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## Poor sleep during early pregnancy increases subsequent risk of gestational diabetes mellitus

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## Abstract

**Objectives:** To examine the relationship between poor sleep quality during pregnancy and the risk of gestational diabetes mellitus (GDM).

**Methods:** A total of 4066 singleton pregnant women from the Tongji Maternal and Child Health Cohort (TMCHC) without overt diabetes before pregnancy were analyzed. Sleep quality and duration during early pregnancy were self-reported by enrolled women at their first antenatal care visit before 16 weeks of gestation. Gestational diabetes mellitus (GDM) was assessed with a 75-g, 2-hour oral glucose tolerance test at 24–28 weeks of gestation. Information about self-reported sleep quality and duration in mid-pregnancy were also collected then. Odds ratios (OR) and 95% CIs were calculated by multivariable logistic regression models, and adjusted for potential confounders to estimate the effect of poor sleep quality and the interaction between sleep quality and duration on the development of GDM. Stratified analyses were performed according to age, parity, family history of diabetes and napping.

**Results:** A total of 335 (8.2%) participants were diagnosed with GDM. Poor sleep quality was reported in 259 (6.4%) women during early pregnancy and 248 (6.1%) in mid-pregnancy. The risk of GDM was increased in women with poor sleep quality during early pregnancy (OR 1.77, 95% CI 1.20–2.61). No association was found between poor sleep quality during mid-pregnancy and the risk of GDM. The risk of GDM was highest in women with poor sleep and longer nighttime sleep duration during early pregnancy (OR 2.27, 95% CI 1.20–4.29) when compared with those who reported good sleep and 7.0–8.5 hours of sleep duration per night. Stratified analysis found that the association between poor sleep quality in early pregnancy and the risk of GDM was stronger among women aged  $\geq 30$  years (OR 2.35, 95% CI 1.35–4.09) and those with a family history of diabetes (OR 4.02, 95% CI 1.54–10.48).

**Conclusions:** Poor sleep quality during early pregnancy was associated with an increased risk of GDM. Screening for and treating sleep problems in early pregnancy could potentially reduce the risk of GDM.

**Keywords:**

Early pregnancy

Gestational diabetes mellitus

Poor sleep quality

ACCEPTED MANUSCRIPT

## Introduction

Gestational diabetes mellitus (GDM) is classified as glucose intolerance of varying degrees of severity with onset or first recognition during pregnancy [1]. It is associated with adverse maternal and neonatal outcomes, including pre-eclampsia, cesarean section, macrosomia, and neonatal hypoglycemia [2]. GDM is also a risk factor for obesity, type 2 diabetes, cardiovascular disease and metabolic syndrome among mothers and their offspring [3–5].

In pregnancy, sleep patterns change and poor sleep quality is a common complaint as pregnancy progresses [6,7]. Evidence from observational and experimental studies has demonstrated associations between poor sleep quality and the risk of impaired glucose metabolism and type 2 diabetes [8–11]. However, existing studies have been limited and somewhat conflicting regarding the association between sleep quality and the development of GDM. Wang et al. found poor sleep during pregnancy, assessed by a modified questionnaire, increased the risk of GDM [12]. Facco et al. did not observe the association when monitoring the daily sleep of pregnant women for a 7-consecutive-day period in mid-pregnancy [13].

Several studies have documented that shorter and longer sleep durations in pregnancy are linked to elevated risk of hyperglycemia and GDM [12–17], but it is still unclear whether an interactive effect exists between poor sleep quality and sleep duration and the development of GDM.

The current study aimed to examine the association between sleep quality during early and mid-pregnancy and subsequent risk of GDM, and further assess the possible interaction of sleep quality and nighttime sleep duration or other potential modifications.

