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Review Article

Chronic sleep loss during pregnancy as a determinant of stress: impact on pregnancy outcome

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ABSTRACT

Short sleep duration, poor sleep quality, and insomnia frequently characterize sleep in pregnancy during all three trimesters. We aimed: (i) to review the clinical evidence of the association between conditions of sleep loss during pregnancy and adverse pregnancy outcomes; and (ii) to discuss the potential pathophysiological mechanisms that may be involved. A systematic search of cross-sectional, longitudinal studies using Medline, Embase, and PsychINFO, and MeSH headings and key words for conditions of sleep loss such as 'insomnia', 'poor sleep quality', 'short sleep duration', and 'pregnancy outcome' was made for papers published between January 1, 1960 and July 2013. Twenty studies met inclusion criteria for sleep loss and pregnancy outcome: seven studies on prenatal depression, three on gestational diabetes, three on hypertension, pre-eclampsia/eclampsia, six on length of labor/type of delivery, eight on preterm birth, and three on birth grow/birth weight. Two main results emerged: (i) conditions of chronic sleep loss are related to adverse pregnancy outcomes; and (ii) chronic sleep loss yields a stress-related hypothalamic–pituitary–adrenal axis and abnormal immune/inflammatory, reaction, which, in turn, influences pregnancy outcome negatively. Chronic sleep loss frequently characterizes sleep throughout the course of pregnancy and may contribute to adverse pregnancy outcomes. Common pathophysiological mechanisms emerged as being related to stress system activation. We propose that in accordance to the allostatic load hypothesis, chronic sleep loss during pregnancy may also be regarded as both a result of stress and a physiological stressor per se, leading to stress 'overload'. It may account for adverse pregnancy outcomes and somatic and mental disorders in pregnancy.

1. Introduction

Pregnancy is one of the most important periods in a woman's life. Despite being a natural phenomenon, pregnancy is accompanied by major physiological, psychological and social changes [1,2]. Sleep disorders are among the most widespread major problems experienced in pregnancy [3–8]. In a recent poll by the National Sleep Foundation, more than 79% of women reported that their sleep had been altered during pregnancy compared to any other time [6].

Sleep restriction, short sleep duration, poor sleep quality, sleep-disordered breathing, and parasomnias have been described as widespread sleep problems during pregnancy [3,5,9–14]. The quantity and quality of sleep of pregnant women have been shown to be altered during pregnancy [3,4,13]. Previous studies have documented trimester-specific changes in sleep architecture [3–6,8–10]. Emerging evidence also indicates that sleep disturbances during pregnancy are associated with women's poor health outcomes [15–17]. In addition, recent data indicate that sleep disturbances are associated with adverse pregnancy outcomes including intrauterine growth restriction and preterm birth [18–20].

As other sleep disorders in pregnancy such as sleep-disordered breathing, and parasomnias have already been covered in detail elsewhere [5,10,11,16,20,21], this study focuses on the available data concerning conditions of sleep loss such as short sleep duration, poor sleep quality, and insomnia with respect to the outcome

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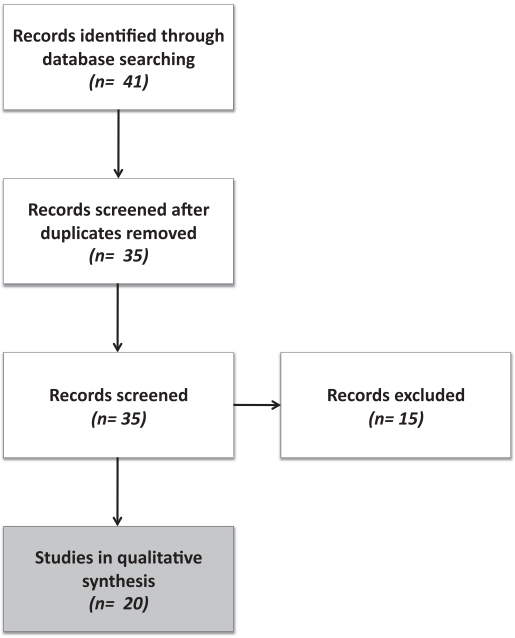

Fig. 1. Flow of information through the different phases of the systematic review.

of pregnancy. It has already been hypothesized that such sleep conditions cause serious consequences, which include depression, diabetes, and various cardiovascular dysfunctions [22–28]. The primary aim of this article is systematically to review the clinical evidence of the association of such sleep conditions and pregnancy outcome. The secondary aim is to discuss the potential pathophysiological mechanisms that may be involved in this interaction. A model of the role of chronic sleep loss in modulating stress response (allostasis) [29–31] and consequences on pregnancy outcome will be proposed.

2. Methods

2.1. Search strategy

A systematic search of Medline, Embase, and PsychINFO was performed. The initial search was conducted in November 2011 with a final search in July 2013. The search strategies used MeSH headings and keywords for 'insomnia', 'poor sleep quality', 'short sleep duration' or 'sleep restriction' and 'pregnancy outcome'.

2.2. Inclusion and exclusion criteria

Studies were included if they: (1) involved human adult pregnant women aged >18 years; (2) were longitudinal observational, case–control, or cross-sectional studies, or meta-analyses; (3) analyzed prevalence and characteristics of disturbed sleep such as insomnia and poor sleep quality, short sleep duration and pregnancy outcome; and (4) were published between January 1, 1960 and July 2013. Studies were excluded if: (1) they did not control for confounding factors such as other sleep disorders or other comorbid disorders (i.e. other sleep disorders, sleep-disordered breathing, restless leg syndrome, depression; (2) they did not analyze data stratified by race and age; (3) they were not available in full text; or (4) they were not available in English.

3. Results

3.1. Selection of articles

Forty-one articles were retrieved, 21 of which were excluded after detailed review as they did not meet the inclusion criteria. Twenty papers were included and their data retrieved (Fig. 1).

Three studies focused on prenatal depression (Table 1), two on gestational diabetes (Table 2), three on hypertension, pre-eclampsia/eclampsia (Table 3), five on the length of labor/type of delivery (Table 4), five on preterm birth (Table 5) and three on fetal growth (Table 6).

