Sleep Medicine 56 (2019) 145–150

Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Original Article

Stress-related sleep reactivity is associated with insomnia, psychopathology and suicidality in pregnant women: preliminary results

Laura Palagini [a, *], Giada Cipollone [a], Isabella Masci [a], Martina Novi [a], Danila Caruso [a], David A. Kalmbach [b], Christopher L. Drake [b]

[a] University Psychiatric Clinic, Department of Clinical and Experimental Medicine, Azienda Ospedaliero Universitaria Pisana- AUOP, Italy
[b] Henry Ford Hospital Sleep Disorders and Research Center, Detroit, MI, USA

ARTICLE INFO

Article history:
Received 7 September 2018
Received in revised form
4 January 2019
Accepted 10 January 2019
Available online 21 January 2019

Keywords:
Pregnancy
Insomnia
Sleep reactivity
Anxiety
Depression
Suicidality

ABSTRACT

Introduction: Depression and anxiety symptoms are commonly experienced by women during pregnancy and may have negative consequences on mothers and newborns. Deterioration of sleep quality throughout pregnancy increases insomnia, which may lead to adverse outcomes including increased psychopathology in the perinatal period. Thus, identifying women at high risk of developing insomnia may have important clinical implications on maternal–fetal outcomes. Stress-related sleep reactivity is a well-established risk factor for future insomnia, depression, and anxiety in general adult samples. However, little is known of sleep reactivity and its relations to sleep and mood pathology in pregnancy. Therefore, we explored sleep reactivity in pregnant women and its relations to prenatal symptoms of insomnia, depression, anxiety, and suicidality.
Method: Sixty-two pregnant women (mean age 33.6 ± 3 years, 20.6 ± 0.6 weeks of pregnancy) were evaluated during their routine visit at the Gynecological Unit of the University of Pisa, Italy, using the Insomnia Severity Index (ISI) for insomnia symptoms, the Ford Insomnia Response to Stress Test for sleep reactivity (FIRST), Edinburgh Postnatal Depression Scale (EPDS) for depressive symptoms, and the Zung Self Rating Anxiety Scale (SAS) for anxiety symptoms. Item #10 of the EPDS was used to assess for suicidality. Differences in means between women with high vs low stress-related sleep reactivity were calculated using t-test or Mann–Whitney U/Wilcoxon test. Linear/multiple regression analyses have been performed to study associations between variables.
Results: Pregnant women with high stress-related sleep reactivity, relative to those with low reactivity, reported greater symptoms of insomnia ($t = 6.5$, 0.004) as well as higher rates of depression (62.0% vs 6.1%, $p < 0.001$), anxiety (55.1% vs 15.1%, $p = 0.030$), and suicidality (17.2% vs 3.0%, $p = 0.025$). Multivariate models revealed sleep reactivity to correlate independently with symptoms of insomnia, depression, and anxiety, when controlling for comorbid symptoms.
Conclusions: In mid-pregnancy, women with high sleep reactivity report elevated symptoms of insomnia, depression, and anxiety, and are more likely to endorse suicidal ideation. As a prognostic marker of future insomnia and psychiatric illness, early detection of high prenatal sleep reactivity holds potential to prevent the development of sleep and mood pathology during pregnancy, thereby potentially improving maternal and child outcomes.

1. Introduction

Pregnancy is one of the most important phases in the life of a woman. Despite being a natural phenomenon, pregnancy is accompanied by major physiological, psychological and social changes and it is widely considered a period of increased vulnerability to psychiatric disorders [1]. Depression is among the most common complications during pregnancy and after delivery such

* Corresponding author. Psychiatric Clinic, Department of Clinical and Experimental Medicine, University of Pisa, Via Roma 67, 56100, Pisa, Italy. Fax: +39 050 992656.
E-mail address: lpalagini@tiscali.it (L. Palagini).

https://doi.org/10.1016/j.sleep.2019.01.009
1389-9457/

that 8.5%–10% of women during pregnancy and from 6.5% to 12.9% in the first post-partum year are clinically depressed [1]. When considering subclinical levels of depression, approximately 50% of women endorse severe depressive symptoms during pregnancy and after delivery [2]. Although depression during pregnancy receives considerable clinical and research attention, rates of anxiety during pregnancy are similarly high, ranging from 25% to 45% [3,4].

When untreated, psychopathology related to pregnancy produces profound adverse effects on maternal health, including suicidal thoughts and behaviors [1,5,6], and may also impact long-term child development throughout adulthood [1,6]. Indeed, children of psychiatrically ill mothers report impaired emotion regulation, increased stress reactivity, and maladaptive cognitions as young as early childhood to adult life [1,6,7]. To improve both mother and child outcomes, at-risk pregnant women must be identified prior to the development of depression or anxiety.

