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Sleep disorders during pregnancy - its prevalence, characteristic and neonatal implications

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Summary:

Introduction and purpose: Each phase of a woman's life, from childhood to menopause, may be associated with a variety of sleep disturbances. The pregnancy is particularly predisposed to develop sleep disorders such as insomnia, restless legs syndrome and sleep-disordered breathing, which require special management.

This article reviews the most common sleep disturbances in pregnancy and discusses epidemiology, pathophysiology, maternal and fetal possible implications and therapeutic options in the pregnant population.

Material and methods of research: The search was conducted using PubMed and Google Scholarship databases available to January 2024.

Results: Although the exact cause of previously mentioned diseases remains uncertain, the impact of hormonal changes, the body mass before pregnancy and weight gaining during gestation on their development is highlighted by researchers. Poor sleep in pregnancy may have negative outcomes for women as well as fetuses and influence the pregnancy course. These sleeping disorders may also contribute to development of other systemic diseases. The management of sleep disturbance in pregnant patients is challenging due to the risk of teratogenicity, pharmacokinetic changes and the dynamic nature of pregnancy, thus nonpharmacologic interventions should be preferred as safer than medications.

Conclusions: Sleep disturbances result in poorer quality of pregnant women's life and have a negative impact on the condition of pregnancy. Thus, this theme should create the need for additional research on the possibilities of prevention and treatment strategies of sleep disorders in pregnant women.

Key words: Pregnancy; Sleep disorders; Insomnia; Restless leg syndrome; Sleep-disordered breathing

1. Introduction

Pregnant women very commonly report issues with sleep quality. Many of these problems derive from sleep disorders during pregnancy. Although their exact cause is unknown, it likely involves physiological changes, especially hormonal ones.

These disorders not only impact sleep quality but may also have long-term negative effects on the health of both the mother and the fetus [1]. In this work, we focused on insomnia, restless leg syndrome and sleep-disordered breathing. Due to the growing interest in this area, we aimed to present the latest information, placing particular emphasis on the impact of these disorders on the health of women and developing fetuses, as well as discussing available treatment methods. This is crucial, especially considering the limited use of medications during pregnancy and the frequent trivialization of these issues. A comprehensive understanding of these matters will contribute to providing better, holistic care for pregnant women.

2. Insomnia

Insomnia is a sleep disorder characterized by difficulties in falling asleep and waking up during the night. Its prevalence is associated with the trimester of pregnancy, with the highest occurrence in the third trimester estimated at 42.4% [2,3]. Potential risk factors for insomnia include overweight or obesity in early pregnancy, improper sleep hygiene, sleeping in the lateral position causing back pain, gastroesophageal reflux, and fetal movement [4,5].

The consequences of insomnia and other sleep disorders in pregnant women are still not fully understood. Li et al. concluded from their meta-analysis that insomnia during pregnancy is not correlated with postpartum depression. However, poor sleep quality, especially in the third trimester, was found to be associated [6]. These findings align with a study by Emamian et al., where the occurrence of insomnia in the perinatal period was linked to the presence of perinatal depressive symptoms [7]. In another meta-analysis, researchers observed that the risk of preterm birth may be elevated in patients with insomnia symptoms [8]. Additionally, this may be associated with increased suicidal risk and distress in the newborn [9] as well as miscarriage [10].

In 2023, two meta-analyses were published in the PubMed database evaluating the impact of cognitive-behavioral therapy (CBT) in the treatment of insomnia in pregnant patients. In the first study by Shang et al., 9 Randomized Controlled Trials (RCTs) were examined to assess the influence of CBT as a first-line treatment. They demonstrated that the application of CBT brings benefits to patients with short-

term insomnia [11]. In the second study conducted by Zheng et al., 8 RCTs were included. They concluded that insomnia severity decreased in patients who underwent CBT [12]. This suggests that one of the contributing factors to insomnia may have a psychological basis.

