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Sleep Deprivation during Pregnancy and Maternal and Fetal Outcomes: Is There a Relationship?

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Abstract

Sleep duration in the population has been declining. Women occupy an increasingly prominent place in the work force without reducing most of their responsibilities at home. Consequently, sleep needs are often pushed to the bottom of women's daily priority list. Prior research has indicated that sleep deprivation is associated with higher levels of pro-inflammatory serum cytokines. This is important because higher plasma concentrations of pro-inflammatory serum cytokine levels are associated with postpartum depression and adverse birth outcomes such as preterm delivery. However, little research has directly examined how sleep deprivation may affect maternal and fetal outcomes. This review summarizes the existing data on the effect of sleep deprivation during pregnancy on maternal and fetal outcomes.

We review supporting evidence for the hypotheses that sleep deprivation during pregnancy increases the risk of preterm delivery and postpartum depression, and that systematic inflammation is the causal mechanism in the association. Prior research on sleep in pregnancy has been limited by varying data collection methods, subjective self-reported sleep measures, small and non-representative samples, cross-sectional designs; descriptive or non-hypothesis driven studies. Future research with longitudinal study designs is needed to allow examination of the effect of sleep deprivation on adverse maternal and fetal outcomes.

Keywords

Sleep; Sleep deprivation; postpartum depression; preterm birth; inflammation

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Introduction

Sleep deprivation has become a major public health concern in the United States because of its detrimental effects on cognitive functioning over time, accidents and errors in the workplace, and alterations in metabolic and endocrine function of individuals [1]. Increasing evidence also suggests that sleep deprivation may increase mortality [1,2]. To date, despite the multiple competing demands women face in modern society [3], 75% of sleep research has been conducted in men [4], although there is increased interest in sleep research in women. To meet the demands and opportunities of our modern society, having adequate sleep is often at the bottom of the priority list for American women who try to balance work and family life [3].

During pregnancy and the postpartum period, women are at particular risk for sleep restriction because of the physical changes of pregnancy and the need to provide frequent infant care. Pregnancy and the postpartum period are also times when women are at a heightened risk of depression [5]. Maternal depression has been well documented to adversely impact maternal-child relationships, parenting practices, family functioning, and children's development and general well-being [5]. Several authors have hypothesized that sleep deprivation may increase the risk of adverse maternal and fetal outcomes. Limited evidence also suggests an association between sleep problems and maternal depression. This article reviews what is currently known about the relationship between sleep duration during pregnancy and maternal and fetal outcomes, with a special emphasis on preterm delivery and postpartum depression.

The prevalence of sleep deprivation

Although sleep needs may vary by age and gender, the National Sleep Foundation has recommended 7 to 8 hours of sleep per 24 hours for adults [6]. Research have shown that sleep duration in healthy young adults stabilized at approximately 8.2 hours after elimination of prior sleep debt [7]. However, studies have indicated that the self-reported sleep duration of Americans has decreased by 1.5 to 2 hours over the past 40 years, to a mean of 7-7.9 hours [8-10]. Average nightly sleep duration has declined even over the past several years. In a population based study of objectively measured sleep patterns in 2000, Jean-Louis and associates [10] reported that adults age 40-64 were sleeping only an average of 6.22 hours. National data also indicate that a greater percentage of adult Americans reported sleeping 6 hours or less in 2004 than in 1985 based on subjective self-report data [8]. Specifically, more than 30% of adult men and women between the ages of 30 and 64 years report sleeping less than 6 hours per night in 2004 [8]. Thus, a substantial proportion of American adults suffer from sleep deprivation.