## Methods

The presented data were drawn from the Tongji Maternal and Child Health Cohort (TMCHC) project, which is a multicenter, population-based, prospective cohort study designed to examine maternal dietary and lifestyle effects on the outcomes of mother-infant pairs in Wuhan, China. From January 2013 to May 2016, women who initiated prenatal care prior to 16 weeks of gestation in three research hospitals of Wuhan and eligible for the study were invited to join the cohort. Women were excluded if they were >16 weeks' gestation, did not speak and read Chinese, and did not intend to receive the following prenatal care or deliver at either of the three research hospitals. A total of 4066 singleton pregnancies without pre-gestational diabetes underwent a 75-g, 2-hour oral glucose tolerance test and were included in this study. All participants provided written, informed consent when recruited to the TMCHC project. This study was approved by the Ethics Review Committee of Tongji Medical College of Huazhong University of Science and Technology in China.

At enrollment, all participants completed a questionnaire regarding sociodemographic, medical, obstetrical, pre-gravid weight and lifestyle characteristics, including pre-gravid smoking and drinking habits, sleep quality, nighttime sleep duration and daytime sleep duration during early pregnancy. Meanwhile, their height and weight were accurately measured by trained staff. Sleep quality and duration in mid-pregnancy were self-reported at their clinic visit during 24–28 weeks of gestation. Insomnia was used to assess the quality of sleep, defined as difficulty initiating or maintaining sleep, or early awakening with inability to return to sleep, together with associated impairment of daytime functioning. The questions

were: “During the past month, how many hours of nighttime and daytime sleep do you get every day?” and “During the past month, how often have you experienced insomnia: frequently (three or more times a week), sometimes (once or twice a week), occasionally (less than once a week) or never?” Based on this information, participants were categorized as poor sleep quality (reported insomnia frequently) and good sleep quality groups. Women who reported no daytime sleep duration were defined as non-nappers and the others were nappers. Nighttime sleep duration in early pregnancy was categorized into three levels ( $<7.0$  hours/night,  $7$  to  $<8.5$  hours/night, and  $\geq 8.5$  hours/night) and further created six categories: (1) women with good sleep quality and sleeping  $<7.0$  hours/night; (2) women with good sleep quality and sleeping  $7$  to  $<8.5$  hours/night; (3) women with good sleep quality and sleeping  $\geq 8.5$  hours/night; (4) women with poor sleep quality and sleeping  $<7.0$  hours/night; (5) women with poor sleep quality and sleeping  $7$  to  $<8.5$  hours/night; and (6) women with poor sleep quality and sleeping  $\geq 8.5$  hours/night.

Pre-pregnancy body mass index (BMI) was calculated using self-reported pre-pregnancy weight (in kg) divided by the subject’s height squared (in  $m^2$ ) measured at the first visit.

Subjects were categorized as underweight ( $BMI < 18.5 \text{ kg/m}^2$ ), normal weight ( $18.8 \leq BMI < 24.0 \text{ kg/m}^2$ ), overweight ( $24.0 \leq BMI < 28.0 \text{ kg/m}^2$ ), or obese ( $BMI \geq 28.0 \text{ kg/m}^2$ ) according to the recommendations of the Working Group on Obesity in China (WGOC) [18]. Owing to the descriptive similarities and small group size, overweight and obese women were combined in the analysis. The rate of gestational weight gain in early pregnancy was defined as:

(weight at enrollment – pre-pregnancy weight)/(weeks of gestation attained at the first antenatal care visit).

At 24–28 weeks of gestation, oral glucose tolerance tests were conducted and the diagnosis of GDM was made according to the criteria of the American Diabetes Association [19] when any of the following plasma glucose values were exceeded: fasting:  $\geq 5.1$  mmol/L (92 mg/dL), 1 hour:  $\geq 10.0$  mmol/L (180 mg/dL), 2 hours:  $\geq 8.5$  mmol/L (153 mg/dL).