Sleep disorders such as insomnia are highly prevalent during pregnancy, particularly during the third trimester [8,9]. Critically, insomnia is a widely recognized risk factor for psychiatric disorders and suicidality [10–12], and is implicated in increasing the risk of depression and anxiety during pregnancy [13–17]. Moreover, suicide is one of the leading causes worldwide of maternal deaths during pregnancy [18,19] and suicidal ideation has been linked to sleep disturbance and insomnia symptoms [20–22]. Thus, early detection of pregnant women at high risk of developing insomnia, depression, and anxiety may have important clinical benefits for maternal-child outcomes: preventing or treating sleep disturbance could be a cost-effective method for preventing maternal psychopathology and associated consequences for the mother and child [9,14,23].

Stress exposure commonly triggers insomnia development [24], although clearly not everyone who is exposed to stress develops insomnia. By extension, the manner in which individuals regulate stress determines whether insomnia develops. The degree to which sleep is disrupted in response to stress exposure is referred to as sleep reactivity [25–27]. Sleep reactivity is a trait characteristic, and individuals with high sleep reactivity (ie, sleep systems easily disrupted by stress) have been shown to be at high risk for developing insomnia as compared to those with low sleep reactivity (ie, more robust sleep systems) [24,27,28]. Notably, high sleep reactivity is linked to greater cognitive-emotional hyperarousal and stress dysregulation [29], and even pre-exists the development of depression and anxiety [27].

Premorbid sleep reactivity accurately identifies adults at elevated risk for future insomnia, depression, and anxiety [27]. However, little is known about sleep reactivity levels or correlates in pregnant women. Given the prognostic value of sleep reactivity in general samples, characterizing sleep reactivity in pregnant women holds immense potential. In the present study, we collected cross-sectional self-report data on sleep reactivity, insomnia, depression, anxiety, and suicidality from 62 women in mid-pregnancy. We hypothesized that pregnant women with high sleep reactivity would report higher symptom levels of insomnia, depression, and anxiety. In addition, we hypothesized that highly sleep reactive pregnant women would be more likely to endorse suicidality as compared to women with low sleep reactivity. Finally, we ran multivariate analyses to explore specificity of associations among sleep reactivity, insomnia, depression, and anxiety during mid-pregnancy.

2. Methods

2.1. Selection of subjects and distribution of psychometric questionnaire

The current study included a subsample of participants from a larger, ongoing research study investigating the effects of prenatal sleep disorders and psychopathology on acute and long-term mother-child outcomes. Subjects were recruited during their first routine evaluation at the Gynecological Unit of the University of Pisa, from January 2017 through January 2018, during the first trimester of pregnancy. Our assessment represented the baseline evaluation of the longitudinal ongoing project aiming to follow up women from pregnancy to the 12th month after childbirth.

The inclusion criteria were: age >18 years; willingness to sign an informed consent to the study. The exclusion criteria were poor knowledge of the Italian language or other limitations related to Italian communication. The Ethics Committee of the University of Pisa approved the study protocol. The analyses of the present study refer to women who completed all the questionnaires necessary for the purpose of this study. All women were administered with a set of questionnaires that included the Ford Insomnia Response to Stress Test (FIRST) [25] to investigate stress-related sleep reactivity, the Insomnia Severity Index (ISI) [30] to evaluate insomnia symptoms, the Edinburgh Postnatal Depression Scale (EPDS) to measure depressive symptoms [31] the Zung Self-Rating Anxiety Scale (SAS) [32] to explore anxiety symptoms. Suicidality was evaluated with the Item number 10 of the EPDS according to literature recommendation [33]. Al subjects completed socio-demographic questionnaire, which included age, educational level, marital, and socioeconomic status and employment.

2.2. Sleep scales

Sleep reactivity was calculated with the Ford Insomnia Response to Stress Test (FIRST) [25]. The FIRST is a self-administered questionnaire that provides an indicator of an individual's overall level of "sleep reactivity" or the degree to which the person is vulnerable to sleep disturbance when exposed to stress. The questionnaire includes items relevant to situational sleep-disturbing stimuli (For example: "When you experience the following situations, how likely is it for you to have difficulty sleeping?", "After a stressful experience during the day?"; "After an argument?") with a 4-point Likert scale (1 = not likely; 4 = very likely). The sum yields a global FIRST score ranging from 9 to 36. A higher score indicates a higher level of sleep reactivity to the stimuli and, according to the authors' recommendations, FIRST scores $\geq$16 indicate elevated sleep reactivity [25] For the Italian version see Palagini et al., 2016 [34]. The FIRST was validated as a valuable tool to evaluate sleep reactivity during pregnancy [35].