In examining the decline in average sleep time in the general population, American women may be bearing more of the burden of sleep deprivation than men, even though objective sleep studies had reported that women may have better sleep quality than men in general [11,12]. Sleep deprivation will be referred to here as preventing individuals from obtaining their usual amount of sleep within a 24-hour period [13]. In a questionnaire-based study of 529 young adults (mean age 32.4 years), Lindberg and coworkers observed a significantly longer self-reported total sleep time and estimated hours of sleep they need among females compared to male subjects [11]. Furthermore, it was found that the difference between the two above-mentioned variables was significantly higher among women compared to men, indicating a higher level of sleep deprivation among women [11]. Similarly, in a population-based study, Hublin and associations reported that 24% of women in the study experienced insufficient sleep compared to 16% in men. In sufficient sleep was defined as a difference of 1 hour between the self-reports of the total sleep time and the estimated hours of sleep needed [14]. Women in today's society have grown to occupy a more prominent place in the work force, without

reducing most of their responsibilities at home. Women struggle to balance family and work demands and are increasingly time-pressed and pulled in multiple directions with work, play groups, household responsibilities, care of family members, school activities, and other responsibilities [3]. Consequently, sleep is often pushed to the bottom of women's daily priority lists, with women in the 2007 NSF survey reporting more frequently that they ran out of time for sleep (52%) than other work, family or leisure activities [15]. This also manifests in the observation that one in four women report suffering from daytime sleepiness, and nearly 50% indicate that they have driven while drowsy [16].

Effect of Sleep Deprivation

In 2004, the U.S. Surgeon General observed that sleep disorders, sleep deprivation, and sleepiness affect as many as 70 million Americans and result in \$16 billion in annual health-care expenses and \$50 billion in lost productivity [17]. The effects of sleep deprivation are cumulative, such that a mild reduction in sleep duration each night could, over time, result in significant functional deficits [18]. Chronic sleep deprivation has detrimental effects on fat and glucose metabolism, inflammatory processes, learning and cognitive functioning, social relationships, job performance, mental health, and overall quality of life [1,19,20]. Furthermore, at the cellular level, even a single brief episode of acute sleep restriction (4–8 hours) is associated with robust declines in immune cell activity [20]. Prior research has demonstrated that sleep deprivation alters the immune response and significantly increases circulating levels of inflammatory markers such as interleukin-1 (IL-1), IL-2, IL-6, tumor necrosis factor (TNF) α , and C-reactive protein [20-23]. In addition, epidemiologic data support the finding that prolonged sleep restriction (less than 6 hours per night) or prolonged extended sleep duration (more than 9 hours sleep per night) are associated with increased mortality [2]. For example, Hublin et al reported that short sleep (< 7 hours) duration increased risk of mortality by 26% in men and 21% in women compared to individuals with average length of sleep (7-8 hours) per 24 hours but the gender difference in the effect of short sleep on the risk of mortality was not statistically significant [2]. In the same study, long sleep (> 8 hours) duration also increased risk of mortality by 24% in men and 17% in women compared to individuals with average length of sleep (7-8 hours) per 24 hours [2].

Sleep duration during pregnancy

Sleep in women is affected by physiologic changes in neuroendocrine hormones, body temperature, mood, and emotional state during puberty, the menstrual cycle, pregnancy and menopause [24]. In the past decade, sleep patterns and problems in women in the childbearing years have received increased research interest. However, few studies have focused on pregnancy. Using subjective sleep data, Hedman and coworkers surveyed 325 pregnant Finnish women and found that the mean hours of total self-reported sleep per 24 hours before pregnancy was 7.8 hours [25]. Total sleep time increased during the first trimester to 8.2 hours, decreased during the second trimester to 8.0 hours, and remained unchanged from antepartum sleep time at 7.8 hours in late pregnancy [25]. In a cross-sectional survey of 127 pregnant women at varying gestational ages, Mindell and Jacobson [26] observed similar findings of self-reported mean total sleep time during weekdays of 7.7 hours during pregnancy. Furthermore, in the Mindell study, women reported that the average amount of sleep they needed was 8.2 hours, greater than the self-reported mean total sleep time, indicating the presence of sleep deprivation during pregnancy.