3.2. Chronic sleep loss during pregnancy and adverse pregnancy outcome: clinical evidence

In the USA, more than one million pregnancies each year result in adverse outcomes that increase maternal and infant morbidity [31–36]. Even if only few investigations have focused on this issue, emerging evidence indicates that conditions of sleep loss may have a role in adverse outcome of pregnancy. Changes in sleep pattern during pregnancy have been widely described in all three trimesters of pregnancy since 1968 [for overviews see 3–10]. Conditions of sleep loss such as short sleep duration [37–39], poor sleep quality [4,13,38–51], poor sleep efficiency with an increase in time spent awake during the night [13,42,46], and insomnia [38,52] characterize the sleep of pregnant women during the period of pregnancy. The most frequent adverse outcomes include conditions related to mother morbidity such as prenatal depression, gestational diabetes, and pre-eclampsia. In addition, abnormal duration of labor, type of delivery, intrauterine growth restriction, and preterm birth have been considered adverse pregnancy outcomes.

Prenatal depression prevalence estimates range from 10% to 25% [53–57], and it is a significant risk factor for miscarriage, preterm birth, and low birth weight [53,58–62]. Sleep disturbances are more frequent in depressed than in non-depressed women during pregnancy, especially in early gestation [57,63–65]. Although few studies have investigated the role of sleep loss in the development of depressive symptoms during pregnancy [51,66,67] (Table 1), they show that it may constitute a risk for developing

Table 1
Sleep loss and prenatal depression.

Authors	Study design	Study population	Week of gestation	Sleep evaluation	Main findings
Skouteris et al. [66]	Longitudinal	273 pregnant women	From 14th week until delivery every 8 weeks	PSQI BDI	Poor sleep quality earlier in pregnancy predicted higher levels of depressive symptoms at later stage of pregnancy
Skouteris et al. [67]	Longitudinal	252 pregnant women	Mid/late pregnancy	PSQI BDI	Sleep problems are risk factors for increased depressive symptoms during pregnancy
Kamysheva et al. [51]	Longitudinal	252 pregnant women	Early–mid 2nd trimester and late 3rd trimester	BDI PSQI	Poor sleep quality is a risk for depressive symptoms early–mid 2nd trimester, late 3rd trimester

PSQI, Pittsburgh Sleep Quality Index; BDI, Beck Depression Inventory.

Table 2
Sleep loss and gestational diabetes.

Authors	Study design	Study population	Week of gestation	Sleep evaluation	Main findings
Qiu et al. [70]	Cross-sectional	1290 pregnant women	14th	Sleep questionnaires	GD risk was increased among women sleeping ⩽4 h vs 9 h/night. RR = 5.6 (1.31–23.69)
Reutrakul et al. [71]	Cross-sectional	169 pregnant women	2nd trimester	Sleep questionnaires PSQI	SD inversely correlated with glucose values ($r = -0.21$, $P < 0.01$) Each hour of reduced sleep time was associated with a 4% increase in glucose levels SD <7 h/night increases risk of developing GD

GD, gestational diabetes; RR, relative risk; SD, sleep duration.

Table 3
Sleep loss and hypertension, pre-eclampsia.

Authors	Study design	Study population	Week of gestation	Sleep evaluation	Main findings
Ekholm et al. [74]	Cross-sectional	9 women with pre-eclampsia 8 women with normal pregnancy		Sleep questionnaires	Sleep is impaired in pre-eclamptic subjects
Edwards et al. [75]	Cross-sectional	25 pre-eclamptic women 17 women with normal pregnancies		Polysomnography	Pre-eclamptic subjects had markedly altered sleep architecture, with a markedly increased percentage of NREM SWS Longer latency to REM sleep and reduced time spent in REM compared to normal pregnancy
Williams et al. [76]	Prospective cohort study	1272 pregnant women	Early pregnancy	Sleep questionnaires	Sleep duration ⩽6 h/night in early pregnancy was associated with increased mean 3rd trimester blood pressure

REM, rapid eye movement sleep; NREM, non-REM sleep; SWS, slow wave sleep.

Table 4
Sleep loss, length of labor and type of delivery.

Authors	Study design	Study population	Week of gestation	Sleep evaluation	Main findings
Evans et al. [77]	Cross-sectional	99 multiparous women	3rd trimester last 2 weeks	Sleep questionnaires	No relationship between poor sleep quality and length of labor type of delivery
Lee et al. [78]	Cross-sectional	131 pregnant women	3rd trimester last month	48 h wrist actigraphy Sleep questionnaires	SD <6 h; long labor increased risk of cesarean deliveries by 4.5-fold
Naghi et al. [79]	Cross-sectional	88 pregnant women	3rd trimester last 3 weeks	PSQI	Poor sleep quality related to long labor cesarean deliveries
Wangel et al. [80]	Population-based	10,662 pregnant women	3rd trimester last days	Sleep questionnaires	Sleep disorders are risk for emergency cesarean; OR, 1.57 (95% CI, 1.14–2.16)
Zafarghandi et al. [81]	Cross-sectional	457 pregnant women	3rd trimester	Sleep questionnaires	Poor sleep quality/short SD related to long labor cesarean delivery

PSQI, Pittsburgh Sleep Quality Index; SD, sleep duration; OR, odds ratio; CI, confidence interval.

Table 5
Sleep loss and preterm birth.

Authors	Study design	Study population	Week of gestation	Sleep evaluation	Main findings
Strange et al. [89]	Cross-sectional	220 pregnant women	2nd trimester	PSQI EES PSS	Disturbed sleep in pregnancy may be associated with preterm birth
Samaraweera et al. [90]	Case–control	230 pregnant women. 504 controls	1st, 2nd trimesters	Sleep questionnaires	SD <8 h per night is a risk factor for 1st and 2nd trimester miscarriage. OR, 3.80 (95% CI, 1.01–14.3)
Okun et al. [91]	Observational	166 pregnant women	1st, 2nd, 3rd trimesters	PSQI	Poor sleep. Risk of preterm birth: 1st trimester OR, 1.25 (95% CI, 1.04–1.50) 3rd trimester OR, 1.18 (95% CI, 0.98–1.42)
Micheli et al. [92]	Prospective mother–child cohort	10,662 nulliparous women	3rd trimester	Sleep questionnaires	SD <5 h per night is a risk for preterm birth OR, 2.4 (95% CI, 1.0–6.4)
Okun et al. [93]	Cross-sectional	217 pregnant women	20–30	Sleep questionnaires	Poor sleep may contribute to risk for preterm birth

PSQI, Pittsburgh Sleep Quality Index; EES, Epworth Sleepiness Scale; PSS, Perceived Stress Scale; SD, sleep duration; OR, odds ratio; CI confidence interval.