Insomnia severity was evaluated with the Insomnia Severity Index (ISI) [30]. The ISI is a 7-item self-report questionnaire with a two week recall period. The sum yields a global score ranging from 0 to 28. For the purposes of this study, according to the ISI authors' recommendations, an ISI score of 8 or higher indicated insomnia symptoms. The ISI has been validated in previous Italian samples [36]. The ISI has also been used in samples of pregnant women (eg, Ref. [13]).

2.3. Psychiatric scales

Depressive symptoms were assessed using the Edinburgh Postnatal Depression Scale (EPDS). The EPDS is a 10-item, widely used screening scale for depression during pregnancy [31]. The EPDS items asked participants to rate how they felt during the previous seven days. Response categories were scored 0, 1, 2, or 3 for each item according to increased severity of the symptoms. Items 3 and 5–10 were reversed scored. According to the author's recommendations, we used the EPDS score >10 as indicative of depressive symptoms [31]. Suicidal ideation was defined based on item 10. Item 10 asked participants to rate the frequency of "the thought of harming myself has occurred to me" in the past seven days as "yes,

quite often," "sometimes," "hardly ever," or "never." For suicidal ideation, participants who gave a response of "yes, quite often," "sometimes," or "hardly ever" were categorized as "yes," but categorized as "no" when endorsing the response category "never." When evaluating the relationship between EPDS and suicidality, the EPDS score was re-calculated and item 10 was excluded to avoid multicollinearity. The EPDS has been previously used in Italian samples [33].

Anxiety symptoms were assessed with the Zung Self-rating Anxiety Scale (SAS): the SAS is a 20-item self-report assessment, divided into four groups of manifestations: cognitive, autonomic, motor and central nervous system symptoms. Each question is scored on a Likert-type scale of 1–4. The total score ranges from 0 to 80. The presence of clinically relevant anxiety symptoms is indicated by SAS scores >44 [32,37].

2.4. Statistical analysis

The statistical analyses were performed using NCSS (2008). Results were expressed as Mean ± Standard Deviation (SD). The Shapiro Wilk Test was used to check the normality of the variables. To test our hypotheses, we compared pregnant women with high vs low sleep reactivity for group differences in symptoms of insomnia, depression, and anxiety, and endorsement of suicidality; specifically, we conducted t-tests for normally distributed variables, or the Mann–Whitney U/Wilcoxon Test for non-normally distributed variables. Categorical variables were analyzed via the $\chi 2$ test. Following these analyses, we conducted series of univariate and multivariate regression models to identify factors uniquely associated with our four primary clinical outcomes: insomnia, depression, anxiety, and suicidality; linear models were used to predict continuous outcomes, whereas logistic models were used to predict binary outcomes. Specifically, significant predictors in univariate models were subsequently entered into a multivariate model. These multivariate models identified factors that were independently associated with the clinical outcome of interest while controlling for potential confounds.

3. Results

3.1. Descriptive statistics

See Table 1 for full sample characteristics. Of the 100 potential participants evaluated, 62 pregnant women (mean age 33.2 ± 4.6 years) were included in the study. Thirty-eight subjects did not complete participate in this study. Reasons for non-participation included disinterest in participating, scheduling conflicts, and continued obstetric care outside the University Hospital (as noted above, the parent project is a longitudinal study, thus inability to participate in the full study was exclusionary). Most subjects had a partner, were employed, and had a medium-to-high level of education and socio-economic status. Twenty-nine subjects (46.7%), presented with high stress-related sleep reactivity and, accordingly, 27.9% of the full sample reported elevated insomnia symptoms. Over one-third of the sample also endorsed severe symptoms of depression (33.3%) and anxiety (34.4%), and 9.6% of the sample endorsed suicidality.

We then compared pregnant women with high sleep reactivity (FIRST $\geq$ 16) vs pregnant women with low sleep reactivity (FIRST < 16). Subjects with high sleep reactivity reported higher symptom levels of insomnia and depression. An association wherein highly reactive sleepers endorsed greater anxiety approached significance ($p = 0.059$). Chi-square analyses showed that pregnant women with high sleep reactivity more likely to screen positive for depression ($\chi^2 = 1.4$ $p < 0.001$). Along these

Table 1
Demographic and psychometric variables.

