

Chapter 2

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.

We now know 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 rare until recently as well, and now is 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.

The recent findings of the association of sleep duration and mortality have shown some gender differences as well, with both sexes having higher mortality if they slept 5 or less hours or 10 or more hours but these extremes of sleep were only a risk factor for cardiovascular morbidity and mortality in women [3].

H.P. Attarian (✉)

Department of Neurology, Sleep Medicine, Northwestern University,
Chicago, IL 60611, USA

e-mail: h-attarian@northwestern.edu

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

Insomnia

The complaint of insomnia is more prevalent in women. Several studies looking at different aspects of insomnia have confirmed this fact. Bixler et al. in 1979 published the results of their survey of 1,006 Los Angeles metropolitan area where they looked at the prevalence of sleep disorders in general. They found a 42.5% prevalence of insomnia. Trouble falling asleep was 14.4%, and difficulty with frequent nighttime awakenings was 22.9%. Women, especially postmenopausal women, were more affected than men [4]. Karacan and colleagues also reported a similar prevalence in their community survey, with again a female preponderance [5]. Liljenberg et al. surveyed randomly selected members of the population aged 30–65 years from two geographically different rural parts of central Sweden: 7.1% of the women and 5.1% of the men reported difficulty in falling asleep; 8.9% of women and 7.7% of men reported trouble with nocturnal awakenings. 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 it was 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 [6]. Morgan et al. surveyed 1,023 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 [7]. 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 it was 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 [6]. In one Brazilian town, the prevalence of insomnia was 38.9%, being higher among women (45.3%) than among men (28.8%) [8]. In Hong Kong, females were found to be about 1.6 times at higher risk for insomnia than males [9]. In Kuwait, it was found that 14.6% of boys and 20.3% of girls reported difficulty initiating sleep, while 8.6% of boys and 15.7% of girls reported difficulty maintaining sleep. Girls had higher mean scores in most of a 12-point insomnia scale items [10]. In Germany, the prevalence of severe insomnia was found to be 5% in women vs. 3% in men [11]. Over the years, multiple other survey-based studies have

come up with robust data to support the increased prevalence of insomnia in women in different adult population groups in several other countries as well and among the elderly [12, 13] (the Netherlands, Greece, the UK, India, Japan, France, Spain, Korea, Sweden, Canada, China) [14–26]. Women are also more likely to use sleep aids for insomnia and have more insomnia-related depression [27].

National Sleep Foundation started their annual polls in 1995, and every year they have demonstrated about 1.5–2/1 female to male preponderance of different insomnia complaints. The poll of 2007 focused primarily on women and their sleep habits. They phone surveyed a random sample of 1,003 women ranging from 18 to 64 years old between September 12 and October 28, 2006, and 29% of women reported rarely if ever getting a good night's sleep, with an additional 32% reporting a good night's sleep only a few times a week. Sixty-seven percent reported having sleep problems at least a few nights a week, while 46% reported it happening almost every night. Among the respondents, 11% had the diagnosis of insomnia and 7% were being treated for it, but full 29% used some sort of sleep aid every night or almost every night. The older the women the more likely it was that they suffered from insomnia. Other risk factors included menopause, pregnancy, RLS, snoring, and other medical problems. 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 [28]. That out of 522 female staff nurses those with insomnia had increased tobacco use compared to those who slept well [29]. Substance use was also reported in a US study among shift-working nurses with insomnia [30]. Shift work in women is therefore a significant risk factor for insomnia and subsequent tobacco and alcohol use. More women complain of ambient noise-related sleep disruptions than men (78.3% vs. 48.6%) as shown in an Indian study of the impact of noise in urban areas on health [31], and women's sleep is more prone to disruption due to job-related stress [32]. Lastly, single women have more complaints of insomnia than partnered ones according to a US survey of a multiethnic middle age group [33]. Short sleep duration is also associated with central obesity in young women as shown by Theorell-Haglow et al. [34]. African American women were more likely to have poor sleep objectively than Caucasians or Asian Americans after adjusting for other variables [35].

