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Original Review

Common Sleep Disorders: Management Strategies and Pregnancy Outcomes

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Sleep disorders, prevalent in industrialized countries, are associated with adverse health outcomes such as hypertension, diabetes, and obesity. Disturbed sleep during pregnancy is frequently overlooked by health care providers, yet recent studies suggest there is an association between sleep disorders and adverse pregnancy outcomes, including preeclampsia, elevated serum glucose, depression, prolonged labor, and cesarean birth. Growing evidence indicates that the recognition and management of prenatal sleep disorders may minimize adverse pregnancy outcomes and improve maternal and fetal well-being. This focused review of prenatal sleep disturbance literature suggests there are 3 main sleep disorders of interest: breathing-related sleep disorders (ie, habitual snoring and obstructive sleep apnea), restless legs syndrome, and insomnia. These sleep disorders are common in pregnancy and have maternal and fetal consequences if left untreated. This article describes sleep disorders of pregnancy, elucidates their relationship with maternal and neonatal outcomes, and presents current evidence regarding diagnostic and management strategies.

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Epidemiologic studies suggest that US adults sleep 90 minutes less per night than 100 years ago.[1,2] Women aged 30 to 60 years currently average 6.5 hours of sleep per night.[1] An estimated 11% of adults in the United States report insufficient sleep. Poor sleep ratings are higher in women (12.4%) and non-Hispanic African Americans (13.3%) compared with men and whites, respectively.[1]

Sleep disturbance is defined as either short or long sleep duration with associated poor sleep quality or continuity, which may be related to a sleep disorder. Disturbed sleep is associated with neuroendocrine, metabolic, and inflammatory changes.[1] Sleep disturbance results in alterations in mental functioning, diminished daytime functioning, depression, hypertension, and diabetes[2] and has recently received greater attention because of the growing evidence of its association with adverse maternal and neonatal outcomes when occurring during pregnancy. This article summarizes the results of a literature review conducted to understand the causes and consequences of sleep disturbance during pregnancy. In this article, the most common sleep disorders during pregnancy are described, present research related to sleep and maternal and neonatal outcomes is reviewed, and current diagnosis and management strategies are presented.

BACKGROUND

The incidence of disturbed sleep is higher during pregnancy compared with the nonpregnant population. Up to 97% of pregnant women report disturbed sleep,[3–5] particularly in the third trimester of pregnancy.[4] Perhaps because of the high percentage of sleep problems during pregnancy, disturbed sleep is frequently treated as a common discomfort, and its importance to maternal and fetal health is overlooked. With refinement of diagnostic criteria, recent studies have linked sleep disturbances with adverse pregnancy outcomes.[6] Thus, management of sleep disturbances may decrease the incidence and severity of pregnancy-related health problems.

METHODS

With the assistance of a trained health librarian, a systematic literature search relative to sleep disorders during pregnancy was conducted in March 2012. Databases included PubMed and MEDLINE. Key search terms included "sleep," "sleep disorders," and "pregnancy" in all applicable combinations. The initial search included all published articles regardless of year. Subsequently, we focused on publications from January 2000 to the present to ensure clinical relevance. Articles that described sleep characteristics during pregnancy, sleep-related pregnancy outcomes, or sleep management strategies qualified for inclusion. We identified 3 sleep disorders that frequently occur during pregnancy: 1) breathing-related sleep disorders, 2) restless legs syndrome, and 3) insomnia. Subsequently, searches with these and related terms were conducted to fully capture the literature. Publications that met the following criteria were included in the final review: 1) written in English, 2) published in peer-reviewed journals, and 3) relevant to the topic. Empirical literature addressing sleep during pregnancy such as research studies (any design), reviews, and observational and case studies were included. Opinions and editorials were excluded. Special attention was paid to research linking sleep disorders with pregnancy outcomes and publications describing management strategies.

RESULTS

A total of 396 published articles from 2000 to 2012 were identified from the database search. Many were only secondarily

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Quick Points

- Breathing-related sleep disorders, restless legs syndrome, and insomnia are prevalent during pregnancy and are independently associated with adverse pregnancy outcomes.
- Growing evidence suggests that effective management of sleep disorders may improve pregnancy outcomes.
- To promote optimal health of pregnant women and fetuses, clinicians need to evaluate sleep quality and quantity during office visits.
- Simple sleep hygiene and lifestyle changes can mitigate many of the effects of poor sleep during pregnancy.

related to sleep during pregnancy and thus contributed no new information. Of these, 152 articles were selected for inclusion. About one-fifth of the selected studies were cohorts, descriptive/comparative studies, or literature reviews. Eighteen percent were prospective case-control studies, and 10% were cross-sectional surveys. Randomized controlled trials made up about 3%, whereas meta-analyses, clinical guidelines, pilot studies, and case studies made up less than 10% all together. Table 1 lists the diagnostic criteria and risk factors for each of the 3 sleep disorders that are common during pregnancy.

Breathing-Related Sleep Disorders

Several diagnostic codes have been developed that describe criteria for breathing-related sleep disorders, a group of sleep disorders also referred to as sleep-disordered breathing and sleep-related breathing disorders. We have chosen to use the term *breathing-related sleep disorder* throughout this article, as this is the term used by both the Ninth Revision of the *International Classification of Diseases* (*ICD*-9) and the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (*DSM*-4), and we believe it more clearly describes the disorder.

Breathing-related sleep disorders are characterized by irregularities of respiratory pattern (eg, pauses in breathing) and/or the quantity of ventilation during sleep. Breathing-related sleep disorders include snoring; upper airway resistance syndrome, which is irregular breathing during sleep with increased effort to breathe in the absence of hypoxia; and obstructive sleep apnea (OSA), which is defined as irregular breathing during sleep with repeated episodes of apnea or hypopnea secondary to obstruction of air flow in the upper airway.[11] The association between breathing-related sleep disorders and hypertension, cardiovascular disease, chronic fatigue syndrome, and fibromyalgia has been established in general adult populations.[8] Understanding short- and long-term health consequences in pregnant women is in its infancy. Snoring, a common prenatal sleep disorder, arises in an estimated 9% of nonpregnant women.[17] In contrast, the rates of snoring in pregnant women range from 11% to 35%.[17,18] Although most studies conclude that pregnancy increases the risk of snoring,[17–19] findings are based on self-reported measures that lack objective validation.