	Pregnant women Total sample 1rst trimester (n = 62)	Pregnant women FIRST≥16 (n = 29)	Pregnant women FIRST <16 (n = 33)	t or $\chi 2$ (df = 2)	*p*
Age (years)					
mean ± SD	33.2 ± 4.6	34.2 ± 2	32.2 ± 2.2	1.4	0.372
Gestational week	20.6 ± 0.6	19.1 ± 0.6	21.6 ± 0.6	1.6	0.453
Marital status					
Married/de facto % (n°)	96.7 (60)	96.5 (28)	96.9 (32)	0.005[a]	0.729
Employment status					
employed % (n°)	98.3 (59)	93.1 (27)	96.9 (32)	1.8[a]	0.883
Level of education					
diploma and higher % (n°)	83.8 (52)	79.3 (23)	87.8 (29)	0.8[a]	0.298
Socio-economic status					
medium/high % (n°)	96.7 (60)	96.5 (28)	96.9 (32)	0.005[a]	0.729
FIRST score sleep reactivity					
mean ± SD	33.3 ± 4.0	21.6 ± 4.9	12.2 ± 2.3	9.5	**<0.001**
ISI score					
mean ± SD	4.9 ± 4.4	7.7 ± 4.5	2.6 ± 2.4	6.5	**0.004**
EPDS score					
mean ± SD	7.6 ± 4.9	11.8 ± 2.8	3.9 ± 2.8	7.2	**<0.001**
SAS score					
mean ± SD	39.2 ± 15.9	41.4 ± 6.2	37.4 ± 8.9	1.9	0.059
Symptoms of insomnia % (n°)	27.9 (17)	34.4 (10)	21.2 (7)	4.7[a]	0.083
Depressive symptoms % (n°)	33.3 (20)	62.0% (18)	6.1% (2)	1.4[a]	**<0.001**
Anxiety symptoms % (n°)	34.4 (21)	55.1% (16)	15.1% (5)	1.06[a]	**0.030**
Suicidality % (n°)	9.6 (6)	17.2% (5)	3.0% (1)	5.05[a]	**0.025**

Data are reported as mean ± standard deviation-SD and percentage. FIRST: Ford Insomnia Response to Stress Test for sleep-reactivity, ISI: Insomnia Severity Index, EPDS: Edinburgh Postnatal Depression Scale, SAS: Zung Self Rating Anxiety Scale. Symptoms of insomnia: ISI>8, Depressive symptoms: EPDS≥10, Anxiety symptoms: SAS>40. Suicidality: item 10 EPDS ≥1.

[a] chi-square coefficient.

lines, highly reactive sleepers were more likely to endorse anxiety ($\chi^2 = 1.06$ p = 0.030) and suicidal ideation ($\chi^2 = 5.05$, p = 0.025)) as compared to low reactive sleepers. The rate at which highly reactive sleepers endorsed higher rates of insomnia relative to low reactivity sleepers did not reach significance (34.4% vs 21.2%, $\chi^2 = 4.07$, p = 0.083); see Table 1 for full results.

No significant differences emerged on socio-demographic data or gestational week.

3.2. Identifying factors uniquely associated with prenatal insomnia

After establishing that insomnia, depression, anxiety, and suicidality differs between pregnant women with high vs low sleep reactivity, we next conducted a series of univariate and multivariate regression models to identify independent correlates of clinical outcomes (ie, insomnia, depression, anxiety, and suicidality). With insomnia as the dependent variable, univariate linear regression models showed that insomnia was associated with sleep reactivity, anxiety symptoms, and depression symptoms; see Table 2. However, when entering all three independent variables into a multivariate model, only sleep reactivity (B = 0.33, p < 0.001) and depression symptoms (B = 0.30, p = 0.001) were uniquely associated with insomnia symptoms, whereas anxiety was no longer significantly related (p = 0.06).

3.3. Identifying factors uniquely associated with prenatal depression

With depression symptoms as the dependent variable, univariate linear regression models showed that depression was correlated with sleep reactivity, anxiety symptoms, and insomnia symptoms; see Table 2. However, when entering all three independent variables into a multivariate model, only anxiety symptoms (B = 0.23, p = 0.023) and insomnia symptoms (B = 0.54, p < 0.001) were uniquely associated with depression symptoms, whereas sleep reactivity was no longer significantly related (p = 0.0631).

3.4. Identifying factors uniquely associated with prenatal anxiety

With anxiety symptoms as the dependent variable, univariate linear regression models showed that anxiety was associated with sleep reactivity, depression symptoms, and insomnia symptoms; see Table 2. However, when entering all three independent variables into a multivariate model, only sleep reactivity (B = 0.27, p < 0.048) and depression symptoms (B = 0.40, p = 0.019) were uniquely associated with depression symptoms, whereas insomnia symptoms were no longer significantly related (p = 0.792).