### ***Statistical analyses***

Descriptive statistics were used to characterize the study population according to the categories of sleep quality in early and mid-pregnancy. Continuous variables were expressed by mean  $\pm$  SD or median ( $P_{25}$ ,  $P_{75}$ ), and categorical variables were expressed by frequency ( $n$ ) and percentages (%). Chi-squared analysis, independent sample  $t$ -tests, Mann-Whitney U tests, and Wilcoxon signed-rank tests were used to analyze the relationships between variables. Multivariable logistic regression was used to assess the relationship between sleep quality and GDM, adjusting for the following confounding variables: maternal age, pre-pregnancy BMI, family history of diabetes, parity, education, smoking before pregnancy, and rate of gestational weight gain in early pregnancy. A second model was further adjusted for nighttime sleep duration and napping in corresponding pregnancies. Multivariable logistic regression also was performed to examine the interplay between sleep quality and duration in early pregnancy in affecting the development of GDM. To assess the potential modification effect of maternal age ( $<30$ ,  $\geq 30$  years), pre-gravid BMI ( $<24.0$ ,  $\geq 24.0$  kg/m<sup>2</sup>), parity (nulliparity, multiparity), family history of diabetes (yes, no), and napping (yes, no),



interaction terms were examined by log-linear model and repeating the multivariable logistic regression in the corresponding subgroup. OR and 95% CI were reported;  $p < 0.05$  was considered statistically significant. Analyses were performed using SAS 9.4 software.

## Results

### *Participants' demographic characteristics*

As shown in Table 1, among the 4066 study participants, 335 (8.2%) were diagnosed with GDM. Poor sleep quality was reported in 259 (6.4%) women during early pregnancy and 248 (6.1%) in mid-pregnancy. Participants' nighttime sleep durations in early pregnancy were significantly longer than in mid-pregnancy. Women who reported poor sleep quality tended to have less nighttime sleep duration, both in early and mid-pregnancy. Women who were older and multiparas were more likely to have poor sleep quality in early and mid-pregnancy, and those with lower education levels were more likely to have poor sleep quality in early pregnancy. Higher mean pre-gravid BMI and smoking before pregnancy were only associated with poor sleep quality during early pregnancy, and family history of diabetes was only linked to poor sleep quality in mid-pregnancy. In women with and without poor sleep separately in early and mid-pregnancy, no significant differences were found in gestational age at the time of enrollment and glucose screening test, ethnicity, rate of gestational weight gain, average personal income, drinking, and daytime sleep duration in either early or mid-pregnancy.

### *Poor sleep quality in early pregnancy but not in mid-pregnancy was associated with increased risk of GDM*

The results of unadjusted and adjusted logistic regression analyses between sleep quality in different pregnancies and GDM are shown in Table 2. Women with poor sleep quality during

early pregnancy had higher risk of GDM compared with those who reported good sleep quality (OR 1.96, 95% CI 1.36–2.83). After adjusting for potential confounders, including pre-gravid BMI, maternal age, family history of diabetes, parity, education, smoking before pregnancy and the rate of weight gain in early pregnancy, the association remained significant (OR 1.70, 95% CI 1.16–2.50). The association became slightly elevated after further adjusting for nighttime sleep duration and napping during early pregnancy. Regardless of using unadjusted or adjusted models, no significant association was found between sleep quality in mid-pregnancy and the risk of GDM.

### ***Sleep duration and quality in early pregnancy and risk of GDM***

To further assess the interaction of sleep duration and quality in early pregnancy on the development of GDM, nighttime sleep duration was categorized into three levels. Compared to women with good sleep and 7.0 to <8.5 hours/nighttime sleep, after adjustment for pre-gravid BMI, maternal age, family history of diabetes, parity, education, smoking before pregnancy and the rate of weight gain in early pregnancy, those with poor sleep and nighttime sleep duration  $\geq 8.5$  hours/night had the greatest risk of GDM (OR 2.32, 95% CI 1.23–4.38). The association remained significant, although slightly decreased, after further adjusting for napping during early pregnancy (OR 2.27, 95% CI 1.20–4.29) (Table 3).

### ***Potential effect modification for the impact of poor sleep during early pregnancy on the development of GDM***

Stratified analyses were performed to assess the potential effect modification for the impact of poor sleep during early pregnancy on the development of GDM. Significant interactions between maternal age, parity, family history of diabetes and sleep quality during early pregnancy were observed (all  $p$  for interaction  $< 0.05$ ). Women aged  $\geq 30$  years and who reported poor sleep during early pregnancy had increased risk of developing GDM (OR 2.35,

95% CI 1.35–4.09) compared with those with good sleep. Significant association between poor sleep and the risk of GDM was observed among nulliparas (OR 1.77, 95% CI 1.13–2.77), but not multiparas (OR 1.56, 95% CI 0.70–3.48). The association between poor sleep quality during early pregnancy and risk of GDM was strongest in women with a family history of diabetes (OR 4.02, 95% CI 1.54–10.48). No significant interaction was found with pre-gravid BMI and napping during early pregnancy (all  $p$  for interaction  $>0.05$ ).

