Differences between Men and Women in the Clinical Presentation of Patients Diagnosed with Obstructive Sleep Apnea Syndrome

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Study Objectives: Obstructive sleep apnea syndrome (OSAS) results from recurrent episodes of breathing cessation during sleep. Epidemiologic studies have shown that OSAS is more prevalent in men than women (4% vs 2%). Previous studies have explored gender-related differences in upper airway anatomy and function, hormone physiology, and polysomnographic findings. The aim of this study is to assess differences in clinical presentation between women and men with OSAS.

Design: Retrospective chart review analysis.

Setting: Tertiary university-based medical center

Participants: 130 randomly selected women with OSAS matched individually with 130 men with OSAS for age, body mass index, apnea-hypopnea index, and Epworth Sleepiness Scale score.

Interventions: N/A.

Measurements and Results: Data were obtained from questionnaires and in-laboratory polysomnographic studies. There were no differences between the genders for age (48.0 ± 1.1 years [mean ± SEM] for women vs 47.6 ± 1.0 years for men), body mass index (40.4 ± 0.7 kg/m² for women vs 40.0 ± 0.6 kg/m² for men), apnea-hypopnea index (36.8 ± 3.3/hour for women vs 36.0 ± 3.0/hour for men), or Epworth Sleepiness Scale score (12.45 ± 0.53 for women vs 12.84 ± 0.47 for men). Although snoring and sleepiness were similarly common in women and men, women more often described their main presenting symptoms as insomnia (odds ratio: 4.20; 95% confidence interval: 1.54-14.26) and were much more likely to have a history of depression (odds ratio: 4.60; 95% confidence interval: 1.71-15.49) and hypothyroid disease (odds ratio: 5.60; 95% confidence interval: 2.14-18.57). Women presented less often with a primary complaint of witnessed apnea (odds ratio: 0.66; 95% confidence interval: 0.38-1.12), consumed less caffeine per day (3.3 cups in women vs 5.2 cups in men; P = .0001), and admitted to less alcohol consumption (odds ratio: 0.36; 95% confidence interval: 0.18-0.70).

Conclusions: At the time of OSAS diagnosis, women with OSAS are more likely to be treated for depression, to have insomnia, and to have hypothyroidism than are men with the same degree of OSAS.

Key Words: Sleep apnea, gender differences, clinical presentation, signs and symptoms, depression, insomnia, hypothyroidism

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INTRODUCTION

OBSTRUCTIVE SLEEP APNEA SYNDROME (OSAS) IS A COMMON DISORDER AFFECTING BETWEEN 2% AND 4% OF THE MIDDLE-AGED ADULT POPULATION. Patients with this diagnosis have repetitive episodes of breathing cessation, followed by awakenings from sleep. It has been documented that OSAS is a significant risk factor in the development of other clinical diseases including hypertension,3,7 cardiac arrhythmias,6 myocardial infarction,4,6 stroke,4,7 decreased cognitive abilities, and excessive daytime somnolence and is associated with an increase in the frequency of motor vehicle accidents.

Although it is well documented that men have a higher incidence of sleep apnea than do women (4% vs 2%),9 little information is known about the differences between men and women upon first clinical presentation. This greater sleep-apnea prevalence in men has raised the concern that a selection bias for referral and identification of the diagnosis may favor men. The Wisconsin sleep cohort study estimated that sleep apnea was undiagnosed in more than 90% of women with moderate to severe sleep apnea.10 In addition, the study suggested that there was or might be a significantly higher 5-year mortality for women with sleep-disordered breathing than for women without the diagnosis. Several studies have tried to provide an explanation for the male predominance in the prevalence of sleep apnea, including differences in the anatomic size of the airway,9,12 greater collapsibility of the upper airway,11 greater increase in upper airway resistance in men,13 or hormonal changes in women.14,15 The disparity in clinical prevalence can possibly be explained by other factors, such as difference in clinical presentation of symptoms,16,17 different tolerance of symptoms, differing amount of usage of medical services, or bias by physicians expecting a higher male predominance. We hypothesized that even when sleep-apnea severity is similar in men and women with OSAS, the clinical presentation might be different, perhaps explaining why sleep apnea in women is apparently underdiagnosed. We thus compared the clinical presentation in 130 pairs of women and men with OSAS who were individually matched for age, body mass index (BMI), apnea-hypopnea index (AHI), and, as a measure of subjective sleepiness, scores on the Epworth sleepiness scale (ESS).18

