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Changes in Sleep and Depressive Symptoms in The Perinatal Period: A Case Series of Four Japanese Mothers

Kumiko Kido[1], Mari Matsuo[2], Yuko Uemura[1], Atsuko Shiota[3], Satoshi Tada[1]

1 Kagawa Prefectural University of Health Sciences, Japan
2 Bokko Birth Home, Japan
3 Kagawa University, Japan
Corresponding author: kkumiko0305@gmail.com

ABSTRACT

Background: Late maternal deaths have been associated with psychiatric disorders such as perinatal depression and their prevention is an important issue within perinatal healthcare. Sleep disturbance can be a chronic stressor, and chronic stress can lead to depression. Sleep disturbances during pregnancy, as a lifestyle factor, are associated with postpartum depression. Depression could be assessed using prostaglandin D2 (PGD2) levels. Compared to sleep prior to pregnancy, shorter sleep duration and poorer sleep efficiency in the postpartum period have been reported. The association of breastfeeding, sleep habits, baby care, stress and depressive symptoms have not been examined.
Purpose: This case series describes changes in sleep quality, stress, and depressive symptoms of perinatal women.
Methods: This was a longitudinal case study. Pregnant women, who consented to participate, were followed between the third trimester of pregnancy and four month postpartum. This study was approved by the Ethical Review Committee of the Kagawa Prefectural University of Health Sciences (No.350).
Results: The Japan Pittsburgh Sleep Quality Index (JPSQI) scores decreased over the postpartum period. However, there were temporarily higher JPSQI scores in the early postpartum period. Sleep duration and sleep efficiency improved two months postpartum. No participant scored ≥9 on the Japanese version of the Edinburgh Postnatal Depression Scale (J-EPDS) from the third trimester of pregnancy to four months postpartum. Two samples had temporarily higher J-EPDS scores from two weeks to one month postpartum, showing a sharp drop at two months postpartum. The Patient Health Questionnaire-9 (PHQ-9) scores and urine biopyrin (UBP) levels decreased, while PGD2 levels increased over the postpartum period.
C**onclusion**: Sleep quality and depressive symptoms improved over time postpartum. Improved sleep quality reduces stress, as shown by decreased levels of an oxidative stress marker with improved sleep quality. PGD2 and UBP are useful biomarkers to assess sleep quality and stress, respectively.

Keywords: *chronic stress; sleep quality; perinatal depression; prostaglandin D2; urine biopyrin*

Corresponding email: *kkumiko0305@gmail.com*
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BACKGROUND

The incidence of late maternal death (death of a woman due to direct or indirect obstetric causes more than 42 days but less than 1 year after childbirth; ICD-11) has increased compared to that of early maternal death, especially in the last decade (Kassebaum et al., 2014; Kyu et al., 2018). Late maternal death is reported to be related to mental health problems, such as postnatal depression, which develops between 6 weeks and 1 year postpartum (Knight, 2019) thus, identifying the risk factors for postnatal depression is crucial.

In Japan, the Edinburgh Postnatal Depression Scale, Japanese version (J-EPDS), has been used to identify symptoms of postnatal depression and prevent them at early stages. The assessment is usually carried out at the 2-week and 1-month postpartum follow-up visits, but no routine assessment is carried out between 6 weeks and 1 year postpartum, when the risk of postpartum depression may be high. It also reported that since the EPDS is a self-administered questionnaire, 20.7% of the women may not answer honestly if they have confidence in their coping skills, for fear of the consequences of their answers, or for fear of health service interventions (Forder et al., 2020; Ghaedrahmati et al., 2018). Identified five risk factors for postpartum depression: psychological, obstetrical, biological, social, and lifestyle factors. As lifestyle factors, insomnia during pregnancy (Dorheim et al., 2014) and sleep disturbance have been reported to be associated with postnatal depression (Ross et al., 2005; Zinga et al., 2005). Furthermore, sleep disturbance is an essential component in the pathophysiology of anxiety-related disorders (Cox & Olatunji, 2020), and psychiatric treatments for improving sleep have been provided to patients with depression (Suzuki & Tamaki, 2018). There are also sex differences in the symptoms of depression, where a higher number of women than men report sleep disturbances (Hyde & Mezulis, 2020). Postpartum depression and sleep disturbance have been found to be highly linked after adjusting for the following risk factors of depression: history of depression, depression during pregnancy, poor relationship with a partner, and stressful life events. Additionally, there is a report that a history of depression or sleep disorders, mixed feeding for infant, first birth, premature birth, and sex of the child (male) were factors associated with poor sleep quality in postpartum women (Dorheim et al., 2009).

