### **Research Paper**





# Association of Sleep Quality and Duration With Preterm Birth: The Qazvin Maternal and Neonatal Metabolic Study (QMNMS)

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#### **ABSTRACT**

**Background:** Preterm birth (PB) is a worldwide gestational problem. Poor sleep quality and short duration have been reported as possible predisposing factors of PB in some studies.

Objective: This study was conducted to investigate the roles of sleep quality/duration in the occurrence of PB.

Methods: This longitudinal study was performed on pregnant women with gestational age ≤14 weeks. The sleep quality was evaluated using the Pittsburgh sleep quality index (PSQI) at the first visit and women were followed until delivery. A total of 76 women with preterm and 441 women with term delivery were compared regarding the sleep quality components, sleep duration, and long or short sleep duration. The multivariate logistic regression was performed to examine the independent association of sleep quality/duration with PB.

**Findings:** Data from 517 participants were analyzed. PB occurred in 14.7% of participants. No significant difference of 7 items of sleep quality was observed between preterm and non-preterm groups (P>0.05 for each comparison). The total PSQI score in the preterm group was significantly higher (poorer quality) compared to the non-preterm group (5.6±2.1 vs 5.3±2.4, P=0.076). In multivariate logistic regression, each unit of worsening PSQI was independently associated with a 20% higher risk of PB occurrence. Sleep duration was not associated with PB either in unadjusted or adjusted models.

Conclusion: No relationship was observed between poor sleep quality (defined as PSQI>5) and PB; however, based on our results, poorer sleep quality (as a continuous variable) can be an independent risk factor for PB.

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#### 1. Introduction

reterm birth (PB) is a worldwide gestational problem [1]. The neonates born prematurely, especially those born before 32 gestational weeks, have higher rates of mortality and admission to the neonatal intensive care unit [2]. In addition, premature infants are at higher risk of lifelong medical and neurodevelopmental disabilities [3]. Despite improvements in other pregnancy complications, most studies have shown that the rate of PB has been rising in recent decades [4].

Regarding the above-mentioned considerations, it is necessary to identify predisposing factors for PB. Some well-documented risk factors exist for PB, such as pre-pregnancy body mass index (BMI), smoking during pregnancy, and personal history of PB [5, 6]. However, the role of non-traditional factors, such as sleep-related parameters remains controversial [7].

In recent decades, an increasing emphasis has been placed on the significance of sleep quality and duration in maintaining health. According to the present data, the sleeping process is beyond a simple resting of the body [8]. During sleep, the accumulated free radicals are metabolized and damaged tissues are restored [9]. Moreover, significant changes in the sympathetic tone and hormone secretion take place [10]. These changes help maintain tissue health.

The association of sleep abnormalities with Gestational Diabetes Mellitus (GDM), preeclampsia, and PB has been previously evaluated [11]. Regarding the association of PB with sleep-related parameters, these data are inconsistent, especially in the case of sleep duration, and these associations seem to be influenced by other factors, such as racial and psychological factors [12, 13].

Considering the aforementioned issues, the present study was designed to explore the impact of sleep quality/duration of the first trimester on PB, considering other crucial parameters, such as depression.

#### 2. Materials and Methods

#### **Participants**

This prospective longitudinal study (Qazvin Maternal and Neonatal Metabolic Study [QMNMS]) was carried out on women referred to Qazvin obstetrics/gynecology clinic for prenatal care from September 2018 to May 2020 in Qazvin Province, Iran.

This study was designed to evaluate adverse pregnancy outcomes. To calculate the sample size with proper power, we considered the pregnancy outcome of preeclampsia with the least prevalence. Considering the prevalence of preeclampsia of about 6% [14], power of 80%, d=0.02,  $\alpha$ =0.05, attrition of 20%, and early abortion rate of about 10% [15], a minimum sample size of 717 participants was calculated; however, regarding adequate resources, we recruited 821 participants into the study.

