



Gender differences in obstructive sleep apnea syndrome: a clinical study of 1166 patients

Esther Quintana-Gallego^{a,*}, Carmen Carmona-Bernal^a, Francisco Capote^a,
 Ángeles Sánchez-Armengol^a, Georgina Botebol-Benhamou^b, Juan Polo-Padillo^c, José Castillo-Gómez^a

^aDepartment of Pneumology, Virgen del Rocío University Hospital, Seville, Spain

^bDepartment of Clinical Neurophysiology, Virgen del Rocío University Hospital, Seville, Spain

^cDepartment of Statistic, Seville University, Seville, Spain

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Summary The objective of this study was to compare the frequency of some sociocultural, clinical, and anthropometric data between men and women in a sample of 1745 patients referred to a Sleep Unit for symptoms of obstructive sleep apnea (OSA). A standardized questionnaire was administered and anthropometric data were measured. Patients underwent a polysomnography (during a night or a nap) or an overnight home cardiorespiratory polygraphy. A total of 1166 patients (male/female ratio 4.9:1) fulfilled criteria of OSA (apnea–hypopnea index ≥ 10). Women were employed, habitual drivers or workers at risk occupations in a lower percentage than men. Women came to the clinical interview accompanied by their partner less frequently than men. The frequency of snoring and daytime hypersomnolence was similar in both genders, although witnessed apneas were more frequent in males. Fatigue, morning headaches, insomnia, depression and use of sedatives were more frequent in women than in men. Women were older than men, more obese (although with an obesity pattern less centrally distributed), and referred hypertension more frequently. It is concluded that it is likely that women with OSA may be underdiagnosed due to circumstances related to the family lifestyle and sociocultural factors in addition to different OSA clinical expression.

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Introduction

Obstructive sleep apnea syndrome (OSA) is a serious public health burden because it has adverse physical, psychological, and socioeconomic consequences. Different studies have shown that people with this condition have an increased risk for traffic accidents,^{1,2} hypertension,^{3,4} cardiovascular mor-

bidity,⁵ and impaired health-related quality of life.⁶

It is estimated that the prevalence of OSA in the overall population is 1–6%.^{7,8} Sleep-disordered breathing has been assumed to be a condition associated predominantly with men.⁹ Community-based studies have shown that the male to female ratio for OSA is in the range of 2:1 or 3:1.¹⁰ In the epidemiological study of Young et al.,¹¹ it was estimated that 2% of adult women and 4% of adult men fulfilled diagnostic criteria of OSA, i.e., apnea–hypopnea index (AHI) ≥ 5 and daytime hypersomnolence. The possible mechanisms

*Corresponding author. C/Triana n 11, 2-4, Tomares, Seville 41940, Spain. Tel.: +34-95-5012191, fax: +34-95-5012199.

Email-address: mqg01se@saludalia.com (E. Quintana-Gallego).

underlying the differences in the prevalence of OSA in men and women are not fully understood. Sex differences in the structure and physiological behaviour of the upper airway, in craniofacial morphology, and in the pattern of fat deposition have been proposed to account for a higher male risk of OSA.^{12,13} On the other hand, differences in sex-specific OSA prevalence by age suggest that sex hormones play an important role in the natural history of OSA. Gender differences in the prevalence of sleep-disordered breathing in the pediatric and adolescent age groups have not been observed^{14,15} compared to an increase in the male/female ratio in the middle age group. Menopause is a risk factor for sleep-disordered breathing,¹⁶ and the prevalence of OSA in the elderly is similar in men and women.¹⁷ Finally, the influence of other risk factors like alcohol consumption, and smoking has been associated with a higher prevalence of OSA in men.¹⁸

However, the male predominance reported for OSA in epidemiological studies is more marked in the clinical setting, with estimates of the male/female ratio as high as 8–10:1.^{19,20} This suggests that there is a clinical under-recognition of OSA in females which could be due to differences in sociocultural factors and/or clinical expression of OSA between males and females, although this hypothesis has not been well studied. This study was therefore performed to compare the frequency of some sociocultural, clinical, and anthropometric parameters between men and women in a sample of patients with suggestive symptoms of OSA referred to a Sleep Unit.

Patients and methods

A total of 1745 patients with symptoms suggestive of OSA who were consecutively referred during 30 months to our Sleep Unit were retrospectively evaluated. This Sleep Clinic belongs to an acute care teaching hospital in Seville, Spain, with a referral area's size of 750,000 subjects. The study included the administration of a standardized questionnaire, a complete physical examination, and a sleep study.