METHODS

Study Design

The population analyzed for this study consisted of patients with OSAS (and upper airway resistance syndrome; UARS) diagnosed at the Sleep Disorders Centre, St. Boniface General Hospital in Winnipeg, Manitoba. All patients had undergone a
comprehensive overnight polysomnographic study, which included electroencephalogram, electrocologram, electromyogram (submental and anterior tibialis), electrocardiogram, nasal pressure and oronasal CO\(_2\) for airflow monitoring, continuous earlobe oxygen pulse oximetry, and respiratory inductance plethysmography. Sleep staging was done using standard criteria.\(^{19}\) Apnea was defined as cessation of airflow at the nose and mouth for a period of more than 10 seconds. Hypopnea was defined as a reduction in airflow of at least 50% for more than 10 seconds associated with a fall in oxygen saturation of at least 4%.

From a large clinical database, a computer program selected, at random, women with documented breathing disorders during sleep. Each female case was matched to a male case in the database for age, BMI, AHI, and ESS score. In order to obtain at least 100 sets of matched data for each clinical feature, 130 matched subjects were required. Thus, we generated a cohort of female and male cases matched for age, apnea severity, and subjective sleepiness.

Data for various clinical features commonly associated with sleep disorders were obtained from detailed clinical questionnaires submitted by the patient at the time of the initial referral, as well as from the initial assessment by one of the authors (MK). The questionnaires were standardized for the information collected. For each case, we determined the main presenting sleep complaints, sleep disorder symptoms, medical symptoms, and past medical history.

**Statistical Analysis**

Qualitative data from the matched subjects was analyzed by calculating odds ratio (OR) using the Newcombe method for comparison of proportions and 95% confidence intervals (CI) were calculated using Confidence Interval Analysis Software version 2.05.\(^{20}\) In addition, percentages of women or men found with each clinical characteristic were reported and rounded to the nearest percentage. For quantitative data, the mean ± SEM was calculated, and unpaired student \(t\) tests were performed for each study characteristic. Two-tailed \(p\) values of less than .05 were considered statistically significant.

**RESULTS**

**Matching of Gender Pairs**

Random cases of women and matched men were selected from our clinical database to ensure that at least 100 cases could be analyzed for each clinical feature. This was done to ensure sufficient statistical power. The least number of matched responses for each gender for a particular characteristic included 104 pairs, and the maximum number of matched pair responses was 130 pairs. The mean values for age (48.02 ± 1.06 years for women vs 47.58 ± 1.00 years for men; \(p = .14\)), BMI (40.41 ± 0.66 kg/m\(^2\)) for women vs 40.05 ± 0.62 kg/m\(^2\)) for men; \(p = .24\)), AHI (36.83 ± 3.29/hour for women vs 35.96 ± 3.00/hour for men; \(p = .11\)) and ESS score (12.45 ± 0.53 for women vs 12.84 ± 0.47 for men; \(p = .60\)) were nonsignificant, indicating a good population match (Table 1). In addition, no statistically significant difference between the groups was noted in the number of minutes spent below an oxygen saturation of 90% prior to treatment, although initial design for selection of the population match did not include this parameter. Thus, men and women had sleep apnea that was similar for apnea severity and subjective sleepiness and had similar degrees of extreme obesity, as classified by the National Institutes of Health.\(^{21}\)

**Clinical Presentation of Sleep Apnea in Women and Men**

**Main Presenting Complaints**

We determined the main reason for referral. Women and men were equally likely to have snoring, observed apnea, and daytime sleepiness as their main presenting complaints (Table 2a). However, women who had a diagnosis of OSAS or UARS more commonly described their main sleep problem as insomnia: 17% for women vs 5% for men; OR for women, 4.2 (95% CI, 1.54-14.26).