Using objective sleep measures, other studies found that pregnant women sleep about 30 minutes less than they subjectively report [27-29]. Hence, it is important to utilize objective sleep measurement tools such as polysomnography or actigraphy to reduce measurement error in estimating sleep duration. In one study, Lee and colleagues [29] assessed the sleep patterns

of 33 women during pregnancy with in-home polysomnography and reported that mean total sleep time increased from 6.8 hours at pre-pregnancy baseline to 7.4 hours by 11-12 weeks gestation. However, mean total sleep time returned to the baseline level of 6.9 hours at 36 weeks gestation. Although polysomnography may have underestimated pre-pregnancy sleep duration because of the first night effect, this pattern is similar to self-reported assessments of total sleep time that demonstrate an increase in total sleep time during the first trimester and a decrease in sleep time during the third trimester [30]. Using actigraphy, Elek and associates [27] examined the length of sleep during the last trimester of pregnancy in 24 nulliparous couples and observed that the mean hours of sleep were 7.3, 7.6, and 7.3 at the seventh, eighth, and ninth month of pregnancy, respectively. In contrast to these observations, Hertz and colleagues [31] reported total sleep time per 24 hours did not differ between 12 pregnant women and 10 non-pregnant controls (6.2 hours vs. 6.3 hours, respectively) at 30-38 weeks gestation. However, these findings were based on cross-sectional one-night polysomnography data of women at varying gestation ages and did not account for intra-individual variation in sleep time before pregnancy and during the antepartum period.

To summarize, descriptive studies of sleep duration throughout pregnancy have found an increase in total sleep time and daytime sleepiness during the first trimester which suggests that sleep needs may increase in early pregnancy [25-28,31]. In contrast, the third trimester is characterized by a decrease in sleep time [25,28,29,31,32]. Although previous studies suggest an increase in sleep need in early pregnancy, the optimal duration of sleep in pregnancy is unknown. The change in sleep needs are likely due to the physical and hormonal changes of pregnancy. The variation in measured sleep duration during pregnancy across studies is likely due to methodological differences, including failure to account for frequency and duration of daytime naps and use of subjective vs. objective assessment of sleep.

Effect of sleep deprivation on maternal and fetal health

Despite the potential adverse effect of sleep deprivation on maternal and fetal outcomes, little research has investigated the prevalence of and risk factors for sleep deprivation during pregnancy and the postpartum period, or the relationship between sleep and pregnancy outcomes. Limited research has indicated that poor sleep may be detrimental to the labor and delivery process. In a prospective observational study of 131 healthy primiparous women in their ninth month of pregnancy, Lee and Gay [28] used both objective (48-hour actigraphy) and subjective (sleep log and questionnaire) sleep measures to test the hypothesis that fatigue and sleep disturbance in late pregnancy were associated with labor duration and delivery type. They discovered that women averaging less than 6 hours of sleep per night during the last month of pregnancy had a significantly longer mean duration of labor (29 hours vs. ≥ 20 hours) and a higher rate of cesarean births (< 6 hours: 37%; 6-6.9 hours: 34%; 7+ hours: 11%, p -value < 0.05) than women getting more than 6 hours of sleep [28]. However, whether decreased sleep duration was the proximate cause of longer labor, or reflective of physical or emotional stressors that may also impact labor duration, was not examined. In a descriptive correlational study of 35 nulliparous women, Beebe and Lee [33] used wrist actigraphy monitors to measure sleep duration in the last 5 days of pregnancy and assessed its relationship with pain perception and fatigue during early labor. They observed that less total sleep time on the night before hospitalization was associated with elevated perception of pain and discomfort during labor [33].

Researchers have also investigated the relationship between sleep duration and risk of adverse pregnancy outcomes in physician trainees. Training in medicine is characterized by long hours and intense psychological stress, particularly during the residency years. In one study of 45 university-affiliated residency programs, Osborn and associates found that one half of the female residents (physicians in training) averaged at least one night per week without sleep

during the first and second trimester, and 44% averaged one night per week without sleep during the third trimester [34]. In the same study, pregnant medical residents were more likely to experience preterm labor compared to the wives of male medical residents [34]. Using a nationally representative sample of 4,412 women residents who worked long hours and often suffer more sleep deprivation, Klebanoff et al reported that women residents, compared to wives of their male classmates, had higher rate of preterm labor (11% vs. 6%) and preeclampsia (8.8% vs. 3.5%). Furthermore, the study examined pregnancy outcomes of a subset of women residents who work 100 hours or more per week during pregnancy and were likely to experience sleep deprivation due to long work hours. It was observed that women residents who worked 100 hours or more per week during first trimester of pregnancy had a 9.8% risk of preterm delivery, as compared with 4.6% for residents who worked less than 100 hours per week ($p = 0.0012$) [35].