Table 2
Univariate and multivariate linear regression models predicting symptoms of insomnia, depression, and anxiety in pregnant women.

ISI	Univariate		Multivariate	
	B (SE)	p	B (SE)	p
FIRST	**0.34** (0.08)	**<0.001**	**0.33** (0.10)	**<0.001**
SAS	**0.17** (0.07)	**0.017**	0.13 (0.06)	0.064
EPDS	**0.32** (0.10)	**0.001**	**0.30** (0.12)	**0.001**
EPDS	Univariate		Multivariate	
	B (SE)	p	B (SE)	p
FIRST	**0.24** (0.09)	**0.028**	0.05 (0.10)	0.631
SAS	**0.26** (0.20)	**0.034**	**0.23** (0.07)	**0.019**
ISI	**0.32** (0.13)	**<0.001**	**0.54** (0.01)	**<0.001**
SAS	Univariate		Multivariate	
	B (SE)	p	B (SE)	p
FIRST	**0.35** (0.16)	**0.022**	**0.27** (0.20)	**0.048**
EPDS	**0.26** (0.20)	**0.002**	**0.40** (0.24)	**0.019**
ISI	**0.17** (0.07)	**0.017**	0.05 (0.26)	0.792

Results of the univariate and multivariate regression analyses between variables. ISI: Insomnia Severity Index, FIRST: Ford Insomnia Response to Stress Test for sleep-reactivity, SAS: Zung Self Rating Anxiety Scale, EPDS: Edinburgh Postnatal Depression Scale. B = unstandardized regression coefficient, SE: Standard Error. Significance in bold.

3.5. Identifying factors uniquely associated with prenatal suicidality

Lastly, we conducted a series of univariate and multivariate logistic regression models to identify factors uniquely associated with prenatal suicidality; see Table 3 for full results. Univariate logistic regressions models showed that greater levels of sleep reactivity (p = 0.030), depressive symptoms (p = 0.017), and insomnia symptoms (p = 0.0006) are associated with increased odds of endorsing suicidality, whereas anxiety was not (p = 0.074). In a multivariate model, only depression symptoms were uniquely related to suicidality such that a 1-point increase in EPDS scores corresponded to almost a two-fold increase in odds of endorsing suicidal ideation. Sleep reactivity (p = 0.372) and insomnia symptoms (p = 0.372) were not significant in the multivariate model.

4. Discussion

In a sample of women in mid-pregnancy, we compared sleep and mood pathology levels between women with high vs low stress-related sleep reactivity. Pregnant women with high sleep reactivity reported greater severity for insomnia, depression, and anxiety, and were more likely to engage in suicidal ideation as compared to those with low sleep reactivity. These findings extend prior knowledge of sleep reactivity to pregnant women and highlight the pathogenicity of sleep reactivity during pregnancy. Given that sleep and mood commonly deteriorate as pregnancy progresses [15,17,38], identification of women in early pregnancy who are at-risk for developing insomnia or psychiatric illness during pregnancy is critical to improve maternal and child outcomes. Given that high sleep reactivity preexists these conditions that are endemic to the perinatal period, the present study identifies sleep reactivity as a potential premorbid marker for future pathology in this highly vulnerable population.

Over a quarter of women in our study reported elevated insomnia symptoms during early pregnancy. These rates are higher than the general population, but not as high as what is observed in later stages of pregnancy [13,38]. Similarly, over one-third of pregnant women in our study endorsed elevated levels of depression and anxiety, and nearly 10% endorsed recent thoughts of self-harm. These rates are concerningly high although not as elevated as what is observed in late pregnancy [2,3]. As risk for sleep disorders and psychiatric illness increases in late pregnancy [38], it is likely that rates of insomnia, depression, anxiety, and suicidality will increase as our subjects' progress through pregnancy. As such, it is imperative to identify during early pregnancy the women who will likely be at highest risk for developing these disorders later in pregnancy or after childbirth.

Nearly half of pregnant women in our study were classified as having elevated sleep reactivity. Sleep reactivity was linked to insomnia symptoms, depressive symptoms, anxiety symptoms, and even suicidality. Insomnia severity endorsed by highly sleep reactive pregnant women was nearly twice as large as those reported by women with low sleep reactivity. Moreover, multivariate analyses revealed that sleep reactivity and depression are both independently associated with prenatal insomnia symptoms. This finding not only emphasizes the interconnectedness of prenatal sleep reactivity, depression, and insomnia, but also suggests that the link

Table 3
Univariate and multivariate logistic regression models predicting suicidality in pregnant women.