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 adolescents [36] and adults. A few studies looking at the prevalence of insomnia in prepubertal children have not demonstrated this gender difference [37–40]. This could very well be due to 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 [41], and dysmenorrhea is associated with decreased sleep efficiency and worsening daytime functioning [42]. Luteal phase is also associated with increased mood problems [41]. Due to both unique hormonal changes and mechanical problems (including backache, urinary frequency, heartburn, fetal movement, and spontaneous awakenings), significant number of women experience insomnia during pregnancy [43]. Insomnia starts becoming prevalent in the 23–24 weeks of gestation. By the third trimester, only

1.9% of women fail to experience nocturnal awakenings [43]. This is indirectly reflected in studies from Europe that show increasing use of benzodiazepines as pregnancy progresses (8.3% in the first trimester, 14.2% in the second trimester, and 23.7% in the third). These papers, however, do not differentiate between benzodiazepine use for insomnia vs. anxiety [44, 45].

Despite the complaint of insomnia, partially due to napping and partially due to “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 h during the first trimester, compared to the prepregnancy period, has been reported, and a mean increase of more than 30 min of total nocturnal sleep time was recorded at 11–12 weeks of gestation in 33 women who underwent in-home polysomnography prior to conception and during each trimester of pregnancy [43]. Shorter sleep duration in the first year postpartum is also associated with increased adiposity up to 3 years postpartum in the form of higher waist circumference and higher retention of pregnancy weight [46]. And, lastly, there is a high level of sleep disturbance (42–54%) [47–50] in menopausal women. The odds of complaining of severe insomnia was 2- to 3.5-fold higher in menopausal women compared to premenopausal women, and hysterectomy specifically is an independent risk factor for insomnia [51]. Insomnia worsens as menopause progresses [52]. Caucasian menopausal women have slightly higher chance of sleep maintenance issues, but there are no real significant differences across different ethnic groups when it comes to overall prevalence of insomnia in menopause [53, 54].

Insomnia was associated with higher levels of anxiety, depression, stress, higher systolic and diastolic blood pressures, greater waist/hip ratios, and significant economic burden in the form of absenteeism, consumption of medical services, and decreased productivity [55].

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, and it is unclear whether receiving hormone replacement therapy prevents this [47, 49]. Interestingly, when subjective and objective sleep measures were compared in peri- and postmenopausal women, perimenopausal and postmenopausal women, relative to premenopausal women, were less satisfied with their sleep, but did not have diminished sleep quality measured by polysomnography [56]. In conclusion, although prevalence rates of insomnia varies 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.

Hypersomnia or Excessive Daytime Sleepiness

The complaint of hypersomnia, regardless of cause, is more prevalent in women as well. This has been confirmed time and time again 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 [57]. A Japanese study showed a prevalence of EDS 13.3% in women and 7.2% in men [58]. Similar results of a higher prevalence in women were found in Brazil [59]. This gender difference appears to be a phenomenon of the adolescent and postadolescent population. Adolescent girls reported slightly but significantly more sleep per night than boys (5–20 min) according to two-cross sectional surveys of adolescents [60, 61], while in another study that followed 3,134 adolescents for 1 year the female sex was one of the risk factors for curtailed sleep [62, 63].

These two findings may not be as contradictory as they appear on the surface, as girls may need to sleep more but because of societal restrictions are getting less sleep than their male counterparts. Studies from other countries have shown curtailed sleep time in preadolescent boys vs. girls or no difference between the sexes, suggesting a cultural component to the number of hours of sleep children get [64, 65].

Long sleep duration in middle aged women, but not in men, is a risk factor for weight gain as demonstrated in a Finnish public health study that followed 7,332 individuals for up to 7 years [66]. This also could be due to middle aged women being more sleep deprived than their male counterparts, therefore reporting longer catch up sleep. In the elderly group, women who napped regularly or slept more than 9 h a day were at a higher risk for mortality from causes other than cancer [67].

Idiopathic hypersomnia with long sleep time tends to have a female preponderance of 2/1 [68]. Children have not demonstrated this gender difference in the complaint of EDS in various ethnic groups [69]. 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 sex dizygotic twins [70]. In pregnancy, EDS is a common first-trimester complaint that may precede the realization of pregnancy [43].

