



Editorial

Sleep disorders in pregnancy



A recent epidemiologic study with a small sample size ($n = 248$) in southern Taiwan suggested that the prevalence of poor sleepers (Pittsburgh Sleep Quality Index score > 5) was 58% for second-trimester women and 66% for third-trimester women. The study also showed that women who were unemployed reported significantly higher prevalence of poor sleep quality than those who were employed.¹

Sleep disturbance, a substantial health problem, is defined as either short or long sleep duration with associated poor sleep quality or continuity, which may be related to a sleep disorder. This can result in alterations in mental functioning, diminished daytime functioning, depression, hypertension, and diabetes. The phenomenon of sleep disturbance has also received considerable attention because evidence indicates that sleep disturbance is associated with adverse maternal and neonatal outcomes when occurring during pregnancy, including low birth weight, intrauterine growth retardation, preterm birth, and operative birth.² Sleep disturbance is associated with neuroendocrine, metabolic, and inflammatory changes²; therefore, we are pleased to be in the position to comment on the article of Gunduz et al,³ entitled *Sleep disturbance in the last trimester of pregnancy and inadequate vitamin D: is there a relationship?*, published in the current issue of the *Journal of the Chinese Medical Association*. Furthermore, we wish to more widely introduce this relatively common and important issue—sleep disturbance, which is often neglected in the routine of clinical practice.

First, similar to the report from southern Taiwan, the median value of the Pittsburgh Sleep Quality Index score was a high of 6.2, and the prevalence of Turkish women with sleep disturbance was estimated to be 43.5%.³ Both showed that sleep disturbance is extremely common in pregnant women.

The authors tried to investigate the relationship between sleep disturbance and serum level of vitamin D in pregnant women, but found an absence of any association. The discussion of vitamin D is often limited to calcium homeostasis, especially on issues of bone health,^{4,5} although more recent knowledge might expand the conversation to cover cardiovascular, neurological, dermatologic, and immunologic systems, and possibly neoplasm therapy. Vitamin D rarely involves or is associated with psychiatric problems, including sleep disorders. Therefore, it is not surprising that the authors would obtain the negative report of absence of

association between sleep disorders and inadequate vitamin D.³ Based on the results of the authors, it would be interesting to know whether there really is an absence of association between sleep disorders and inadequate vitamin D. We highlight this question based on the following. In Taiwan, sleep disorders and sleep-related breathing disorders are common in hemodialysis patients,⁶ although we were not aware of any vitamin D as causation or association for sleep disturbance in hemodialysis patients. However, the publication did hint at the possibility. In fact, sleep disturbance is a complicated disease, which can be separated into at least three subgroups, including sleep-disordered breathing (habitual snoring and obstructive sleep apnea), restless legs syndrome, and pure types of insomnia. Therefore, without a clear demonstration of what types of sleep disturbances are in the current study, it is difficult to make the conclusion.

Second, we would like to introduce *sleep disturbance in pregnancy*. The topic of sleep disorder in pregnant women is seldom reported in Taiwan, and any discussion and education on the issue is extremely rare. Although the reasons for this omission are unknown, it may be secondary to a general unfamiliarity with the diagnosis and management of pregnant women with sleep disturbance. Of course, the other possibility is that obstetricians have frequently just neglected this disorder and instead were more inclined to use sleep-promoting medications. A recent review by Okun et al⁷ reported that medications, including benzodiazepines, hypnotic benzodiazepine receptor agonists, antidepressants, and antihistamines, did not show any correlation of increased risk of congenital malformations, however, benzodiazepines and hypnotic benzodiazepine receptor agonists may increase rates of preterm birth, low birth weight, and/or small-for-gestational-age infants. The results from a recent nationwide population-based study in Taiwan could provide a further reference of value.⁸ Wang et al⁸ compared the risk of adverse pregnancy outcomes in 2497 women who received zolpidem (hypnotic benzodiazepine receptor agonists, pregnancy category C) and 12,485 randomly selected mothers who did not receive the drug. The results showed that the adjusted odds ratios (OR) for adverse pregnancy outcomes, including low birth weight infants, preterm births, small-for-gestational-age infants, and cesarean delivery, were all higher in mothers who received zolpidem treatment during pregnancy relative to the randomly selected controls,

with an OR of 1.39 [95% confidence interval (CI) 1.17–1.64], 1.49 (95% CI 1.28–1.74), 1.34 (95% CI 1.20–1.49), and 1.74 (95% CI 1.59–1.90), respectively. Therefore, the authors concluded that the risk of adverse pregnancy outcomes was higher in pregnant women treated with zolpidem than in those without similar treatment.⁸ Based on the above-mentioned report, benzodiazepines (pregnancy category D) and hypnotic benzodiazepine receptor agonists (pregnancy category C) should be used cautiously in pregnant women.

Finally, because antihistamines are highly soporific, which makes them desirable for pregnancy-related sleep disturbances, and it has been reported that approximately 92% of pregnant women occasionally self-treat with over-the-counter sleep aids, in particular diphenhydramine (pregnancy category B) and doxylamine (pregnancy category A),⁹ antihistamines might be an alternative choice.

In conclusion, sleep disturbance during pregnancy could be an important health issue, although it is often missed. There is currently no prescription protocol that exists for the treatment of sleep problems in pregnancy.⁷ To avoid the potential teratogenic effect, obstetricians might consider using non-pharmacologic treatments to address sleep complaints, including cognitive behavioral treatment for insomnia and exercise. Ultimately, antihistamines may be one of the best choices of medication, however, no studies have confirmed the efficacy of their use for sleep complaints. More research is needed to investigate more carefully the treatment of sleep disturbance in pregnancy.

Conflicts of interest

The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

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