## Discussion

In this large cohort of pregnant women, a significantly positive association was found between poor sleep quality during early pregnancy and the incidence of subsequent GDM. Compared to women with good sleep in early pregnancy, those with poor sleep quality in early pregnancy had a 77% increased risk of developing GDM later. To date, evidence for the association between sleep quality and the risk of GDM is limited. However, previous studies have well-documented the association between poor sleep quality and type 2 diabetes [9,20–23]. A meta-analysis study reported that poor sleep quality, such as difficulty initiating sleep and difficulty maintaining sleep, was significantly associated with an increased risk of type 2 diabetes [21]. The mechanism involved in this association may be related to impaired glucose tolerance. A laboratory study found that among young adults, all-night selective suppression of slow-wave sleep, which was regarded as the most “restorative” sleep stage, without any change in total sleep duration resulted in a 25% decrease in insulin sensitivity [10]. A significant association between decreased sleep quality and increased hemoglobin A1c levels has also been observed in a previous study [24]. Hence, the association between poor sleep quality and the risk of GDM is biologically plausible.

A few recent studies have suggested associations between sleep quality and the risk of impaired glucose tolerance and GDM [12,15,25]. In a cohort of 686 Asian singleton pregnant

women, poor sleep quality assessed by the Pittsburgh Sleep Quality Index (PSQI) was associated with an elevated risk of GDM [15]. Reutrakul et al. explored, using four validated sleep questionnaires, the association between sleep disturbances and glucose tolerance, and found an inverse correlation between reported sleep duration and glucose values from the 50-g oral glucose tolerance test ( $r = -0.21$ ,  $p < 0.01$ ) such that each hour of reduced sleep duration was linked to a 4% glucose increase [25]. In the present study, poor sleep quality in early pregnancy was linked to an increased risk of GDM; however, the association was not found in mid-pregnancy. Consistent with this result, Facco et al. recently reported that sleep quality measures were not associated with GDM at 16 and 21 weeks of gestation; the daily sleep of pregnant women was monitored using wrist actigraphy for a 7-consecutive-day period [13].

Existing data show that short and long sleep duration are associated with type 2 diabetes and GDM [12,14,16,21]. Either long sleep duration or short sleep due to sleep restriction or sleep problems in pregnancy could contribute to impaired glucose tolerance by dysregulating appetite hormones, such as leptin and ghrelin, which may disrupt energy homeostasis, and result in weight gain [26–28]. The current study assessed the interaction of sleep quality and duration in early pregnancy on the development of GDM, and noted that women with poor sleep combined with nighttime sleep duration  $\geq 8.5$  hours/night in early pregnancy had the highest risk of GDM. This may be because women with longer sleep duration are those who suffer from more-frequent and serious poor sleep so they compensate for this by spending more time sleeping. Poor sleep during early pregnancy requires more clinical attention, especially among those who need longer nighttime sleep duration. Screening for sleep problems and improving sleep in early pregnancy may help to prevent the development of GDM.

The current study also found that the adverse effects of poor sleep on the development of GDM were stronger among women aged  $\geq 30$  years and those with a family history of diabetes. The risk factors of GDM, advancing maternal age, and family history of diabetes may enhance the adverse effects of poor sleep on the development of GDM. In the present study, statistically significant interaction terms for parity and poor sleep quality were observed; however, the association between poor sleep and the risk of GDM was only found among nulliparas. The interaction between parity and poor sleep during early pregnancy may be related to maternal age. Evidence has indicated that age is negatively linked with self-reported sleep quality and duration assessed by the Pittsburgh Sleep Quality Index [29]. In addition, some poor sleep reported by parous women may be due to childcare-relevant factors rather than pregnancy; this may explain the lesser association between poor sleep during early pregnancy and the risk of GDM in multiparas.