The estimated prevalence of OSA is 2% in nonpregnant women and 0.6% in premenopausal women.[1] In contrast, in 2 prospective studies using self-report OSA symptom measures, women with single gestations reported higher risks for OSA compared with nonpregnant populations. One study reported a 10% risk for developing OSA in pregnancy. Olivarez et al administered 2 of the sleep disorder validated questionnaires to women during the second and third trimesters of pregnancy (N = 220). They found 25% of respondents had OSA symptoms.[20,21] Consensus on the diagnostic criteria for prenatal OSA is lacking; therefore, true prevalence rates are unknown.

Easily administered self-report surveys, such as the Berlin Sleep Questionnaire,[22] have been used to screen for breathing-related sleep disorders during pregnancy. A definitive breathing-related sleep disorder diagnosis requires polysomnography (ie, sleep study), typically in an overnight sleep laboratory. Polysomnography consists of multiple physiologic assessments during sleep, including brain electrical activity; eye, jaw, and leg muscle movement; electrocardiography; respiratory airflow and effort (chest and abdominal excursion); and oxygen saturation.

Physiologic and hormonal changes of pregnancy such as weight gain and displacement of the diaphragm by an enlarging uterus contribute to breathing-related sleep disorders.[23,24] In addition, increased estrogen causes edema of the mucous membranes that contributes to nasal congestion and reduced pharyngeal dimensions, which also are associated with breathing-related sleep disorders.[9,24]

Adverse Outcomes of Breathing-Related Sleep Disorders in Pregnancy

Growing evidence suggests there is a relationship between breathing-related sleep disorders and hypertensive disease of pregnancy.[18,19,25,26] For example, a retrospective study of 447 women with singleton pregnancies found snoring was associated with gestational hypertension and/or preeclampsia (adjusted odds ratio [OR], 1.82; 95% confidence interval [CI], 1.16-2.84), independent of body mass index (BMI), gestational weight gain, neck circumference, smoking, alcohol use, and age. This same study found an adjusted odds ratio of 8.00 (95% CI, 2.71-23.55) for women with witnessed sleep apnea and associated hypertensive disease of pregnancy, defined as blood pressure readings on day of birth of greater than 140/90 mm Hg, regardless of proteinuria, compared with women without witnessed sleep apnea.[18] A larger, cross-sectional study of 1000 randomly selected recent postpartum women reported a 2-fold higher risk of hypertension and/or preeclampsia in those with symptoms of breathing-related sleep disorders after adjusting for age, BMI, diabetes, chronic hypertension, renal disease, smoking,

Table 1. Sleep Disorders of Pregnancy, Diagnostic Criteria, and Risk Factors

Type of Sleep Disorder	*ICD*-9 Code	Diagnostic Criteria	Risk Factors
Breathing-related sleep disorder	780.51	*DSM-IV*: Sleep disruption leading to excessive sleepiness or insomnia due to a sleep-related breathing condition (eg, obstructive or central sleep apnea syndrome). Symptoms may include snoring, pauses in breathing, and/or gasping during sleep and/or daytime fatigue/somnolence. The sleep disruption is not accounted for by a mental disorder, direct physiologic effects of a substance (eg, drug of abuse, medication), or another general medical condition.[7]	Obesity[8] High GWG[9] Smoking[8] Drug or alcohol use[10] Prior history of snoring[9] Large neck circumference[9]
Obstructive sleep apnea (OSA)	327.23	*ICSD-2*: A type of breathing-related sleep disorder. "Diagnosis confirmed by obstructive events (apneas, hypopnea, and respiratory events related to arousals) on PSG of ≥ 15 events/hr or ≥ 5/hr in a patient who reports [symptoms[a]]."[10]	
Restless legs syndrome (RLS)	333.94	*ICSD-2* criteria: 1. Strong urge to move the legs, usually accompanied by discomfort. 2. The urge to move and discomfort occur during inactivity. 3. Movement such as stretching or walking immediately relieves the symptoms, but they recur with subsequent inactivity. 4. Symptoms occur primarily in the evening/night.[11]	RLS prior to pregnancy[12] Family history of RLS[12] Folate/ferritin deficiency[12] Childhood history of "growing pains"[12] Obesity[13]
Insomnia (primary or comorbid)	780.52	*DSM-IV*: Difficulty initiating or maintaining sleep or nonrestorative sleep, for at least one month, which causes significant distress or daytime impairment.[7] *ICSD-2*: Complaint of difficulty falling asleep, difficulty maintaining sleep, waking too early, or experiencing sleep that is chronically nonrestorative or poor in quality with accompanying daytime impairment.[11]	Chronic pain[14] Passive smoke exposure[4] Neurologic disorders[14] African American[14] Shift work[15] Depression[16] Stress[16]

Abbreviations: *DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, 4th edition*; GWG, gestational weight gain; hr, hour; ICSD-2, *Second Edition of the International Classification of Sleep Disorders*; PSG, polysomnography; RLS, restless legs syndrome.
[a]Symptoms include unintentional sleep episodes during wakefulness, daytime sleepiness, unrefreshing sleep, fatigue, insomnia, waking up breath holding, gasping or choking; or the bed partner describing loud snoring, breathing interruptions, or both during patient's sleep.

and multifetal gestation (adjusted OR, 2.3; 95% CI, 1.4-4.0).[25] Similarly, O'Brien et al conducted a prospective, cohort study of 1719 US pregnant women and, after adjusting for confounders, found that pregnancy-onset habitual snoring, but not chronic habitual snoring, was independently associated with gestational hypertension (OR, 2.36; 95% CI, 1.48-3.77) and preeclampsia (OR, 1.59; 95% CI, 1.06-2.37).[27]