Table 6
Sleep loss and fetal growth.

Authors	Study design	Study population	Week of gestation	Sleep evaluation	Main findings
Abeysena et al. [94]	Cross-sectional	885 pregnant women	From 16th week until delivery	Sleep questionnaires	SD <8 h per night increased the risk of LBW: OR, 2.84 (95% CI, 1.49–5.40)
Bonzini et al. [95]	Meta-analysis: effect of shift work on LBW and SGA	Pregnant women on shift work			Risk of LBW: OR, 1.27 (95% CI, 0.93–1.74) Risk of SGA: OR, 1.12 (95% CI, 1.03–1.22)
Zafarghandi et al. [81]	Cross-sectional	457 pregnant women	3rd trimester	Sleep questionnaires	Short SD was related to Apgar score and birth weight

SD, sleep duration; LBW, low birth weight; OR, odds ratio; CI, confidence interval; SGA, small for gestational age.

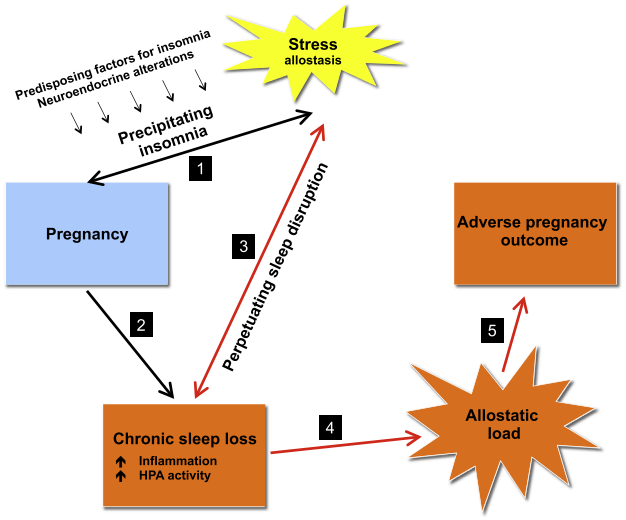

Fig. 2. Proposed model: conditions of stress during pregnancy result in an activation of allostasis. If the allostatic reaction occurs in a woman with predisposing factors for insomnia, some neuroendocrine alterations (1) result in chronic sleep loss (2). The latter is typically associated with a chronic activation of both the inflammation and hypothalamic–pituitary–adrenal axis (HPA). Given the bidirectional relationship between sleep and stress system (3), conditions of sleep loss may lead to a vicious circle (1–2–3) by auto-amplifying prolonged/exaggerated inflammatory responses which, in turn, may generate a state of allostatic load (4). The latter condition may account for adverse pregnancy outcomes (5).

antenatal depression. Gestational diabetes is also a frequently occurring medical condition during pregnancy [68] and is associated with an increased risk of complications for both mother and child [68,69]. Although only few studies have investigated the role of disturbed sleep due to glucose tolerance in pregnancy, they have found that short sleep duration may increase the risk of gestational diabetes [70,71] (Table 2).

Hypertension and pre-eclampsia also have a variable incidence ranging from 5% to 10% of pregnancies [72,73]. Pre-eclampsia and eclampsia are major causes of maternal and perinatal morbidity and mortality [72,73]. Although few studies have investigated the relationship between both sleep duration and quality with trimester-specific blood pressures and hypertensive disorders in pregnancy [74–76] (Table 3), they show that both short sleep duration and poor sleep quality may have a role in developing hypertensive disorders during pregnancy. Few studies have evaluated the relationship between sleep loss, insomnia, and length of labor [77–81] (Table 4). According to these findings, both short sleep duration and poor sleep quality may increase the risk of both labor duration and cesarean delivery.

Preterm birth is also a major health concern, accounting for 75% of perinatal mortality and more than half of long-term morbidity [82–85]. Preterm birth is hypothesized to be a multifactorially caused phenomenon [86]; indeed maternal sleep disruption is emerging as a significant factor for developing it [87,88]. Studies evaluating the relationship between sleep loss and preterm birth [89–93] (Table 5) show that both poor sleep quality and short sleep duration may contribute to preterm birth. In addition, some research in the available literature has studied the relationship between conditions of sleep loss during pregnancy and birth growth [81,94,95] (Table 6). From these data, we may hypothesize that both mothers' sleep duration and quality may negatively affect neonates' Apgar score, birth weight, or gestational age. Low birth weight is a marker of suboptimal prenatal environment, which is known to exert lifelong effects on organ structure and organization of physiologic systems [96,97].

3.3. Chronic sleep loss during pregnancy and adverse pregnancy outcome: psychobiological hypotheses

Common pathophysiological mechanisms in the relationship between sleep loss and negative pregnancy outcome emerged as being related to stress system activation. Whereas previous research has shown that sleep quality and insomnia are antecedent to depressive symptoms [28,98], some authors argued that the relationship between sleep disorders and depression during pregnancy may be more complex [64–67]. Based on animal and human data, it was previously thought that an alteration of the hypothalamic–pituitary–adrenal (HPA) axis may be a potential underlying mechanism for the relationship between sleep problems and prenatal depression [99,100]. Other authors have sustained the hypothesis that depression and disturbed sleep may be associated with increased proinflammatory system activity [101,102], and that this may be considered also during pregnancy [65,91]. Other authors have hypothesized that these mechanisms, i.e. HPA axis and proinflammatory system alterations, are also involved in the association between sleep loss and both the development of diabetes [17,103–107] and hypertension [18,27] during pregnancy. In addition, a sleep disorder-related alteration in systematic inflammation has been hypothesized as the causal mechanism in the pathogenesis of adverse pregnancy outcomes, including length of labor [18,87], type of delivery [18,87], preterm birth [18,87], and intrauterine fetal growth [18].