Additionally, proper improvement of sleep hygiene can also help patients with insomnia symptoms. In a study involving patients with a BMI ≥25 kg/m2 and a sleep duration of <6.5 hours, behavioral sleep intervention was shown to reduce the severity of insomnia symptoms [13].

It is worth investigating how physical activity affects insomnia in pregnant women, especially considering a meta-analysis that demonstrated an improvement in sleep quality with physical activity in perinatal women [14]. Another study directly indicated that physical activity in pregnant women had a positive impact on sleep quality [15]. Furthermore, the fact that a woman takes a nap during the day may also influence insomnia. Naps lasting from 15 to 59 minutes during the day in the second trimester had a positive effect on sleep in women [16]. Despite evidence that evening light exposure in the third trimester may negatively impact sleep duration [17], using blue light-blocking glasses did not affect sleep quality in women [18]. There is also evidence that supplementation with Lactuca sativa L. seeds may be helpful in reducing symptoms. In a double-blind randomized placebo-controlled trial involving 100 patients, half of them were given 1000 mg of lettuce seed or placebo. After 2 weeks, patients taking the supplement showed an improvement in the quality of sleep [19].

Melatonin supplementation could potentially have a positive impact as well. Although it seems to be a safe treatment, it is still not adequately researched, and there is insufficient scientific evidence [20].

This is particularly important because most medications used in the treatment of insomnia are not suitable for use during pregnancy due to their harmful effects on the fetus.

Data on the impact of many groups of drugs that may have potentially positive effects in the treatment of insomnia are still limited. Their use should be considered individually, taking into account the well-being of the patient, the fetus, and the risk of side effects. It is also important to note that the medications used may be present in the breast milk of breastfeeding mothers. In specific situations, zopiclone and trazodone may be considered due to their biochemical properties

[21]. It is crucial to differentiate whether insomnia is caused by pregnancy or if it is also a symptom, for example, of a recurrence of depression [22].

3. Restless leg syndrome

Restless legs syndrome (RLS) is a movement disorder characterized by an urge to move the legs and peculiar, unpleasant sensations (paraesthesias) in the lower limbs, especially at rest. Rarely it can also occur in the arms. The symptoms appear usually during periods of rest or inactivity (in the evening and at night) and patients feel relief in movement [23]. RLS might be primary (idiopathic) or secondary to pregnancy or many of systemic diseases including iron deficiency and chronic renal insufficiency. [24] The prevalence of this disorder during pregnancy varies depending on the gestational week (the highest occurrence was noticed in the third trimester) and decreases after delivery [25,26]. It is two to three times higher than in the standard population [27]. The cross-sectional study conducted by Jurjević et al., which sought to examine the relationship between gestational age and RLS development in pregnant women, revealed that before 16th week of pregnancy RLS occurred in 7.1% of pregnant women and after 16 weeks of pregnancy in 22.6% of them [28].

Generally, the cause of RLS remains still uncertain, but it is probably due to central nervous system dopaminergic dysfunction and other undefined contributing mechanisms [24]. Mendes et al. conducted a bibliographic search to reveal the pathogenesis of RLS in pregnancy. The most covered hypothesis linking RLS and pregnancy were hormonal fluctuations and iron metabolism dysfunction. Hormonal changes such as increased levels of estrogen, progesterone, prolactin and thyroid hormones may influence dopamine and constitute a possible explanation for RLS in pregnancy. Occurring during gestation, decrease in iron, ferritin, serum folate and hemoglobin levels may influence the pathogenesis of the syndrome. Moreover, vitamin D, zinc and magnesium deficiency, which may also occur during pregnancy, appear to have a connection with RLS. Turan et al. observed that in all trimesters decreased levels of ferritin, folic acid, vitamin B12 and hemoglobin were associated with RLS occurrence. In the second and third trimesters of pregnancy low magnesium and high creatinine levels were connected with this disorder and in the third trimester the relationship between higher