EPDS Item # 10 – Suicidality	Univariate				Multivariate			
	B (SE)	O.R.	C.I. 95%	p	B (SE)	O.R.	C.I. 95%	p
FIRST	**0.13** (0.06)	1.14	1.013–1.147	**0.030**	0.06 (0.11)	1.06	0.825–1.672	0.372
SAS	0.12 (0.06)	1.12	0.988–1.285	0.074	–	–	–	–
EPDS	**0.56** (0.23)	1.75	1.107–2.770	**0.017**	**0.54** (0.22)	1.72	1.106–1.729	**0.016**
ISI	**0.37** (0.13)	1.45	1.111–1.892	**0.006**	0.16 (0.18)	1.17	0.825–1.672	0.372

Results of the univariate and multivariate logistic regression analyses among variables. Suicidality-item 10 EPDS-Edinburgh Postnatal Depression ≥1, yes/no. ISI: Insomnia Severity Index, FIRST: Ford Insomnia Response to Stress Test for sleep-reactivity, SAS: Zung Self Rating Anxiety Scale, EPDS: Scale. B = unstandardized regression coefficient. S.E.: Standard Error; O.R.: Odds Ratio; C.I. 95%: confidence interval at 95%. Significance in bold.

between prenatal anxiety and insomnia may be accounted for by sleep reactivity and/or depression during this period.

Notably, we observed that sleep reactivity was linked to psychiatric illness during pregnancy. Highly reactive sleepers endorsed elevated depressive symptoms compared to those with low sleep reactivity, reflecting that pregnant women with high sleep reactivity are more than 10 times as likely to endorse depression. Along these lines, highly reactive sleepers were over five times as likely to endorse thoughts of self-harm during pregnancy as compared to low reactive sleepers. Multivariate analyses revealed, however, that sleep reactivity was not uniquely related to depressive symptoms or suicidality when controlling for anxiety and insomnia. Prior research in general adult samples offers mixed results regarding whether sleep reactivity is directly related to depression development [39,40] or if its effects are largely mediated by insomnia and sleep disturbance [28]. Thus, it is possible that the link between sleep reactivity and depression symptoms during pregnancy may be facilitated by insomnia or even anxiety. Future research is needed to examine prospective relationships among these factors across pregnancy.

Differences in anxiety rates were similar such that highly reactive sleepers were 3–4 times more likely to endorse clinical anxiety than pregnant women with low sleep reactivity. Unlike depression and suicidality, sleep reactivity remained a significant predictor of anxiety symptoms in multivariate analysis. This finding suggests that sleep reactivity may be directly linked to anxiety symptoms during pregnancy, even when accounting for co-occurring insomnia and depression.

Collectively, our findings show that women in mid-pregnancy with high sleep reactivity endorse greater insomnia, depressive symptoms, anxiety, and even suicidality than pregnant women with low sleep reactivity. To maximize potential for early detection of disease-risk, future studies should determine whether high sleep reactivity in early pregnancy corresponds to increased risk for developing insomnia, depression, anxiety, and suicidality during pregnancy or even after childbirth. Indeed, high sleep reactivity predicts future insomnia, depression, and anxiety in the general adult population [28,39–41]. Thus, highly sleep reactive pregnant women may be a targetable population for preventive efforts against insomnia and psychiatric illness. Given that most pregnant women in developed countries engage in routine prenatal care, many women can be assessed for sleep reactivity in the first or early portion of the second trimester. Highly sleep reactive pregnant women may be referred to for preventive care or monitored more closely by their obstetrician or midwife at routine visits for early signs of sleep and mood pathology to ensure early intervention.

Prior prospective evidence shows that sleep reactivity directly influences insomnia development, whereas its effects on future depression may be mediated, at least in part, by sleep disturbance and insomnia [28,40] These data are consistent with the present findings showing that sleep reactivity was not directly linked to depressive symptoms or suicidality when accounting for the effects of co-occurring anxiety and insomnia. Thus, the most effective preventive care and early interventions may focus on promoting healthy sleep habits and target early emerging sleep symptoms; research is needed to explore the viability of this care approach. Since highly reactive sleepers are sensitive to myriad sources of stress [27], many pregnancy related factors likely contribute to sleep distress including physical discomfort in bed, pain, mental stress, sleep breathing difficulties, and comorbid illness. Therefore, highly sleep reactive pregnant women may benefit from referrals to sleep clinics where specialists can monitor symptoms, differentially diagnose, identify contributing factors, and create a personalized treatment plan.