3.4. Chronic sleep loss during pregnancy as a determinant of stress: a proposed model

We propose that conditions of chronic sleep loss that are experienced during pregnancy may be considered both a result of stress and as a stressor per se according to the allostatic load hypothesis (Fig. 2). Conditions of stress during pregnancy may result in the activation of allostasis, and, if the allostatic reaction occurs in a woman with both predisposing factors for insomnia and some neuroendocrine alterations, it may result in chronic sleep loss. The latter is typically associated with the chronic activation of both the inflammation and HPA axis. Given the bidirectional relationship between sleep and stress system, conditions of sleep loss may lead

to a vicious circle by auto-amplifying prolonged/exaggerated inflammatory responses which, in turn, may generate a state of allostatic load. We propose that in the same manner, the latter condition may account for all the different conditions of pregnancy adverse outcome related to sleep loss.

Pregnancy is a time of increased stress [108–111]. It has been hypothesized that maternal stress represents a significant cause of maternal and perinatal morbidity and mortality [31,112–115]. Psychosocial factors such as socio-economic status, work status, marital status, level of education, access to prenatal care, substance abuse, ethnicity, cultural background, and quality of relationships with partners and parents have been identified as determinants of stress during pregnancy [31].

This conceptualization of insomnia suggests the importance of the '3P' model (predisposing, precipitating, and perpetuating factors) [116]. Predisposing factors are present before insomnia is manifested, and it is hypothesized that they interact with precipitating factors, i.e. stressful life events over time, to increase the risk of insomnia. Mounting evidence confirms that higher levels of stress are indeed associated with more disrupted sleep [116–122], both of which are associated with immune and neuroendocrine dysregulation and increased morbidity [22,123,124]. Within this context, sleep disorders during pregnancy may be considered a stress response to an increased level of stress in pregnancy (Fig. 2). Conditions of stress during pregnancy may result in the activation of the stress system and the allostasis. The stress system is essentially an alarm system that is activated each time a discrepancy between expectations and reality is generated. The allostasis is the adaptive response of the organism to a stressful condition, i.e. environmental or internal stimuli. It is produced by the joint activities of the central and autonomic nervous systems, the HPA axis, and the immune system [22,29]. However, if the stressful condition becomes chronic, it may produce the so-called 'allostatic state', characterized by an increased activity of the mediators on their target cells that leads to receptor desensitization and tissue damage, thus reflecting the situation known as 'allostatic load' [22,123,124]. This may cause serious consequences, which include insomnia, depression, and various cardiovascular dysfunctions, which, in turn, could sustain the above-mentioned negative effects of sleep loss on different aspects of pregnancy (Fig. 2).

Sleep loss, due to environmental, genetic, biological, and psychosocial factors reciprocally interacting, may be considered a typical condition of allostatic load [22,29], which promotes severe physiologic, neurobiologic, and behavioral consequences [for review, see 22] involving increased arterial blood pressure, reduced parasympathetic tone, increased proinflammatory cytokines, and increased oxidation [22,29]. Within this framework, conditions of sleep loss have therefore been considered as a neurobiologic and physiologic stressor per se [22,29]. In animal models, and in men and non-pregnant women, sleep loss has been associated with the development of cardiovascular disease [24,26], hypertension [27], insulin resistance and Type 2 diabetes [103–107], as well as with an increased risk for depression [28,98]. All these negative changes induced by sleep loss could sustain some negative outcome for pregnancy such as pre-eclampsia and gestational diabetes, through an allostatic 'overload' mechanism [23–27]. Sleep loss may affect nervous structures that play a major role in producing and maintaining allostatic load: amygdala and hippocampus interpret what is stressful and regulate responses [125,126]. It has been hypothesized that the hippocampus–amygdala alteration may represent one of the possible pathophysiological mechanisms of depression [123]. Consequences of disrupted sleep include a reduction in neurogenesis which, in turn, endangers hippocampal integrity and thereby, via HPA axis dysregulation, contributes to the pathophysiology of depression [22,29,123,124].

Within this hypothesis, perinatal depression could also be an expected outcome of sleep loss as allostatic factor. Thus, a sustained overactivation of the stress system could be a possible mechanism underlying the relation between sleep deprivation, short sleep duration, insomnia, and negative pregnancy outcome. Because sleep plays key homeostatic functions counterbalancing the negative effects of stress, its alterations – including sleep loss and disruption – yield an overactivation of the HPA axis, of the sympathetic nervous system, and of the proinflammatory system [22]. Maternal sleep disruption could then act as a stressor per se activating the stress system. Hence, according to the allostatic load hypothesis, we propose that conditions of chronic sleep loss may also be considered as one of the psychological/physiological stressors determinants of stress during pregnancy. It may lead to a vicious circle, inducing the occurrence of the allostatic load (Fig. 2) and thereby contribute to adverse pregnancy outcomes. Thus, a sustained overactivation of the stress system may be a mechanism underlying the relationship between sleep deprivation, short sleep duration, insomnia, and negative pregnancy outcome. Because sleep plays key homeostatic functions in counterbalancing the negative effects of stress, its alterations, including sleep loss and disruption, yield an overactivation of the HPA axis, of the sympathetic nervous system, and of the proinflammatory system [22].

In summary, we propose that conditions of chronic sleep loss experienced during pregnancy may be considered both a result of stress and a stressor per se (Fig. 2). This may account in the same frame for conditions of adverse pregnancy outcomes related to sleep loss.