The participants were included in the study from the first antenatal care visit. Pregnant women aged  $\geq 20$  years who had a gestational age of  $\leq 14$  weeks based on the last menstrual period or sonography were included in the study. The participants with Diabetes Mellitus (DM) or undiagnosed overt DM as well as hypertension before pregnancy were excluded from study.

After the study objectives were explained to them, all participants gave their written informed consent to participate in the study. This study was approved by the Ethics Committee of Oazvin University of Medical Sciences (Code: IR.QUMS.REC.1394.819). The data were gathered during three prenatal visits, the first antenatal visit at ≤ 14th gestational week, during the 22th-24th gestational weeks, and during the first 6 weeks postpartum. PB was defined as delivery at  $\leq 37^{th}$  gestational week. In the first antenatal visit, the sleep quality was evaluated using the Pittsburgh sleep quality index (PSQI) questionnaire. This questionnaire includes 19 items assessing seven components of sleep quality, sleep latency, sleep disturbances, habitual sleep efficiency, subjective sleep quality, sleep duration, using sleep medications, and daytime dysfunction. Poor sleep quality has been defined as a total PSQI score of more than [16]. The participants filled out the questionnaire after receiving adequate descriptions from two trained interviewers. The details of the study methodology have been previously published [17].

#### Statistical analysis

Statistical analysis was carried out using SPSS software, version 24. The normality of quantitative data was evaluated using the Kolmogorov-Smirnov test. The t-test and chi-square test were used to compare quantitative and categorical data, respectively. Logarithmic transformation was conducted before comparing the data with non-normal distribution using t test.

The multivariate logistic regression analysis was performed to assess the independent relationship of variables, including poor sleep quality, mean night sleep duration, night sleep duration of <7 h, and night sleep duration of <10 h (as independent variables) with the occurrence of PB (as the dependent variable). In model 1, adjustments were made for age, parity, education level, job (employed vs. non-employed), current smoking status, history of PB, and history of GDM. In model 2, adjustments were made for physical activity and depression scores as well as model 1 variables. P<0.05 were considered significant.

#### 3. Results

After excluding participants with abortion, missing follow-up and or missing data (n=304), the data of 517 participants were analyzed. PB was reported in 76 participants (14.7%). Table 1 presents the baseline characteristics of the participants categorized by PB outcome. No significant difference was observed regarding age, smoking status, history of PB, depression, and total physical activity scores between preterm and non-preterm groups.

Table 1. Baseline characteristics of participants categorized by preterm birth status

Variables –		Mean±S	_	
		Term Delivery (n=441)	Preterm Delivery( n=76)	Р
Age (y)		29.8±4.8	29.8±4.7	0.989
	Age≤25 y	84(19.0)	12(15.8)	
Age groups	25 <age≤40 td="" y<=""><td>350(79.4)</td><td>64(84.2)</td><td></td></age≤40>	350(79.4)	64(84.2)	
	Age>40 y	7(1.6)	0	
Employment status (employed)		94(21.3)	17(22.4)	0.891
	Primary school graduate,	3(0.7)	0	
Education	High school/diploma	136(30.8)	24(31.6)	
	University	302(68.5)	52(68.40	
Smoking		4(0.9)	0	0.403
Gravidity		1.8±0.9	1.7±0.9	0.418
Gestational age† (wk)		8.7±0.2	8.4±0.2	0.361
Pre-pregnancy BMI (kg/m²)		25.1±4.1	25.1±4.3	0.976
	Normal BMI	239(54.1)	40(52.6)	
Pre-pregnancy BMI groups††	Overweight	145(32.8)	28(36.9)	
	Obese	57(13.1)	8(10.5)	
Preterm labor history***		11(4.6)	3(8.3)	0.342
Depression score		8.7±5.3	8.2±5.6	0.274
Physical activity		6.6±1.0	6.7±1.3	0.883

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The data were collected by two trained interviewers. Quantitative data are presented as Mean±SD. Logarithmic transformation was used to compare the quantitative date with non-normal distribution. BMI: Body mass index.