Interestingly though, men tend to report falling asleep unintentionally more than women do. In a survey aimed at Chinese medical students, 20.3% of men vs. 8.8% of women reported habitually falling asleep in class [71].

Obstructive Sleep Apnea Syndrome

In the landmark study published in *New England Journal of Medicine* in 1993, Young et al. studied 602 employed men and women 30–60 years of age. The estimated prevalence of sleep-disordered breathing defined as an apnea–hypopnea 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 apnea–hypopnea score of 5 or higher and daytime hypersomnolence). Male sex and obesity were strongly associated with the presence of sleep-disordered breathing [72].

Most population-based studies estimate a sex-specific prevalence of two- to threefold greater risk for men compared with women [73], but little progress has been made in understanding the reasons for the risk difference. This male preponderance has been shown in groups as young as 2–6 years of age where, across three ethnic groups (Caucasian, Black, and Hispanic), boys were 2.9 times more likely to have obstructive sleep apnea than girls [74]. This held true for Chinese preadolescents as well where the prevalence of OSA in boys was 5.8% vs. 3.8% in girls [75], in Brazilian children 7–11 years of age [76], 3/2 in Turkish children 7–13, and in Turkish adolescents (1.5/1) [77].

The role of sex hormones in OSA pathogenesis has been hypothesized to account for this disparity [78]. Clear sex 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 [79]. However, no conclusive findings have emerged [79].

Bixler et al. in 2001 further studied the gender difference in the prevalence of OSA and sleep-disordered breathing (an apnea–hypopnea score of 10 or higher and daytime hypersomnolence). The overall incidence for women was 1.2%, and for men was 3.9%. Premenopausal women had a prevalence of 0.6%, and postmenopausal women had a prevalence of 1.9%. When they further subdivided postmenopausal women into two groups, one on HRT and the other not on HRT, they discovered that the prevalence in the first group was only 0.5% vs. 2.7% in the second [80]. This difference between those with and without HRT (especially estrogen) was also demonstrated in another study in 2003 [81]. Age also has an impact 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 1.1%, and in the age group 65–100 3.1% [80]. Weight also has an impact in increasing the prevalence of OSA in women but not to the degree it does in men. Again, in their study, Bixler et al. demonstrated that women with a BMI of under 32.3 kg/cm² had a prevalence of 0.4% and women with BMI equal or more than 32.3 kg/cm² had a prevalence of 4.8% [80]. This is in concordance with previous studies that have shown the prevalence among obese women (BMI over 27.3 kg/m²) to be 3–7% [82, 83]. In contrast, the impact of weight in men is much more pronounced. The prevalence for obese men (BMI over 27.8 kg/m²) is 40–76.9% [82, 83]. 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 [84]. Studies have shown an OSAS prevalence of 17%–69.9% (depending on the definition of OSA used) in women with PCOS [84–86]. OSA is independently associated with higher risk of metabolic syndrome (central obesity, hypertriglyceridemia, and low high density lipoprotein [HDL]) in women, both pre- and postmenopause. The prevalence of metabolic syndrome increases from 10.5% in women without OSA to 57.1% in those with severe OSA. Moreover, the apnea–hypopnea index (AHI), the nadir oxygen saturation, and the oxygen desaturation index (ODI) are each independently associated with metabolic syndrome [87].

Habitual alcohol intake also increases the risk of OSA in women by twofolds after controlling for other variables [88]. Compared to men with similar OSA severity, women are heavier users of health care resources because of poor perceived health status and the overuse of psychoactive drugs [89].

Pregnancy is another situation where women are at particular risk for OSA [79]. There are, unfortunately, very few studies addressing this. Twenty-seven percent of otherwise healthy women report snoring in the third trimester [43]. 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 [90]. Both frequency and loudness of snoring, and episodes of awakening with a choking sensation, appear to increase during pregnancy, with half of the women in one study reporting snoring and 14% reporting choking awakenings at 35–38 weeks of gestation, vs. 37% and 4%, respectively, at 8–12 weeks of gestation [79]. 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 [91]. There is evidence that the impact of pregnancy on snoring resolves within several months after delivery [79].

