	50.7 (34–69.3)	48 (30.7–66.7)	48 (30.4–67.6)	54 (38.2–71.2)	< 0.01
– AHI (apnea/hypopnea index)	13 (4–29)	1.45 (0–3)	13.9 (9–23.7)	26.8 (15.5–42)	< 0.001
– T90 (%)	1.15 (0.1–8.5)	0 (0–0.2)	2.1 (0.3–14.3)	3.9 (0.8–15.7)	0.01
– SO_2 mean (%)	93.3 (91.9–95)	95 (93.6–96)	92.9 (91.3–94.4)	92.8 (91.5–94.3)	0.47
Severity of OSA (%)					
– AHI ≥ 5–< 15	272 (34.5)		157 (51.6)	115 (23.8)	< 0.001
– AHI ≥ 15–< 30	248 (31.5)		97 (32)	151 (31.2)	0.9
– AHI ≥ 30	268 (34)		50 (16.4)	218 (45)	< 0.001

Data are presented as median (25–75% percentiles), or *n* (%)

TNREM total stages N1 + N2 + N3; *TREM* total amount of REM sleep

*Differences between G2 and G3

$p < 0.001$), restless leg syndrome (coefficient 0.59, OR 1.80, p 0.001), and ESS (coefficient 0.77 OR 2.16, $p < 0.001$).

Excessive diurnal somnolence was associated with age (coefficient − 0.0012, OR 0.99, p 0.019), BMI (coefficient 0.033, OR 1.03, p 0.022), AHI (coefficient 0.017, OR 1.02, $p < 0.001$), mean SO_2 (coefficient 0.13, OR 1.14, p 0.007), insomnia (coefficient − 0.42, OR 0.66, p 0.012), and tiredness (coefficient 0.77, OR 2.16, p 0.001).

Sleep onset insomnia was significantly related with age (coefficient − 0.015, OR 0.98, p 0.017), female gender (coefficient − 0.53, OR 0.59, p 0.0035), use of sedatives or antidepressants (coefficient 0.47, OR 1.60, p 0.006), frequent awakenings (coefficient 0.99, OR 2.70, $p < 0.001$), sleeping movements (coefficient 0.99, 2.69, $p < 0.001$), restless leg syndrome (coefficient 0.47, OR 1.60, p 0.01), tiredness (coefficient 0.58, OR 1.77, p 0.001), and ESS (coefficient − 0.66, OR 0.52, p 0.001).

Maintenance insomnia showed a meaningful relationship with AHI (coefficient − 0.021, OR 0.95, p 0.003), use of sedatives or antidepressants (coefficient 0.72, OR 2.06, p 0.001), frequent awakenings (coefficient 2.25, OR 9.5, $p < 0.001$), and tiredness (coefficient 0.70, OR 2.02, p 0.001).

Subjective cognitive complaints correlated with AHI (coefficient − 0.012, OR 0.99, p 0.026), T90 (coefficient 0.018, OR 1.02, p 0.004), insomnia (coefficient 0.47, OR 1.60, p 0.004), sleeping movements (coefficient 0.35, OR 1.42, p 0.02), frequent awakenings (coefficient 0.36, OR 1.44, p 0.02), tiredness (coefficient 0.48, OR 1.62, $p < 0.001$), ESS (coefficient 0.78, OR 2.17, $p < 0.001$), consumption of sedatives or antidepressants (coefficient 0.49, OR 1.64, p 0.002), and comorbidities (coefficient 0.44, OR 1.55, p 0.045).

Nocturia presented a marked association with age (coefficient 0.040, OR 1.04, $p < 0.001$), BMI (coefficient 0.039, OR 1.04, p 0.001), mean SO_2 (coefficient − 0.11, OR 0.89, p 0.001), insomnia (coefficient − 0.43, OR 0.65, p 0.02), frequent awakenings (coefficient 1.92, OR 6.8, $p < 0.001$), and sleeping movements (coefficient 1.19, OR 3.28, $p < 0.001$).