The mechanism for how breathing-related sleep disorders are related to hypertension in pregnancy has not been elucidated. Theories include: 1) chronic hypoxemia may increase the risk for fetal growth restriction and preeclampsia; 2) intermittent episodes of hypoxia may cause endothelial dysfunction that is also a component of the etiology of preeclampsia; and/or 3) higher levels of oxidative stress markers are found in women who snore, and oxidative stress markers may also be a trigger for placental changes that lead to preeclampsia.[26,28,29]

In nonpregnant populations, breathing-related sleep disorders are more common in persons with type 2 diabetes. A limited number of studies have demonstrated a positive relationship between breathing-related sleep disorders and gestational diabetes (GDM).[9,17,25,30] For example, a prospective study of healthy pregnant women found that the risk for OSA, as assessed by the Berlin Sleep Questionnaire,[22] was associated with a 3-fold increased rate of GDM (n = 26) when they were compared with those without GDM (n = 116), as measured by glucose testing (OR, 3.0l; 95% CI, 1.2-7.4) using univariate analysis.[30] Women with higher prepregnant BMI were significantly more likely to have both GDM and greater risk for OSA.[30]

A larger cross-sectional study of 1000 women that adjusted for BMI at birth, age, smoking status, and multifetal pregnancy reported a 2-fold increased risk of GDM with breathing-related sleep disorder symptoms: snoring

(adjusted OR, 2.1; 95% CI, 1.3-3.4); gasping/snorting (adjusted OR, 2.4; 95% CI, 1.4-4.3); and choking/stopped breathing (adjusted OR, 2.0; 95% CI, 0.9-4.3).[25] These findings suggest there is an association between breathing-related sleep disorders and GDM, independent of other GDM risk factors.

Other outcomes, including mode of birth, Apgar scores, preterm birth (PTB), and birth weight, have also been evaluated. A recent review of prenatal breathing-related sleep disorders concluded that the evidence of a link between habitual snoring and OSA with unplanned cesarean birth and Apgar score is limited.[23] There is, however, a trend toward more PTBs (less than 37 weeks' gestation) in women who snore habitually or have sleep apnea symptoms.[23] A prospective study of 1091 Greek women in the third trimester with singleton pregnancies found that severe snoring, measured by self-report, was associated with low birth weight (<2500 g; relative risk [RR], 2.6; 95% CI, 1.2-5.4) and intrauterine growth restriction, defined as birth weight less than 10% of predicted weight for gestation (RR, 2.0; 95% CI, 1.0-3.9). However, after adjusting for maternal age, education, smoking, and prepregnant BMI,[31] PTB was not associated with severe snoring in this study.[31]

Taken together, these studies suggest women are predisposed to developing breathing-related sleep disorders during pregnancy. Growing evidence indicates there may be a relationship between breathing-related sleep disorders and various adverse pregnancy outcomes, specifically preeclampsia and gestational diabetes, although the relationship has not been determined to be causal at this time. Standard criteria, research measures, and clinical tools (subjective and objective) are needed to better understand the impact of breathing-related sleep disorders on pregnancy outcomes.

Management of Breathing-Related Sleep Disorders

Several studies have evaluated the effects of treatment for breathing-related sleep disorders and pregnancy outcomes. Table 2 summarizes adverse pregnancy outcomes related to breathing-related sleep disorders and management strategies that have been evaluated. The most effective treatment for OSA is continuous positive airway pressure (CPAP).[8] CPAP uses air pressure to keep the upper airway open during sleep, thus preventing airway occlusion. CPAP works by pumping room air through a compressor that is connected by a hose to a mask that is worn over or against the nose. Reduced cardiac output, peripheral vascular resistance, and persistent high blood pressure at night have been associated with both OSA and preeclampsia.[9,32] There is some evidence that these

Table 2. Sleep Disorders, Associated Pregnancy Outcomes, and Management Strategies

Sleep Disorder	Associated Pregnancy Outcomes	Management (Options That Have Support in the Literature)
Breathing-related sleep disorder	Gestational hypertensive disorders[8] Gestational diabetes[30] Unplanned cesarean birth[25] Low birth weight[31] IUGR[31] Neonatal ICU admission[30]	Depends on extent of disorder, but may include: CPAP[34] Nasal strips or stenting[35] Sleep hygiene: avoidance of sedatives, elevation of the head, avoiding supine position[23] Control gestational weight gain Referral to specialist
Restless legs syndrome	Daytime sleepiness[36] Poor quality of life[35] Poor daytime functioning and safety[36] Depression[4]	Sleep hygiene and lifestyle changes: consistency of time to bed and time to rise; avoid alcohol, caffeine, nicotine; warm baths prior to bed; daily moderate exercise (but not just before bed)[12] Massage, acupuncture [37] Treat folate and iron deficiencies[38] Medications (see Table 3) Referral to specialist
Insomnia (primary or comorbid)	Daytime functioning and safety[16] Depression and anxiety in later pregnancy and postpartum[6,16,39] Pain perception in early labor, longer labor, and operative birth[40,41] PTB[31]	Sleep hygiene and lifestyle changes as noted under RLS Acupuncture may be helpful[3] Relaxation techniques such as yoga, massage[39] Treatment of depression, if present[16] Light therapy[40] Medications (see Table 3) Referral to specialist

Abbreviations: CPAP, continuous positive airway pressure; ICU, intensive care unit; IUGR, intrauterine growth restriction; PTB, preterm birth; RLS, restless legs syndrome.

adverse nocturnal physiological changes may be improved with regular CPAP use.[32] Research studies evaluating the efficacy of CPAP in pregnancy, however, are limited by small samples.[32,33]