4. Conclusions

Conditions of sleep loss such as short sleep duration, poor sleep quality, and increase in time spent awake during the night, frequently characterize the sleep of pregnant women during all three trimesters. Emerging evidence indicates that conditions of sleep loss in pregnancy are associated with adverse pregnancy outcome such as prenatal depression, gestational diabetes, pre-eclampsia, abnormal length of labor, cesarean delivery, alteration in fetal growth, and preterm birth. Indeed, the empirical evidence is still scarce and further rigorous studies are needed to reach definite conclusions. Potential pathophysiological mechanisms, which various authors have described as being involved in the relationship with adverse pregnancy outcomes, include both the HPA axis and the proinflammatory system alteration. In accordance with the allostatic load conceptualization, we propose that conditions of chronic sleep loss in pregnancy may be regarded as a result of stress and as a physiological stressor per se, leading to stress 'overload'. It may impair the HPA axis and the proinflammatory system, leading to such important negative pregnancy outcomes. This model may therefore account for all the different conditions of adverse pregnancy outcomes related to sleep loss. Thus, we propose that conditions of sleep loss should be included among the determinants of stress already identified during pregnancy (Fig. 2). Within this framework, sleep disorders during pregnancy need to be systematically assessed and treated. Prenatal screening and intervention for relevant biopsychosocial risk factors may be useful in preventing stress-related perinatal complications and should include sleep disorders. Guidelines for pharmacological and cognitive behavioral treatments of sleep disorder need to be developed for all the sleep disorders that could contribute to conditions of sleep loss during pregnancy.

Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2014.02.013.