**Symptoms of Sleep Disorders**

The presence or absence of symptoms of sleep disorders was then determined. Women with OSAS were less likely to be aware of witnessed apnea (55% for women vs 70% for men; OR for women, 0.55 [95% CI, 0.31-0.97]). No significant difference between genders was found in prevalence of sleep-related symptoms, including excessive daytime sleepiness, restless leg symptoms, choking on awakening at night, dreaming on sleep onset, cataplexy, sleep paralysis, snoring, dreaming during naps, or number of naps (Table 2a).

**Medical Symptoms**

Analysis of medical symptoms revealed that women complained more of cardiac palpitations (39% for women vs 21% for men; OR for women, 2.47 [95% CI, 1.32-4.84]) and ankle edema (58% for women vs 35% for men; OR for women, 2.71 [95% CI, 1.52-5.03]) (Table 2a). No statistically significant differences were seen in symptoms of heartburn, choking on awakening, or headaches between the genders.

No statistically significant difference in the duration of symptoms of heart palpitations or ankle edema was found (Table 2b). In men, the snoring began, on average, at age 34 years; witnessed apnea at age 39; and daytime sleepiness at age 41. In women, snoring began at age 36 years, witnessed apnea at age 42, and sleepiness at age 43.

**Medical Diagnoses and Medication Usage in OSAS Patients**

Information about the patient’s medical history and medication usage was obtained from the patient, the submitted questionnaire, and a list of medications provided by the patient.

**Psychiatric Disorders**

Women with OSAS more commonly had a diagnosis of depression (21% for women vs 7% for men; OR for women, 4.60

<table>
<thead>
<tr>
<th>Table 1—Study Population Demographics*</th>
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<tbody>
<tr>
<td><strong>Women</strong></td>
</tr>
<tr>
<td>No.</td>
</tr>
<tr>
<td>Age, y</td>
</tr>
<tr>
<td>BMI, kg/m(^2)</td>
</tr>
<tr>
<td>AHI, No./h</td>
</tr>
<tr>
<td>ESS score</td>
</tr>
<tr>
<td>Percentage of sleep time</td>
</tr>
<tr>
<td>SaO(_2) &lt; 90%</td>
</tr>
</tbody>
</table>

*Data are expressed as mean (SEM) except as indicated. There were no differences between men and women for these variables. BMI refers to body mass index; AHI, apnea-hypopnea index; ESS, Epworth Sleepiness Scale.
Women more frequently had a previous diagnosis of hypothyroidism on presentation than men (22% for women vs 4% for men; OR for women, 5.60 [95% CI, 2.14-18.57]) and were much more likely to be taking thyroid replacement medication (20% for women vs 5% for men; OR for women, 4.33 [95% CI, 1.74-12.87]). Women also presented more often with a previous diagnosis of asthma or allergies (35% for women vs 22% for men; OR for women, 1.90 [95% CI, 1.06-3.50]) and were found to be taking significantly more asthma medications (17% for women vs 7% for men; OR for women, 2.63 [95% CI, 1.12-6.85]).

As was likely expected, women were more commonly taking sex hormone medications (16% for women vs 2% for men; OR for women, 10.50 [95% CI, 2.57-92.37]). No significant difference in the prevalence of reported diagnosis of cardiac diseases, hypertension, or diabetes mellitus was found between the sexes.

Social History of Patients with OSAS

Significantly more men admitted to regular alcohol consumption compared with women (29% for women vs 50% for men; OR for women, 0.36 [95% CI, 0.18-0.70]). Men consumed more caffeinated beverages per day (5.24 cups/day for men vs 3.26 cups/day for women; p < .001). However, no significant difference between the genders was found on examination of past or present smoking history (23% for women vs 25% for men) or pack years of cigarettes consumed (21.6 pack years in women vs 23.3 pack years in men). A positive history of sleep disorders in family members was also found to not differ significantly between the sexes (38% for women vs 25% for men).