Morning headaches were associated with age (coefficient − 0.021, OR 0.98, p 0.005), gender (coefficient − 1.15, OR 0.32, $p < 0.001$), ESS (coefficient 0.75, OR 2.11, p 0.001), insomnia (coefficient 0.83, OR 2.28, p 0.001), and restless leg syndrome (coefficient 0.93, OR 2.52, $p < 0.001$). Figures 2 and 3 show the influence of gender on the symptoms associated with OSA.

Discussion

In our population that included patients without OSA to avoid leaving out of the analysis patients who could potentially have had airway resistance syndrome (AHI < 5 plus sleepiness), we observed that gender was an independent, explanatory variable of several specific and nonspecific OSA-related symptoms. After adjusting for age, BMI, and AHI, women were less likely to report snoring, habitual or loud snoring, and apneas than males. After controlling for multiple variables, female gender was an independent predictive factor of tiredness, sleep onset insomnia, and morning headaches. On the other hand, the report of excessive daytime sleepiness, nocturia, maintenance insomnia, and subjective cognitive complaints did not show a significant association with gender.

Table 4 Symptoms gender differences in obstructive sleep apnea

	All	Non OSA	OSA		*p**
Nocturnal symptoms			Female	Male	
Snoring					
– Yes	922 (85.1)	203 (68.6)	248 (81.6)	471 (97.3)	< 0.001
– No	162 (14.9)	93 ((31.4)	56 (18.4)	13 (2.7)	< 0.001
Loud snoring	580 (53.5)	104 (35.1)	140 (46.1)	336 (69.4)	< 0.001
Habitual snoring	709 (65.4)	131 (44.3)	187 (61.5)	391 (80.8)	< 0.001
Apnea	359 (33.1)	37 (12.5)	77 (25.3)	245 (50.6)	< 0.001
Sleep onset insomnia (1)	262 (24.2)	89 (30.1)	94 (30.9)	79 (16.3)	< 0.001
Maintenance insomnia (2)	264 (24.4)	104 (35.1)	76 (25)	84 (17.4)	< 0.01
Insomnia (1 or 2)	372 (34.3)	133 (44.9)	120 (39.5)	119 (24.6)	< 0.001
Frequent awakenings	393 (36.3)	132 (44.6)	107 (35.2)	154 (31.8)	0.32
Nocturia	312 (28.8)	69 (23.3)	100 (32.9)	143 (29.5)	0.31
Diaphoresis	191 (17.6)	45 (15.2)	58 (19.1)	88 (18.2)	0.75
Sleeping movements	469 (43.3)	138 (46.6)	134 (44.1)	197 (40.7)	0.35
Nightmares	121 (11.2)	52 (17.6)	30 (9.9)	39 (8.1)	0.39
Diurnal symptoms					
Tiredness	544 (50.2)	150 (50.7)	177 (58.2)	217 (44.8)	< 0.01
Excessive daytime somnolence (Epworth > 10)	402 (37.1)	101 (34.1)	97 (31.9)	204 (42.1)	< 0.01
Morning headache	111 (10.2)	40 (13.5)	47 (15.5)	24 (5)	< 0.001
Concentration problems	512 (47.2)	150 (50.7)	172 (56.6)	190 (39.3)	< 0.001
Memory loss	574 (53)	171 (57.8)	187 (61.5)	216 (44.6)	< 0.001
Attention deficit	536 (49.4)	158 (53.4)	176 (57.9)	202 (41.7)	< 0.001
Subjective cognitive complaints (1, 2, and 3)	411 (37.9)	122 (41.2)	138 (45.4)	151 (31.2)	< 0.001

*Chi-square test

Our observations are supported by early publications. It has been reported that male gender constitutes an independent risk factor for typical symptoms of OSA, such as habitual or loud snoring [10, 22] and witnessed apnea [4, 6, 9, 10], after adjusting for covariables such as age, BMI, alcohol consumption or sedatives, cigarette smoking, and/or AHI. Several potential explanations may account for these findings. We speculated that during the development of the obstructive respiratory event, males could develop a higher intrathoracic negative pressure than females. Thus, the higher forces applied to the vibratory structures of the upper airway could cause more intense and perceptible respiratory sounds. In line with this theory, Itasaka [23] and Stoohs [24] observed that, in subjects with OSA, the intensity of snoring showed a strong positive correlation with inspiratory effort evaluated by esophageal pressure. It has also been described that men had significantly more and longer apneas than their female counterparts [25]. Therefore, women could perceive more easily the breathing pauses than males and so report it to their bedpartner. Third, women may consider their own snoring "unladylike" and therefore be less likely to mention it [2]. In addition, women are more likely to attend clinical appointments on their own, whereas men often do so with their partner [14]. Consequently, information from a partner on snoring and witnessed apneas may be less readily available for women. Finally, the definitions used for habitual or loud snoring are not uniform in published studies and this could add another source of variation in symptom reporting.