This study had several strengths. Firstly, it was a multicenter, population-based, prospective cohort study with a large sample size. Secondly, it explored separately the relationship between sleep quality in early and mid-pregnancy and the risk of GDM, and assessed the interaction of sleep quality and duration in early pregnancy on the risk of GDM. It also assessed the interaction of several covariates (maternal age, parity, pre-gravid BMI, family history of diabetes, and napping). Nevertheless, this study also had some limitations. First, sleep quality was assessed by self-reported questionnaires, which may have resulted in under-estimation or over-estimation because of recall bias. Further studies to assess the relationship between sleep during pregnancy and GDM using objective measures of sleep are warranted. Another limitation was that the questionnaires did not involve screening for snoring, which has been associated with an elevated risk of GDM [30]. Lastly, diet and physical activities, which are potential confounders for GDM risk, were not adjusted for in

the current study when assessing the association between sleep quality and GDM.

## Conclusion

Women with poor sleep quality during early pregnancy were associated with an elevated risk of GDM. Women with poor quality of sleep and longer nighttime sleep duration in early pregnancy were more likely to develop GDM. The association between poor sleep and the development of GDM was stronger among women aged  $\geq 30$  years, nulliparas, and those with a family history of diabetes. Screening for and treating sleep disturbances in early pregnancy could potentially improve pregnancy outcomes.

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CZ and NY designed the research. CZ, RC, XZ, SX, QL, WC, WW, XL, JW, CL, MX, GS contributed to the acquisition of data for the study. LH, XY and NY supervised the study conduct. CZ and NY contributed in the statistical analysis. CZ wrote the manuscript under supervision of NY. All authors critically reviewed drafts and approved the final manuscript.

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**Table 1.** Demographics characteristics of the study population ( $n = 4066$ ).

Characteristics	Overall ( $n = 4066$ )	Sleep quality during early pregnancy			Sleep quality during mid-pregnancy		
		Poor ( $n = 259$ )	Good ( $n = 3807$ )	$P$	Poor ( $n = 248$ )	Good ( $n = 3818$ )	$P$
Gestational age at enrollment, weeks	$12.5 \pm 1.6$	$12.4 \pm 1.6$	$12.5 \pm 1.6$	0.418	$12.5 \pm 1.7$	$12.5 \pm 1.6$	0.928
Gestational age at the glucose screening test, weeks	$26.2 \pm 1.9$	$26.3 \pm 1.7$	$26.2 \pm 1.9$	0.969	$26.2 \pm 1.7$	$26.3 \pm 1.9$	0.731
Ethnicity (Han Chinese)	3961 (97.4)	255 (98.5)	3706 (97.3)	0.276	246 (99.2)	3715 (97.3)	0.069
Nulliparity	3415 (84.0)	200 (77.2)	3215 (84.4)	0.002	187 (75.4)	3228 (84.5)	<0.001
Rate of gestational weight gain in early pregnancy, kg/week	$0.09 \pm 0.20$	$0.08 \pm 0.22$	$0.09 \pm 0.20$	0.505	$0.08 \pm 0.24$	$0.09 \pm 0.20$	0.321
Pre-pregnancy BMI, kg/m <sup>2</sup>	$20.8 \pm 2.6$	$21.3 \pm 2.9$	$20.8 \pm 2.6$	0.001	$20.9 \pm 2.6$	$20.8 \pm 2.6$	0.546
16.8~	767 (18.9)	34 (13.1)	733 (19.3)	0.011	46 (18.5)	721 (18.9)	0.850
18.5~	2836 (69.7)	185 (71.4)	2651 (69.6)		171 (69.0)	2665 (69.8)	
24.0~37.8	463 (11.4)	40 (15.4)	423 (11.1)		31 (12.5)	432 (11.3)	
Maternal age, years	$28.3 \pm 3.4$	$29.0 \pm 4.3$	$28.2 \pm 3.4$	<0.001	$29.0 \pm 3.7$	$28.2 \pm 3.4$	0.001
Family history of diabetes	302 (7.8)	27 (10.4)	299 (7.9)	0.140	30 (12.1)	296 (7.8)	0.015
Education level, schooling years							