In summary, on the basis of the limited data, there appears to be an association between short sleep duration and adverse maternal and fetal outcomes. Specifically, women who are sleep deprived during pregnancy may experience longer labor, more pain and discomfort during labor, higher rates of preterm labor and cesarean section. Given the magnitude of the potential adverse impact of sleep deprivation on maternal and fetal outcomes during pregnancy, it is important to understand the prevalence of and risk factors for sleep deprivation in pregnancy. In the general population, risk factors for sleep deprivation include low income level, living alone, low self-perceived societal status, minority race/ethnicity, urban environment, and long work hours [36]. Although it is likely that similar risk factors exist for pregnant women, whether pregnancy-specific risk factors exist is unknown [37]. A greater understanding of these risk factors could aid health professionals in identifying women who are at higher risk of sleep deprivation so that timely interventions could be made to maximize maternal and fetal well-being.

Sleep Deprivation during Pregnancy and Risk of Spontaneous Preterm Delivery

Preterm Delivery as a major public health issue—Preterm birth refers to infants delivered at less than 37 weeks of gestation. The obstetric precursors that lead to preterm birth are: 1) delivery for maternal or fetal indicators (e.g. pre-eclampsia, placenta previa, antepartum bleeding, or threatening fetal asphyxia), in which labor is either induced or the infant is delivered via pre-labor caesarean section; 2) spontaneous preterm labor with intact membranes, and 3) preterm premature rupture of the membranes, regardless of whether delivery is vaginal or by caesarean section [38]. Births that follow spontaneous preterm labor and preterm premature rupture of the membranes are together referred to spontaneous preterm births [38]. The current preterm delivery rate in the US is 12% to 13%, increased from 9.5% in 1981, despite advancement of our knowledge in risk factors and mechanisms related to preterm labor and interventions designed to reduce it [38].

Preterm delivery is the leading cause of perinatal morbidity and mortality; it accounts for 75% of perinatal mortality and more than half of long-term morbidity [38]. It is also an independent risk factor for postpartum depression. Mothers of premature babies may awaken frequently at night well beyond the postpartum period because it takes premature babies much longer compared to term babies before they sleep through the night [39]. The resulting disrupted maternal sleep could increase the risk of postpartum depression [39].

Rationale for sleep deprivation as a determinant of spontaneous preterm delivery with inflammation as a causal mechanism—As 50% of preterm births are due to unknown causes, the mechanisms of preterm delivery remain poorly understood. Several mechanisms or pathways to preterm delivery have been proposed. They include infection or inflammation, utero-placental ischemia or hemorrhage, uterine overdistension, stress, and

other immunologically mediated processes [38]. There are also numerous maternal or fetal risk factors that have been associated with preterm birth, including maternal demographic characteristics, nutritional status, pregnancy history, present pregnancy characteristics, psychological characteristics, adverse behaviors, infection, uterine contractions and cervical length, and biological and genetic markers (Table 1) [38]. One potential risk factor that has received little attention in preterm birth research is sleep deprivation during pregnancy.

To examine potential mechanisms for the relationship between sleep and adverse maternal-fetal health outcomes, Okun and associates [40] showed that self-reported short sleep duration and poor sleep efficiency in both mid and late pregnancy in 19 healthy women were associated with higher levels of IL-6, a pro-inflammatory serum cytokine. It has been postulated that inflammatory cytokines may play a key role in mechanisms initiating labor that contribute to the etiology of spontaneous preterm birth [41,42]. Prostaglandin plays a major role in uterine contractions and inflammatory cytokines could stimulate prostaglandin production in gestational tissue, causing cervical ripening and promoting uterine contractions [43]. In support of this hypothesis, women who delivered prematurely have been found to have elevated amniotic fluid concentrations of inflammatory cytokines [41,42]. In one study, Arntzen and coworkers [41] obtained amniotic fluid samples from 3 groups of women – 39 women who delivered prematurely with established labor, 25 women who delivered prematurely via cesarean section without preterm labor, 33 women who delivered vaginally at term – to compare levels of inflammatory cytokines including TNF, IL-1, IL-6, IL-8 and soluble TGF β receptors. Elevated levels of IL-1, IL-6, and IL-8 were found in women in premature labor with no signs of infection, compared to samples from women who were not in parturition [41]. Similarly, Hillier and associates [42] observed increased levels of IL-6 and IL-1 in amniotic fluid samples from 32 women who delivered at or before 24 weeks of gestation compared to 18 women who delivered after 34 weeks.