Most publications from clinical or community populations have found that women with OSA complain more of tiredness or fatigue than their male counterparts, independently of other confounders [7, 8, 13]. Several hypotheses may be raised to try to explain this observation. Prior studies have indicated that women are frequently more likely to report physical symptoms [26–28]. Also, cultural differences may make men less willing than women to admit that they have any of the problems we asked about, or there may be a real gender-based neurophysiologic bias in the way daytime effects of disturbed sleep are perceived. An unexpected finding was the lack of association between tiredness and OSA severity indicators such as AHI, and various measurements of oxygen desaturation. Nevertheless, other investigators have published similar findings [8, 39–42]. The absence of association between OSA and fatigue suggests that this subjective complaint may be produced by other factors. However, the fact that the sensation of tiredness or fatigue is relieved in some patients

Table 5 Stepwise multiple logistic analysis

DV: dependent variable IV: independent variables	Variables included in the model	Coefficient	OR	95% CI	*p*
DV: Snoring. IV: age, gender, BMI, AHI	Gender	1.40	4.06	2.59–6.35	< 0.001
	BMI	0.038	1.04	1.01–1.08	0.039
	AHI	0.067	1.07	1.05–1.09	< 0.001
DV: Habitual snoring. IV: age, gender, BMI, AHI	Gender	0.85	2.34	1.76–3.1	< 0.001
	BMI	0.076	1.08	1.05–1.11	< 0.001
	AHI	0.026	1.03	1.02–1.04	< 0.001
DV: Loud snoring. IV: age, gender, BMI, AHI	Age	− 0.0095	0.99	0.98–0.99	0.041
	Gender	0.76	2.14	1.63–2.8	< 0.001
	BMI	0.031	1.03	1.01–1.06	0.015
	AHI	0.025	1.03	1.02–1.034	< 0.001
DV: Apnea. IV: age, gender, BMI, AHI	Age	− 0.015	0.98	0.97–0.99	0.004
	Gender	0.89	2.44	1.8–3.3	< 0.001
	AHI	0.035	1.03	1.03–1.045	< 0.001
DV: Tiredness. IV: age, gender, BMI, AHI, mean SO_2, T90, min. SO_2, EDS, comorbidities, sedative/antidepressant, insomnia, restless leg syndrome, frequent awakenings, sleeping movements	Age	− 0.014	0.99	0.97–0.99	0.02
	Gender	− 0.55	0.57	0.44–0.75	0.001
	Insomnia	0.83	2.29	1.74–3.03	< 0.001
	Restless leg syndrome	0.59	1.80	1.30–2.50	0.001
	EDS	0.77	2.16	1.65–2.82	< 0.001
DV: EDS. IV: age, gender, BMI, AHI, mean SO_2, T90, min. SO_2, comorbidities, tiredness, sedative/antidepressant, insomnia, restless leg syndrome, frequent awakenings, sleeping movements	Age	− 0.012	0.99	0.98–0.99	0.019
	BMI	0.033	1.03	1.01–1.06	0.022
	AHI	0.017	1.02	1.01–1.03	< 0.001
	Mean SO_2	0.13	1.14	1.04–1.26	0.007
	Insomnia	− 0.42	0.66	0.48–0.91	0.012
	Tiredness	0.77	2.16	1.64–2.84	0.001
DV: Sleep onset insomnia. IV: age, gender, BMI, AHI, mean SO_2, T90, min. SO_2, comorbidities, sedative/antidepressant, restless leg syndrome, frequent awakenings, sleeping movements, tiredness, EDS	Age	− 0.015	0.98	0.97–0.99	0.017
	Gender	− 0.53	0.59	0.41–0.84	0.0035
	Sedative/antidepressant	0.47	1.60	1.15–2.24	0.006
	Frequent awakenings	0.99	2.70	1.94–3.76	< 0.001
	Sleeping movements	0.99	2.69	1.93–3.77	< 0.001
	Restless leg syndrome	0.47	1.60	1.12–2.30	0.01
	Tiredness	0.58	1.77	1.27–2.47	0.001
	EDS	− 0.66	0.52	0.36–0.74	0.001
DV: Maintenance insomnia. IV: age, gender, BMI, AHI, mean SO_2, T90, min. SO_2, comorbidities, sedative/antidepressant, restless leg syndrome, frequent awakenings, sleeping movements, tiredness, EDS	AHI	− 0.021	0.95	0.96–0.99	0.003
	Sedatives/antidepressant	0.72	2.06	1.43–2.94	0.001
	Frequent awakenings	2.25	9.5	6.6–13.8	< 0.001
	Tiredness	0.70	2.02	1.41–2.90	0.001
DV: Subjective cognitive complaints. IV: age, gender, BMI, AHI, mean SO_2, T90, min. SO_2, comorbidities, EDS, tiredness, sedative/antidepressant, insomnia, restless leg syndrome, frequent awakenings, sleeping movements	AHI	− 0.012	0.99	0.97–0.99	0.026
	T90	0.018	1.02	1.01–1.03	0.004
	Insomnia	0.47	1.60	1.16–2.20	0.004
	Sleeping movements	0.35	1.42	1.06–1.90	0.02
	Frequent awakenings	0.36	1.44	1.06–1.96	0.02
	Tiredness	0.48	1.62	1.22–2.15	< 0.001
	EDS	0.78	2.17	1.62–2.90	< 0.001
	Sedatives/antidepressant	0.49	1.64	1.21–2.22	0.002
	Comorbidities	0.44	1.55	1.01–2.36	0.045
DV: Nocturia. IV: age, gender, BMI, AHI, mean SO_2, T90, min. SO_2, comorbidities,	Age	0.040	1.04	1.03–1.05	< 0.001
	BMI	0.039	1.04	1.01–1.07	0.001
	Mean SO_2	− 0.11	0.89	0.83–0.95	0.001

