Poor sleep quality in early pregnancy increases the risk of developing gestational diabetes mellitus: a propensity score matching analysis

Xu Zhou · Xiang Hong · Kaiping Huang · Xiaoling Ding · Hong Yu · Jun Zhao · Yan Xuan · Tao Yan · Bei Wang

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Abstract

Purpose This study aimed to demonstrate the relationship between poor sleep quality in early pregnancy and the risk of developing gestational diabetes mellitus (GDM).

Methods We conducted a nested case–control study and performed a 1:3 propensity score (PS) matching to match pregnant women with GDM to women without GDM. After PS matching, logistic regressions were carried out to describe the association between sleep quality (assessed by Pittsburgh Sleep Quality Index [PSQI]) and the risk of GDM. We also performed a second analysis to explore the association in groups divided according to maternal age.

Results A total of 535 women were enrolled in this study. Of 456 women with complete data, the incidence of GDM was 12.1% (55/456). After PS matching, we found poor sleep quality (PSQI > 5) in early pregnancy was a statistically significant risk factor for GDM (OR 2.03; 95% CI 1.02–4.01; p-value = 0.043). The association of poor sleep quality (PSQI > 5) with GDM was significant among women less than 35 years old (OR 2.72; 95% CI 1.22–6.43; p-value = 0.018) but not among women more than or equal to 35 years old after adjusting for all covariates.

Conclusion Poor sleep quality in early pregnancy is associated with higher risk of developing GDM, especially for women under 35 years old. Screening expectant mothers with sleep problems in the first trimester is suggested.

Keywords Sleep quality · Gestational diabetes mellitus · Early pregnancy · Nested case–control study · Propensity score matching

Introduction

Gestational diabetes mellitus (GDM) refers to a common disease of glucose metabolism that occurs in expectant mothers [1, 2]. GDM has become a burden to the public health care system since the increasing prevalence of obesity and the aging of pregnant women [2]. Previous studies have demonstrated that GDM affects both mothers and babies [3–5]. It increases the incidence of hypertensive disorder complicating pregnancy (HDCP), macrosomia, fetal distress, and neonatal hypoglycemia [2, 6, 7]. In addition, women with GDM have a higher risk of developing type 2 diabetes mellitus (T2DM) and cardiovascular disease after giving birth, and their offspring are more likely to develop T2DM or become obese after being adults [7]. Existing research evidence on the etiology of GDM has failed to clarify the underlying mechanism, but clinical and epidemiological evidence clearly illustrates that the occurrence of GDM is a result of the combined effects of environmental
and genetic factors. However, currently recognized risk factors for GDM, such as maternal age ≥ 35 years, obesity, family history of diabetes, and personal history of GDM, do not exist in nearly half of patients with GDM [8]. Therefore, it is important to find out modifiable risk factors for the prevention of GDM.

Sleep disturbances are common during pregnancy due to body morphing, hormone shifting, and stress and depression symptoms [9–12]. The relationship between sleep and diabetes has also been a topic of interest in recent years. Previous studies have demonstrated that sleep disorders are related to obesity, cardiovascular disease, and insulin resistance in the non-pregnant population. Poor sleep quality is correlated with the development of diabetes and metabolic syndrome while sleeping either less than 6 h or more than 8 h is also positively correlated with the risk of diabetes [13–16]. Regarding the pregnant population, the results of the meta-analysis by Reutrakul et al. [17] showed that women who slept less than 7 h (objectively measured) were more likely to develop GDM (OR 1.70; 95% CI 1.24–2.33). Those results are consistent with findings in self-reported sleep conditions. Women with sleep duration < 6.25 h had a higher blood glucose level and a higher risk of developing GDM (OR 2.84; 95% CI 1.25–6.44), when compared with women with sleep duration > 6.25 h. However, few studies have explored the association between sleep quality during early gestation and the risk of developing GDM. The sleep conditions in early pregnancy may have predictive value on GDM. In this study, we hypothesized that women with poor sleep quality during their early gestation may have a higher risk of developing GDM.

**Materials and methods**

**Study population**

We performed a nested-control study to explore the association between sleep quality and the risk of GDM. The cases and controls in this study were drawn from the Prospective Fertility and Pregnancy Study Cohort (PFPSC). The overall goal of PFPSC is to identify risk factors that affect fertility and birth outcomes. This study was conducted at the Maternal and Child Health Center, Gulou District, Nanjing City, Jiangsu Province. We recruited women in their early pregnancy from April 2019 to March 2020. Pregnant women were enrolled if they met inclusion criteria. The eligibility criteria included: (1) ≤ 20 weeks of pregnancy; (2) no serious mental illness, able to answer the questionnaire. Women were ineligible if they had diabetes, hypertension, or other chronic diseases requiring medication. All women understood the pros and cons of this study and signed informed consent. This study passed the ethical review of the Ethics Committee of Zhongda Hospital affiliated to Southeast University (Reference number: 2018ZDSYLL116-P01).

