

Sleep and Its Disorders in Pregnancy

Sunil Sharma MD, FCCP; Rose Franco MD, FCCP

INTRODUCTION

By their third trimester of pregnancy, 97% of women report sleep disturbance. Sleep can be altered during pregnancy due to several reasons, including mechanical and hormonal. The importance of quality sleep and the negative impact of sleep disturbances in pregnancy are under-recognized by both patients and physicians. This is in part due to limited literature on this topic. The true incidence of sleep disorders in pregnancy is not known; however, due to growing awareness of the importance of sleep and sleep disorders in pregnancy, "Pregnancy Associated Sleep Disorders" is now recognized as a distinct clinical entity in the international classification of sleep disorders. In this review we will present a consolidated literature review on sleep changes in pregnancy and sleep disorders that may develop or be worsened in pregnancy.

SLEEP DEBT OF PREGNANCY

Pregnancy can and does result in profound changes in sleep quality. This is the result in part of mechanical factors such as low back pain, restless legs, leg cramps, nocturia, and abdominal discomfort. By the third trimester, 97% of women polled reported sleep disruptions.¹ Studies of the sleep architecture of the pregnant woman demonstrate increased light sleep (stage 1 sleep) and suppression of dream sleep (REM sleep), as well as more awakenings.² This can affect not only the sufferer's energy level but can also negatively impact their mood. Postpartum mothers typically spend 3 hours less a night asleep than they did prepregnancy.³ First-time mothers complain the most of disturbed sleep and mood changes.⁴ Mothers of pre-term infants have the most wake after sleep onset time (WASO) in the post-

partum period.⁵ Poor sleep preterm can add to the sleep debt that occurs during the first weeks of postpartum. Wilkie and Shapiro found an association between accumulated sleep loss during the first week of postpartum and depressed mood.⁶ The relationship between poor sleep and postpartum depression is difficult to decipher. Large prospective studies utilizing mood surveys are needed to fully understand the link. Much of the sleep disruption of the new mother is unavoidable (child care) and therefore experienced health care providers continue to counsel their patients to "sleep while the baby sleeps."

EFFECT OF HORMONES

There is marked increase in the levels of progesterone and estrogens in pregnancy. Estrogen decreases REM sleep.⁷⁻⁹ Estrogen can cause edema of upper airway mucosa, contributing to an increase in upper airway resistance.

Progesterone, on the other hand, has been shown to increase non-REM sleep.¹⁰ Progesterone increases ventilation and respiratory alkalosis. Respiratory alkalosis can lead to instability in respiratory pathways, which may become unbalanced in sleep.¹¹ The resulting hypocapnia has been shown to lead to episodes of central apneas during non-REM sleep in non-pregnant subjects,^{12,13} however this has not been directly tested in pregnancy. Conversely, increased levels of progesterone may protect upper airway patency.¹⁴

Progesterone shares binding sites on corticosteroid-binding globulin.¹⁵ Hence, an increase in progesterone levels in pregnancy also increases levels of free cortisol.¹⁶ Pregnant women who sleep poorly have been found to have a low cortisol-melatonin ratio. Conversely, the ratio is reported to be high in psychiatric depression causing disturbed sleep.¹⁷ It has been hypothesized that determining the cortisol-melatonin levels may help differentiate primary sleep disturbance from depression-induced sleep disturbances.^{18,19} Studies have not revealed any changes in Melatonin levels compared to non-pregnant states.²⁰

Doctors Sharma and Franco are with the Department of Pulmonary and Critical Care Medicine, Medical College of Wisconsin, Milwaukee, Wis. Please address correspondence to Sunil Sharma, MD, FCCP, Department of Pulmonary and Critical Care Medicine, 9200 W Wisconsin Ave, Milwaukee, WI 53226-3596; e-mail ssharma2@mcw.edu.

SNORING IN PREGNANCY

Small population survey studies have revealed a more than 4-6 times increase in the incidence of snoring in pregnancy (14%-23%)^{21,22} as compared to nonpregnant women (4%). The true incidence is suspected to be higher as women tend to under-report snoring.²³ In special circumstances the incidence is much higher and the relevance more important. Edwards et al documented 100% incidence of upper airway flow limitation in preeclamptic women. They also reported an increase in blood pressure during sleep (nondippers), which improved with nasal continuous positive airway pressure (CPAP).¹¹ A Swedish population survey study of 502 pregnant women reported that snoring women had a 2-fold greater incidence of hypertension, preeclampsia, intrauterine growth restriction, and lower APGAR scores at birth.²² Douglas et al used acoustic reflection to measure upper airway dimensions and documented that preeclamptic women had upper airway narrowing in both upright and supine position,²⁴ characteristics that are consistently seen in obstructive sleep apnea sufferers.