DISCUSSION

OSAS has been considered to be predominantly a disease of obese middle-aged men, and it is generally accepted that the disorder is twice as common in men than women.2 A few studies have shown that women who have morbid obesity,22 hypercapnia,23,24 or are postmenopausal24 have a higher propensity to be diagnosed with sleep apnea. However, few studies have exam-
ined the differences in clinical presentation between the genders to ascertain if these differences could potentially explain whether an underrepresentation of OSAS exists in the female population and if so, why. In most previous studies, men and women with OSAS had differing apnea severity (women having a lower AHI) and differing weights (with women having a greater BMI). In this study, we controlled for severity of apnea, severity of subjective sleepiness, BMI, and age by matching individual female cases with male cases by these parameters. The average men and women were both extremely obese (obesity class III).21 This study reveals that there are several differences in clinical presentation between the genders in patients with OSAS when apnea severity, subjective sleepiness, BMI, and age are controlled.

Walker et al16 compared 686 consecutive patients (111 women and 575 men) with OSAS preoperatively, to determine gender-related symptoms, controlling for respiratory disturbance index (RDI), apnea index, hypopnea index, BMI, and age. Their male patients were younger, had significantly lower BMI, and higher respiratory disturbance index and apnea index before treatment when compared with women. Assessment of the type of presenting symptoms revealed that women reported more headaches on awakening (p = .001) and that men more often noted snoring on a nightly basis (p = .01), as well as observed apneic episodes (p = .001). Young et al22 similarly found that women presented with more “atypical symptoms,” (ie, morning headaches and depression), and this may divert the treating physician to concentrate on alternative diagnoses and ignore the possibility of sleep apnea in the differential diagnoses.

Previous studies comparing sex differences have matched populations for age, age and BMI, age and respiratory disturbance index, or age and AHI. Walker et al16 reported that women had higher BMI compared with men of similar age at presentation. Millman et al,23 on the other hand, compared women and men of similar age and BMI and discovered that men had more statistically severe apnea compared to women when matched for BMI and age (AHI, 51.5/hour for men vs 34.4/hour for women; p < .05). Ware et al24 compared women and men with OSAS matched for BMI, showing an increased AHI for men and concluded that women are more obese than men for a given BMI. Similarly, Walker et al16 concluded from their study that women could be more obese than men with the same severity of apnea. Examination of women and men with OSAS evaluated preoperatively, using multivariate modeling techniques to match patients for RDI, apnea index, hypopnea index, BMI, and initial symptoms revealed that there were no differences noted in number of symptoms based on gender.16 However, this study did show that certain clinical characteristics were more commonly reported in each sex, despite a similar diagnosis of OSAS. We determined in men and women with OSAS matched for apnea severity, subjective sleepiness, age, and BMI whether there were differences in gender-related presenting complaints, sleep symptoms, medical symptoms, and past medical history.

### Presenting Complaints

Snoring, observed apnea, and excessive daytime sleepiness are generally considered to be the most common presenting complaints in OSAS; they were indeed the most common in the men and women, and there was no difference in the prevalence of these as presenting symptoms. Insomnia, however, was much more likely to be a presenting complaint in women than in men. Insomnia is not considered a common symptom in OSAS, and it was not in men. Women, however, were much more likely to complain of insomnia than men. The retrospective study by Krakow et al25 showed that problematic insomnia symptoms were seen in about 50% of patients with a sleep-related breathing disorder. Those patients were more likely to have a psychiatric condition and to be treated with hypnotics or psychotropic medications. These authors reported no gender differences between the patients with and without insomnia. Ambrogetti et al26 examined 22 women with OSAS who were matched with men for age (±5 years) and respiratory disturbance index (<15/hour, 16-40/hour, 41-70/hour, and > 70/hour). All women who were referred to the sleep laboratory for evaluation of snoring underwent a sleep study to minimize any selection bias based on clinical presentation. A subgroup of the women from this study were found to have no complaints of apnea, choking, arousals, or restless sleep; had normal blood pressure; and complained only of morning headache (p = .04), fatigue (p < .01), and difficulty initiating sleep (p < .01). Similar to our findings, no difference in daytime sleepiness between sexes was noted, but women reported a 2-times increased frequency of difficulty initiating sleep (p < .01). In our study, about 1 in 5 of the women with OSAS had a presenting complaint of insomnia, compared to about 1 in 20 men. The reason for this is unclear.

