

Epidemiology of Sleep Disorders in Women

Hrayr P. Attarian

HISTORICAL PERSPECTIVES

Sleep medicine as a field was not established until the early 1970s after the discovery of obstructive sleep apnea syndrome (OSAS) in Europe in 1965 (1,2) and the establishment of the first sleep laboratory at Stanford in 1972. The term *polysomnography* was coined by Dr. Jerome Holland at Stanford, in 1974, to describe the studies that were done during all-night sleep.

In the early years of sleep medicine, sleep centers concentrated on diagnosing and treating OSAS and less frequently narcolepsy. Both conditions were thought rare, in fact OSAS was initially described as a rare disorder of overweight men.

It is now known that OSAS is a very common disorder that affects both men and women (premenopausal women less than postmenopausal women) and can affect both overweight and normal weight people.

Restless legs syndrome (RLS), another well-described sleep disorder, was thought of as being rare until recently as well. RLS is now known to be quite prevalent, especially in women.

In addition, the increased recognition and acceptance of insomnia, a condition more prevalent in women, as a sleep disorder in its own right have established the fact that sleep disorders are quite common and are not gender-specific disorders of the male population.

In this chapter, I discuss the prevalence of the complaint of difficulty sleeping and excessive daytime sleepiness (EDS) in women. I also discuss the gender differences in the prevalence of the two most common sleep syndromes: OSAS and RLS.

INSOMNIA

As several studies looking at different aspects of insomnia have confirmed, insomnia is more prevalent in women. Bixler et al., in 1979, published the results of their survey of 1006 women in the Los Angeles metropolitan area, where they looked at the prevalence of sleep disorders in general. Bixler et al. found a 42.5% prevalence of insomnia. Trouble falling asleep was 14.4% and difficulty with frequent night-

time awakenings was 22.9%. Women, especially postmenopausal women, were more affected than men (3). Karacan and colleagues also reported a similar prevalence in their community survey, again showing a female preponderance (4). Liljenberg et al. surveyed randomly selected members of the population aged 30 to 65 years from two geographically different rural parts of central Sweden. Difficulty falling asleep was cited by 7.1% of the women and 5.1% of the men and nocturnal awakenings were reported in 8.9% of women and 7.7% of men. Using a stringently defined concept of insomnia as a disorder of initiating sleep (DIS), the prevalence rate of insomnia among women was 1.1% and among men 0.5%. Defining insomnia as a disorder of maintaining sleep (DMS), the prevalence among both women and men was 1.1%. Defining insomnia as a disorder of initiating and maintaining sleep (DIMS), the prevalence rate was 1.7% among women and 1.4% among men. Liljenberg concluded that the reason for the lower prevalence of insomnia in this study was because they used more stringent criteria for the definition of insomnia (5). Morgan et al. surveyed 1023 randomly chosen elderly members of the community in Nottinghamshire, England and discovered subjective insomnia at least *sometimes* in 37.9% of the sample, with women having a higher prevalence than men (6). For example, in Sweden, Liljenberg reported the following in 1988: females significantly more often reported difficulty in falling asleep (7.1% of the women and 5.1% of the men). Among women, 8.9% and among men, 7.7% of individuals reported trouble with nocturnal awakenings. Using a stringently defined concept of insomnia as a DIS, the prevalence rate of insomnia among women was 1.1% and among men 0.5%. Defining insomnia as a DMS, the prevalence among both women and men was 1.1%. Defining insomnia as a DIMS, the prevalence rate was 1.7% among women and 1.4% among men (5). In one Brazilian town, the prevalence of insomnia was 38.9%, being higher among women (45.3%) than men (28.8%) (7). In Hong Kong, females were found to be about 1.6 times at higher risk for insomnia than males (8). In Kuwait, it was found that 14.6% of boys and 20.3% of girls reported difficulty initiating sleep, whereas 8.6% of boys and 15.7% of girls reported difficulty maintaining sleep. Girls had higher mean scores in most of the 12-point insomnia scale items (9). In Germany, the prevalence of severe insomnia was found to be 5% in women vs 3% in men (10). Over the years, multiple other survey-based studies have presented robust data to support the increase prevalence of insomnia in women in different adult population groups in several other countries as well (Netherlands, United Kingdom, India, Japan, and Canada) (11–17).