The questionnaire was divided into four sections: (1) demographics; (2) personal history, including job situation (employed, unemployed, retired), risk occupations (when to fall asleep put one's or others' life at risk), habitual driving, obesity, cardiovascular disease (hypertension, ischemic heart disease and/or cerebrovascular events), alcohol consumption, cigarette smoking, and the

use of some medications (such as sedatives, muscular relaxants, antidepressant drugs); and (3) nocturnal and daytime symptoms suggestive of OSA as well as non-specific symptoms. The fact that the patient was accompanied by his/her partner was also recorded. Nocturnal symptoms included snoring (categorized as absent, sometimes, usually, and unknown), breathing pauses during sleep (absent, sometimes, usually, and unknown), awakenings, and other symptoms that may occur during sleep, such as nicturia and insomnia. Daytime symptoms included daytime hypersomnolence (categorized as absent, mild, moderate, severe), morning fatigue, morning headache, and depression. The patient's subjective assessment of hypersomnolence was graded according to the scale of Epworth. (4) Anthropometric measurements included weight, height, neck circumference (in the standing position at the level of the cricothyroid membrane), waist circumference (at the midpoint between the anterior superior iliac spine and the lower costal arch), hip circumference (at the level of the greater trochanters). The body mass index (BMI), defined as the weight in kilograms divided by the square of the height in meters, and waist-to-hip ratio were calculated. Subjects with a BMI equal or greater than 30 kg/m² were considered obese.

Patients underwent an overnight polysomnography, a nap polysomnography, or an overnight home polygraphy. These sleep studies were selected according to geographical criteria, that is, whether or not sleep studies at home were feasible because of the patient's place of residence, and in case of the daytime polysomnography, when the patient was considered that he/she was able to take a nap for at least 3 h.

The polysomnography consisted of continuous polygraphic recordings using standardized equipment (Somnostar 4100, Sormedics) with surface leads for electroencephalography (C3/A2, C4/A1, O1/A1 and O2/A1 placements), electrooculography, submental electromyography, and electrocardiography. Non-invasive sensors were used for nasal and oral airflow (thermistor), chest and abdominal respiratory movements (thoracic and abdominal belts), and oxyhemoglobin saturation (finger pulse oximetry). An abnormal breathing event was defined as a complete cessation of airflow for ≥ 10 s (apnea) or a $\geq 50\%$ reduction in respiratory airflow accompanied by a decrease of $\geq 4\%$ in oxyhemoglobin saturation (SaO₂) and/or an electroencephalographic arousal (hypopnea). Oxygen desaturation was defined as a drop $\geq 4\%$ in SaO₂ compared to baseline. An arousal was defined according to the American Sleep Disorders Associa-

tion.²¹ The total number of scored apneas and hypopneas divided by the number of hours of sleep (AHI) was determined for each participant.

The overnight home polygraphy was performed using a portable ambulatory device (Apnoescreen I, Erich Jaeger GmbH & CoKg, Wuerzburg, Germany) that monitored the oronasal airflow (thermistor), SaO₂ and heart rate (digital pulse oximeter), body position (mercury sensor), and actigraphy (wristband with activity sensor). Analysis was carried out manually. Apnea was defined as a complete cessation of airflow for ≥ 10 s, hypopnea as $\geq 50\%$ reduction in respiratory airflow accompanied by a decrease of $\geq 4\%$ in SaO₂, and oxygen desaturation was defined as a drop $\geq 4\%$ in SaO₂ compared to baseline. The respiratory disturbance index (RDI) was defined as the number of respiratory events (apneas and hypopneas) per hour of recording.

The diagnosis of OSA was established in patients with AHI ≥ 10 in the overnight or nap polysomnography and in patients with RDI ≥ 10 in the overnight home polygraphy.

Statistical analysis

Patients were divided into two groups according to sex and differences between them were statistically analyzed for each of the symptoms and measurements described above. Statistical analyses and calculations were performed using the Statistical Package for the Social Sciences (SPSS) for Windows (version 10.0) (SPSS Inc., Chicago, IL, USA). All results are reported as mean \pm standard distribution (SD) or numbers and percentages. Comparison of quantitative variables were carried out by using the Student's *t*-test for independent samples and the chi-square (χ^2) test was used for the comparison of categorical variables. Statistical significance was set at $P < 0.05$.

Results

Of the 1745 patients with suggestive clinical symptoms of OSA included in the study, 1386 were

Table 1 Gender differences in 1166 patients with OSA.