One randomized controlled trial found that women with severe preeclampsia (N = 24) treated with CPAP had improvements in cardiac output and a reduction in total peripheral vascular resistance.[32] In addition, decreased cardiac output during sleep was correlated with lower fetal weight ($P < .001$) in the 24 women with severe preeclampsia as well as 15 nulliparous controls. In another study, 12 pregnant women diagnosed with either OSA or upper airway resistance disorder before pregnancy or in the first trimester were given CPAP to use nightly. Sleep and physiologic measures were assessed using polysomnography and sleep questionnaires at 3 times: before CPAP treatment, at 24 to 26 weeks' gestation, and at 32 to 34 weeks' gestation.[33] CPAP use reduced the number of apnea-hypopnea events. Investigators concluded that CPAP was safe, effective, and well tolerated during pregnancy.[33] Other interventions for breathing-related sleep disorders during pregnancy are discussed in the literature, but effectiveness during pregnancy has not been evaluated. For example, control of gestational weight gain, head elevation, avoidance of the supine position during sleep, and limited use of alcohol and sedatives have been recommended.[24,25] Nasal strips have been shown to be beneficial for upper airway resistance syndrome in nonpregnant persons.[35]

Not all treatments prescribed for the general population are recommended during pregnancy. The use of oral appliances has not been examined in pregnant women. Oral appliances are devices that advance the mandible or hold the tongue forward during sleep to allow for unobstructed breathing. Although considered less effective than CPAP for the treatment of moderate or severe OSA, oral appliances are prescribed for mild OSA or if CPAP cannot be tolerated.[8] Oral appliances work best when the person wearing them is in a supine position, a position that is not recommended for pregnant women.[42] Finally, the risks associated with surgery during pregnancy (eg, preterm birth, thromboembolic complications) preclude the use of elective surgical treatments. If a breathing-related sleep disorder is suspected during pregnancy, referral to a sleep center for further evaluation and treatment is recommended. Pregnant women with a history of OSA and CPAP use should be encouraged to continue CPAP and to seek ongoing evaluation at a sleep center because of changing oxygen requirements.[33]

Restless Legs Syndrome

Restless legs syndrome (RLS), also referred to as Willis Ekbom disease, is characterized by intensely uncomfortable sensations in the legs at rest or in the horizontal position that are relieved through leg movement.[43] Those with RLS describe the sensation in their limbs as creepy, crawly, jittery, and burning. These symptoms occur primarily in the evening and at night. The incidence in the general population is 3.5% to 10%.[37] Restless legs syndrome is more common in women and older adults. It is associated with renal disease, depression, anxiety, and diabetes mellitus.[44] Restless legs syndrome is linked to delayed sleep onset, sleep deprivation, and daytime fatigue, which influence the quality of life, safety, and workplace productivity.[36] Compared with nonpregnant women, pregnant women have a higher incidence of RLS. Between 27% and 30% of pregnant women experience RLS; symptoms are most severe in the third trimester.[45] New-onset RLS affects 13% to 20% of pregnant women,[37] but symptoms usually abate after birth for those who have new onset during pregnancy. For those with prepregnancy RLS, symptoms often worsen during pregnancy. Restless legs syndrome is often underdiagnosed in part because of clinicians' lack of awareness.[4,45]

The symptoms of RLS are easily confused with leg cramps, which occur at about the same rate.[46] Leg cramps are involuntary muscle contractions that often occur at night and are relieved by flexion of the extremity, whereas RLS symptoms, although also occurring at night, are nerve-type sensations of the legs and are not relieved by stretching.[46] Diagnosis of RLS can be ascertained via a thorough sleep history, including the 4 diagnostic criteria noted in Table 1. Patients who answer affirmatively to all criteria have RLS.

Hormonal changes associated with pregnancy have been studied as possible etiologies of new-onset RLS during pregnancy, but results have been inconclusive.[43] One small longitudinal study of 10 pregnant women with RLS matched with 9 women serving as controls found that women with RLS had higher levels of estradiol during pregnancy compared with controls ($P < .05$).[43] Yet no relationship was found between RLS and other hormones (ie, prolactin, progesterone, testosterone, follicle-stimulating hormone, and luteinizing hormone).[43]

Most sleep experts agree that iron (ferritin) or folate deficiency and/or malabsorption during pregnancy are associated with RLS in pregnant women.[12,38] Iron deficiency alters dopamine transporter functioning. Dopamine levels are in part responsible for sleep onset and wakefulness as well as smooth, purposeful muscle movement and activity. The altered dopamine transporter functioning associated with iron deficiency may account for the possible connection between iron deficiency indicators and RLS.[38]

In a secondary analysis of a sleep/fatigue longitudinal study of pregnant women, Lee et al assessed folate and ferritin levels at 5 times: before conception (n = 41), each trimester (n = 32, 32, and 30 in the first, second, and third trimesters, respectively), and postpartum (n = 31), and pregnant women who developed RLS (n = 7) were compared with healthy pregnant controls (n = 23).[38] Women with RLS had lower preconception folate and ferritin levels than healthy counterparts (between-group statistical analysis not reported) and lower folate throughout pregnancy (third trimester: $t = 2.4$, $P = .03$), although these values remained within normal limits.[38] In one quasiexperimental study, however, the association between iron, ferritin, and hemoglobin with RLS (n = 19) was not supported.[43] Small sample size in the studies of iron measures and RLS during pregnancy may have contributed to the discrepant findings.

Restless Legs Syndrome and Adverse Outcomes

Few studies have addressed outcomes in pregnant women with RLS. One longitudinal study found a higher rate of

Table 3. Medications for Sleep Disorders That Are Considered Safe in Pregnancy

Medications: Generic (Brand)	Clinical Considerations
Restless legs syndrome	
Ferrous sulfate plus vitamin C	Avoid in women with GI disease[45]
Codeine	OK for short-term use; CNS depression; maternal opioid dependence; neonate withdrawal[48]
Gabapentin (Neurontin)	CNS depression; pregnancy outcome data limited[48]
Zolpidem (Ambien)	CNS depression; abnormal thinking/behavior change; hazardous sleep-related activity; neonatal respiratory depression and withdrawal when used at end of pregnancy.[48]
Insomnia	
Codeine	OK for short-term use; CNS depression; maternal opioid dependence; neonate withdrawal[48]
Zolpidem (Ambien)	CNS depression; abnormal thinking/behavior change; hazardous sleep-related activity; neonatal respiratory depression and withdrawal when used at end of pregnancy.[48]
Diphenhydramine (Benadryl)[a]	Withdrawal symptoms and respiratory depression have been reported in newborns exposed in utero[48]
Doxylamine (Unisom)[a]	CNS depression[48]