The National Sleep Foundation started its annual polls in 1995 and every year the polls have demonstrated about 1.5–2/1 female-to-male preponderance of different insomnia complaints. The most recent poll published on the foundation's website on March 29, 2005 polled 1506 adults by phone on a variety of sleep habits. Slightly more than half (51%) of men vs 57% of women complained of any symptom of insomnia at least a few nights a week. Difficulty falling asleep (taking one 30 minutes or longer to fall asleep) was present in 26% of women and only 17% of men. Sleep maintenance issues (awake a lot during the night) were also more common in women (35%) than men 28%. Early morning awakenings were reported in

24% of women and 19% of men. A study in Japan surveyed 555 nurses for symptoms of insomnia. The prevalence of insomnia among shift-working nurses (29.2%) was three to four times higher than that in the general population (18). The same group also discovered increased tobacco use in those with insomnia among a group of 522 female staff nurses (19). Substance use was also reported in a US study among shift-working nurses with insomnia (20). Shift work in women is therefore a significant risk factor for insomnia and subsequent tobacco and alcohol use.

It is therefore clearly established that insomnia is a much more prevalent complaint in women than men. This gender difference seems to be present only in adults. A few studies looking at the prevalence of insomnia in prepubertal children have not demonstrated this gender difference (21–24). This could very well be the result of hormonal changes occurring during the menstrual cycle, during pregnancy, and after menopause. It has been well documented that there is an increase in subjective sleep complaints during the late luteal phase (25) and dysmenorrhea is associated with decreased sleep efficiency and worsening daytime functioning (26). Luteal phase is also associated with increased mood problems (25). As a result of both unique hormonal changes and mechanical problems (including backache, urinary frequency, heartburn, fetal movement, and spontaneous awakenings), a significant number of women experience insomnia during pregnancy (27). Insomnia starts becoming prevalent in weeks 23–24 of gestation. By the third trimester, only 1.9% of women fail to experience nocturnal awakenings (27). Despite the complaint of insomnia, partially resulting from napping and partially from “sleeping in,” there is an overall increase in total sleep time in pregnancy, despite a reduction in sleep efficiency. A mean increase in sleep duration of 0.7 hours during the first trimester, compared with the prepregnancy period has been reported and a mean increase of more than 30 minutes of total nocturnal sleep time was recorded at 11 to 12 weeks of gestation in 33 women who underwent in-home polysomnography prior to conception and during each trimester of pregnancy (27). Finally, there is a high level of sleep disturbance (occurring in about 42%, according to one study [28]) in menopausal women. A total of 521 women were studied in the above-mentioned study and insomnia was associated with higher levels of anxiety, depression, stress, higher systolic and diastolic blood pressures, and greater waist-to-hip ratios. Although cross-sectional analyses indicate that sleep disturbance may be independent of menopausal status, transition into postmenopausal status is associated with deleterious changes in sleep among women not receiving hormone replacement therapy [HRT]; 28). Interestingly when subjective and objective sleep measures were compared in peri- and postmenopausal women, these women, relative to premenopausal women, were less satisfied with their sleep, but did not have diminished sleep quality measured by polysomnography (29).

HYPERSONMIA OR EXCESSIVE DAYTIME SLEEPINESS

The complaint of hypersomnia, regardless of cause, is more prevalent in women as well. This has been confirmed repeatedly in different populations around the world. One of the most important studies done in Sweden showed a prevalence of

EDS (23.3% in women and 15.9% in men), despite the fact that women generally reported longer total sleep time. They also looked at psychological status and discovered a higher prevalence of anxiety in women; however, this alone was not enough to explain the more prevalent complaint of EDS (30). A Japanese study showed a prevalence of EDS 13.3% in women and 7.2% in men (31). Similar results of a higher prevalence in women were found in Brazil (32). This gender difference appears to be a phenomenon of the adolescent and postadolescent population. Children have not demonstrated this gender difference in the complaint of EDS in various ethnic groups (33). Even in special groups, such as patients with major depression, EDS was more prevalent in women than men (the study was conducted in matched opposite gender dizygotic twins) (34). In pregnancy, EDS is a common first-trimester complaint that may precede the realization of pregnancy (27).