<16	1654 (40.7)	130 (50.2)	1524 (40.0)	0.001	114 (46.0)	1540 (40.3)	0.080
≥16	2412 (59.3)	129 (49.8)	2283 (60.0)		134 (54.0)	2278 (59.7)	

## Average personal income , CNY

<5000	1504 (37.0)	106 (40.9)	1398 (36.7)	0.299	95 (38.3)	1409 (36.9)	0.624
≥5000	2502 (61.5)	148 (57.1)	2354 (61.8)		151 (60.9)	2351 (61.6)	
Unsure/declined	60 (1.5)	5 (1.9)	55 (1.4)		2 (0.8)	58 (1.5)	
Smoking before pregnancy	117 (2.9)	13 (5.0)	104 (2.7)	0.033	10 (4.0)	107 (2.8)	0.262
Drinking before pregnancy	55 (1.4)	5 (1.9)	50 (1.3)	0.405	5 (2.0)	50 (1.3)	0.351
Daytime sleep duration in early pregnancy, h/day	1.0 (0.5, 2.0)	1.0 (0.5, 2.0)	1.0 (0.5, 2.0)	0.465	1.0 (0.5, 2.0)	1.0 (0.5, 2.0)	0.163
Daytime sleep duration in mid-pregnancy, h/day	1.0 (0.5, 1.5)	1.0 (0, 1.5)	1.0 (0.5, 1.5)	0.332	1.0 (0, 1.5)	1.0 (0.5, 1.5)	0.221
Nighttime sleep duration in early pregnancy, h/day	8.0 (8.0, 9.0)	8.5 (7.0, 8.5)	8.0 (8.0, 9.0)	<0.001	8.0 (7.5, 9.0)	8.0 (8.0, 9.0)	<0.001
Nighttime sleep duration in mid-pregnancy, h/day	8.0 (7.5, 9.0)	8.0 (7.0, 8.5)	8.0 (7.5, 9.0)	<0.001	7.5 (6.5, 8.5)	8.0 (8.0, 9.0)	<0.001
GDM	335 (8.2)	37 (14.3)	298 (7.8)	<0.001	24 (9.7)	311 (8.1)	0.395

BMI = body mass index; CNY = Chinese Yuan; GDM = gestational diabetes mellitus; SD = standard deviation; 1 CNY ≈ 0.16 US\$; h/day =

hours per day.

Data are mean  $\pm$  SD or  $n$  (%) or median (P<sub>25</sub>, P<sub>75</sub>).

$p$ -values for differences in participant characteristics across categories of sleep quality were obtained by independent sample  $t$ -test and Mann-Whitney U test for continuous variables and Chi-squared test for categorical variables.

ACCEPTED MANUSCRIPT

**Table 2.** Associations of poor sleep quality during early and mid-pregnancy with gestational diabetes mellitus.

Sleep quality	GDM	Crude OR (95% CI)	Model I* OR (95% CI)	Model II** OR (95% CI)
During early pregnancy				
Good	298 (7.8)	1	1	1
Poor	37 (14.3)	1.96 (1.36, 2.83)	1.70 (1.16, 2.50)	1.77 (1.20, 2.61)
During mid-pregnancy				
Good	311 (8.1)	1	1	1
Poor	24 (9.7)	1.21 (0.78, 1.87)	1.13 (0.73, 1.77)	1.13 (0.72, 1.77)

CI = confidence interval; GDM = gestational diabetes mellitus; OR = odds ratio.

Data are *n* (%) or OR (95% CI).

\*OR and 95% CI estimated with multivariable logistic regression adjusted for pre-gravid

BMI, maternal age, family history of diabetes, education, smoking before pregnancy, parity and the rate of weight gain in the first trimester.

\*\*OR and 95% CI estimated with multivariable logistic regression adjusted for model I plus nighttime sleep duration and napping during corresponding pregnancy.