thyroid-stimulating hormone, higher free T4 levels and RLS was noticed. The authors also distinguished predictive factors including present and before conception Body Mass Index (BMI), gravida, low ferritin level, low vitamin B12, low folate, RLS history before conception and family history of RLS [26]. The research conducted by Shidhanie et al. on Omani women indicated the significant relationship of RLS development and weight gain during pregnancy. Particularly those women, who gained >12 kg, were more likely to be affected by RLS [29]. Present understanding also highlights a strong role of family history in RLS occurrence [30]. In the already mentioned study RLS appeared in 11,4% of women without RLS in the family and in 74,2% pregnant women with family history of this disorder. There was no statistically significant connection between RLS and the number of previous pregnancies in pregnant women observed [28]. RLS is a very common reason for insomnia in pregnancy [31]. Additionally, in comparison to the women without RLS, those affected by this disorder are more likely to have poor sleep quality, poor daytime function and excessive daytime sleepiness [32]. As Gupta et al. indicated, RLS is also associated with some pregnancy complications such as preeclampsia and increased incidence of Cesarean sections [33].

Kondori et al. suggested that first-line management of RLS should include nonpharmacologic methods. Authors listed 5 treatment options that were found to be beneficial: moderate-intensity exercise, yoga, massage, sequential compression devices, avoidance of aggravating causes of RLS and treatment of obstructive sleep apnea. In iron deficiency, its supplementation should be also considered [31].

Most medications in RLS treatment have been used due to the evidence from non-pregnant patients, thus standard therapy of this disorder during gestation is still not established [27]. However, about one-third of patients require pharmacologic treatment for RLS in pregnancy. Medications that may be considered as a therapeutic option include: dopamine agonists, off-label used gabapentin and other GABA analogues, not-FDA approved, but also off-label used in refractory RLS benzodiazepines and non-benzodiazepine benzodiazepine receptor agonists and reserved for very severe and very refractory RLS opioids. If it is possible pharmacologic treatment should be avoided in the first trimester [31].

It is worth noticing that medical treatment should be based on a balance between the benefit of relieving the symptoms and the risk for mother and fetus as well,

but in some severe cases of the disease, it may require medications [27]. In general, there is complete remission of symptoms after delivery observed, however in some cases patients may be still affected [33]. Goecke et al. observed that from the group of 119 pregnant women with RLS, 23 of them (19.3%) remained affected by this disorder 12 weeks after childbirth. The authors also pointed out that women with pregnancy-related RLS experienced baby blues more frequently, while no effect on the development of postpartum depression was observed [34]. However, it is noteworthy that women with RLS onset before pregnancy, who revealed moderate to severe symptoms, were more likely to develop both antenatal and postnatal depression [35]. Also the association between RLS in pregnant women and gestational diabetes and hypertension was observed [34].

4. Sleep-disordered breathing

Sleep-disordered breathing (SDB) is a condition that tangles pregnancy with unknown prevalence as scientists estimate that many women with this disease remain undiagnosed [36]. As stated by the Antony et al. scales used to measure sleepiness: Berlin questionnaire and Epworth sleepiness scale are not useful tools during the pregnancy as they tend to have a high false referral rate [37]. However, it is known that the incidence is constantly rising mostly because of the fact that more women that become pregnant are obese. This disorder encompasses a broad spectrum of sleep- related disorders such as snoring or obstructive sleep apnea which leads to sleepiness during the day and increasing exhaustion [38].

Louis et al. in their research highlighted the factors that could contribute to the higher risk of SDB. Basen on the questionnaires filled by the 3264 and 2512 women in early and mid pregnancy, respectively, they concluded that age, body mass index and repeated snoring (≥3 days per week) can be considered as reliable predictors [39].

Pien et al. in their study focused on the risk factors for women in the third trimester. Their findings indicate that higher starting BMI and maternal age are linked with the bigger chance of SDB [40].