**Data collection**

At the time of enrolment, all eligible pregnant women were asked to complete a questionnaire survey, including their demographic information and two standardized questionnaires to assess their perception of stress and sleep quality respectively. At 26–28 weeks of gestation, all participants underwent a 75-g oral glucose test (OGTT) after overnight fasting. Plasma glucose levels were measured before, 1 h and 2 h after administration of oral glucose. GDM was defined using the International Association of the Diabet es and Pregnancy Study Groups (IADPSG) diagnostic criteria: ≥ 5.1 mmol/L (92 mg/dL) for fasting glucose and/or ≥ 10.0 mmol/L (180 mg/dL) for 1 h plasma glucose and/or ≥ 8.5 mmol/L (153 mg/dL) for 2 h plasma glucose [18].

**Standardized questionnaires**

The perceived stress scale (PSS) [19] was used to assess the stress perception of pregnant women. The PSS can assess a person’s subjective experience of stress during the past month and is validated for pregnant women in China [20]. The PSS-14 version was used in this study. There are 14 items in total, and the score of each item ranges from 0 to 4. PSS-14 has two dimensions: positive scoring constitutes the dimension of anxiety, while reverse scoring constitutes the dimension of out of control. The sum of these two dimensions is the total score for PSS-14, with a higher score indicating increased stress status.

We chose the Pittsburgh sleep quality index (PSQI) [21] scale to assess the subjective sleep quality of pregnant women during the past month. The coefficient of reliability and validity are 0.85 and 0.83, respectively [21]. Previous research has shown the reliability and validity of the scale are satisfied among pregnant and non-pregnant women [22]. This scale contains 18 self-assessment items that participate in scoring (comprising 9 self-assessment questions) and 5 other-evaluated items that do not participate in scoring. In this study, only the first 18 items were used to measure and assess the sleep quality of pregnant women. Those items consist of 7-dimensional factors: factor 1: subjective sleep quality; factor 2: sleep latency (how long it takes to fall asleep); factor 3: sleep duration; factor 4: habitual sleep efficiency (the percentage of time in bed that one is asleep); factor 5: sleep disturbances; factor 6: use of sleeping medication; factor 7: daytime dysfunction. Each factor is scored on a scale of 0 to 3. The cumulative score of each factor is the total score of PSQI, which is between 0 and 21 points. The higher the PSQI score, the worse the quality of sleep. PSQI
score > 5 is considered as having poor sleep quality [21]. In this study, we also explored the association of sleep duration and the risk of GDM, because in practice this dimension is easier to monitor and effect change on.

**Statistical methods**

To compare baseline characteristics between the GDM group and the control group, we used independent Student t-tests and chi-squared tests to analyze continuous and categorical maternal characteristics, respectively. Covariates were maternal age, pre-pregnancy BMI, gestational week, gravidity, maternal passive smoking, family history of hypertension (women with a family history of diabetes were excluded from this analysis due to sparse data), adverse pregnancy history, and PSS scores. Although the nested-control study design has been considered as a cost-effective study design, it may suffer statistical efficiency. To deal with the potential problem of confounding, we performed a 1:3 propensity score (PS) matching accordingly for women who developed GDM or not. We constructed the nearest neighbor matching, which runs through the list of women with GDM and selects the closest eligible controls to be paired with each woman with GDM. All covariates above were selected as variables for the PS model. We calculated standardized mean differences (SMD) between unmatched groups and matched groups. SMD < 10% indicates trivial effect between groups, while 10–34% indicates small effect [23]. After PS matching, we conducted logistic regressions to describe the association between sleep quality and the risk of developing GDM. Further analysis to assess the specific sleep problem was also performed in terms of sleep duration. In addition, we conducted stratified analysis classified by women’s age (less than 35 vs. more than or equal to 35 years old).

Data were entered into Epidata 3.1 by double entry and all statistical analysis was conducted with R version 4.0.3 software. All statistical tests were two-sided tests at the 5% level, and p-value < 0.05 was considered significant.

**Results**

**Characteristics of enrolled pregnant women**

Of 535 enrolled pregnant women, 456 women had complete information for all statistical analyses (Fig. 1). The average age of these 456 women was 29.7 ± 4.2, and their average gestational age was 14.2 ± 3.7. In our study, the overall incidence of GDM was 12.1% (55/456). After 1:3 propensity score matching, there were 55 matched pairs.