At present, we are unaware of clinical studies that have directly examined the effect of sleep deprivation on the risk of preterm delivery. As previously described, arduous residency training among female physician trainees was associated with increased risk of preterm labor and preterm delivery [34,35]. Sleep deprivation as a result of long work hours may be a cause of the higher risk for adverse birth outcomes in female residents; however, neither subjective nor objective measures of sleep duration were collected. *More studies are needed to examine whether sleep deprivation is causal to the development of preterm labor and the specific mechanisms involved.*

Sleep Deprivation during Pregnancy and Risk of Postpartum Depression

Postpartum Depression—Depression can develop at any point in a woman's life, and it occurs across educational, economic, and racial or ethnic groups [44]. The onset of depression frequently occurs during the childbearing years [44]. Past research suggests that the rate of the onset of depression increases by three-fold in the months after childbirth [44], and depression is one of the most common complications of the prenatal and postpartum periods [44]. While childbirth is often a joyous event, it is also a time of great change in a woman's life. The increased demands of infant care, changes in family and marital relationships, and impact on work and social activities can all create significant stress.

Postpartum depression is defined as an episode of depression arising within 4 weeks of delivery and can last up to 6 months in duration [44]. Symptoms of depression include a persistent sad mood, loss of interest or pleasure in activities that were once enjoyed, significant change in appetite or body weight, sleep disturbance, physical slowing or agitation, fatigue or loss of energy, feelings of worthlessness or inappropriate guilt, difficulty concentrating, and recurrent thoughts of death or suicide [44,45]. Although symptoms of postpartum depression are similar to depression at any other times, they also include difficulty sleeping when the baby sleeps,

worrying about hurting the baby, feelings of inadequacy in the maternal role, and concerns for the well-being of the infant [44]. It is important to note the distinction between postpartum blues and postpartum depression. Postpartum blues refers to a mild and transient form of depression, with a duration of 3-7 days after delivery [44]. In contrast, postpartum depression is a clinical syndrome of moderate to severe depressive symptoms that lasts longer than postpartum blues and has a greater impact on the family [44].

Depression in new mothers is common: approximately 10% to 15% of childbearing women experience postpartum depression [44,45]. Among high risk populations, the prevalence of postpartum depression can reach 40% to 50% [44]. Various mechanisms for development of postpartum depression have been suggested. They include the progressive increase in progesterone and estrogen levels during pregnancy and dramatic fall in these hormones levels in the first few postpartum days, history of previous depression, lack of social support, low socioeconomic status, marital or relationship conflict, overly high expectations of the baby and motherhood, unexpected difficulties with labor and delivery, or childcare stress, infant temperament, and a sudden shift in attention from the mother to the baby (Table 2) [44-46]. Postpartum depression is an important public health problem because significant personal costs are associated with depression, including loss of life by suicide, impaired social and physical functioning, and increased morbidity from medical illness [44,45]. Children of parents with a history of depression are also more likely to display problems ranging from difficult temperaments, noncompliance and aggression, to poor self-esteem, poor peer relations, depressed mood, insecure attachment patterns, and attention deficits [45,47].

Rationale for sleep deprivation as a determinant of Postpartum Depression with inflammation as a causal mechanism—In addition to the recognized risk factors for postpartum depression, another potential factor that seems obvious but which has received little attention is sleep deprivation. Past epidemiologic studies have indicated an association between sleep disturbance and depression [48-52]. Increased rates of major depression have been observed in individuals with sleep complaints compared with those with no sleep complaints – 31.1% for those with insomnia, 25.3% for those with hypersomnia, and 54.3% for those with both insomnia and hypersomnia [48]. A longitudinal cohort study with a median follow-up period of 34 years found that male medical school students without a history of depression during medical school who reported insomnia or having difficulty sleeping under stress were at increased risk (RR: 2.0 and RR:1.8, respectively) of developing major depression [49]. In a study of sleep loss among adolescents, children who reported decreased amounts of sleep were more likely to develop symptoms of depression and reduced self-esteem [50]. Although studies of sleep disturbances and insomnia based on less reliable self-report data in many populations have suggested a relationship between sleep disturbances and symptoms of depression, the association between sleep deprivation and postpartum depression has been largely untested.