The hormones prostaglandin D2 (PGD2) and prostaglandin E2 (PGE2) are strongly associated with sleep in humans. They are involved in the regulation of slow-wave sleep (SWS: non-rapid eye movement [REM] sleep, deep sleep) and paradoxical sleep (PS: REM sleep, shallow sleep). When the levels of PGD2 increase, there is an increase in SWS and PS durations, whereas an increase in PGE2 levels leads to a decrease in their durations (Hayaishi, 1988). SWS is essential for the recovery of cortical functional connectivity (eliminating fatigue) and is also associated with the pathogenesis of depression. Some studies have reported that changes in PGD2 levels are associated with depressive symptoms (behavior) (Chu et al., 2017), and it is possible that depression reflecting sleep quality can be assessed by PGD2 levels. Urinary tetranor-PGDM (t-PGD2) is easily measured and has been shown to be indicative of PGD2 levels in humans (Zhou et al., 2020).

In Japan, Hirose et al found that in the perinatal period, women with depressive symptoms had a decreased length of sleep and poor sleep quality at 1 month postpartum (Hirose, 2000). Recent studies have reported symptoms of depression and anxiety in postpartum mothers with sleep problems in the first month after childbirth (Adachi et al., 2018) as well as the possibility of sleep disturbances inducing postpartum depression in first-time mothers (Fujioka et al., 2016). There is limited evidence of a link between maternal postpartum depression and sleep, and professionals may not pay much attention

to the sleep status of postpartum mothers, as it is natural for a postpartum woman to sleep intermittently during the night while feeding her baby. The EPDS, a risk assessment scale for postnatal depression, has only one measure for mother's sleep: "I have been so unhappy that I have had difficulty sleeping". The question consists of two components, "I have been so unhappy" and "I have had difficulty sleeping." The question consists of two components, "unhappiness" and "difficulty sleeping/falling asleep," with varying answers depending on the focus of the respondent, and it does not clarify whether sleep disturbance is impaired in quantity or quality.

Sleep is regulated by the biological clock (circadian rhythm) and by homeostatic functions. During the postpartum period, sleep is significantly affected by parenting and breastfeeding. A Study examined the sleep status of women during pregnancy, and at 1 and 4 months postpartum (Inui et al., 2008). They found that the sleep duration of pregnant women was longer than that of non-pregnant women, but the sleep-wake rhythm of postpartum mothers was 24 hours, although the sleep duration was shortened by mid-waking and sleep efficiency was poor. In other words, the sleep-wake pattern of postpartum women seems to be significantly different from that of non-pregnant women although the circadian rhythm is maintained. However, they did not examine the presence of depressive symptoms in the participants nor did they investigate whether the women were breastfeeding, sleeping with the baby, or caring for other children.

Sleep disturbance can be a chronic stressor. Chronic stress can lead to depression (Chiba et al., 2012). Urine biopyrin (UBP), a marker of oxidative stress, is a simple and useful indicator of chronic stress (Tada et al., 2020). The levels of oxidative stress markers have been reported to correlate with intensity of depressive symptoms (Miyaoka et al., 2005). UBP levels have been found to be high in pregnant women with high psychological stress (Matsuzaki et al., 2006), indicating that oxidative stress markers may be useful as objective measures of depression.