Table 1 showed baseline characteristics of two groups before and after PS matching. Before PS matching, expectant mothers’ characteristics varied considerably by GDM. We found participants with GDM had higher maternal age and greater proportion of family history of hypertension and abnormal pre-pregnancy BMI, while
their gestational week and PSS score were statistically lower than that in the control group. After PS matching, the 55 matched pairs were analyzed for differences in the distribution of all measured covariates. We found there were no significant differences between the two matched groups ($p > 0.05$) (Table 1). Across 8 covariates, the SMDs were less than 10% in absolute value except for SMD for family history of hypertension, which was 10.9% (Fig. 2). Since 10% < SMD < 34% indicates small effect [23], and we found there was no statistically significant difference in the family history of hypertension, we considered the covariate balance was acceptable. We also plotted a density plot to show propensity scores of two groups before and after PS matching, which also demonstrated a successful balancing between the two matched groups (Fig. 3).

### Table 1 Baseline characteristics by GDM before and after propensity score (PS) matching

| Covariate                  | Before PS match | After PS match |
|----------------------------|-----------------|----------------|
|                            | Control ($N=401$) | GDM ($N=55$) | $P$-value | Control ($N=165$) | GDM ($N=55$) | $P$-value |
| Maternal age, mean ± SD    | 29.5 ± 4.1      | 30.9 ± 4.9     | < 0.001   | 30.8 ± 4.3       | 30.9 ± 4.9     | 0.814 |
| Pre-pregnancy BMI, n (%)   |                 |               |          |                 |               |          |
| 18.5 – 25                  | 312 (77.8)      | 37 (67.3)     | < 0.001   | 104 (63.0)      | 37 (67.3)     | 0.820 |
| < 18.5                     | 56 (14.0)       | 4 (7.3)       | 30 (18.2) | 4 (7.3)         |               |          |
| ≥ 25                       | 33 (8.2)        | 14 (25.5)     | 31 (18.8) | 14 (25.5)       |               |          |
| Gestational week, mean ± SD| 14.2 ± 3.6      | 13.6 ± 3.7    | < 0.001   | 13.8 ± 3.3      | 13.6 ± 3.7    | 0.752 |
| Gravidity, n (%)           |                 |               |          |                 |               |          |
| 1                          | 177 (44.1)      | 27 (49.1)     | 0.581     | 83 (50.3)       | 27 (49.1)     | 0.870 |
| ≥ 2                        | 224 (55.9)      | 28 (50.99)    | 82 (49.79)| 28 (50.9)       |               |          |
| Maternal passive smoking, n (%) | 394 (98.3) | 54 (98.2) | 1.000 | 162 (98.2) | 54 (98.2) | 1.000 |
| Yes                        | 7 (1.8)         | 1 (1.8)       | 3 (1.8)   | 1 (1.8)         |               |          |
| Family history of hypertension, n (%) | 344 (85.8) | 40 (72.7) | 0.022 | 128 (77.6) | 40 (72.7) | 0.416 |
| No                         | 57 (14.2)       | 15 (27.3)     | 37 (22.4) | 15 (27.3)       |               |          |
| Yes                        | 266 (66.3)      | 34 (61.8)     | 0.610     | 109 (66.1)      | 34 (61.8)     | 0.532 |
| Adverse pregnancy history, n (%) | 135 (33.7) | 21 (38.2) | 0.526 | 56 (33.9) | 21 (38.2) | 0.532 |
| No                         |                 |               |          |                 |               |          |
| Yes                        |                 |               |          |                 |               |          |
| PSS, mean ± SD             | 20.21 ± 7.1     | 18.33 ± 7.3   | < 0.001   | 18.9 ± 7.5      | 18.3 ± 7.3    | 0.579 |

**Fig. 2** Standardized mean differences in covariates between two groups before and after propensity score matching.
Sleep quality and the risk of GDM

In this study, poor sleep quality was defined as a sum score of PSQI > 5. We found 63.8% (291/456) women suffering from sleep problems.

Table 2 showed the results of ORs and 95% CI for poor sleep quality and the risk of developing GDM. Before PS matching, we found women with poor sleep quality had a greater risk of developing GDM than those without sleep problems, but this association had no statistical significance when adjusted for all covariates (OR 1.71; 95% CI 0.88–3.48). Results were consistent in other statistical models. After PS matching, we found this association was more obvious than that before matching, and there was statistical significance between poor sleep quality and the risk of developing GDM (OR 2.03; 95% CI 1.02–4.01).