References

[1] Sevil U, Bakıcı A. Identification of the physical health problems and affecting factors in pregnancy. Health Soc J 2002;12:56–62.
[2] Yanıkkerem E, Altıparmak S, Karadeniz G. Review of the physical health problems experienced in pregnancy. Family and community education. Culture Res J 2006;3:35–42.
[3] Lee KA. Alterations in sleep during pregnancy and postpartum: a review of 30 years of research. Sleep Med Rev 1998;2:231–4.
[4] Mindell JA, Jacobson BJ. Sleep disturbances during pregnancy. J Obstet Gynecol Neonatal Nurs 2000;29:590–7.
[5] Pien GW, Schwab RJ. Sleep disorders during pregnancy. Sleep 2004;27:1405–17.
[6] National Sleep Foundation. Summary of Findings of the 2007 Sleep in America Poll. Available at: http://sleepfoundation.org/media-center/press-release/sleep-america-poll-summary-findings.
[7] Hunter LP, Rychnovsky JD, Yount SM. A selective review of maternal sleep characteristics in the postpartum period. J Obstet Gynecol Neonatal Nurs 2009;38:60–8.
[8] Kempler L, Sharpe L, Bartlett D. Sleep education during pregnancy for new mothers. BMC Pregnancy Childbirth 2012;12:155.
[9] Santiago JR, Nolledo MS, Kinzler W, Santiago TV. Sleep and sleep disorders in pregnancy. Ann Intern Med 2001;134:396–408.
[10] Sahota PK, Jain SS, Dhand R. Sleep disorders in pregnancy. Curr Opin Pulm Med 2003;9:477–83.
[11] Bourjeily G, Ankner G, Mohsenin V. Sleep-disordered breathing in pregnancy. Clin Chest Med 2011;32:175–89.
[12] Ibrahim S, Foldvary-Schaefer N. Sleep disorders in pregnancy: implications, evaluation, and treatment. Neurol Clin 2012;30:925–36.
[13] Hertz G, Fast A, Feinsilver SH, Albertario CL, Schulman H, Fein AM. Sleep in normal late pregnancy. Sleep 1992;15:246–51.
[14] Manconi M, Govoni V, De Vito A, Economou NT, Cesnik E, Mollica G, et al. Pregnancy as a risk factor for restless legs syndrome. Sleep Med 2004;5:305–8.
[15] Parry BL, Martinez F, Maurer E, Lopez A, Sorenson D, Meliska C. Sleep rhythms and women's mood: Part I. Menstrual cycle, pregnancy and postpartum. Sleep Med Rev 2006;10:129–44.
[16] Izci-Balserak B, Pien GW. Sleep-disordered breathing and pregnancy: potential mechanisms and evidence for maternal and fetal morbidity. Curr Opin Pulm Med 2010;16:574–82.
[17] O'Keeffe M, St-Onge MP. Sleep duration and disorders in pregnancy: implications for glucose metabolism and pregnancy outcomes. Int J Obes 2013;37:765–70.
[18] Okun ML, Roberts JM, Marsland AL, Hall M. How disturbed sleep may be a risk factor for adverse pregnancy outcomes. Obstet Gynecol Surv 2009;64:273–80.
[19] O'Brien LM. Sleep disruption and adverse pregnancy outcomes. BMC Pregn Childbirth 2012;12:11.
[20] August EM, Salihu HM, Biroscak BJ, Rahman S, Bruder K, Whiteman VE. Systematic review on sleep disorders and obstetric outcomes: scope of current knowledge. Am J Perinatol 2012;30:323–34.
[21] Facco FL. Sleep-disordered breathing and pregnancy. Semin Perinatol 2011;35:335–9.
[22] McEwen BS. Sleep deprivation as a neurobiologic and physiologic stressor: allostasis and allostatic load. Metabolism 2006;55:20–3.
[23] Spiegel K, Knutson K, Leproult R, Tasali E, Van Cauter E. Sleep loss: a novel risk factor for insulin resistance and Type 2 diabetes. J Appl Physiol 2005;99:2008–19.
[24] Mullington JM, Haack M, Toth M, Serrador JM, Meier-Ewert HK. Cardiovascular, inflammatory, and metabolic consequences of sleep deprivation. Prog Cardiovasc Dis 2009;51:294–302.
[25] Gangwisch JE, Heymsfield SB, Boden-Albala B, Buijs RM, Kreier F, Pickering TG, et al. Sleep duration as a risk factor for diabetes incidence in a large U.S. sample. Sleep 2007;30:1667–73.
[26] Spiegelhalder K, Scholtes C, Riemann D. The association between insomnia and cardiovascular diseases. Nat Sci Sleep 2010;2:71–8.
[27] Palagini L, Bruno RM, Gemignani A, Baglioni C, Ghiadoni L, Riemann D. Sleep loss and hypertension: a systematic review. Curr Pharm Des 2013;19:2409–19.
[28] Baglioni C, Battagliese G, Feige B, Spiegelhalder K, Nissen C, Voderholzer U, et al. Insomnia as a predictor of depression: a meta-analytic evaluation of longitudinal epidemiological studies. J Affect Disord 2011;135:10–9.
[29] Meerlo P, Sgoifo A, Suchecki D. Restricted and disrupted sleep: effects on autonomic function, neuroendocrine stress systems and stress responsivity. Sleep Med Rev 2008;12:197–210.
[30] Han KS, Kim L, Shim I. Stress and sleep disorder. Exp Neurobiol 2012;21:141–50.
[31] Cardwell MS. Stress: pregnancy considerations. Obstet Gynecol Surv 2013;68:119–29.
[32] Lumley J. Defining the problem: the epidemiology of preterm birth. BJOG 2003;110:3–7.
[33] Peacock JL, Bland JM, Anderson HR. Preterm delivery: effects of socioeconomic factors, psychological stress, smoking, alcohol, and caffeine. BMJ 1995;311:531–5.
[34] Sibai BM. Risk factors, pregnancy complications, and prevention of hypertensive disorders in women with pregravid diabetes mellitus. J Matern Fetal Med 2000;9:62–5.
[35] March of Dimes. Pregnancy complications. 2006. Available at: http://www.marchofdimes.com/pregnancy/pregnancy-complications.aspx#.
[36] Hollander MH, Paarlberg KM, Huisjes AJ. Gestational diabetes: a review of the current literature and guidelines. Obstet Gynecol Surv 2007;62:125–36.
[37] Elek SM, Hudson DB, Fleck MO. Expectant parents' experience with fatigue and sleep during pregnancy. Birth 1997;24:49–54.
[38] Kızılırmak A, Timur S, Kartal B. Insomnia in pregnancy and factors related to insomnia. Scient World J 2012;2012:197093.
[39] Hutchison BL, Stone PR, McCowan LM, Stewart AW, Thompson JM, Mitchell EA. A postal survey of maternal sleep in late pregnancy. BMC Pregn Childbirth 2012;12:144.
[40] Karacan I, Heine W, Agnew HW, Williams RL, Webb WB, Ross JJ. Characteristics of sleep patterns during late pregnancy and postpartum periods. Am J Obstet Gynecol 1968;101:579–86.
[41] Brunner DP, Munch M, Biedermann K, Huh R, Borbely AA. Changes in sleep and sleep electroencephalogram during pregnancy. Sleep 1994;17:576–82.
[42] Waters MA, Lee KA. Differences between primigravidae and multigravidae mothers in sleep disturbances, fatigue, and functional status. J Nurse Midwifery 1996;41:364–7.
[43] Baratte-Beebe KR, Lee K. Sources of mid sleep awakenings in childbearing women. Clin Nurs Res 1999;8:386–97.
[44] Lee KA, Zaffke ME, McEnany G. Parity and sleep patterns during and after pregnancy. Obstet Gynecol 2000;95:14–8.
[45] Hedman C, Pohjasvaara T, Tolonen U, Suhonen-Malm AS, Myllylä VV. Effects of pregnancy on mothers' sleep. Sleep Med 2002;3:37–42.
[46] Greenwood KM, Hazendonk KM. Self-reported sleep during the third trimester of pregnancy. Behav Sleep Med 2004;2:191–204.
[47] Okun ML, Hall M, Coussons-Read ME. Sleep disturbances increase interleukin-6 production during pregnancy: implications for pregnancy complications. Reprod Sci 2007;14:560–7.
[48] Neau JP, Texier B, Ingrand P. Sleep and vigilance disorders in pregnancy. Eur Neurol 2009;62:23–9.
[49] Facco FL, Kramer J, Ho KH, Zee PC, Grobman WA. Sleep disturbances in pregnancy. Obstet Gynecol 2010;115:77–83.
[50] Naud K, Ouellet A, Brown C, Pasquier JC, Moutquin JM. Is sleep disturbed in pregnancy? J Obstet Gynaecol Can 2010;32:28–34.
[51] Kamysheva E, Skouteris H, Wertheim EH, Paxton SJ, Milgrom J. A prospective investigation of the relationships among sleep quality, physical symptoms, and depressive symptoms during pregnancy. J Affect Disord 2010;123:317–20.
[52] Fernández-Alonso AM, Trabalón-Pastor M, Chedraui P, Pérez-López FR. Factors related to insomnia and sleepiness in the late third trimester of pregnancy. Arch Gynecol Obstet 2012;286:55–61.
[53] Dunkel Schetter C, Tanner L. Anxiety, depression and stress in pregnancy: implications for mothers, children, research, and practice. Curr Opin Psychiatry 2012;25:141–8.
[54] Bonari L, Pinto N, Ahn E, Einarson A, Steiner M, Koren G. Perinatal risks of untreated depression during pregnancy. Can J Psychiatry 2004;49:726–35.
[55] Field T, Diego M, Dieter J, Hernandez-Rief M, Schanberg S, Kuhn C, et al. Prenatal depression effects on the foetus and the newborn. Infant Behav Dev 2004;27:216–29.
[56] Field T, Diego M, Hernandez-Reif M. Prenatal depression effects on the fetus and newborn: a review. Infant Behav Dev 2006;29:445–55.
[57] Field T, Diego M, Hernandez-Reif M, Figueiredo B, Schanberg S, Kuhn C, et al. Chronic prenatal depression and neonatal outcome. Int J Neurosci 2008;118:95–103.
[58] Dayan J, Creveuil C, Marks MN, Conroy S, Herlicoviez M, Dreyfus M, et al. Prenatal depression, prenatal anxiety, and spontaneous preterm birth: a prospective cohort study among women with early and regular care. Psychosom Med 2006;68:938–46.
[59] Li D, Liu L, Odouli R. Presence of depressive symptoms during early pregnancy and the risk of preterm delivery: a prospective cohort study. Hum Reprod 2009;24:146–53.
[60] Grote NK, Bridge JA, Gavin AR, Melville JL, Iyengar S, Katon WJ. A meta-analysis of depression during pregnancy and the risk of preterm birth, low birth weight, and intrauterine growth restriction 21. Archs Gen Psychiatry 2010;67:1012–24.
[61] 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 2007;30:127–33.
[62] DiPietro J, Novak MF, Costigan KA, Atella LD, Reusing SP. Maternal psychological distress during pregnancy in relation to child development at age two. Child Dev 2006;77:573–87.