Abbreviations: CNS, central nervous system; GI, gastrointestinal.
[a]Sleep aids such as these are not recommended in the treatment of chronic insomnia.[58]

depressed mood, as measured by the Profile of Mood States survey instrument ($t = 2.6$, $P = .012$), and delayed sleep onset, as determined by polysomnography ($t = 2.4$, $P = .019$), in pregnant women with RLS compared with those without RLS.[38] Although the impact of RLS on pregnancy outcomes has not been well studied, sleep deprivation during pregnancy, a known consequence of RLS, has been linked to adverse outcomes.[6]

Management of Restless Legs Syndrome

The goal of treatment is to decrease RLS symptoms and improve sleep; therefore, treatment depends on the incidence and severity of symptoms. Efficacy of RLS treatment is derived from small trials of 15 to 20 participants.[12] New-onset RLS will almost always subside after birth, so reassurances about the temporary nature of RLS may be comforting. Sleep hygiene and lifestyle changes are helpful. Regular sleep schedule, avoidance of dietary stimulants, stretching, and moderate exercise except immediately before bedtime have been recommended.[12,45] Massage therapy and acupuncture may be helpful, but more conclusive evidence is needed.[37]

Serum ferritin, serum folate, and a complete blood count should be assessed and abnormal results treated.[38,45] If serum ferritin levels are less than 50 mcg/L, ferrous sulfate (325 mg) plus vitamin C (500 mg) 3 times per day is recommended. When the ferritin level is higher than 50 mcg/L and symptoms decline, administration of ferrous sulfate and vitamin C should be discontinued.[46]

Table 3 and Table 4 summarize medications often used and medications not recommended for use by pregnant women for RLS and insomnia. There are no recommended medications for treating breathing-related sleep disorders during pregnancy. When RLS symptoms are severe, short-term use of medications with safety records in pregnancy may be effective in limiting symptoms.[43,44] For example, opioids such as codeine and antiepileptics such as gabapentin (Neurontin) and zolpidem (Ambien) are options for managing distressing RLS symptoms.[46,47] Dopamine agonists such as ropinirole (Requip) and pramipexole (Mirapex) are used for nonpregnant RLS patients with severe symptoms,[12,45,46]

Table 4. Medications for Sleep Disorders That Are Contraindicated in Pregnancy

Medications: Generic (Brand)	Reasons for Contraindication
Restless legs syndrome	
Dopamine agonists, such as ropinirole (Requip) or pramipexole (Mirapex)	Teratogenic effects in animal studies; no adequate well-controlled studies in pregnant women; early embryonic loss and postnatal growth inhibition in animal studies; ↓ maternal serum prolactin[48]
Insomnia	
Ramelteon (Rozerem)	Teratogenic effects in animal studies; may cause disturbance of reproductive hormonal regulation; no adequate well-controlled studies in pregnant women[48]
Melatonin	May reduce glucose tolerance; may alter hormone levels[48]
Ethanol	Teratogenic effects in humans; neonatal withdrawal; FAS; safe amount during pregnancy has not been determined[48]

Abbreviations: ↓, decreases; FAS, fetal alcohol syndrome.

but it is recommended that these drugs not be used during pregnancy.[46,47]

Insomnia

Insomnia is characterized as difficulty initiating or maintaining sleep, early-morning awakening, nonrestful sleep, or a combination of these complaints.[11] Frequency, duration, and daytime sequelae define the severity of the disorder. Comorbid insomnia (previously referred to as secondary insomnia) is associated with medical or psychiatric conditions, whereas, primary insomnia does not co-occur with other illnesses. Daytime consequences of insomnia include excessive sleepiness, low energy, irritability, negative mood,[11] and more work injuries, car accidents, and sick days.[1] Approximately 40% of individuals with insomnia also suffer from depression,[49] suggesting insomnia may exacerbate depression and vice versa. Sleep is essential to emotional well-being; thus, sleep and depression have a complex and bidirectional interconnection.

Transient or intermittent insomnia from periods of stress, life crises, or illness is common. More than a third of adults report occasional insomnia in the last year, and 10% have had significant daytime impairment or distress because of insomnia.[14,49] More than 80% of pregnant women experience insomnia symptoms at some point during pregnancy,[3,5,14] with the highest prevalence of insomnia and most wakefulness after sleep onset occurring in the third trimester.[3,5] A diagnosis of insomnia is usually made via self-report sleep history. Sleep diaries are a simple way for health care providers to ascertain duration and patterns of sleep over a week or more. A daily sleep diary provides information about bedtime, sleep onset, nocturnal awakenings, awake time, and subjective evaluation of sleep quality.[49]

Common discomforts experienced by pregnant women, including lower back pain, nocturia, fetal movement, breast tenderness, and leg cramps,[46,50] negatively affect sleep quality and quantity.[50,51] The interplay of increased estrogen and progesterone is thought to contribute to insomnia during gestation. Estrogen and progesterone influence sleep stages, nocturnal breathing, and other hormonal levels (eg, cortisol-melatonin ratio).[14] Higher levels of estrogen decrease the time in rapid eye movement sleep, an essential stage of sleep architecture. Progesterone and cortisol share binding sites on corticosteroid-binding globulin. Therefore, an increase of progesterone levels during pregnancy leads to higher levels of free cortisol, which increases arousal.[52]

Insomnia and Adverse Outcomes

The social implications of insomnia during pregnancy and postpartum include disruption in a woman's relationship with her partner and family and interference with mother-infant bonding.[53] Established daytime consequences of insomnia in the general public (eg, functioning and safety) are likely to apply to pregnant women; however, literature is limited. Sleep deprivation early in pregnancy may be associated with mood disturbance later in pregnancy or postpartum.[54] Inflammatory markers have been hypothesized as the underlying mechanism in this association.[6] Persons with insomnia have higher levels of proinflammatory cytokines,[55] which are also seen in women who have preterm births, postpartum depression, and other adverse pregnancy outcomes.[6,31,54]

An association between insomnia and hypertension and diabetes in the general population has been found, and proinflammatory markers such as cytokines and C-reactive proteins are considered mediators.[55] Although insomnia, gestational diabetes, gestational hypertension, and preeclampsia are also each associated with higher levels of proinflammatory markers,[6,17] these adverse pregnancy outcomes have not yet been directly associated with insomnia during pregnancy.