<sup>†</sup> Geatatinal age at enrollment into the study; †† Normal BMI, BMI ≤ 25 kg/m²; overweight, 25<BMI ≤ 30 kg/m²; obese, BMI>30 kg/m².

Table 2. Comparison of sleep quality's components and duration between preterm and non-preterm birth groups

Sleep quality components								
	Mean	_						
Variables —	Term Delivery (n =441)	Preterm Delivery (n =76)	P P					
Subjective sleep quality	0.9±0.6	0.9±0.4	0.157					
Sleep latency	1.1±0.9	1.2±0.9	0.785					
Sleep duration	0.4±0.7	0.5±0.7	0.617					
Habitual sleep efficiency	0.3±0.6	0.3±0.7	0.251					
Sleep disturbances	1.2±0.5	1.3±0.4	0.515					
Use of sleep medications	0.03±0.2	0.08±0.5	0.089					
Daytime dysfunction	1.4±0.8	1.4±0.9	0.338					
PSQI score	5.3±2.4	5.6±2.1	0.076					
Poor sleep quality†	256 (58.0)	49 (64.5)	0.303					
Night sleep duration (h)	8.7±1.3	8.7±1.4	0.939					
Night sleep duration <7 h	29 (6.6)	3 (3.9)	0.378					
Night sleep duration >10 h	52 (11.8)	7 (9.2)	0.509					

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PSQI: Pittsburgh sleep quality index. The quantitative data are presented as Mean±standard deviation. The quantitative data with non-normal distribution transformed to logarithmic values before comparing by t test.

Table 3. The crude and adjusted associations of poor sleep quality and sleep duration with the occurrence of preterm birth

Variables	OR (95% CI)	Б	OR (95% CI)	- P -	OR (95% CI)	- Р
	Crude	– P –	Model 1		Model 2	
PSQI score	1.1 (0.9-1.2)	0.246	1.2 (1.0-1.4)	0.039	1.2 (1.0-1.4)	0.017
Poor sleep quality†	1.3 (0.8-2.2)	0.304	1.6 (0.7-3.3)	0.263	1.7 (0.7-3.6)	0.214
Night sleep duration	1.0 (0.8-1.2)	0.977	1.0 (0.8-1.4)	0.908	1.0 (0.7-1.4)	0.889
Night sleep duration <7h	0.6 (0.2-1.9)	0.383	0.8 (0.2-3.7)	0.778	0.8 (0.2-3.7)	0.776
Night sleep duration >10h	0.5 (0.1-2.3)	0.379	0.5 (0.1-2.5)	0.416	0.7 (0.1-2.7)	0.471

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PSQI: Pittsburgh sleep quality index; OR: Odds ratio; CI: Confidence interval.

Model 1, adjusted for age, parity, education level, job (employed vs non-employed), current smoking, previous history of PB, and previous history of gestational diabetes. Model 2, model 1 plus depression and physical activity score.

<sup>†</sup> PSQI score>5.

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The sleep quality components and duration were compared between PB and non-PB groups and the results are presented in Table 2. The frequency of poor sleep quality in PB and non-PB groups were not significantly different (64.5% vs 58.0%, respectively, P=0.303). No significant difference was observed in the seven items of sleep quality between PB and non-PB groups. The total PSQI score was higher (poorer quality) in the PB group compared to the non-PB one, however, the significance was borderline (5.6±2.1 vs. 5.3±2.4, P=0.076). The mean of night sleep duration and short/long sleep duration showed no difference between PB and non-PB groups (P=0.939).

Table 3 presents the crude and adjusted associations of PSQI and sleep duration with PB. Each higher PSQI 9 score (poorer sleep quality) was associated with 1.2 times higher risk of PB in both adjustment models (P<0.05). The associations of poor sleep quality and night sleep duration with PB were not significant before and after adjusting for variables of models 1 and 2.