[63] Swanson LM, Pickett SM, Flynn H, Armitage R. Relationships among depression, anxiety, and insomnia symptoms in perinatal women seeking mental health treatment. J Women's Health 2011;20:553–8.
[64] Jomeen J, Martin CR. Assessment and relationship of sleep quality to depression in early pregnancy. J Reprod Infant Psychol 2007;25:87–99.
[65] Okun ML, Kiewra K, Luther JF, Wisniewski SR, Wisner KL. Sleep disturbances in depressed and nondepressed pregnant women. Depress Anxiety 2011;28:676–85.
[66] Skouteris H, Germano C, Wertheim EH, Paxton SJ, Milgrom J. Sleep quality and depression during pregnancy: a prospective study. J Sleep Res 2008;17:217–20.
[67] Skouteris H, Wertheim EH, Germano C, Paxton SJ, Milgrom J. Assessing sleep during pregnancy: a study across two time points examining the Pittsburgh Sleep Quality Index and associations with depressive symptoms. Women's Health Issues 2009;19:45–51.
[68] American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2009;32:62–7.
[69] Gilmartin AB, Ural SH, Repke JT. Gestational diabetes mellitus. Rev Obstet Gynecol 2008;1:129–34.
[70] Qiu C, Enquobahrie D, Frederick IO, Abetew D, Williams MA. Glucose intolerance and gestational diabetes risk in relation to sleep duration and snoring during pregnancy: a pilot study. BMC Women's Health 2010;10:17.
[71] Reutrakul S, Zaidi N, Wroblewski K, Kay HH, Ismail M, Ehrmann DA, et al. Sleep disturbances and their relationship to glucose tolerance in pregnancy. Diabetes Care 2011;34:2454–7.
[72] Bhattacharya DM, Campbell S. The incidence of severe complications of preeclampsia Hypertens Pregn 2005;24:181–90.
[73] Von Dadelszen P, Menzies J, Payne B, Mage L. Predicting adverse outcomes in women with severe pre-eclampsia. Semin Perinatol 2009;33:152–7.
[74] Ekholm EM, Polo O, Rauhala ER, Ekblad UU. Sleep quality in pre-eclampsia. Am J Obstet Gynecol 1992;167:1262–6.
[75] Edwards N, Blyton CM, Kesby GJ, Wilcox I, Sullivan CE. Pre-eclampsia is associated with marked alterations in sleep architecture. Sleep 2000;23:619–25.
[76] Williams MA, Miller RS, Qiu C, Cripe SM, Gelaye B, Enquobahrie D. Associations of early pregnancy sleep duration with trimester-specific blood pressures and hypertensive disorders in pregnancy. Sleep 2010;33:1363–71.
[77] Evans ML, Dick MJ, Clark AS. Sleep during the week before labor: relationships to labor outcomes. Clin Nurs Res 1995;4:238–49.
[78] Lee KA, Gay CL. Sleep in late pregnancy predicts length of labor and type of delivery. Am J Obstet Gynecol 2004;191:2041–6.
[79] Naghi I, Keypour F, Ahari SB, Tavalai SA, Khak M. Sleep disturbance in late pregnancy and type and duration of labour. J Obstet Gynaecol 2011;31:489–91.
[80] Wangel AM, Molin J, Ostman M, Jernström H. Emergency cesarean sections can be predicted by markers for stress, worry and sleep disturbances in first-time mothers. Acta Obstet Gynecol Scand 2011;90:238–44.
[81] Zafarghandi N, Hadavand S, Davati A, Mohseni SM, Kimiaiimoghadam F, Torkestani F. The effects of sleep quality and duration in late pregnancy on labor and fetal outcome. J Matern Fetal Neonatal Med 2012;25:535–7.
[82] Ananth CV, Vintzileos AM. Medically indicated preterm birth: recognizing the importance of the problem. Clin Perinatol 2008;35:53–67.
[83] Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. Lancet 2008;371:75–84.
[84] Institute of Medicine of National Academies Consensus Report. Preterm birth: causes, consequences, and prevention. Washington, DC: US National Academy of Sciences; 2006.
[85] Martin JA, Kirmeyer S, Osterman M, Shepherd RA. Born a bit too early: recent trends in late preterm births. Atlanta: National Center for Health Statistics Data Brief; 2009. p. 1–8.
[86] Williamson DM, Abe K, Bean C, Ferre C, Henderson Z, Lackritz E. Current research in preterm birth. J Women's Health 2008;17:1545–9.
[87] 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;14:107–14.
[88] Beebe KR, Lee KA. Sleep disturbance in late pregnancy and early labor. J Perinat Neonatal Nurs 2007;21:103–8.
[89] Strange LB, Parker KP, Moore ML, Strickland OL, Bliwise DL. Disturbed sleep and preterm birth: a potential relationship? Clin Exp Obstet Gynecol 2009;36:166–8.
[90] Samaraweera Y, Abeysena C. Maternal sleep deprivation, sedentary lifestyle and cooking smoke: risk factors for miscarriage: a case control study. Aust NZ J Obstet Gynaecol 2010;50:352–7.
[91] Okun ML, Schetter CD, Glynn LM. Poor sleep quality is associated with preterm birth. Sleep 2011;34:1493–8.
[92] Micheli K, Komninos I, Bagkeris E, Roumeliotaki T, Koutis A, Kogevinas M, et al. Sleep patterns in late pregnancy and risk of preterm birth and fetal growth restriction. Epidemiology 2011;22. 738–4.
[93] Okun ML, Luther JF, Wisniewski SR, Sit D, Prairie BA, Wisner KL. Disturbed sleep, a novel risk factor for preterm birth? J Women's Health 2012;21:54–60.
[94] Abeysena C, Jayawardana P, Seneviratne R. Effect of psychosocial stress and physical activity on low birth weight: a cohort study. J Obstet Gynaecol Res 2010;36:296–303.