Table 5 (continued)

DV: dependent variable IV: independent variables	Variables included in the model	Coefficient	OR	95% CI	*p*
insomnia, frequent awakenings, sleeping movements	Insomnia	− 0.43	0.65	0.45–0.93	0.02
	Frequent awakenings	1.92	6.8	4.7–9.7	< 0.001
	Sleeping movements	1.19	3.28	2.35–4.57	< 0.001
DV: Morning headache. IV: age, gender, BMI, AHI, mean SO_2, T90, min. SO_2, comorbidities, sedative/antidepressant, insomnia, EDS, tiredness, restless leg syndrome	Age	− 0.021	0.98	0.96–0.99	0.005
	Gender	− 1.15	0.32	0.20–0.50	< 0.001
	EDS	0.75	2.11	1.38–3.23	0.001
	Insomnia	0.83	2.28	1.49–3.50	0.001
	Restless leg syndrome	0.93	2.52	1.62–3.92	< 0.001

EDS excessive daytime somnolence

who use CPAP adequately is a strong argument for a causal relationship between sleep apnea and this symptomatology [43, 44].

There is contradictory information in the literature regarding the influence of gender on the report of excessive daytime sleepiness (EDS) in subjects with OSA. Although men more frequently had sleepiness than women (see Table 4), in the multiple regression model, the gender was not a predictor of EDS. This finding was maintained even when the cut-off point to define EDS was changed to greater than 9 or 11 (data not shown). In line with our finding, some authors [4, 6] have observed, in models fitted by confounders, that the complaint of excessive daytime sleepiness was not related to gender. A similar finding was reported in a community population study [29]. However, other studies have reported that both women [8] and men [7] with OSA are more likely to report sleepiness. These discrepancies could be related to the way EDS was defined, differences in the variables included in the predictive models of EDS or study population characteristics. Baldwin et al. [7] considered sleepiness as either "feeling frequently or almost always sleepiness during the day" or an ESS greater than 10. While an ESS greater than 10 was related with male gender (adjusted OR = 0.77; CI, 0.66–0.90 for women), the statement "feeling frequently or almost always sleepiness during the day" was not significantly associated with gender (adjusted OR = 1.06; CI, 0.86–1.32). On the other hand, the study by Chervin et al. [8] did not include BMI as a predictor of EDS in the multiple regression analysis and it was described as an independent predictor of EDS [29].