Insomnia is known to be more common in women than in men, and insomnia is a feature often seen in depression (see below), which is also known to be more common in women. Insomnia in women may be associated with an increased prevalence of sleep apnea, and, therefore, the diagnosis of OSAS should be entertained in women who present with sleepiness and complaints of insomnia. However, insomnia and depression are linked and are common in women; therefore, it may be impossible to know whether the exaggerated differences in prevalence of these features that were observed in the study represent selection bias or a true difference in presentation between men and women.

### Sleep Symptoms

Although there was no difference in witnessed apnea as a main complaint between the genders, we found that women with OSAS were less likely than men to state that apnea had been witnessed in them. Ambrogetti et al28 also noted that women were less likely to be aware of witnessed apneic events. Similarly we found that women had a 0.55 OR for knowledge of witnessed apneas. An explanation for this finding may be that women who are bedpartners of men with breathing problems during sleep may be more sensitive to the disruptive behavior and may relate their observations more readily, whereas men either sleep despite

<table>
<thead>
<tr>
<th>Table 3—Medical Diagnoses Present in Women and Men Diagnosed with Obstructive Sleep Apnea Syndrome</th>
<th>Women, %</th>
<th>Men, %</th>
<th>Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypothyroidism</td>
<td>22</td>
<td>4</td>
<td>5.60 (2.14-18.57)*</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>17</td>
<td>9</td>
<td>1.91 (0.88-4.39)</td>
</tr>
<tr>
<td>Cardiac disease</td>
<td>12</td>
<td>15</td>
<td>0.77 (0.34-1.67)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>35</td>
<td>42</td>
<td>0.74 (0.41-1.31)</td>
</tr>
<tr>
<td>Asthma/allergies</td>
<td>35</td>
<td>22</td>
<td>1.90 (1.06-3.50)*</td>
</tr>
<tr>
<td>Depression</td>
<td>21</td>
<td>7</td>
<td>4.60 (1.71-15.49)*</td>
</tr>
</tbody>
</table>

*Statistically significant odds ratio using Newcombe's method for paired proportions, with values in parentheses indicating 95% confidence intervals. The odds ratio presented is the likelihood of a woman with obstructive sleep apnea syndrome (OSAS) versus a matched man having a diagnosis OSAS.
standing with results of the Smith et al study in which there was a significantly less prevalent (2:1 for men) in the community sample. Both genders in the laboratory group reported similar symptoms: snoring, gasping, snorting, and apneas; however, in the community sample, only men were more likely to report these symptoms. The authors felt that underreporting of symptoms possibly occurred, as these symptoms were felt to be “socially unacceptable.” Our studies did not show any significant differences in the genders in the parameters of snoring or choking.

Medical Symptoms

We found that the prevalence of ankle edema was high in both genders (58% for women, 35% for men), and women were more likely to have ankle edema than men. Because the patients were much heavier and had more severe sleep apnea (AHI) and severe nocturnal hypoxemia (percentage of sleep time with an SaO₂ < 90%) than typical OSAS patients, they might more frequently present with ankle edema. However, the reason for the sex difference in prevalence of ankle edema is not clear.

Medical Disorders

Extreme obesity is known to be associated with an extremely high risk of diabetes, cardiovascular disease, and hypertension, and, indeed, that is what was found in both our men and women with OSAS. There was no difference between men and women already having these diagnoses at the time OSAS was first diagnosed.