OBJECTIVE

Studies to describe changes in sleep quality and quantity during pregnancy and the postpartum period and the associated changes in stress markers and depressive symptoms have not been conducted in Japan. This case series aimed to describe how these change for Japanese mothers in the perinatal period.

METHODS

Study design

This was a longitudinal case series. The participants were followed from the third trimester of pregnancy to four months postpartum.

We posed the following research question: How are the following variables associated with the status of sleep, depression, and stress in women during the perinatal period?

(1) Japan Pittsburgh Sleep Quality Index (JPSQI) scores, a measure of sleep status as a composite of sleep duration and sleep efficiency;

(2) EPDS and Patient Health Questionnaire-9 (PHQ-9), as a measure of depression status;

(3) PGD2, as a marker of depression reflecting sleep quality;

(4) UBP, as a marker of psychological stress.

The study lasted from August 2021 to February 2022.

Selection of study subjects and data collection

Pregnant women aged over 20 years (in the second trimester of pregnancy) who provided consent to participate were asked to complete the following: basic questions (framed with reference to the five risk factors – psychological, obstetric, biological, social

and lifestyle factors – reported by (Ghaedrahmati et al., 2018), sleep diary, JPSQI, PHQ-9, and J-EPDS.

Sample size

Although there were no previous studies to calculate the sample size, we invited 20 pregnant women to participate, and four agreed.

Inclusion and exclusion criteria

The inclusion criteria were ability to communicate in Japanese and answer the questionnaire. The exclusion criteria were age <18; need for a language translator; and presence of obesity, allergies, or asthma (as these conditions could affect the PGD2 assay).

Procedure

Pregnant women who provided oral consent to participate in the study were given a consent form and withdrawal form. Once we received the signed consent forms, the following questionnaires were administered: basic questions, sleep diary, JPSQI, PHQ-9, and J-EPDS. In addition, early morning urine samples were collected for UBP and PGD2 assays. The survey forms and urine sample were collected in the following schedule:

1st submission: Third trimester

2nd submission: Fourth postpartum day

3rd submission: 2-week postpartum health examination

4th submission: 1-month postpartum health examination

5th and subsequent submissions: After the 1-month postpartum health examination until the participant wished to engage with the study.

Analysis Method

We present graphs of our descriptive data from the four participants.

Ethics Considerations

This study was approved by the Ethical Review Committee of Kagawa Prefectural University of Health Sciences (No.350).

RESULTS

The characteristics of the participants are shown in Table 1.

Table 1. The characteristics of the participants

	Sample 1	Sample 2	Sample 3	Sample 4
Age (years)	26	33	21	32
First time baby	No	Yes	Yes	No
Unfortunate life events	No	No	No	No
Unexpected pregnancy	No	No	No	No
Marital contentment	9	NA	10	6
0 to 10 Completely unsatisfied; 0 to completely satisfied:10				
Nutritional method	1	0	0	1
Complete Breastfeeding, 1; mixed feeding ,0				
sleeping habit	1	1	1	0
Together (with mother), 1; separately, 0				

NA: no answer

Two of the four participants were first-time mothers. No mother reported an adverse event during the data collection period. All bore expected pregnancies. Marital contentment ranged from 6 to 10, with none clearly unsatisfied. There was an equal number of mothers who performed complete breastfeeding and mixed feeding. Three mothers shared a bed with their children, and one slept separately from the baby.

Changes in the JPSQI scores from the third trimester of pregnancy to the postpartum period for each sample are shown in Figure 1. The JPSQI scores decreased over the postpartum period. No regularity changes were observed in the JPSQI sores in the third trimester of pregnancy until the postpartum period. However, sample 1 and sample 4 had temporarily higher JPSQI score in the early postpartum period.

The changes in sleep efficiency and sleep duration of the JPSQI are shown in Figures 2–3. Sleep efficiency means actual sleep time expressed as a percentage of time in bed (expressed as %). Poor sleep efficiency means that the time awake is repeated in frequency while in bed. For example, the sleep efficiency tends to be poorer during the postpartum period, as mothers are more likely to be frequently interrupted in their sleep by the crying babies to feed.

