



# **Sleep and Pregnancy: Future Perspectives from Circadian and Precision Medicine**

Antonio Del Casale <sup>1,\*</sup>, Jan Francesco Arena <sup>1</sup>, Paolo Girardi <sup>1</sup> and Gloria Angeletti <sup>2</sup>

- <sup>1</sup> Department of Dynamic and Clinical Psychology and Health Studies, Faculty of Medicine and Psychology, Sapienza University of Rome, 00185 Rome, Italy; janfrancesco.arena@uniroma1.it (J.F.A.)
- <sup>2</sup> Department of Neuroscience, Mental Health and Sensory Organs (NESMOS), Faculty of Medicine and Psychology, Sapienza University of Rome, 00189 Rome, Italy
- \* Correspondence: antonio.delcasale@uniroma1.it

## 1. Introduction

Ten years ago, the Society for Women's Health Research highlighted sleep as a significant area of interest in women's health research. Pregnancy, characterized by profound physiological and anatomical changes, significantly affects various aspects of women's health, including sleep [1].

The physiological changes that occur during pregnancy are multisystemic, including increased cardiac output, reduced systemic vascular resistance, respiratory function changes, glomerular filtration, significant hormonal changes, and musculoskeletal modifications [2]. On the one hand, these alterations considerably affect sleep architecture; on the other hand, they might increase a person's susceptibility to specific sleep disorders, such as sleep-disordered breathing (including obstructive sleep apnea syndrome, snoring, obesity hypoventilation syndrome), insomnia, and restless leg syndrome [3].

Nevertheless, the importance of sleep during pregnancy extends far beyond the quality of life, affecting the course of pregnancy in terms of both maternal and fetal health outcomes. Recent evidence supports a potential causal relationship between sleep duration and adverse pregnancy and perinatal outcomes, including stillbirth, low birth weight, and perinatal depression [4]. These findings underscore the need for the thorough understanding and effective management of sleep disturbances in expectant mothers.

The pathophysiology of sleep disturbances is closely linked with circadian rhythms, which arise from the interaction between endogenous physiological oscillations and external environmental factors, and regulate most biological functions [5]. During pregnancy, the key maternal circadian signals include melatonin and glucocorticoids, which synchronize fetal and maternal circadian rhythms [6]. Given that circadian rhythms are vital not only for adults but also for fetal development [7], they represent a shared foundation influencing the bidirectional relationship between sleep and reproductive health outcomes in women.

## 2. Pregnancy, Sleep, and Health

Pregnancy significantly impacts the quality of sleep women obtain, with up to 45.7% of pregnant women reporting a poor quality of sleep which tends to worsen between the second and third trimester [8]. Factors such as fetal movements, nocturia, uterine contractions, and positional discomfort contribute to sleep disturbances. However, these disturbances may serve as warnings for the early detection of maternal and/or fetal disorders.

Various sleep disorders can increase the risk of complications for both the mother and the fetus, such as pre-eclampsia, gestational hypertension, gestational diabetes mellitus, cesarean section, preterm birth, a fetus/infant large for its gestational age, a low birth weight, and stillbirth [9]. The authors of one paper discussed how sleep disturbances may act; through the desynchronization of circadian rhythms, changes in neurotransmitter



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**Copyright:** © 2024 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). release patterns, oxidative stress, and the inflammatory response [9], which has already been identified as a pivotal pathway linking maternal sleep and health [10].

In psychiatry, sleep disturbances are generally recognized as a consolidated risk factor for the development of depressive disorders [11] and show a direct relationship with depressive symptoms, increasing the risk of developing postpartum depression when present during pregnancy [12]. In 2014, with the article "No health without perinatal mental health" [13], Louise M. Howard et al. introduced a series of reviews [14–16] focused on the epidemiology and treatment of perinatal mental disorders. This work underlined how the treatment of perinatal mental disorders concretely addresses both mothers and children's mental and physical well-being. Among the risk factors for new-onset anxiety and the exacerbation of anxiety are comorbid sleep disorders [17], which is consistent with existing evidence for postpartum depression and bipolar disorder [18]. Further evidence is needed to investigate the role of sleep disturbance in the onset and course psychotic disorders [19]. Nevertheless, the effect of sleep disturbance of clinical sleep assessments during pregnancy [20].

Since sleep influences physical and mental health, and vice versa, it could become a promising "finger on the pulse" of pregnancy for clinicians. Monitoring changes in sleep habits and sleep quality may help clinicians tailor screening programs to every woman and carry out further investigation, with sleep disturbance considered as a key clinical variable. Existing evidence indicates that sleep can affect the risk of adverse pregnancy outcomes, suggesting that the predictive role of sleep disturbances may be even more significant in women with specific characteristics (e.g., BMI > 24 kg/m<sup>2</sup>, pre-pregnancy sleep disturbances, or new-onset sleep disturbances during the third trimester, etc.) [9].

Interestingly, circadian rhythms influence mental health [21], reproductive health [22], and a wide range of human diseases [23], with melatonin serving as the primary chronobiological marker. This hormone, produced by the pineal gland, functions through receptor-dependent mechanisms, but it is particularly significant during pregnancy due to its receptor-independent antioxidant and anti-inflammatory properties. Notably, the placenta is capable of autonomously synthesizing melatonin, thereby supporting maternal melatonin blood levels [24]. The daily oscillation of endogenous molecules affects the perinatal period longitudinally, with the relevant effects for newborns retained after delivery through lactation [25]. Therefore, the impact of sleep on the health of women and children may extend well beyond pregnancy, necessitating a more comprehensive consideration of the perinatal period.

Ultimately, our focus should be directed towards treatment and prevention. Sleep hygiene education, behavioral interventions, and specific pharmacological treatments used during pregnancy are available and effective [26], underscoring the importance of raising awareness about this issue.

Pregnancy is an intricate and complex period in a woman's life. We aim to highlight the emerging role of sleep in maternal and fetal health, which could help both mothers and their doctors sleep soundly.

### 3. Conclusions

Sleep disturbances can affect pregnancy outcomes and/or highlight the onset of perinatal physical and mental disorders. Therefore, understanding their underlying mechanisms and identifying at-risk women by assessing their sleep quality during pregnancy is a promising strategy for improving maternal and fetal health. The complex relationship between sleep and pregnancy necessitates the use of a multidisciplinary approach to manage sleep disturbances effectively. Understanding the physiological, hormonal, and circadian changes that occur during pregnancy will better inform clinical practices and improve maternal and fetal health outcomes. Studying sleep in greater depth could substantially advance the burgeoning fields of precision medicine and precision psychiatry. Future research should focus on identifying at-risk populations, improving screening programs for both physical and mental disorders during pregnancy, preventing maternal–fetal complications, and evaluating the safety and efficacy of therapeutic interventions. Moreover, the emerging role of circadian rhythms highlights the need for studies evaluating the possible application of circadian medicine to this important period of a woman's life. By understanding the intricate mechanisms of sleep and its impact on health, clinicians can devise targeted strategies that not only address sleep disorders but also improve overall health outcomes, particularly in vulnerable populations such as pregnant women. Enhanced precision in these medical approaches promises to mitigate risks, optimize therapeutic efficacy, and ultimately improve both maternal and fetal well-being.

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