It has been reported that female gender is an independent predictor of insomnia in general and clinical population after adjusting for numerous confounding variables [4, 6, 7, 15]. However, little attention has been paid to the relationship between subtype of insomnia and gender. We found that sleep onset insomnia, but not maintenance insomnia, was independently associated with female gender. This finding could indicate that OSA would not be a cause of initial insomnia. Given that OSA is a disorder that occurs after sleep onset, it would seem more likely that sleep maintenance insomnia would be causally connected with OSA. Indeed, Chung

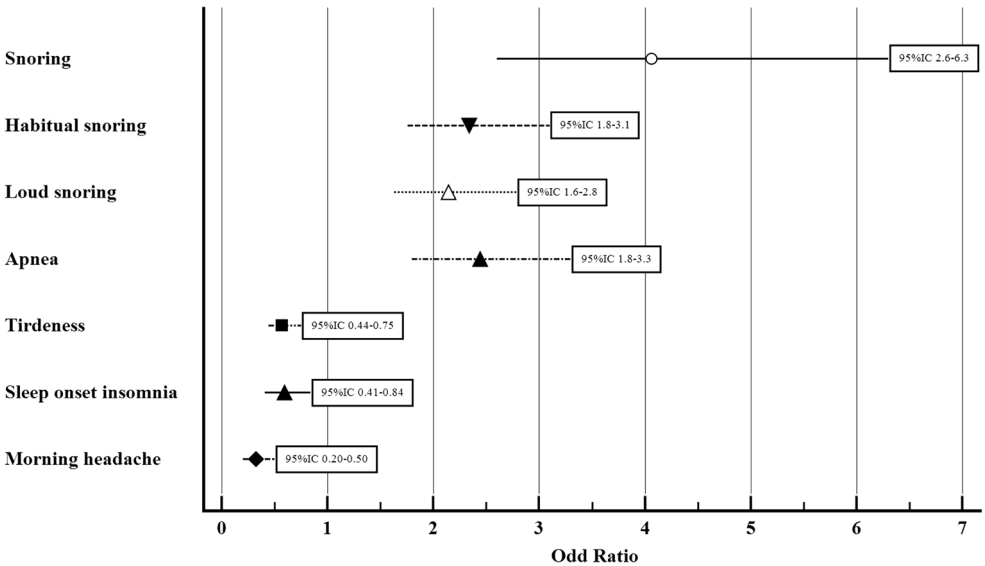

Fig. 2 Forest plot showing the probability of reporting OSA symptoms according to gender. Men had more chance of manifesting snoring, habitual snoring, loud snoring, and apnea than women, and less likelihood of referring tiredness, sleep onset insomnia, and morning headache