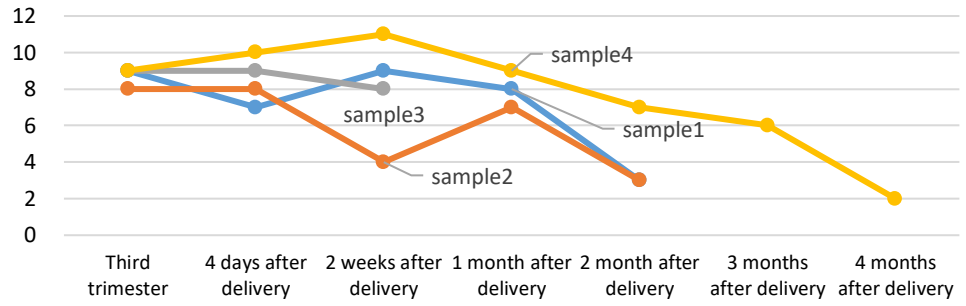

Figure1 Changes in the JPSQI

Figure2 Changes in the sleep duration

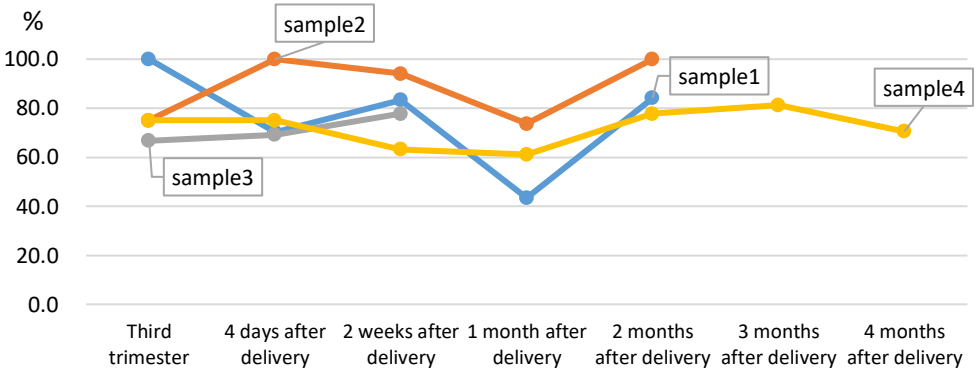

Figure 3 Changes in the sleep efficiency

Sleep duration and sleep efficiency improved in the first two months after delivery for samples 1, 2, and 4. However, only sample 4 showed a slight deterioration in sleep duration up to four months postpartum.