Sleep deprivation in the third trimester also has been correlated with the perception of higher levels of pain in early labor,[40] longer labor, and operative birth.[41] Beebe and Lee[40] assessed rest-activity cycles and total sleep time using actigraphy, a wrist accelerometer device,[2] in 35 nulliparous women. They found reduced total sleep time during the 5 days before labor onset and lower total sleep time the night before labor onset. Less total sleep time the night before labor was associated with perception of a higher level of pain in early labor among women in spontaneous labor ($n = 20$; $r = -0.47$, $P < .05$).[40] Similarly, a prospective study of 131 primigravidas in their last month of pregnancy using both actigraphy and sleep diaries found that women who report less than 5 hours of sleep per night had longer labors and were 4.5 times more likely to have cesarean births.[41]

Micheli and colleagues studied 1091 pregnant women and found higher rates of PTB with decreased sleep duration. In a prospective cohort study from 2007 to 2009, women who reported at least 5 hours of sleep per 24 hours at 28 to 32 weeks' gestation had higher rates of PTB (RR, 1.7; 95% CI, 1.1-2.8) and even higher risk for medically indicated PTB (RR, 2.4; 95% CI, 1.0-6.4).[31] Taken together, these studies suggest an urgent need to address insomnia in pregnancy because of the health and financial implications of longer labor, cesarean births, and preterm births.

Management of Insomnia

Early intervention is recommended so that management strategies have sufficient time to impact sleep.[5] A comprehensive medical history can determine the sort of insomnia (eg, onset, maintenance, early awakening) and reveal environmental and behavioral factors, which help guide insomnia management. Identifying risk factors and ruling out other sleep disorders are essential to appropriate treatment.[17,41] The goal of management is to provide adequate quality and quantity of restful sleep. Sleep counseling focusing on sleep hygiene, dietary modifications, and sleep positioning can be helpful.[3,40] Research related to acupuncture,[3] massage, yoga,[5] and exercise[14] suggests these therapies may be effective treatments for insomnia during pregnancy.

Augmenting insomnia treatment with treatment for comorbid depression may alleviate both insomnia and depressive symptoms.[16] In a small convenience sample of 12 pregnant women with depressive symptoms, a chronobiologic multistage intervention composed of partial sleep deprivation and light therapy showed promising adherence and therapeutic results for treating both depression and insomnia.[56]

Pharmacologic treatments for insomnia during pregnancy should be short term because of the potential risk to the fetus. Low-dose opioids have been used and zolpidem (Ambien), a sedative-hypnotic, is not contraindicated in pregnancy.[14] Other prescription drugs used in the nonpregnant population are best avoided or used with extreme caution during pregnancy. Ramelteon (Rozerem), a melatonin receptor agonist for treatment of sleep-onset insomnia, may affect reproductive hormones, and its effect on the human fetus is not known.[57]

Although widely used as self-remedies, nonprescription antihistamine-/analgesic-type medications (over-the-counter sleep aids), herbal substances, and nutritional substances (eg, valerian and melatonin) are not recommended in the treatment of chronic insomnia.[58] Antihistamines (eg, Benadryl) and doxylamine (eg, Unisom) appear to be safe in pregnancy, although evidence for efficacy and safety is limited to a few studies.[58] Melatonin may alter hormone levels; evidence for use in pregnancy is unavailable.[57] Pregnant women need to be aware that nonprescription sleep aids cause central nervous system depression and drowsiness. Finally, alcohol is known to be harmful to the fetus, and there is no known safe dose.[57]

CLINICAL IMPLICATIONS OF PRENATAL SLEEP DISORDERS

Growing evidence suggests there is an association between disturbed sleep and adverse pregnancy outcomes, including hypertensive disorders in pregnancy, GDM, depression, longer and more painful labor, medically indicated PTB, and unplanned cesarean birth. The interaction between sleep and these outcomes is not fully understood but may be related to certain proinflammatory markers.[9,31] Successful treatment of sleep disorders in pregnancy has improved outcomes in a limited number of small studies (ie, CPAP use by women with preeclampsia improved nighttime cardiac output, which is related to intrauterine growth restriction[32]; treatment for insomnia decreased depression during pregnancy[56]).

Findings of this literature review suggest that clinicians 1) become aware of the importance of adequate, restful sleep during pregnancy and 2) take the time to investigate sleep quality, quantity, patterns, and daytime functioning during routine prenatal visits. Detailed questioning is warranted for women who report disturbed sleep and daytime consequences. Women at risk for hypertensive disorders of pregnancy, GDM, and PTB at the onset of pregnancy and women with comorbid conditions that are risk factors for sleep disorders, such as obesity and depression, may need more comprehensive screening. For example, overweight or obese pregnant women can benefit from assessment of snoring, gasping, choking, or irregular breathing. Pregnant women with depression or anxiety should be asked about insomnia symptoms.

Several sleep screening tools are available for gathering key data about women's sleep; however, additional validation in pregnant women is needed. For instance, the Adult Sleep Assessment is easily completed and provides broad information using only 7 sleep-related items.[59] Documentation of sleep using a sleep diary is another way to recognize problem areas. The root cause of the sleep problem(s) often can be identified through a thorough assessment. Once the problem is identified, targeted behavior or lifestyle changes to improve sleep can be discussed. Medications may be necessary. Referral to a sleep specialist or sleep center for further testing is warranted if symptoms of other sleep disorders are identified (eg, obstructive sleep apnea) or if suggested lifestyle changes are ineffective. Referral to a mental health provider is indicated when depression/anxiety is suspected.