In conclusion, although prevalence rates of insomnia vary from study to study (depending on the definition of insomnia used) and from one geographical area to another, the female preponderance is always the one constant.

OBSTRUCTIVE SLEEP APNEA SYNDROME

In the landmark study by Young et al. in 1993, published in the *New England Journal of Medicine*, 602 employed men and women 30 to 60 years old were studied. The estimated prevalence of sleep-disordered breathing (SDB) defined as an apnea-hypopnea index [AHI] score of 5 or higher, was found to be 9% for women and 24% for men. They also estimated that 2% of women and 4% of men met the minimal diagnostic criteria for the sleep apnea syndrome (an AHI score of 5 or higher and daytime hypersomnolence). Male sex and obesity were strongly associated with the presence of SDB (35).

Most population-based studies estimate a gender-specific prevalence of two- to threefold greater risk for men compared with women (36), but little progress has been made in understanding the reasons for the risk difference.

The role of sex hormones in OSA pathogenesis has been hypothesized to account for this disparity (37). Clear gender differences in upper airway shape and genioglossal muscle activity during the awake state, in craniofacial morphology, and pattern of fat deposition have been proposed to account for a higher male risk of OSA as well (38). However, no conclusive findings have emerged (38).

In 2001, Bixler et al. further studied the gender difference in the prevalence of OSA and SDB (an AHI score of 10 or higher and daytime hypersomnolence). The overall incidence for women was 1.2% and for men 3.9%. Premenopausal women had a prevalence of 0.6% and postmenopausal women had 1.9%. When they further subdivided postmenopausal women into two groups one on HRT and one not on HRT, they discovered that the prevalence in the first group was only 0.5% vs 2.7% in the second (39). This difference between those with and without HRT (especially estrogen) was also demonstrated in another study in 2003 (40). Age also plays a role on the prevalence of sleep apnea in women. In the same landmark study, Bixler et al. demonstrated that the prevalence in women 20–44 was 0.7%, in women 45–64 it was 1.1%, and in the 65- to 100-year-old age group it was 3.1% (39). Weight also has an impact in increasing the prevalence of OSA in women but not to the degree

it does in men. Again, Bixler et al. demonstrated that women with a body mass index (BMI) below 32.3 kg/cm² had a prevalence of 0.4% and women with a BMI equal to or more than 32.3 kg/cm² had a prevalence of 4.8% (39). This is in concordance with previous studies that have shown the prevalence among obese women (BMI >27.3 kg/m²) to be 3–7% (41,42). In contrast, the impact of weight in men is much more pronounced. The prevalence for obese men (BMI >27.8 kg/m²) is 40–76.9% (41,42). Interestingly enough, this male prevalence is what is seen in a group of women with polycystic ovarian syndrome (PCOS). Women with PCOS have hirsutism, obesity, infertility, and enlarged polycystic ovaries. They also have increased androgen production and disordered gonadotropin secretion, it results in chronic anovulation (43). Studies have shown an OSAS prevalence of 17–69.9% (depending on the definition of OSA used) in women with PCOS (43–45).

Pregnancy is another situation where women are at particular risk for OSA (38). Unfortunately, there are very few studies addressing this subject. Twenty-seven percent of otherwise healthy women report snoring in the third trimester (27). Three hundred fifty pregnant women and 110 age-matched nonpregnant women were surveyed at two US Army hospitals. Frequent snoring was reported in 14% of the pregnant women vs 4% of the nonpregnant women (46). Both frequency and loudness of snoring, and episodes of awakening with a choking sensation, appear to increase during pregnancy, with 50% of the women in one study reporting snoring and 14% reporting choking awakenings at 35 to 38 weeks of gestation, vs 37 and 4%, respectively, at 8 to 12 weeks of gestation (38). Another survey of 502 Swedish women at the time of delivery found that 23% reported snoring often or always during the week before delivery, whereas only 4% reported snoring before pregnancy. Most of the time, the snoring increased during the third trimester (47). There is evidence that the impact of pregnancy on snoring resolves within several months after delivery (38).