Variable	Men, <i>n</i> = 970	Women, <i>n</i> = 196	<i>p</i> value
Age (years)	52.9 \pm 11	57.8 \pm 9.5	0.000
BMI (kg/m ²)	32.5 \pm 5	36.5 \pm 7	0.000
Neck circumference (cm)	43.7 \pm 3.3	39.4 \pm 3.3	0.000
Waist-to-hip ratio	0.99 \pm 0.06	0.89 \pm 0.05	0.000
Obesity	669 (69)	164 (83.9)	0.000
Personal history			
Be employed	566 (58.4)	53 (27.2)	0.000
Habitual driver	796 (82.1)	23 (11.7)	0.000
Risk occupations	90 (9.3)	2 (1)	0.000
Smoking	354 (36.5)	23 (11.7)	0.000
Alcohol consumption	512 (52.8)	26 (13.3)	0.000
Sedatives	167 (12.1)	55 (28.1)	0.000
Hypertension	427 (44.1)	136 (69.4)	0.000
Cerebrovascular accident	41 (4.2)	7 (3.6)	NS
Ischemic heart disease	175 (18)	41 (20.9)	NS
Accompanied by his/her partner	806 (83.1)	103 (52.6)	0.000
Clinical findings			
Snoring	938 (96.8)	188 (95.9)	NS
Breathing pauses	691 (72.1)	132 (67.3)	0.002
Awakenings	538 (55.5)	152 (77.6)	0.000
Daytime hypersomnolence	821 (84.6)	168 (85.7)	NS
Epworth scale, score	11.4 \pm 4.5	12 \pm 5.1	NS
Insomnia	145 (15)	57 (29.5)	0.000
Fatigue	563 (58.1)	149 (76)	0.000
Morning headache	293 (30.3)	125 (63.8)	0.000
Depression	123 (12.7)	70 (35.7)	0.000

Data are presented as n°. % or mean \pm SD.

men and 359 women. The percentage of males and females was similar in patients undergoing an overnight polysomnography (79.5% vs. 20.5%), a nap polysomnography (80.8% vs. 19.2%), and an overnight home polygraphy (78.8% vs. 21.2%). A total of 1166 patients fulfilled polysomnographic or polygraphic criteria of OSA. There were 970 men and 196 women (male/female ratio of 4.9:1). The diagnosis of OSA was established in 233 patients by an overnight polysomnography, in 342 by a nap polysomnography, and in 591 by an overnight home polygraphy. Characteristics of the study population are shown in Table 1.

A significantly higher percentage of men were employed and had risk occupations than women. Females drove less frequently than men. Moreover, toxic habits (smoking and alcohol consumption) were also significantly more common in men, although the use of sedatives and antidepressants was more common among women. A higher percentage of men (83.1%) than women (52.6%) were accompanied by their partner to the clinical interview ($p = 0.000$).

With regard to main OSA symptoms, the frequency of snoring and daytime somnolence was similar in men and women, but breathing pauses during sleep were more frequent in males than in females (72.1% vs. 67.3%, $p = 0.000$). On the other hand, awakenings, insomnia, morning fatigue, morning headache, and depression were significantly more common in females than in males.

Mean age in women was significantly higher than in men. Obesity was significantly more frequent among women, although men showed a more central body fat distribution than women in view of a greater neck circumference (43.7 ± 3.3 vs. 39.4 ± 3.3 cm, $p = 0.000$) and waist-to-hip ratio (0.99 ± 0.06 vs. 0.89 ± 0.05 , $p = 0.000$). Regarding cardiovascular morbidity, hypertension was significantly more frequent in women (69.4%) than in men (44.1%) ($p = 0.000$) (Table 1).

Discussion

Results of the present study show that the diagnosis of OSA in women is established more frequently than in early clinical series,^{20,22} although it continues to be made in a lower percentage than is expected according to epidemiological studies.^{11,16} This underdiagnosis may be due to some sociocultural factors in addition to different clinical expression of OSA among women.

In the first series reported in the literature and due to the limited number of women included, it

was considered that sleep-disordered breathing only occurred in postmenopausal women, with morbid obesity and hypercapnia, with a male/female ratio estimated of 8:1.^{22,23} The typical profile of a patient with OSA, which it is still to be considered at the present time, is an obese, middle-aged men with habitual snoring and daytime hypersomnolence.²⁴ However, in well-designed population-based epidemiological studies with larger samples, it was observed that the male/female ratio for sleep-disordered breathing was around 2:1, 3:1.^{7,11} The reasons for the lower diagnosis of OSA in women than in men are not fully understood. A possible reason for this discrepancy between clinical and epidemiological studies is that the clinical significance and the potential of morbidity for having a high AHI in the general population is lower in females. Another reason, however, is that sociocultural factors or differences in clinical expression of this disorder would result in less and later consultations of women, or alternatively their clinical picture could be less recognized by primary care physicians and therefore OSA may be underdiagnosed. The present results support the later hypothesis.