A statistically significant difference in medical diagnoses was seen when comparing the genders. Hypothyroidism was more commonly diagnosed in women with OSAS, and women more commonly used thyroid medications, compared to men. About 1 in 5 of our women with OSAS had been previously diagnosed with hypothyroidism. It is known that hypothyroidism may cause sleep apnea, but it is not clear whether hypothyroidism is more common in a cohort of sleep apnea cases than in a control population. Kapur et al. reported a group of 336 OSAS cases. The group reported that women under age 50 years with prior hypothyroidism had the highest relative risk (2.9) of OSAS, but the association was not statistically significant even for this subgroup (95% CI, 0.74-11.36). However, the number of women in that series was about half of the number in our series, and the severity of the apnea and the BMI of the women with OSAS was not reported, so it is difficult to compare their cases to ours.

Women in our study population were more often noted to be taking asthma medications (puffers), which appeared to be consistent with results of the Smith et al study in which there was a higher OR for women with chronic obstructive pulmonary diseases (2.8 for women vs 1.3 for men. Our patients were obese, and, recently, some reports have suggested that obese women are more likely to have asthma. The reason for this potentially important link is unknown.

Psychiatric Disorders

We found that more women with OSAS on initial presentation for sleep studies were already diagnosed with depression and were using psychiatric medications. There is a strong link between depression and OSAS, and it is unclear whether the depression that is diagnosed is a manifestation of sleepiness or whether OSAS causes a mood disorder. Smith et al. examining a different cohort of women with OSAS in our center and using an administrative database, found that women with OSAS were more likely to have been treated for depression compared to their population controls (OR, 1.5; 95% CI, 0.9-2.6) than were men with OSAS when compared to their controls (OR, 1.3; 95% CI, 0.9-1.9), but these findings did not reach statistical significance. Pillar et al. also found significantly higher scores for both depression and anxiety in women compared with men, when both age groups and respiratory disturbance index were assessed. In addition, they found that women with severe OSAS had higher depression scores than those women with mild OSAS.

Obesity

Our women and men with OSAS (chosen at random from our database) were extremely (class III) obese. Throughout the world, obesity is becoming a major public health problem. Among adults in the United States, about 19.9% of men and 24.9% of women have a BMI greater than 30, and the rate is similar in other countries. In the decade ending with the year 2000, the prevalence of people with BMIs exceeding 40 tripled. It has been reported that about 30% of the population with a BMI exceeding 30 has sleep apnea, and 50% of those with a BMI greater than 40 have sleep apnea. Thus, the worldwide epidemic of obesity is causing an increased prevalence of sleep apnea. Since obesity is more common in women than in men, it is likely that if current trends continue, there will be a dramatic increase in OSAS in women. It is thus important that clinicians appreciate that women with OSAS may present differently than do men.

Limitations of This Study

The population studied represents those who had been referred to a sleep clinic and therefore does not represent the general population. The women with OSAS had more severe OSAS than in other series; our cases had severe apnea and, on average, had class III obesity.

This study was conducted using a retrospective medical chart review, and a structured questionnaire was used for data analysis. Although a structured questionnaire is more suitable for rigorous statistical analysis than is an unstructured questionnaire, a structured questionnaire limits responses of both genders; subsequently, the findings may represent gender differences in the prevalence of the listed symptoms. An unrestricted response opportunity might have resulted in other gender-related symptoms and findings.

CONCLUSIONS

There are some differences in the clinical presentation of breathing disorders during sleep between the sexes. Especially striking, in comparison to men, is the previous history of depression and hypothyroid disease and the presenting complaint of insomnia in women. Men were more likely to have a history of witnessed apnea, consume more caffeinated beverages, and admit to greater alcohol consumption.

Based on these findings, clinicians should appreciate that a
higher degree of suspicion of sleep apnea is needed when evaluating the symptoms of women because women may clinically present differently than men. Clinicians should consider a diagnosis of OSAS in all obese (especially class III) women with a history of insomnia, depression, or hypothyroidism.

REFERENCES