CONCLUSIONS

Breathing-related sleep disorders, restless legs syndrome, and insomnia are common sleep disorders of pregnancy that can have adverse consequences for both mother and fetus. Proinflammatory markers, higher in persons with sleep disorders during pregnancy, may be linked to adverse pregnancy outcomes. Treatment of sleep disorders in pregnancy has been shown to improve outcomes in a limited number of small studies.[33,56] Pregnant women will benefit from the routine assessment of sleep using brief, validated tools. Nonpharmaceutical management options, such as counseling on sleep hygiene and lifestyle changes, are safe and effective treatment options. Medications are available but not recommended as first-line management. The benefits of medications must be weighed against potential risks in individual cases. Additional studies are needed to understand the relationship between disturbed sleep and adverse outcomes of pregnancy. Large, well-designed studies are warranted to test various treatment options for women with sleep disturbance during pregnancy.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to disclose.

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REFERENCES

1. National Sleep Foundation. Women and Sleep Research. 2009. Available at: http://www.sleepfoundation.org/article/sleep-topics/ pregnancy-and-sleep. Accessed October 12, 2009.
2. Ram S, Seirawan H, Kumar S, Clark G. Prevalence and impact of sleep disorders and sleep habits in the United States. *Sleep Breath.* 2010;14:63-70.
3. deSilva J, Nakamura M, Cordeiro J, Kulay L. Acupuncture for insomnia in pregnancy– a propective, quasi-randomized controlled study. *Acupunct Med.* 2005;23:47-51.
4. Facco FL, Kramer J, Ho KH, Zee PC, Grobman WA. Sleep disturbances in pregnancy. *Obstet Gynecol.* 2010;115:77-83.