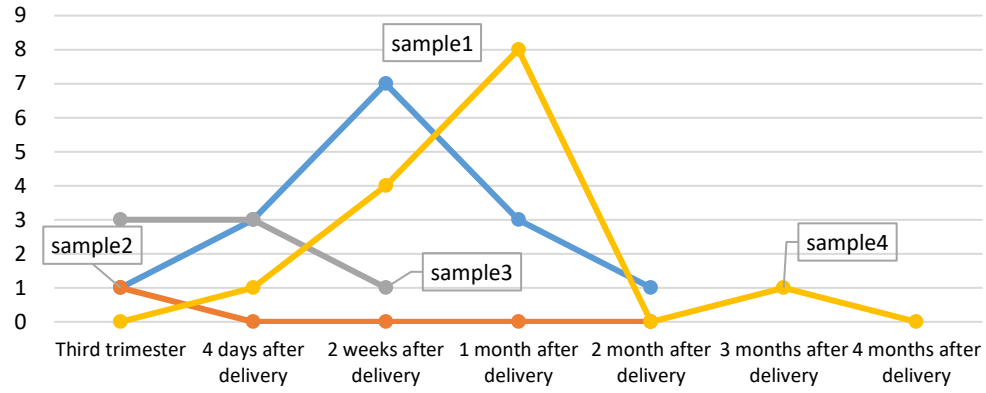

Figure4 Changes in the J-EPDS

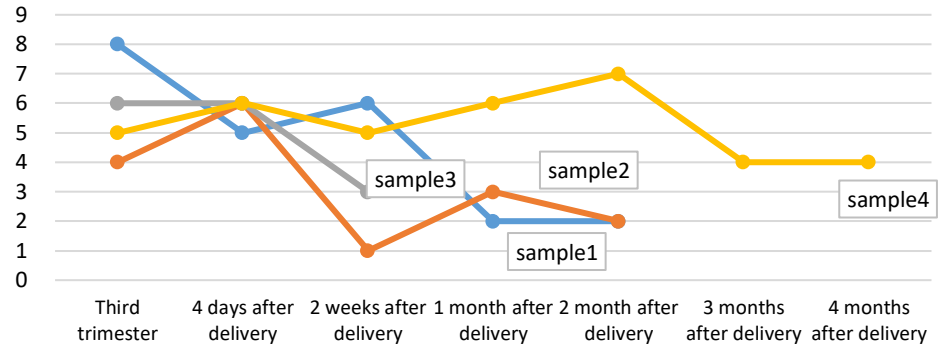

Figure5 Changes in the PHQ-9

No participant scored ≥9 on the J-EPDS in the third trimester of pregnancy through 4 month postpartum. PHQ-9 scores ≥5 (mild or high depression) were reported by three (75%) women in the third trimester, three (75%) in the early postpartum period, and two (50%) at 2 weeks postpartum. No overall trend was observed in the J-EPDS scores in the third trimester of pregnancy until the postpartum period. Samples 1 and 4 had transiently increased J-EPDS scores from two weeks to one month postpartum, then showed a sharp drop at two months postpartum. The PHQ-9 scores decreased over the postpartum period.

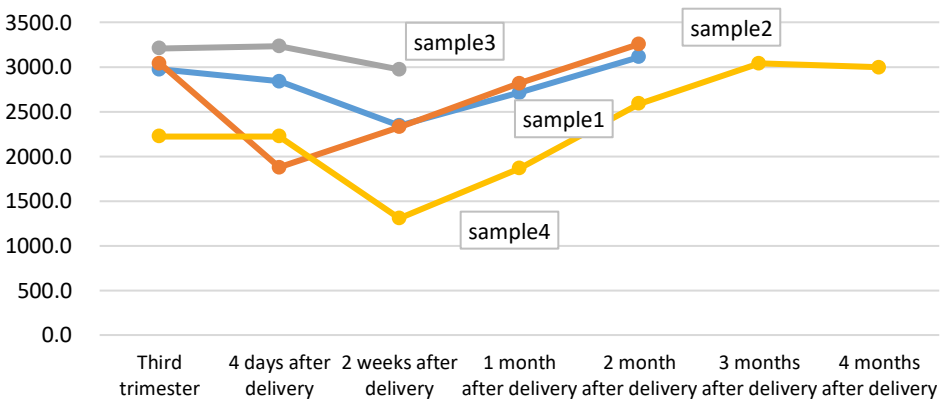

Figure 6 Changes in the PGD2

The PGD2 levels increased over the postpartum period. At two months postpartum, it was higher than at third trimester of pregnancy. In the same period, the UBP levels decreased.