SLEEP-DISORDERED BREATHING IN PREGNANCY

The incidence and prevalence of obstructive sleep apnea (OSA) during pregnancy is unknown. Despite physiological changes conducive to development of OSA during pregnancy as discussed above, some factors may have a protective effect against OSA. Elevated levels of progesterone increase respiratory drive and pharyngeal muscle tone.²⁵ Reductions in REM sleep time, the sleep stage most readily affected by sleep apnea,²⁶ and a tendency to sleep in the lateral decubitus position in late pregnancy may also protect against sleep apnea. Additionally, pregnancy-induced respiratory alkalosis predisposes to sleep onset central sleep apnea, which may create sleep onset insomnia.

Large prospective trials measuring the effects of pregnancy on sleep apnea are lacking; however several reports suggest that pregnancy may precipitate or worsen obstructive sleep apnea.²⁷⁻²⁹ Fiensilver et al³⁰ recorded decreased basal oxygen saturation in sleep as well as a significant increase in number of episodes of desaturations in late pregnancy compared to controls. While recent data suggest that normal pregnancy in a normal weight woman is not associated with precipitation of sleep apnea, the same study found significantly more sleep disordered breathing in obese mothers than subjects with normal weight.³¹ Unfortunately, as the population gets more and more obese (60% of adults

are overweight in the United States), the obese pregnant woman will become the more common patient.

Maternal and Fetal Complications Associated with Sleep-Disordered Breathing (SDB) in Pregnancy

Snoring has been associated with maternal hypertension and preeclampsia.^{22,24} With the strong link between sleep-disordered breathing and hypertension in the general population,³² it is possible that SDB may actually induce hypertension/preeclampsia during pregnancy; however this needs to be explored further. Reports available on fetal outcome in women with snoring or OSA demonstrated adverse outcomes including intrauterine growth restriction.^{22,24,33-35,37}

Treatment of SDB in Pregnancy

Weight loss often proves beneficial in reducing or eliminating sleep apnea in obese patients.³⁹ Nasal CPAP has been used successfully in pregnant women with Obstructive Sleep Apnea Syndrome (OSAS) with good outcome.^{38,41,42} Those pregnant women with OSA who had infants of normal birth weight tended to have been diagnosed and treated with CPAP before the third trimester.^{38,40}

In order to reduce the risk for OSAS in pregnancy, health care providers should counsel their overweight patients considering pregnancy about the risks associated with obesity in the pregnant state.

Sleeping in the lateral decubitus position can be adjunctive therapy for sleep apnea. Tracheostomy has been performed in severe cases of OSAS.³⁶ This form of treatment is best reserved for life-threatening sleep apnea. There is some evidence that nocturnal oxygen may be safely used in sleep apnea^{43,44} and may reduce frequency of apneas and improve oxygenation⁴⁵ but should only be used as a last resort for those intolerant to CPAP and under the supervision of a knowledgeable physician. Oxygen can actually prolong the apneas and does not improve sleep quality. For those patients who have already been diagnosed and are being treated for OSA who become pregnant, the return of snoring, daytime sleepiness, and new hypertension may signal subtherapeutic CPAP and should prompt the physician to reevaluate the CPAP effectiveness.

RESTLESS LEG SYNDROME (RLS)

Restless Leg Syndrome is a common condition. Twenty five percent of pregnant women have experienced this condition.^{46,47} The International RLS Study Group defines RLS as (1) the urge to move legs, usually accompanied or caused by uncomfortable and unpleasant sensation in the legs, which are (2) worse during