Konstanty- Kurkiewicz et al. in their study aimed at assessing the frequency and potential risk factors of SDB on 312 women in the third trimester of pregnancy aged 17-46 observed a significant number of inspiratory airflow limitation

episodes mostly together with snoring. Authors noted that the higher risk was assessed with the greater weight gain during pregnancy. Authors stressed on the importance of careful observation of pregnant women in terms of SDB [41]. The most common symptoms during the night include : frequent or loud snoring, gasping, insomnia, nighttime heartburn, restless sleep, short or too long sleep, restless legs. Typical daytime symptoms are tiredness, lack of energy, sleepiness, feeling depressed, anxious or irritated, troubles with concentration [42].

Potential outcomes of SDB concern both the pregnant women and fetal. Studies on this subject are so far limited. However, it is known that SDB is significantly correlated with pregnancy-induced hypertension, pre-eclampsia and gestational diabetes [43].

Franklin et al. confirmed the higher risk of gestational hypertension (14% vs. 6%) and pre-eclampsia (10% vs. 4%) in pregnant women that experienced habitual snoring during pregnancy compared with the one that did not report that [44]. The association between pregnancy snoring and the risk of hypertension and pre-eclampsia was confirmed also by the O'brien et al [45]. Reutrakul et al. highlighted that SDB are also at risk of developing gestational diabetes mellitus. On the basis of the Epworth Sleepiness Scale that was introduced to 169 pregnant women 41% had excessive daytime sleepiness, 64% had poor sleep quality, 25% snored frequently, 29% had increased risk of sleep-disordered breathing, 52% experienced short sleep. Every hour of reduced sleep time was associated with a 4% increase in glucose levels in the OGTT test. Their conclusion was that women especially at risk were the ones with SDB risk factors, frequent snoring and sleep that lasted less than 7 hours per day [46].

When it comes to neonatal implications, current data remains unclear. Most of the studies state that currently there is no proven significant connection between fetal growth and mother's SDB [47,48]. However, there are some findings that suggest there could be a correlation among them. Franklin et al. in their study on 502 pregnant women reported that repeated snoring was at the higher risk of having a fetus with the growth retardation [44].

It is noteworthy that while the frequency of SDB is constantly rising there are still many knowledge gaps about mechanisms and most effective treatments [49]. Recently, Huynh et al. tested the efficacy of mandibular advancement splints in pregnant women during pregnancy and 6 months after giving birth. The results

were unclear and not unambiguous. Authors also noted that women in postpartum tend to use the device less often [50]. So far, in the spectrum of treatment there is also CPAP - continuous positive airway pressure as some studies indicate its positive effects [51]. Poyares et al. in their randomized study tested the efficacy of CPAP during the first eight weeks of pregnancy and this strategy led to better blood pressure control and also was linked with the lessen frequency of pregnancy complications [52].

To conclude, sleep disordered breathing seems to be highly prevalent and grossly underdiagnosed. Ergo, further studies are needed to develop the best possible treatment.

5. Conclusion

Healthy sleep without disturbances is crucial for human's health. As poor sleep during pregnancy affects not only women's wellbeing but there is also a growing evidence of it having implications to the baby, we conclude that pregnant patients should be carefully diagnosed in terms of sleep-related disorders. Existing knowledge points that sleep complaints should be closely analyzed and each case should be individually examined in order to determine whether the specific treatment should be obtained. While choosing the right intervention, its influence on the fetus must be taken into account as some of the knowable treatments may be riskful for its health, therefore whenever it is realizable non pharmacological treatment should be superior to the drug-based therapies.

Author Contributions:

Conceptualization, K.W. and M.W.; methodology K.W; software, K.W.; check, M.W., K.W. and S.T.; formal analysis, S.T.; investigation, M.W.; resources, S.T; data curation, S.T.; writing - rough preparation, K.W. M.W. and S.T.; writing - review and editing, K.W. S.T and M.W.; visualization, S.T.; supervision, K.W.; project administration, M.W. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest

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