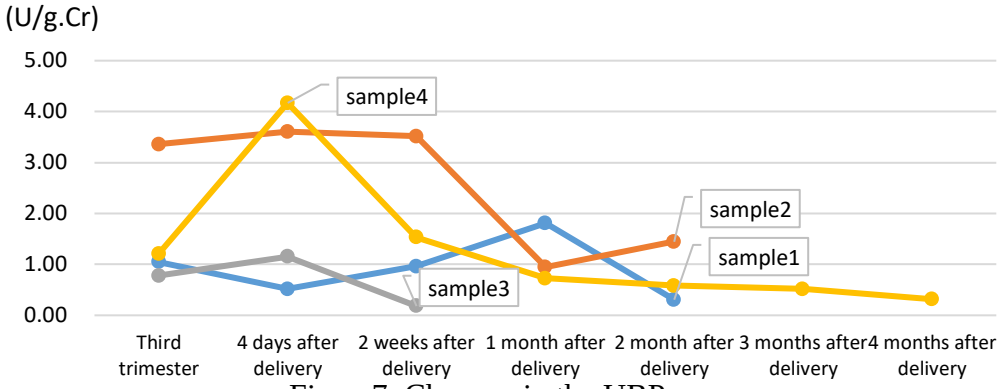

Figure7 Changes in the UBP

The entire samples' sleep diaries are presented in Table 2. An intermittent sleeping pattern can be ovserved from the third trimester of pregnancy to the postpartum period due to parenting of the baby. After delivery, the mother cared for the child seven to 14 times a day. With the exception of one, the number of parenting tasks performed by the mothers did not decrease over time. Additionally, they rarely slept during daytime despite intermittent sleep during the night.

Table2. The entire samples' sleep diaries

Sample No.	The timing of the study	PM 0	1	2	3	4	5	6	7	8	9	10	11	AM 12	1	2	3	4	5	6	7	8	9	10	11	Frequency of ✔
1	Third trimester																									
	4 days after delivery	NA																								
	2 weeks after delivery																									
		✔	✔	✔		✔	✔	✔						✔	✔	✔		✔	✔	✔				✔	✔	14
	1 month after delivery																									
		✔	✔	✔		✔			✔	✔		✔	✔		✔	✔	✔			✔	✔				✔	14
	2 month after delivery																									
						✔	✔				✔			✔				✔	✔				✔			7
2	Third trimester																									
	4 days after delivery																									
							✔	✔						✔	✔	✔	✔				✔	✔				8
	2 weeks after delivery																									
						✔				✔			✔				✔			✔		✔		✔		7
	1 month after delivery																									
		✔			✔	✔					✔	✔	✔	✔					✔		✔		✔			10
	2 month after delivery																									
		✔		✔			✔				✔			✔		✔		✔		✔		✔	✔	✔		11
3	Third trimester																									
	4 days after delivery																									
		✔	✔	✔	✔	✔		✔			✔	✔		✔	✔				✔	✔			✔	✔	✔	15
	2 weeks after delivery																									
		✔	✔	✔	✔			✔		✔	✔	✔			✔		✔		✔	✔			✔	✔		14
	1 month after delivery																									
		✔	✔	✔	✔	✔		✔	✔	✔	✔			✔		✔			✔	✔			✔			14
4	Third trimester																									
		✔						✔		✔												✔			✔	5
	4 days after delivery																									
			✔		✔		✔			✔	✔			✔			✔	✔			✔					9
	2 weeks after delivery																									
		✔		✔	✔	✔	✔	✔	✔		✔				✔	✔		✔				✔	✔	✔		14
	1 month after delivery																									
				✔			✔		✔		✔				✔					✔	✔		✔			8
	2 months after delivery																									
		✔		✔			✔		✔						✔	✔	✔				✔					8
	3 months after delivery																									
		✔	✔			✔	✔	✔	✔	✔						✔						✔			✔	10
	4 months after delivery																									
			✔			✔		✔	✔						✔							✔	✔		✔	✔	9

	Lying on the bed.
	Slept deeply
✔	Woke up for nursing and/or feeding the baby
NA	Not submitted sleep diary