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 [79]. 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 nonsnoring control subjects [92]. The mechanisms underlying the increase in snoring during pregnancy are uncertain, but may include excess weight gain [79], diffuse pharyngeal edema of pregnancy, or the effect of sleep deprivation on pharyngeal dilator muscle activity [79].

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 1,672. RLS is characterized by uncomfortable, tingling, crawling, burning, prickly limb sensations associated with an irresistible urge to move the limbs to obtain relief, typically occurring while sedentary or at sleep onset [93]. Hanson et al. in their series in 2003 found a female to male ratio of 2:1 [93]. These results were replicated in the UK by Van De Vijver et al. in 2004 [94]. Similarly, increased prevalence of RLS in women was found in several other studies [95–97]. This female preponderance, however, seems to be limited to adults as trials among adolescents have not shown a difference

between the sexes (prevalence and correlates of RLS in adolescents). 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, 1.98; 95% confidence interval, 1.25–3.13), two children (odds ratio, 3.04; 95% confidence interval, 2.11–4.40), and three or more children (odds ratio, 3.57; 95% confidence interval, 2.30–5.55) [98]. There was also a gradually increasing risk of RLS with increasing age that was demonstrated in all of the above studies [99]. 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. It develops more frequently during the third trimester and disappears within the first month after delivery in most cases. One of oldest RLS studies reported a prevalence of 19.5% in 500 pregnant women. Four weeks after delivery, only three women still had RLS symptoms [100]. A large Japanese study involving 16,528 pregnant women reported an RLS prevalence of 19.9%. The prevalence of RLS increased with the length of pregnancy: 15% in the first trimester and 23% in the last trimester [101]. Another Italian study of 606 women using more standardized screening questionnaires reported a prevalence of 26.6%, with almost 2/3 of women never having experienced RLS prior to their pregnancy [102].

A similar study from Brazil reported an RLS prevalence of 13.5% in 524 women; 94.4% were in the second or third trimester. RLS prevalence and severity increased by trimester [103]. Yet another large survey of 1,022 pregnant women living in a French town showed that 24% of women were affected by RLS during their pregnancy. The disease was strongly related to the third trimester of pregnancy [104]. Women who had transient RLS during their pregnancy had a fourfold increased risk of developing chronic RLS [105, 106]. These studies were all done in the US and Europe, where the overall prevalence of RLS is estimated to be 10.0%–12.9% [107, 108].

In Asia, the prevalence of RLS is much lower at 3% or less [109–111]. 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 F/M of 7/1 [112]. A Japanese study targeting pregnant women found the prevalence in this particular group to be 19.9% [101].

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

Periodic limb movement disorders (PLMD), on the other hand, do not have as robust a sex predilection, with isolated PLMD being equal in both sexes [113] while PLMD with RLS is more prevalent in women [114].

Other Sleep Disorders

Not much is available about gender differences in other sleep disorders except for the rare condition sudden unexpected nocturnal death syndrome, which tends to be significantly more prevalent in men. In REM parasomnias for example, REM

sleep behavior disorder tends to be more prevalent in men (M/F=2/1) [115, 116] while recurrent sleep paralysis and hypnic hallucinations separately or together do not have a gender predilection, and nightmares are more prevalent in women [117–120].

A recent study from Portugal found that girls ages 7–10 had a higher prevalence of bruxism (56.5%) than boys (43.5%) of the same age [121]. In adults, however, there seemed to be no difference between genders in the prevalence of bruxism [122]. Two epidemiologic studies reported higher prevalence of sleep-walking in women [122, 123], but sleep terrors did not show a gender predilection [124], nor did other parasomnias such as catathrenia, sleep eating, and confusional arousals [125].

Circadian rhythm sleep disorders seem to vary with sex as well. Teenage girls reach the peak of their adolescent delay in their sleep phase by age 17 while boys reach the peak by age 21. The prevalence of delay, however, is about the same regardless of gender. Premenopausal adult women, however, tend to have significantly more advanced sleep phase than men of the same age [126, 127].

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 while its prevalence increases during pregnancy and menopause.

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

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