5.Field T, Diego M, Hernandez-Reif M, Figueiredo B, Schanberg S, Kuhn C. Sleep disturbances in depressed pregnant women and their newborns. *Infant Behav Dev.* 2006;30:127-133.
6.Chang JJ, Pien GW, Duntley SP, Macones GA. Sleep deprivation during pregnancy and maternal and fetal outcomes: is there a relationship? *Sleep Med Rev.* 2010;14:107-114.
7.American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4th ed. Washington, DC: The American Psychiatric Association; 2000.
8.Champagne KA, Kimoff RJ, Barriga PC, Schwartzman K. Sleep disordered breathing in women of childbearing age & during pregnancy. *Indian J Med Res.* 2010;131:285-301.
9.Izci-Balserak B, Pien GW. Sleep-disordered breathing and pregnancy: potential mechanisms and evidence for maternal and fetal morbidity. *Curr Opin Pulm Med.* 2010;16:574-582.
10.Epstein LJ, Kristo D, Strollo PJ Jr, et al. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. *J Clin Sleep Med.* 2009;5:263-276.
11.American Academy of Sleep Medicine (AASM). *International Classification of Sleep Disorders*. 2nd ed. Westchester, IL: American Sleep Disorders Association; 2005.
12.Ryan M, Slevin JT. Restless legs syndrome. *Am J Health Syst Pharm.* 2006;63:1599-1612.
13.Gao X, Schwarzschild MA, Wang H, Ascherio A. Obesity and restless legs syndrome in men and women. *Neurology.* 2009;72:1255-1261.
14.Miller EH. Women and insomnia. *Clin Cornerstone.* 2004;6(Suppl 1B):S8-S18.
15.Swanson LM, Arnedt JT, Rosekind MR, Belenky G, Balkin TJ, Drake C. Sleep disorders and work performance: findings from the 2008 National Sleep Foundation Sleep in America poll. *J Sleep Res.* 2011;20:487-494.
16.Okun ML, Kiewra K, Luther JF, Wisniewski SR, Wisner KL. Sleep disturbances in depressed and nondepressed pregnant women. *Depress Anxiety.* 2011;28:676-685.
17.Facco FL, Grobman WA, Kramer J, Ho KH, Zee PC. Self-reported short sleep duration and frequent snoring in pregnancy: impact on glucose metabolism. *Am J Obstet Gynecol.* 2010;203:142; e141-e145.
18.Perez-Chada D, Videla A, O'Flaherty M, et al. Snoring, witnessed sleep apnoeas and pregnancy-induced hypertension. *Acta Obstet Gynecol Scand.* 2007;86:788-792.
19.Ayrim A, Keskin EA, Ozol D, Onaran Y, Yiidirim Z, Kafali H. Influence of self-reported snoring and witnessed sleep apnea on gestational hypertension and fetal outcome in pregnancy. *Arch Gynecol Obstet.* 2011;283:195-199.
20.Olivarez SA, Ferres M, Antony K, et al. Obstructive sleep apnea screening in pregnancy, perinatal outcomes, and impact of maternal obesity. *Am J Perinatol.* 2011;28:651-658.
21.Pien GW, Fife D, Pack AI, Nkwuo JE, Schwab RJ. Changes in symptoms of sleep-disordered breathing during pregnancy. *Sleep.* 2005;28:1299-1305.
22.Netzer N, Stoohs R, Netzer C, Clark K, Strol K. Using the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome. *Ann Intern Med.* 1999;131:485-491.
23.Bourjeily G, Ankner G, Mohsenin V. Sleep-disordered Breathing in Pregnancy. *Clin Chest Med.* 2011;32:175-189.
24.Kapsimalis F, Kryger M. Obstructive sleep apnea in pregnancy. *Sleep Med Clin.* 2007;2:603-613.
25.Bourjeily G, Raker CA, Chalhoub M, Miller MA. Pregnancy and fetal outcomes of symptoms of sleep-disordered breathing. *Eur Respir J.* 2010;36:849-855.
26.Koken G, Sahin F, Cosar E, et al. Oxidative stress markers in pregnant women who snore and fetal outcomes: A case control study. *Acta Obstet Gynecol Scand.* 2007;86:1317-1321.
27.O'Brien LM, Bullough AS, Owusu JT, et al. Pregnancy-onset habitual snoring, gestational hypertension, and preeclampsia: prospective cohort study. *Am J Obstet Gynecol.* 2012;207:487.e1-e9.
28.Connolly G, Razak AR, Hayanga A, Russell A, McKenna P, McNicholas WT. Inspiratory flow limitation during sleep in pre-eclampsia: comparison with normal pregnant and nonpregnant women. *Eur Respir J.* 2001;18:672-676.
29.Fung AM, Wilson DL, Barnes M, Walker SP. Obstructive sleep apnea and pregnancy: the effect on perinatal outcomes. *J Perinatol.* 2012;32:399-406.
30.Reutrakul S, Zaidi N, Wroblewski K, et al. Sleep disturbances and their relationship to glucose tolerance in pregnancy. *Diabetes Care.* 2011;34:2454-2457.
31.Micheli K, Komninos I, Bagkeris E, et al. Sleep patterns in late pregnancy and risk of preterm birth and fetal growth restriction. *Epidemiology.* 2011;22:738-744.
32.Blyton D, Sullivan C, Edwards N. Reduced nocturnal cardiac output associated with pre-eclampsia is minimized with the use of nocturnal nasal CPAP. *Sleep.* 2004;27:79-84.
33.Guilleminault C, Kreutzer M, Chang JL. Pregnancy, sleep disordered breathing and treatment with nasal continuous positive airway pressure. *Sleep Med.* 2004;5:43-51.
34.Guilleminault C, Palombini L, Poyares D, Takaoka S, Huynh N, El-Sayed Y. Pre-eclampsia and nasal CPAP: Part 1. Early intervention with nasal CPAP in pregnant women with risk factors for pre-eclampsia: Preliminary findings. *Sleep Med.* 2007;9:9-14.
35.Raudenbush B. Stenting the nasal airway for maximizing inspiratory airflow: internal Max-Air Nose Cones versus external Breathe Right strip. *Am J Rhinol Allergy.* 2011;25:249-251.
36.Earley CJ, Silber MH. Restless legs syndrome: understanding its consequences and the need for better treatment. *Sleep Med.* 2010;11:807-815.
37.Balendran J, Champion D, Jaaniste T, Welsh A. A common sleep disorder in pregnancy: restless legs syndrome and its predictors. *Aust N Z J Obstet Gynaecol.* 2011;51:262-264.
38.Lee KA, Zaffke ME, Baratte-Beebe K. Restless legs syndrome and sleep disturbance during pregnancy: the role of folate and iron. *J Womens Health Gend Based Med.* 2001;10:335-341.
39.Breese McCoy SJ. Postpartum depression: an essential overview for the practitioner. *South Med J.* 2011;104:128-132.
40.Beebe K, Lee K. Sleep disturbance in late pregnancy and early labor. *J Perinat Neonatal Nurs.* 2007;21:103-108.
41.Lee KA, Gay CL. Sleep in late pregnancy predicts length of labor and type of delivery. *Am J Obstet Gynecol.* 2004;191:2041-2046.
42.Ferguson K, Cartwright R, Rogers R, Schmidt-Nowara W. Oral appliances for snoring and obstructive sleep apnea: a review. *Sleep.* 2006;29:544-562.
43.Dzaja A, Wehrle R, Lancel M, Pollmacher T. Elevated estradiol plasma levels in women with restless legs during pregnancy. *Sleep.* 2009;32:169-174.
44.Van De Vijver DA, Walley T, Petri H. Epidemiology of restless legs syndrome as diagnosed in UK primary care. *Sleep Med.* 2004;5:435-440.
45.Manconi M, Govoni V, De Vito A, et al. Restless legs syndrome and pregnancy. *Neurology.* 2004;63:1065-1069.
46.Hensley JG. Leg cramps and restless legs syndrome during pregnancy. *J Midwifery Womens Health.* 2009;54:211-218.
47.Djokanovic N, Garcia-Bournissen F, Koren G. Medications for restless legs syndrome in pregnancy. *J Obstet Gynecol Can.* 2008;30:505-507.
48.LexiDrugs Online. In: Rose BD, ed. Waltham, MA: UpTodate; 2012. Available at: http://www.uptodate.com/home/index.html. Accessed June 12, 2012.
49.Roth T. Insomnia: definition, prevalence, etiology, and consequences. *J Clin Sleep Med.* 2007;3(5 Suppl):S7-S10.
50.Lamberg L. Sleeping poorly while pregnant may not be "normal". *JAMA*. 2006;295:1357-1361.
51.Nishihara K, Horiuchi S, Eto H, Honda M. A long-term monitoring of fetal movements at home using a newly developed sensor: An introduction of maternal micro-arousals evoked by fetal movement during maternal sleep. *Early Hum Dev.* 2008;84:595-603.
52.Teran-Perez G, Arana-Lechuga Y, Esqueda-Leon E, Santana-Miranda R, Rojas-Zamorano JA, Moctezuma JV. Steroid hormones and sleep regulation. *Mini Rev Med Chem.* 2012;12:1040-1048.

53.Pires GN, Andersen ML, Giovenardi M, Tufik S. Sleep impairment during pregnancy: possible implications on mother-infant relationship. *Med Hypotheses*. 2010;75:578-582.
54.Skouteris H, Germano C, Wertheim E, Paxton S, Milgrom J. Sleep quality and depression during pregnancy: A propective study. *J Sleep Res*. 2008;17:217-220.
55.Grandner MA, Patel NP, Gehrman PR, Perlis ML, Pack AI. Problems associated with short sleep: bridging the gap between laboratory and epidemiological studies. *Sleep Med Rev.* 2010;14:239-247.
56.Moscovici L, Kotler M. A multistage chronobiologic intervention for the treatment of depression: a pilot study. *J Affect Disord.* 2009;116:201-207.
57.Zammit G. Comparative tolerability of newer agents for insomnia. *Drug Safety.* 2009;32:735-748.
58.Schutte-Rodin S, Broch L, Buysse D, Dorsey C, Sateia M. Clinical guideline for the evaluation and management of chronic insomnia in adults. *J Clin Sleep Med.* 2008;4:487-504.
59.Lee KA, Ward TM. Critical components of a sleep assessment for clinical practice settings. *Issues Ment Health Nurs*. 2005;26:739-750.

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