DISCUSSION

In this study, the sleep diary of all samples demonstrated intermittent sleep in the third trimester of pregnancy until the postpartum period due to feeding the baby. Additionally, they rarely slept during daytime despite intermittent sleep overnight. Sleep disturbance has been reported to be associated with postnatal depression (Ross & Steiner, 2005;Zinga and Born, 2005). A report also suggested that sleep disturbance is a common symptom of perinatal depression and one of the possible early predictors of poor mental health among pregnant women(Fanti and D'Agostino, 2022). In this study, two mothers had temporarily worse sleep quality and higher J-EPDS scores from two weeks to one month postpartum. The J-EPDS is a commonly used measure to assess perinatal depression in Japan, a risk assessment scale for postnatal depression did not assess the sleep quality; "I have been so unhappy" and I have had difficulty sleeping." In this study, the women experienced changes in the sleep status in their perinatal period. If sleep status is related to the degree of depressive symptoms, the J-EPDS score may not be an accurate measure of depression. For example, Item 3 of the PHQ-9—trouble falling or staying asleep or sleeping too much—was reported to be a promising screening tool for sleep disturbance(MacGregor et al., 2012).Therefore, a question about sleep quality linked to depression should be provided to evaluate mothers' depressive condition more accurately. The J-EPDS alone may not be sufficient to assess sleep quality. Additional items are required to evaluate sleep quality linked to perinatal depression.

Previous studies have reported that the following factors impact the link between postpartum depression and sleep disturbances: child's feeding methods, first baby or premature birth, and child's sex (male neonates) (Dørheim et al., 2009). In this study, the numbers of mothers who were performing complete breastfeeding and mixed breastfeeding were the same. Further, there were equal numbers of primipara and multipara, and gender of the baby was unknown, which cannot be comparable to the results of previous studies. However, it can be assumed that the heavy burden of childcare affects the quality of sleep and correlates to depressive symptoms (Song et al., 2008). The sleep diaries in this study revealed that all samples slept intermittently from late pregnancy through the postpartum period due to breastfeeding and other childcare care activities. However, none exhibited severe depressive symptoms, and sleep deprivation due to the burden of parenting may not be the only factor affecting the degree of depression.

In this study, the PGD2 levels increased over the postpartum period. PGD2 is the main hormone associated with sleep. They regulate the SWS (non-REM sleep; deep sleep) and PS (REM sleep; shallow sleep), and there is evidence that the durations of SWS and PS increase with increasing PGD2 levels (Hayaishi, 1988). PGD2 is one of the bioactive substances involved in sleep, body temperature, and pain regulation in mammals (Urade and Hayaishi, 2011). The quality and quantity of sleep improved over this period, suggesting that PGD2 may be an appropriate hormonal indicator of the state of sleep during the postpartum period.

As sleep quality improved, UBP levels, a marker of oxidative stress, decreased. We can infer that improved sleep quality reduces stress among perinatal women. Stress is often assumed to be linked to depression, but a study reported no association between mothers' parenting stress and depression(Barańczuk & Pisula, 2020). Chronic stress heightens vulnerability to depression; nevertheless, the contribution of some confounding factor is essential for the stress to result in depression. In other words, poor sleep quality may increase stress and potentially exacerbate depressive symptoms. This is the first study in which UBP levels were assessed during the perinatal period. Improved sleep quality in women during this period may lead to decreased stress and improved mental

health. The relationships among perinatal depression, stress, and sleep need further investigation.

There is also a link between increasing age and maternal depression (Maghami et al., 2021). In Japan, the number of pregnant women over the age of 35 years has been rising. Therefore, it is necessary to focus on the quality of sleep of women over 35 years of age, and professionals need to engage in health education for improving sleep quality and preventing perinatal depression. Therefore, professionals should take into account the age of women and provide health information on improving sleep quality to help prevent perinatal depression.

CONCLUSION

Women's sleep status changes significantly during the perinatal period. Sleep quality and depressive symptoms improved over the postpartum period. For accurate perinatal assessment of depressive symptoms, an item on sleep status can be added to the standard evaluation. Further, improved sleep quality may reduce stress because a marker of oxidative stress decreased with improved sleep quality. In perinatal women, PGD2 can be used as a hormonal marker to assess sleep quality and UBP as a marker to assess stress.

DISCLOSURE STATEMENT

The authors declare that there are no conflicts of interest.

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