In our series, as in other clinical-based studies,^{25,26} the diagnostic yield of the sleep studies is higher in men (70%) than in women (50%). The reason for this lower diagnostic accuracy in women is unclear. A possible explanation is that a number of women with a RDI less than 10 could have an upper airway resistance syndrome.²⁷

Women included in this study were employed out of home in a much lower proportion than men, similarly that it occurs in Spanish population where 58% of males and 27% of females are employed.²⁸ In addition, there was a lower percentage of women being drivers and also working at risk occupations. For all these reasons, it is probable that the fact of being sleepy during the day may interfere more with work and social life in males, and daytime hypersomnolence may have less repercussions in daily activities in women.

In our series, a higher proportion of men than women smoked, with similar percentages that in our country (43% of males and 17.5% of females).²⁹ Regarding to alcohol consumption, probably reflecting in part that this habit is associated with OSA, the frequency of drinking in men and women is almost twice than in Spanish general population.²⁹ These risk factors may be associated with a higher prevalence of OSA in men. On the other hand, women came to the sleep unit accompanied by their partner in a lower proportion than men, which probably justifies that their nocturnal symptoms could be undetected more frequently than in

males. This finding may be related to the lower proportion of apneas observed among women in the present series.

With regard to OSA symptoms, the frequency of snoring and daytime hypersomnolence was similar in both genders. These data are consistent with some epidemiological studies, in which gender differences in respect to classic OSA symptoms for different AHI cutoff points were not observed.³⁰ However, other symptoms including morning headache and fatigue upon rising were more frequently experienced by women. In a small clinic-based study,³¹ it was also reported that for the same level of somnolence after controlling by age and AHI, daytime headache and asthenia were more frequently found in women. Chervin³² showed that women with OSA reported more "fatigue", "tiredness", and "lack of energy" than male patients. Moreover, we found that depression and insomnia were two other symptoms suffered from a greater proportion of women; in addition the proportion of women taking sedatives was greater. The higher percentages of women with these symptoms may be due to differences in personality between genders. Pillar and co-workers³³ reported higher indexes of depression and anxiety in women, for all age groups and AHI levels, without a clear association between these symptoms and OSA in the female group. Furthermore, the presentation of women with non-specific symptoms, in addition to the classic symptoms, could make physicians turn to other diagnostic possibilities.

The fact that women with OSA in our study were older, more obese, and had hypertension more frequently than men could be associated with that women fail to seek help for suggestive symptoms of OSA or medical care providers fail to respond to these symptoms. It has been shown that some chronic illnesses in women may have a more prolonged and severity course before diagnosis.³⁴ Some other reasons are also possible. Thus, the higher age at the time of diagnosis of OSA in females may be associated to the greater prevalence of sleep-disordered breathing after menopause.¹⁶ On the other hand, the fact that women were more obese may explain that in the female sex a higher BMI is needed to produce OSA because body fat distribution follows a gynecoid pattern in women. This hypothesis is supported by greater indexes of central obesity in men. Some investigations suggest that central distribution of body fat is even a higher risk factor for OSA than BMI.³⁵ The reason for a higher prevalence of hypertension in women observed in the present study is unknown, although the influence of obesity may be plausible. Some data suggest that in women with OSA, the risk

for cardiovascular complications and hypertension is similar than in men.^{3,5,36}

The present findings should be interpreted taking into consideration some limitations of the study, particularly the retrospective design and the use of different diagnostic sleep studies. Full overnight polysomnography is the reference diagnostic method, whereas daytime polysomnography and cardio-respiratory polygraphy are alternative diagnostic procedures.^{37,38} Results of different sleep studies are not interchangeable, so that a particular AHI value in conventional polysomnography is not exactly equivalent to the same AHI value in the other methods. For this reason, correlation studies between polygraphic data and some clinical and anthropometric variables could not be performed. However, the three sleep studies allowed to divide the sample dichotomically into two groups in order to compare the characteristics between men and women in the group that met criteria for OSA according to results of sleep studies. Moreover, the proportion of males and females in each diagnostic group was similar.

In summary, in a large group of patients with OSA, some sociocultural factors and the OSA clinical expression may account in part for gender differences in the prevalence of sleep-disordered breathing observed between the overall population and the clinical series. It is likely that women with OSA are underdiagnosed due to circumstances related to their role in the family and social lifestyle. The influence of a different clinical expression of OSA in women might also contribute to difficulties in initially suspecting this disorder. Further studies addressing gender differences in patients with OSA are needed. Primary care physicians should be aware of sleep apnea in women and the importance of referring women for sleep studies when they complain of symptoms associated with OSA, even if other non-specific symptoms are reported.

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