Similar to studies of insomnia, studies of sleep deprivation in the general, non-gravid population have shown that sleep deprivation increases self-reported feelings of depressed mood, anger, frustration, tension, and anxiety [53,54]. The majority of studies in pregnant and postpartum women also suggest that difficulty sleeping and sleep deprivation are associated with greater depressed mood in the postpartum period [55]. In a longitudinal study, Goyal et al [51] followed 124 primiparous women from their last month of pregnancy through 3 months postpartum. It was observed that self-reported sleep disturbance and depressive symptoms were associated at last month of pregnancy and 3 month postpartum. Women with higher depressive symptom scores had a higher frequency of problem with sleep quantity and quality, trouble falling asleep, more daytime sleepiness, and early awakening [51]. In another study, Lee and associates [56] compared objectively measured sleep patterns for women with positive postpartum affect at 1 postpartum month to women with negative postpartum affect. They observed that women who reported positive postpartum affect had stable total sleep time of

about 7 hours from the last trimester to 1 postpartum month, whereas women with negative mood slept 80 minutes less at 1 postpartum month.

In one study of 38 pregnant women, Wolfson and associates [57] examined self-reported depressive symptoms and sleep patterns from the late pregnancy to 1 year postpartum and observed an association between sleep patterns during late pregnancy and depressive symptoms in the first few weeks postpartum. Although both groups of women reported similar sleep patterns in the postpartum period, mothers who developed greater depressive symptoms at 2 to 4 postpartum weeks had significantly different sleep schedules in late pregnancy compared to non-depressed mothers [57]. On average, mothers who developed postpartum depressive symptoms reported later rise times, longer naps, and more total sleep at the end of their pregnancies [57]. But, interestingly, mothers who developed greater depressive symptoms at 2 to 4 postpartum weeks also experienced decreased total sleep from the end of pregnancy to early postpartum weeks while the non-depressed mothers had an increase in total sleep time during the same time period [57,58]. Even though women who reported having any personal or familial history of depression or other psychological disorders were excluded, some participants with subclinical depression at baseline who were unaware that they had depression may have been included. As a result, the longer total sleep Wolfson et al observed at the end of pregnancy among some mothers with postpartum depression may have been due to antenatal depression. Alternatively, findings from this study may also indicate that women who have greater sleep needs are at increased risk for postpartum depression when these needs are unmet.

These studies suggest that women who experience a greater reduction in sleep time in the postpartum period are likely to be at greater risk for depressive symptoms in the postpartum period. However, findings from most of prior studies are limited by not accounting for daytime naps which is frequent among new mothers during postpartum period as well as self-report nature of sleep measures. Subjective sleep duration measures are liable to misclassification of sleep deprivation. Nonetheless, the misclassification of sleep duration is likely nondifferential with respect to maternal depression status, so any resulting bias should have underestimated the true magnitude of association between sleep and depressive symptoms. Although evidence is accumulating in the association between sleep deprivation and development of depression, paradoxically, past research has also found that acute critically-timed sleep deprivation can have a therapeutic effect on major depression. However, the therapeutic effect of sleep deprivation does not last longer than one or maximally a few days and this intervention seems to work in less than 50% of the patients [59]. More research is needed to clarify the causal link between sleep deprivation and depression.

In addition to sleep duration, other investigators have examined time awake, an indicator of difficulty sleeping, and its effect on mood. Postpartum mothers' increased time awake during the night and poor subjective sleep quality have been strongly associated with increased negative daytime mood, or blues, especially in the first 4 weeks after delivery [60]. Swain and colleagues [60] have shown that compared to non-postpartum women, new mothers had increased dysphoric mood for the first 3 weeks postpartum. However, this significant effect was eliminated once the analysis adjusted for the effect of "amount of time up or time awake during the previous night". In other words, more "time awake" accounted for the observed increased dysphoric mood during the postpartum week. In addition, it was found that dysphoric mood during the first week postpartum was significantly related to time awake during the night [60]. Taken together, it suggests that shorter sleep duration due to more time awake was associated with the observed outcome of dysphoric mood.