[95] Bonzini M, Palmer KT, Coggon D, Carugno M, Cromi A, Ferrario MM. Shift work and pregnancy outcomes: a systematic review with meta-analysis of currently available epidemiological studies. BJOG 2011;118:1429–37.
[96] Bateson P, Barker D, Clutton-Brock T, Deb D, D'Udine B, Foley RA, et al. Developmental plasticity and human health. Nature 2004;430:419–21.
[97] Institute of Medicine (US) Committee on Understanding Premature Birth and Assuring Healthy Outcomes. In: Behrman RE, Butler SA, editors. Preterm birth: causes, consequences, and prevention. Washington, DC: National Academies Press (US); 2007.
[98] Baglioni C, Riemann D. Is chronic insomnia a precursor to major depression? Epidemiological and biological findings. Curr Psychiatry Rep 2012;14:511–8.
[99] Field T, Hernandez-Reif M, Diego M, Schanberg S, Kuhn C. Stability of mood states and biochemistry across pregnancy. Infant Behav Dev 2006;29:262–7.
[100] Field T, Diego M, Hernandez-Reif M. Prenatal depression effects and interventions: a review. Infant Behav Dev 2010;33:409–18.
[101] Irwin M, Clark C, Kennedy B, Christian GJ, Ziegler M. Nocturnal catecholamines and immune function in insomniacs, depressed patients, and control subjects. Brain Behav Immun 2003;17:365–72.
[102] Cyranowski JM, Marsland AL, Bromberger JT, Whiteside TL, Chang Y, Matthews KA. Depressive symptoms and production of proinflammatory cytokines by peripheral blood mononuclear cells stimulated in vitro. Brain Behav Immun 2007;21:229–37.
[103] Knutson KL. Impact of sleep and sleep loss on glucose homeostasis and appetite regulation. Sleep Med Clin 2007;2:187–97.
[104] Knutson KL, Spiegel K, Penev P, Van Cauter E. The metabolic consequences of sleep deprivation. Sleep Med Rev 2007;11:163–78.
[105] Padilha HG, Crispim CA, Zimberg IZ, De-Souza DA, Waterhouse J, Tufik S, et al. Link between sleep loss, glucose metabolism and adipokines. Braz J Med Biol Res 2011;44:992–9.
[106] Engeda J, Mezuk B, Ratliff S, Ning Y. Association between duration and quality of sleep and the risk of pre-diabetes: evidence from NHANES. Diabet Med 2013;30:676–80.
[107] McNeil J, Doucet E, Chaput JP. Inadequate sleep as a contributor to obesity and type 2 diabetes. Can J Diabetes 2013;37:103–8.
[108] Gitau R, Fisk NM, Glover V. Maternal stress in pregnancy and its effect on the human foetus: an overview of research findings. Stress 2001;4:195–203.
[109] Mulder EJ, Robles de Medina PG, Huizink AC, Van den Bergh BR, Buitelaar JK, Visser GH. Prenatal maternal stress: effects on pregnancy and the (unborn) child. Early Hum Dev 2002;70:3–14.
[110] Austin MP, Leader LR, Reilly N. Prenatal stress, the hypothalamic–pituitary–adrenal axis, and fetal and infant neurobehaviour. Early Hum Dev 2005;81:917–92.
[111] O'Donnell K, O'Connor TG, Glover V. Prenatal stress and neurodevelopment of the child: focus on the HPA axis and role of the placenta. Dev Neurosci 2009;31:285–92.
[112] Wadhwa PD, Culhane JF, Rauh V, Barve SS, Hogan V, Sandman CA, et al. Stress, infection and preterm birth: a biobehavioural perspective. Paediatr Perinat Epidemiol 2001;15:17–29.
[113] Wadhwa PD, Culhane JF, Rauh V, Barve SS. Stress and preterm birth: neuroendocrine, immune/inflammatory, and vascular mechanisms. Matern Child Health J 2001;5:119–25.
[114] Ruiz RJ, Fullerton J, Dudley DJ. The interrelationship of maternal stress, endocrine factors and inflammation on gestational length. Obstet Gynecol Surv 2003;58:415–28.
[115] László KD, Liu XQ, Svensson T, Wikström AK, Li J, Olsen J, et al. Psychosocial stress related to the loss of a close relative the year before or during pregnancy and risk of preeclampsia. Hypertension 2013;62:183–9.
[116] Spielman AJ, Caruso LS, Glovinsky PB. A behavioural perspective on insomnia treatment. Psychiatr Clin North Am 1987;10:541–53.
[117] Healey ES, Kales A, Monroe LJ, Bixler EO, Chamberlin K, Soldatos CR. Onset of insomnia: role of life-stress events. Psychosom Med 1981;43:439–51.
[118] Haynes SN, Adams A, Franzen M. The effects of presleep stress on sleep-onset insomnia. J Abnorm Psychol 1981;90:601–6.
[119] Rubman S, Brantley PJ, Waters WF, Jones GN, Constans JI, Findley JC. Daily stress and insomnia. In: Proceedings of the Eleventh Annual Scientific Sessions of the Society of Behavioral Medicine, Chicago, April 18–21; 1990 (abstract).
[120] Morin CM, Rodrigue S, Ivers H. Role of stress, arousal, and coping skills in primary insomnia. Psychosom Med 2003;65:259–67.
[121] Drake C, Richardson G, Roehrs T, Scofield H, Roth T. Vulnerability to stress-related sleep disturbance and hyperarousal. Sleep 2004;27:285–91.
[122] Riemann D, Spiegelhalder K, Feige B, Voderholzer U, Berger M, Perlis M, et al. The hyperarousal model of insomnia: a review of the concept and its evidence. Sleep Med Rev 2010;14:19–31.
[123] McEwen BS, Stellar E. Stress and the individual: mechanisms leading to disease. Archs Intern Med 1993;153:2093–101.
[124] McEwen BS. Protective and damaging effects of stress mediators. N Engl J Med 1998;338:171–9.
[125] Duman RS. Depression: a case of neuronal life and death? Biol Psychiatry 2004;56:140–5.
[126] Drevets WC. Prefrontal cortical–amygdalar metabolism in major depression. Ann N Y Acad Sci 1999;877:614–37.