**Table 3.** The interaction effect of sleep duration and quality during early pregnancy on the development of gestational diabetes mellitus.

Nighttime sleep duration (hours/day)	Sleep quality	GDM	Crude OR (95% CI)	Model I* OR (95% CI)	Model II** OR (95% CI)
7.0 to <8.5	Good	162 (8.2)	1	1	1
7.0 to <8.5	Poor	17 (13.7)	1.77 (1.04, 3.03)	1.53 (0.87, 2.67)	1.53 (0.88, 2.69)
<7.0	Good	13 (9.2)	1.13 (0.63, 2.05)	1.06 (0.58, 1.93)	1.02 (0.56, 1.87)
<7.0	Poor	7 (12.7)	1.63 (0.72, 3.65)	1.15 (0.49, 2.66)	1.09 (0.47, 2.54)
≥8.5	Good	123 (7.2)	0.87 (0.68, 1.11)	1.00 (0.78, 1.29)	1.00 (0.78, 1.29)
≥8.5	Poor	13 (16.2)	2.16 (1.17, 4.01)	2.32 (1.23, 4.38)	2.27 (1.20, 4.29)

CI = confidence interval; GDM = gestational diabetes mellitus; OR = odds ratio.

Data are *n* (%) or OR (95% CI).

\*OR and 95% CI estimated with multivariable logistic regression adjusted for pre-gravid

BMI, maternal age, family history of diabetes, education, smoking before pregnancy, parity and the rate of weight gain in the first trimester.

\*\*OR and 95% CI estimated with multivariable logistic regression adjusted for model I plus napping during early pregnancy.

**Table 4.** Stratified analyses: potential effect modification for the impact of poor sleep during early pregnancy on gestational diabetes mellitus.

Stratification factors	Category	GDM		Adjusted OR <sup>a</sup> (95% CI)	<i>P</i> <sub>int</sub> <sup>b</sup>
		Good sleep	Poor sleep		
Maternal age	<30 years	177 (6.5)	15 (9.1)	1.37 (0.78, 2.43)	0.011
	≥30 years	121 (11.0)	22 (23.4)	2.35 (1.35, 4.09)	
Parity	Nulliparity	241 (7.5)	27 (13.5)	1.77 (1.13, 2.77)	0.037
	Multiparity	57 (9.6)	10 (16.9)	1.56 (0.70, 3.48)	
Pre-gravid BMI, kg/m <sup>2</sup>	16.8~23.9	223 (6.6)	25 (11.4)	1.73 (1.10, 2.72)	0.146
	24.0~37.8	75 (17.7)	12 (30.0)	1.87 (0.84, 4.16)	
Family history of diabetes	No	261 (7.4)	27 (11.6)	1.48 (0.95, 2.31)	0.042
	Yes	37 (12.4)	10 (37.0)	4.02 (1.54, 10.48)	
Napping	No	39 (6.6)	5 (8.3)	1.43 (0.52, 3.90)	0.264
	Yes	259 (8.1)	32 (16.1)	1.79 (1.17, 2.75)	

BMI = body mass index; CI = confidence interval; GDM = gestational diabetes mellitus; OR = odds ratio.

Data are *n* (%) or OR (95% CI).

<sup>a</sup>OR and 95% CI estimated with multivariable logistic regression adjusted for confounding factors (poor sleep vs good sleep).

All covariates are as follows: pre-gravid BMI, maternal age, family history of diabetes, education, smoking before pregnancy, parity, the rate of weight gain in the first trimester, napping and nighttime sleep duration during early pregnancy.

Each of the above groups were adjusted for all covariates except itself.

<sup>b</sup>*p* for interaction estimated with log-linear model.



## Highlights

1. Poor sleep quality during early pregnancy was associated with an increased risk of gestational diabetes mellitus (GDM), especially among women aged  $\geq 30$  years, nulliparas, and those with family history of diabetes.
2. Women with poor sleep quality and longer nighttime sleep duration in early pregnancy were more likely to develop GDM.
3. No significant association was found between poor sleep quality during mid-pregnancy and the risk of GDM.