It has been suggested that sleep disturbances may increase the risk of postpartum depression with inflammation as the underlying mechanism [39,61]. Disturbances in neurochemical transmission and modulation of the hypothalamus-pituitary-adrenal (HPA) axis are proposed

mechanisms by which cytokines may be involved in the pathogenesis of depression [61,62]. Depressive symptoms and increased pro-inflammatory cytokine concentrations have been observed after administration of cytokines to patients afflicted with cancer [63]. The elevation of pro-inflammatory cytokines observed after administration of cytokine therapy such as IL-2 demonstrates immune activation (i.e., inflammation). Development of depressive symptoms after administration of pro-inflammatory cytokines may be due to the roles that cytokines have in facilitation of communication between the immune and central nervous systems [63]. For example, IL-1, IL-6 and TNF are key mediators in immune system-to-brain communication by orchestrating responses such as fever and changes in sleep patterns [64]. Specifically, injection of IL-1 or TNF increases non-rapid eye movement sleep while inhibition of either IL-1 or TNF hinders spontaneous sleep [64]. IL-6 influences the sleep cycle during stress or inflammatory periods, leading to increased daytime sleepiness [22].

Previous studies have looked at levels of these and other pro-inflammatory cytokines in female subjects with major depression or postpartum depression. Sluzewaska and colleagues[65] examined immune-inflammatory markers and their correlates in patients with major depression. They measured plasma concentrations of IL-6, soluble IL-6 receptor (sIL-6R), soluble interleukin-2 receptor (sIL-2R), transferrin receptor (TfR), C-reactive protein (CRP), and alpha 1-acid glycoprotein (AGP), as well as the microheterogeneity of AGP, in 49 patients with major depression during an acute phase of the illness and compared them with levels in 15 normal control subjects. They observed that plasma concentrations of IL-6, sIL-6, sIL-2R, TfR, CRP, and AGP were significantly higher in patients with major depression than in healthy control subjects [65]. Corwin and associates [66] examined the effect of the pro-inflammatory cytokine IL-1 β in postpartum depression, finding that higher levels of IL-1 β were associated with fatigue in women at four weeks postpartum. The authors speculated that the elevated levels of IL-1 β may have an indirect link to postpartum depression through fatigue [66]. In 2000, Maes and associates [67] documented that mothers with postpartum depression had higher levels of inflammation with significantly higher serum IL-6 and IL-1 receptor antagonist concentrations compared to mothers who did not. Inflammation can influence levels of serotonin and catecholamines (norepinephrine, epinephrine, and dopamine), impacting the HPA axis, which controls cortisol levels [61,68]. Once inflammation starts, it triggers the HPA axis to release cortisol, and the release of more pro-inflammatory substances[61].

To summarize, prior research suggests a possible relationship between sleep and depressed mood during the postpartum period. However, comparison of research findings across studies is difficult because of variations in how sleep duration was assessed (e.g., subjective, less reliable self-report questionnaire and sleep log vs. objective polysomnography or actigraphy). In addition, since prior history of maternal depression or other antepartum mood disorders was rarely considered in these studies, the “chicken and the egg” issue has not yet been clearly addressed. It is possible that antepartum depression causes shorter sleep duration during pregnancy, which in turn, increases the likelihood of postpartum depression. Alternatively, a decrease in total sleep time from the antepartum to postpartum periods may also increase the risk of postpartum depression. Further research with objective assessment of maternal sleep parameters and adjustment for antepartum depression or depressive symptoms in the analyses is required for a better understanding of the relation between sleep deprivation during pregnancy and risk of postpartum depression.

Limited research has also suggested an association between sleep duration, inflammation, and postpartum depression. Sleep deprivation increases levels of inflammatory markers such as interleukin-1 (IL-1), IL-2, IL-6, tumor necrosis factor (TNF) α , and C-reactive protein and increased levels of pro-inflammatory cytokines have been observed among women with postpartum depression [20-23]. However, no prior research has directly examined the relationship between sleep duration, levels of pro-inflammatory markers, and risk of

postpartum depression. More research is needed to enhance our understanding of the effect of sleep deprivation on postpartum depression and the physiological mechanisms underlying this relationship.