The present study must be interpreted in light of certain methodological limitations. Foremost, this study was not prospective, thus we cannot establish directionality or causality. Prior prospective research has influenced some of our interpretation of findings, but future research is needed to determine the causality among these factors and to characterize any prognostic utility of sleep reactivity in pregnancy. Secondly, the study consisted of only 62 women in mid-pregnancy. Therefore, rates of insomnia, depression, anxiety, and suicidality may not reflect those of the greater population. Further, the modest sample size may have increased risk for type II errors, particularly in the multivariate models. Taken together, the associations among sleep reactivity, insomnia, and psychopathology should be investigated prospectively in a larger sample to provide a better understanding of how these factors evolve across pregnancy and postpartum to impact maternal and child health.

In conclusion, nearly half of women in mid-pregnancy have highly reactive sleep systems. Women with high sleep reactivity report higher levels of insomnia, depression, and anxiety, and are more likely to have thoughts of self-harm than women with low sleep reactivity. At-risk women can be identified via routine prenatal care, which may allow for opportunity to prevent development of mood or sleep pathology. Future research is needed to clarify how trajectories of insomnia, depression, anxiety, and suicidality differ between highly reactive sleepers and non-reactive sleepers across pregnancy and after childbirth.

Acknowledgement

No grant or funding to acknowledge.

Conflict of interest

Dr. Drake has received research support from Merck & Co., Eisai Co., Aladdin Dreamer, Jazz, Actelion, and Teva, and has served on speakers bureau for Merck & Co. No other financial or non-financial interests exist.

Dr. Kalmbach has received research support from Merck & Co.

Dr Danila Caruso, Dr Giada Cipollone, Dr Isabella Masci, Dr Martina Novi, Dr Laura Palagini: nothing to disclose.

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: https://doi.org/10.1016/j.sleep.2019.01.009.