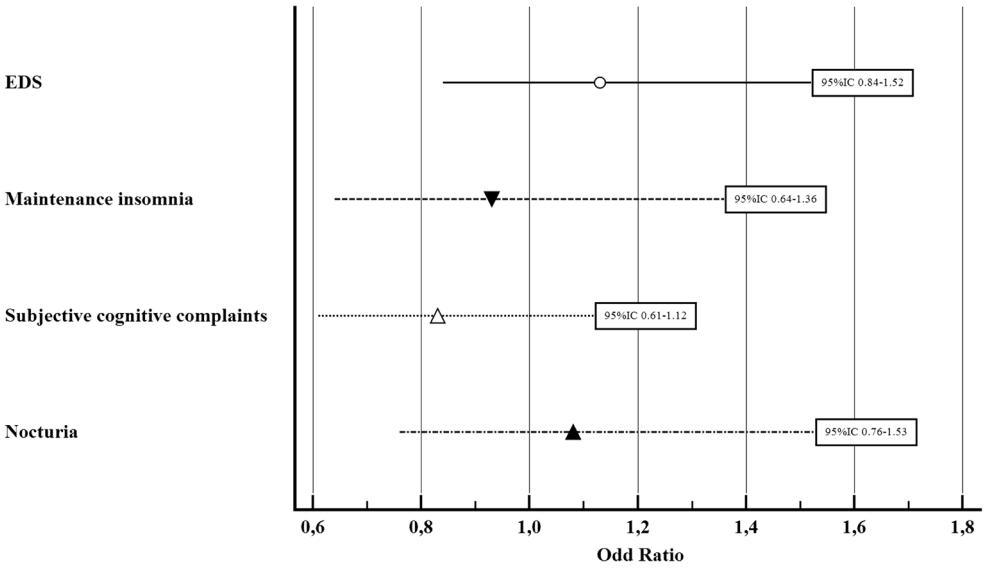

Fig. 3 Forest plot showing the lack of association between EDS (excessive daytime sleepiness), maintenance insomnia, subjective cognitive complaints, and nocturia with gender

et al. [30] showed that the most common insomnia complaint was frequent awakenings during the night and the least common complaint was difficulty falling asleep. Also, after 2 years of CPAP treatment, OSA patients often improve midnight insomnia but not early or late insomnia [31]. Thus, it has been hypothesized that sleep maintenance insomnia has causal links with OSA, but sleep onset insomnia might be an independent co-occurring sleep disorder [30]. However, in a community-based study [7], different subtypes of insomnia were associated with female gender after controlling for multiple variables including the AHI.

We did not find a relationship between subjective cognitive complaints and gender. Our results are consistent with a paper that assessed the relation between habitual snoring, sleep apnea, and cognitive complaints (concentration and memory problems) in an adult population-based sample [32]. After adjusting for potential confounders such as gender, both concentration and/or memory problems were related to depression, insomnia, unintended sleepiness, habitual snoring, and sleep apnea. Similarly, in a large cohort of adults, the relationship between objective neurocognitive tests and severity of OSA did not show any gender influence on cognitive performance [33].

We did not observe any association between gender and nocturia reports. This is in line with a recent systematic review of factors associated with nocturia in community-based cohorts [34]. Also, the Sleep Health Heart Study evaluated the association between nocturia, cardiovascular morbidity, and OSA and no relationship between nocturia and gender was found after adjusting for several covariates [35].

Female gender constituted a risk factor for morning headaches. In addition, we observed no association between the report of morning headaches and the severity of OSA measured through AHI and other indicators of oxygen desaturation. Such findings are in agreement with previous studies [36, 37]. We speculate that these observations may reflect the fact that migraine and tension headaches are more prevalent conditions in women than in men [38].

Clinical importance and limitation

The fact that obstructive sleep apnea has different clinical presentations in women and men may have important clinical implications. First, reliance on snoring or self-reported apnea may result in more men being referred for sleep study than women. Second, the fact that women present more nonspecific symptoms, such as tiredness or insomnia, could make physicians turn to other diagnostic possibilities like anxiety or depression, rather than OSA. Finally, understanding gender differences will contribute to the better clinical recognition of OSA in women as well as the provision of proper health care and therapeutic practice.

The present study presents limitations due to its retrospective design, selection bias, and the fact that the study site was a tertiary care center with its inherent referral bias and limited generalizability.

In summary, after adjusting for numerous covariables, we found that women with OSA were more likely to report tiredness, sleep onset insomnia, and morning headaches, and less likely to complain of typical OSA symptoms (snoring, apneas) compared to men. We did not observe any gender influence in the self-report of daytime sleepiness, subjective neurocognitive complaints, maintenance insomnia, or nocturia.

Further studies describing the clinical manifestations of different severity levels of OSA in men and women will substantially contribute to its identification and treatment in women across a wide disease spectrum.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of our institutional committee and with the 1964 Helsinki declaration and its later amendments.

Informed consent Informed consent was obtained from all individual participants included in the study.

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