Conclusion

Lack of sleep affects our physical and mental health. Although the average sleep duration in the American population has declined for both sexes, research has shown that more women than men report not getting the sleep they need [11]. Pregnant women particularly need sufficient sleep to nourish the development of their infants and the energy they need for the labor and delivery process. Sleep deprivation during pregnancy has been associated with longer labor, elevated perception of pain and discomfort during labor, higher cesarean rates, preterm labor, and higher levels of pro-inflammatory serum cytokines. Limited research has also indicated a possible relationship between sleep deprivation and preterm births and postpartum depressive mood. Nevertheless, prior research on the relationship between sleep deprivation and pregnancy outcomes has been limited by varying data collection methods which create barriers for comparison across studies, small and often non-representative samples, poorly controlled studies, and cross-sectional designs [24]. And A number of studies are descriptive or non-hypothesis driven.

Many women are not allowing themselves enough sleep partially due to lack of knowledge of its adverse effect on their health. Much remains to be learned about the extent of sleep deprivation during pregnancy and its effect on maternal and fetal outcomes. More research is needed to identify the clinical, social, and behavioral risk factors associated with sleep deprivation among pregnant women, and to examine the effect of sleep deprivation on adverse maternal and fetal outcomes. Identification of sleep deprivation during pregnancy will aid clinicians in improved management of patients' health throughout pregnancy and facilitate timely intervention for patients to prevent adverse maternal and fetal outcomes.

Practice Points

1. Even though there has been a decline in average sleep time in the general population, American women may be bearing a greater burden of sleep deprivation than men.
2. The few studies that investigated sleep duration throughout pregnancy have found an increase in total sleep time and daytime sleepiness during the first trimester, whereas the third trimester is characterized by a decrease in sleep time and an increase in the number of nocturnal awakenings.
3. Sleep deprivation during pregnancy has been associated with longer labor, elevated perception of pain and discomfort during labor, higher cesarean rates, preterm labor, and higher levels of pro-inflammatory serum cytokines.
4. Prior research has indicated a possible relationship between sleep and depressed mood

Research agenda

1. More studies are needed to understand the extent of sleep deprivation during pregnancy and its effect on maternal and fetal outcomes.
2. Sleep research in pregnancy women using longitudinal study designs is needed to allow the examination of the cumulative effect of sleep deprivation on adverse maternal and fetal outcomes such as preterm delivery and postpartum depression.

3. Further research with objective assessment of maternal sleep parameters and the adjustment of antepartum depression in the analysis is required for a better understanding of the relation between sleep deprivation during pregnancy and risk of postpartum depression.

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Table 1
Risk factors for preterm delivery

Category	Risk factors
Sociodemographic characteristics	Low and high maternal age, Black race, single marital status, low socioeconomic status
Psychological factors	Higher levels of psychological or social stress, depression, anxiety
Obstetric history and pregnancy characteristics	Short interpregnancy interval (< 6 months), Prior history of preterm birth or low birth weight, multiple second trimester spontaneous abortions, in vitro fertilization pregnancy, multiple gestations, low prepregnancy body-mass index
Medical complications of pregnancy	Placental abnormalities, gestational bleeding, cervical and uterine anomalies, intrauterine infection
Chronic disorders	Cardiopulmonary disease, diabetes mellitus, asthma, hyperthyroidism, epilepsy, hypertension
Substance use and abuse	Cigarette smoking

Table 2
Risk factors for postpartum depression

Category	Risk factors
Socioeconomic characteristics	Low socioeconomic status, limited educational attainment, single marital status, poor marital relationship, social isolation, low levels of social support
Obstetrical factors	Unplanned/unwanted pregnancy, cesarean section delivery, preterm delivery
Psychiatric and psychosocial factors	Low self-esteem, psychological distress, childcare stress, history of previous depression or postpartum depression, anxiety or depression during pregnancy, experiencing stressful life event during pregnancy