rest/inactivity, (3) partially or totally relieved by movement, and (4) worse at night/in the evening.⁴⁸ The sensations usually worsen in the evening and are relieved nearly instantly by movement of the limb. The patient may also develop limb movements that they cannot suppress, especially at bedtime. This results in trouble getting to sleep or staying asleep. RLS is diagnosed based on history in 90% of cases. This condition may respond very well to iron supplementation when the ferritin level is less than 50µg/dL. Some studies have found that lower levels of folate are associated with RLS during pregnancy, which has led to recommendations for treating affected women with folate, although this needs further evaluation.⁴⁹ Most drugs used to treat idiopathic RLS fall into category C (uncertain safety in pregnancy—animal studies show an adverse effect, no human studies) with the exception of Pergolide, which is category B (presumed safety based on animal studies).⁵⁰ Calf stretches, massage, warm or cold compresses, and restriction of carbohydrate-rich foods, nicotine, and caffeine can all help reduce these sensations. Many over-the-counter sleep aids can worsen this condition. Physicians should advise their patients that diphenhydramine and other antihistamine containing medications can worsen these sensations. For the extreme cases, codeine and permax can be used to help improve sleep.

PARASOMNIAS IN PREGNANCY

Parasomnias are sleep disorders arising during sleep. These include sleep talking, sleep walking, teeth grinding, nightmares, and night terrors. While these conditions are common in the general population, there is no evidence that they occur with greater frequency in the pregnant patient. In fact, Hedman et al surveyed 325 pregnant women and reported a decline in frequency of most parasomnias in pregnancy.⁵¹ If the pregnant patient is complaining about one of these conditions, it is likely the result of psychological stress. Often talking about the fears or stressors will result in the nighttime symptoms abating. New onset or increased sleep walking, night terrors, or nightmares may signal an undiagnosed sleep disorder such as RLS, OSA, or snoring with increased awakenings due to upper airway resistance.⁵²

INSOMNIA IN PREGNANCY

Insomnia in pregnancy is very common and is usually due to awakenings after going to sleep (sleep maintenance insomnia). This is again likely due to a combination of physiological changes that occur throughout the

pregnancy. Mechanical factors are especially important in the third trimester and most women experience shortness of breath while supine. This has a significant impact on pregnant women's ability to initiate and maintain sleep.⁴⁵ Brief naps (less than 20 minutes) before 1 PM can be helpful in providing relief of the fatigue. Longer naps closer to bedtime can exacerbate insomnia. Other measures to improve insomnia include practicing relaxation techniques, avoiding caffeine, limiting fluid intake after 6 PM and managing low back pain with massage, local heat application, and pillow support.¹⁶

Additionally, sleep disorders can develop or worsen during pregnancy and may result in increased awakenings. RLS can result in difficulty getting to sleep and staying asleep, and OSAS can result in difficulty staying asleep. Pregnancy-induced respiratory alkalosis predisposes to sleep onset central sleep apnea, which may create sleep onset insomnia. Screening the patient for snoring and restless legs symptoms can help determine if medical intervention is necessary.

PHARMACOLOGY

Administration of pharmacological agents before, during, and after pregnancy can have significant implications for both mother and fetus and hence should be carefully reviewed. Category C agents are best avoided as unknown fetal effect may exist.⁵³

Insomnia should first be addressed with behavior changes, but if no sleep disorder is suspected and the insomnia is resistant to conservative measures, pharmacological agents of choice are diphenhydramine or zolpidem (category B). However, no hypnotics are considered safe in nursing mothers as most are excreted in milk. If the drug is used for prolonged periods, breastfeeding should be discontinued.

Pregnant patients with narcolepsy should avoid stimulants. However Pemoline (category B) can be used if needed. Caution is recommended with this drug because of rare cases of hepatic necrosis.

SSRIs and tricyclic antidepressants are used in major depression in pregnancy under expert guidance but may cause or exacerbate RLS/PLMS. Most antidepressants are category C or D for safety in pregnancy.

CONCLUSION

Pregnancy is a time of great change in a woman's life. Likewise, sleep is altered and may not return to pre-pregnancy quality for several years after the birth of the child. Some sleep disturbances are a harbinger of sleep disorders. If they are not recognized and treated, there

can be significant negative effects for the patient and her unborn child. Sleep apnea syndrome occurs in about 4% of women, and the obese pregnant woman should be screened for snoring severity, nocturnal awakening, and daytime fatigue. If present, a sleep study should be done and CPAP initiated as soon as possible if OSAS is diagnosed. RLS is common in pregnancy and can be a significant cause of sleep disruption. Simple measures and iron supplementation can result in improved sleep and quality of life. Poor sleep pre-term may increase the mother's risk for post-partum depression. Identification of poor sleep habits and sleep disorders can significantly reduce the depressive symptoms.

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