The high prevalence of snoring and choking awakenings during pregnancy suggests that pregnancy may be associated with OSA; however, there are few data regarding the prevalence of OSA during pregnancy (38). In the largest reported study, polysomnography was performed in 11 snoring women early in the third trimester. All had an AHI less than 5, although all had evidence of increased upper airway resistance characterized by either crescendo respiratory effort or abnormal sustained increases in respiratory effort, occurring more commonly than in control subjects who do not snore (48). The mechanisms underlying the increase in snoring during pregnancy are uncertain, but may include excess weight gain (38), diffuse pharyngeal edema of pregnancy, or the effect of sleep deprivation on pharyngeal dilator muscle activity (38).

In conclusion, OSAS is common in women but not as common as in men. Weight, menopause, age, and endocrine disorders have an impact on increasing the prevalence of OSAS in women.

RESTLESS LEGS SYNDROME

RLS, one of the most common sleep disorders, was first described in 1672. RLS is characterized by uncomfortable, tingling, crawling, burning, prickly limb sensa-

tions associated with an irresistible urge to move the limbs to obtain relief, typically occurring while sedentary or at sleep onset (49). In their series of studies done in 2003, Hanson et al. found a female-to-male ratio of 2:1 (49). These results were replicated in the United Kingdom by Van De Vijver et al. in 2004 (50). Similarly, increased prevalence of RLS in women was found in several other studies (51,52). Berger et al. looked at the relationship between parity and increased prevalence of RLS. Nulliparous women had prevalences similar to those among men the risk of RLS increased gradually for women with one child (odds ratio [OR], 1.98; 95% confidence interval [CI], 1.25–3.13), two children (OR, 3.04; 95% CI, 2.11–4.40), and three or more children (OR, 3.57; 95% CI, 2.30–5.55) (53). There was also a gradually increasing risk of RLS with increasing age that was demonstrated in all of the above studies (54). Pregnancy also is a significant risk factor. Pregnant women have at least two or three times higher risk of experiencing RLS than the general population. These data come from few epidemiological studies finding an 11–27% prevalence of RLS during pregnancy. Women affected by pre-existing RLS often complain of worsening symptoms during pregnancy. This is usually a benign form of RLS, with the highest degree of severity in the third trimester and a tendency to disappear around delivery (55).

RLS can also occur with an increasing prevalence in women who had no symptoms prior to pregnancy. Prevalences have been shown to increase from 0% prepregnancy to 12.5% in the first trimester to 23% by the third trimester (27).

The above studies were all done in the United States and Europe, where the overall prevalence of RLS is estimated to be 10–12.9% (56,57).

In Asia, the prevalence of RLS is much lower at 3% or less (58–60). Despite the lower prevalence, the ratio of female to male is high and so is the overall prevalence in pregnancy. One study from India reported a female-to-male ratio of 7:1 (61). A Japanese study targeting pregnant women found the prevalence in this particular group to be 19.9% (62).

This increased prevalence of RLS in women and especially its association with pregnancy has been thought to be related to reduced iron, ferritin, and/or folate levels (27).

RLS is much more prevalent in women, especially with pregnancy and menopause, even in ethnic groups where RLS is relatively uncommon.

CONCLUSION

The complaint of both insomnia and hypersomnia is more prevalent in women. Of the two most common sleep syndromes, OSAS is relatively rare in premenopausal nonpregnant women, whereas its prevalence increases during pregnancy and menopause.

RLS is much more prevalent in women and that prevalence amplifies as women get pregnant and when they reach menopause. Interestingly, parity itself increases the prevalence of RLS in women even after delivery, whereas RLS exacerbations during pregnancy tend to disappear with delivery.

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