References

[1] Dunkel Schetter C, Tanner L. Anxiety, depression and stress in pregnancy: implications for mothers, children, research, and practice. Curr Opin Psychiatr 2012;25:141–8.
[2] McCall-Hosenfeld JS, Phiri K, Schaefer E, et al. Trajectories of depressive symptoms throughout the peri- and postpartum period: results from the first baby study. J Wom Health (Larchmt) 2016;25:1112–21.
[3] Malak SM, Crowley MJ, Mayes LC, et al. Maternal anxiety and neural responses to infant faces. J Affect Disord 2015;172:324–30.
[4] Falah-Hassani K, Shiri R, Dennis CL. The prevalence of antenatal and postnatal co-morbid anxiety and depression: a meta-analysis. Psychol Med 2017;47:2041–205.
[5] Alhusen JL, Ayres L, DePriest K. Effects of maternal mental health on engagement in favorable health practices during pregnancy. J Midwifery Wom Health 2016;61:210–6.
[6] Kendig S, Keats JP, Hoffman MC, et al. Consensus bundle on maternal mental health: perinatal depression and anxiety. Obstet Gynecol 2017;129:422–30.
[7] Leis JA, Heron J, Stuart EA, et al. Associations between maternal mental health and child emotional and behavioral problems: does prenatal mental health matter? J Abnorm Child Psychol 2014;42:161–71.
[8] Wilkerson AK, Uhde TW. Perinatal sleep problems: causes, complications, and management. Obstet Gynecol Clin N Am 2018;45:483–94.
[9] Chaudhry SK, Susser LC. Considerations in treating insomnia during pregnancy: a literature review. Psychosomatics 2018;59:341–8.
[10] Baglioni C, Battagliese G, Feige B, et al. Insomnia as a predictor of depression: a meta-analytic evaluation of longitudinal epidemiological studies. J Affect Disord 2011;135:10–9.
[11] Woznica AA, Carney CE, Kuo JR, et al. The insomnia and suicide link: toward an enhanced understanding of this relationship. Sleep Med Rev 2015;22:37–46.
[12] Pigeon WR, Bishop TM, Krueger KM. Insomnia as a precipitating factor in new onset mental illness: a systematic review of recent findings. Curr Psychiatr Rep 2017;19:44.
[13] Swanson LM, Pickett SM, Flynn H, et al. Relationships among depression, anxiety, and insomnia symptoms in perinatal women seeking mental health treatment. J Wom Health (Larchmt) 2011;20:553–8.
[14] Dørheim SK, Bjorvatn B, Eberhard-Gran M. Can insomnia in pregnancy predict postpartum depression? A longitudinal, population-based study. PLoS One 2014;9:94674.
[15] Palagini L, Gemignani A, Banti S, et al. Chronic sleep loss during pregnancy as a determinant of stress: impact on pregnancy outcome. Sleep Med 2014;15:853–9.
[16] Bei B, Coo S, Trinder J. Sleep and mood during pregnancy and the postpartum period. Sleep Med Clin 2015;10(1):25–33.
[17] Okun ML. Sleep and postpartum depression. Curr Opin Psychiatr 2015;28:490–6.
[18] Lindahl V, Pearson JL, Colpe L. Prevalence of suicidality during pregnancy and the postpartum. Arch Wom Ment Health 2005;8:77–87.
[19] Gavin AR, Tabb KM, Melville JL, et al. Prevalence and correlates of suicidal ideation during pregnancy. Arch Wom Ment Health 2011;14(3):239–46.
[20] Benute GR, Nomura RM, Jorge VM, et al. Risk of suicide in high risk pregnancy: an exploratory study. Rev Assoc Med Bras 2011;57:583–7.
[21] Sit D, Luther J, Buysse D, et al. Suicidal ideation in depressed postpartum women: associations with childhood trauma, sleep disturbance and anxiety. J Psychiatr Res 2015;66–67:95–104.
[22] Gelaye B, Addae G, Neway B, et al. Poor sleep quality, antepartum depression and suicidal ideation among pregnant women. J Affect Disord 2017;209:195–200.
[23] Ross LE, Murray BJ, Steiner M. Sleep and perinatal mood disorders: a critical review. J Psychiatry Neurosci 2005;30:247–56.
[24] Spielman AJ, Caruso LS, Glovinsky PB. A behavioral perspective on insomnia treatment. Psychiatr Clin North Am 1987;10. 541-153.
[25] Drake C, Richardson G, Roehrs T, et al. Vulnerability to stress related sleep disturbance and hyperarousal. Sleep 2004;27:285–91.
[26] Drake CL, Roth T. Predisposition in the evolution of insomnia: evidence, potential mechanisms, and future directions. Sleep Med Clin 2006:333–49.
[27] Kalmbach DA, Anderson JR, Drake CL. The impact of stress on sleep: pathogenic sleep reactivity as a vulnerability to insomnia and circadian disorders. J Sleep Res 2018:12710.
[28] Drake CL, Pillai V, Roth T. Stress and sleep reactivity: a prospective investigation of the stress-diathesis model of insomnia. Sleep 2014;37:1295–304.
[29] Fernández-Mendoza J, Vela-Bueno A, Vgontzas AN, et al. Cognitive-emotional hyperarousal as a premorbid characteristic of individuals vulnerable to insomnia. Psychosom Med 2010;72:397–403.
[30] Morin CM. Insomnia: psychological assessment and management. New York: Guilford Press; 1993.
[31] Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression. Development of the 10-item Edinburgh postnatal depression scale. Br J Psychiatr 1987;150:782–6.
[32] Zung WWK. A rating instrument for anxiety disorders. Psychosomatics 1971;12:371–9.
[33] Mauri M, Oppo A, Borri C, et al. SUICIDALITY in the perinatal period: comparison of two self-report instruments. Results from PND-ReScU. Arch Wom Ment Health 2012;15:39–47.
[34] Palagini L, Manni R. Misurare il sonno. Torino: Minerva Medica; 2016.
[35] Gelaye B, Zhong QY, Barrios YV, et al. Psychometric evaluation of the Ford insomnia response to stress test (FIRST) in early pregnancy. J Clin Sleep Med 2016 Apr 15;12(4):579–87.
[36] Castronovo V, Galbiati A, Marelli S, et al. Validation study of the Italian version of the insomnia severity Index (ISI). Neurol Sci 2016;37:1517–24.
[37] Conti L. Repertorio delle scale di valutazione in psichiatria. Firenze: SEE; 2000.
[38] Santiago JR, Nolledo MS, Kinzler W, et al. Sleep and sleep disorders in pregnancy. Ann Intern Med 2001;134(5):396–408.
[39] Jarrin DC, Chen IY, Ivers H, et al. The role of vulnerability in stress-related insomnia, social support and coping styles on incidence and persistence of insomnia. J Sleep Res 2014;12:1373–8.
[40] Vargas I, Friedman NP, Drake CL. Vulnerability to stress-related sleep disturbance and insomnia: investigating the link with comorbid depressive symptoms. Transl Issues Psychol Sci 2015;1(1):57.
[41] Kalmbach DA, Pillai V, Arnedt JT, et al. Sleep system sensitization: evidence for changing roles of etiological factors in insomnia. Sleep Med 2016;21:63–9.