#### 4. Discussion

In the present study, each unit's worsening sleep quality score was independently associated with a 20% higher risk of PB. Considering the non-significant relationship of sleep quality score with PB in the non-adjusted model, it appears that some variables have concealing effects on this association.

The present data on the relationship between sleep quality and PB are inconclusive. In the meta-analysis conducted by Wang et al., 10 studies (9 cohorts and one cross-sectional study) were evaluated and indicated that the relative risk of PB was 1.54 in pregnant women with poor sleep quality compared to women with good sleep quality [18]. However, there was high heterogeneity between studies. Some investigations found no relationship between poor sleep quality and PB [19], while others reported that the relationship between poor sleep quality with PB varied in different trimesters of pregnancy. In the studies conducted by Okun et al. [20] and Ota et al. [21], sleep quality was evaluated in each trimester of pregnancy. In these two studies, poor sleep quality in earlier gestational weeks had the greatest impact on the risk of PB. On the contrary, in the study conducted by Li et al., poor sleep quality during the second and third trimesters was associated with a significant risk of PB [22]. In our study, although a higher score of sleep quality (poorer quality) was related to PB, the association of poor sleep quality with PB was non-significant, indicating the lack of a specific cut-off for the association of sleep quality with PB.

The data on the relationship between sleep duration and PB are even more inconsistent. In the meta-analysis by Wang et al. (published in 2020), the results of studies published up to September 30, 2018, were analyzed, and the authors found a 23% increase in PB in short-duration sleepers compared with long-duration sleepers [18]. In this meta-analysis, the heterogeneity of the included studies was moderate. However, in two studies with very large sample sizes, which were published after 2018 by Facco et al. [23] and Nakahara et al. [24], no relationship was observed between sleep duration and PB.

There are possible explanations for the results of different studies. PB is a multifactorial pregnancy complication and its incidence varies by geographic region and race [25]. Multiple risk factors exist for PB that can interfere with the relationship between sleep-related parameters and PB [25, 26]. Some socioeconomic and psychological factors, such as education level and depression can affect both sleep quality/duration and PB risk [27, 28]. However, in our study, night sleep duration was not associated with PB either before or after adjusting for these risk factors.

As mentioned above, the risk of PB can be influenced by race [25]. A few studies have compared the impact of sleep quality/duration on PB between groups of different races. In the study by Blair et al., the relationship between sleep quality with PB was investigated in two groups of African American and European American women. Poor sleep quality was associated with a 10-fold increase in the risk of PB in African American women. On the contrary, PB was not predicted by sleep quality in European American women [12].

Regarding the above-mentioned considerations, it appears that the relationship between sleep quality/duration and PB is complex and can be influenced by racial, socioeconomic, and psychological factors. Future study design should be based on comparing prespecified groups in terms of the relationship between sleep quality/duration and PB.

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Our study had limitations and advantages. The main limitation of this research was the evaluation of sleep quality and duration using subjective methods. The second limitation was the lack of pre-specified sociopsychosocial groups to better examine the complex association of sleep quality/duration with preterm delivery. The longitudinal design and acceptable sample size were the advantages of our study.

#### 5. Conclusion

In our study, sleep duration had no association with PB risk even after adjusting for known risk factors for PB. However, each unit's worsening of sleep quality was independently associated with a mild but significantly higher risk of PB.

#### **Ethical Considerations**

#### Compliance with ethical guidelines

This study was approved by the Ethics Committee of Qazvin University of Medical Sciences (code: IR.QUMS.REC.1394.819). All the participants gave their written informed consent to participate in the study.

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#### Authors' contributions

Methodology: Fatemeh Lalooha and Sima Hashemipour; Data collection and Writing-original draft: Fatemeh Lalooha, Sima Hashemipour, and Khadijeh Elmizadeh; Data analysis and interpretation: Sima Hashemipour. All authors read the manuscript and participated in the preparation of the final version.

#### Conflict of interest

The authors declare no competing interests.

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