Table 3 presented the outcomes of sleep duration and the risk of GDM after PS matching. When we considered sleep duration as a continuous variable, no significant correlation

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**Table 2** Odds ratios and 95% CI for poor sleep quality and the risk of GDM

|                | Crude OR (95% CI) | Adjusted OR* (95% CI) | Adjusted OR** (95% CI) | Adjusted OR# (95% CI) |
|----------------|-------------------|-----------------------|------------------------|-----------------------|
| **Unmatched**  |                   |                       |                        |                       |
| Normal (PSQI ≤5) | Ref               | Ref                   | Ref                    | /                     |
| Poor (PSQI >5)  | 1.59 (0.87–3.07)  | 1.47 (0.78–2.89)      | 1.71 (0.88–3.48)       | /                     |
| **Matched**     |                   |                       |                        |                       |
| Normal (PSQI ≤5) | Ref               | Ref                   | Ref                    | Ref                   |
| Poor (PSQI >5)  | 2.01 (1.05–4.03)  | 2.1 (1.07–4.32)       | 2.33 (1.14–4.98)       | 2.03 (1.02–4.01)      |

*ORs were adjusted for maternal age, pre-pregnancy BMI, gestational week, gravidity, maternal passive smoking, family history of hypertension, and adverse pregnancy history
**ORs were additionally adjusted for PSS scores
#OR for the matched group was adjusted for propensity scores

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**Table 3** Odds ratios and 95% CI for sleep duration and the risk of GDM

| Sleep duration | OR     | 95% CI | p-value |
|----------------|--------|--------|---------|
| > 7 h          | Ref    | Ref    | Ref     |
| ≤7 h           | 1.32   | 0.75–2.28 | 0.325   |
was found between sleep duration and the risk of GDM (OR 0.87; 95% CI 0.70–1.07). Results were similar when sleep duration was treated as a category variable, there was also no significant correlation between pregnant women sleeping ≤7 h and the risk of GDM (OR 1.32, 95% CI 0.75–2.28).

**Stratified analysis by maternal age**

Figure 4 presented the comparison of the association of sleep quality with the risk of GDM between two age groups (<35 vs. ≥35 years old). We found the incidence of poor sleep quality (PSQI > 5) among pregnant women ≥ 35 years old (65.9%, 29/44) was higher than pregnant women < 35 years old (59.7%, 105/176). However, the association of sleep quality with the risk of GDM was statistically significant only among pregnant women < 35 years old (OR 2.72; 95% CI 1.22–6.43).

**Discussion**

**Main findings**

In this study, there was a relatively high prevalence (63.8%, 291/456) of poor sleep quality among pregnant women, indicating sleep problems are common during pregnancy. Our findings demonstrated that poor sleep quality in early pregnancy (<20 weeks of pregnancy) increased the risk of developing GDM at 26–28 weeks of pregnancy (OR 2.03; 95% CI 1.02–4.01). Pregnant women, especially during their early pregnancy, are prone to anxiety, stress, and other bad feelings due to weight gain, hormone shifting, morning sickness, etc., which may result in poor sleep quality [24]. Obstetric clinical practice currently focuses on serious psychological diseases such as perinatal depression, while less concerns about common problems, like maternal stress and sleep quality, which may lead to adverse perinatal outcomes. Thus, it is necessary to provide psychological counseling services during routine prenatal care to guide pregnant women to reduce stress and develop good sleep habits, so that problems may be “nipped in the bud.” We also observed a slight protective effect of longer sleep duration on GDM, but the association had no statistical significance possibly due to the small sample size.

After PS matching, we further conducted a stratified analysis by their maternal age. The proportion of poor sleep quality among younger pregnant women (<35 years old) was lower than that among women ≥ 35 years old (59.7% vs. 65.9%). This finding was in accordance with the results of previous meta-analysis, which reported older samples had higher prevalence of PSQI scores ≥ 5 [25]. However, in stratified analysis, the association of poor sleep quality with GDM was statistically significant only among participants <35 years old. In our study, although the prevalence of poor sleep quality (cut-off point = 5) was lower among participants <35 years old, the prevalence of PSQI scores ≥ 10 was higher among younger participants (7.4% vs. 4.6). We assumed that younger pregnant women are more susceptible to sleep quality and experience worse sleep problems during early pregnancy, which increases their risk of developing GDM. It should be noted that the sample size of participants ≥ 35 years old in our research was relatively small, which may affect our finding. Studies with larger sample size are needed to justify our results.

**Comparison with previous studies**

We found poor sleep quality in early pregnancy was associated with increased risk of GDM. Our findings are consistent with the results of previous studies among the non-pregnant T2DM population [26–29], and extend previous findings to show that poor sleep quality during pregnancy is also associated with hyperglycemia. On a mechanistic level, previous studies have proposed several pathophysiological links between sleep disturbances and impaired glucose tolerance [30, 31]. Sleep deprivation, as well as obstructive sleep apnea (OSA), are associated with greater sympathetic nervous system activity [32], a dysregulation of proinflammatory cytokine levels [31] and cortisol secretion [33], which in turn leads to a decline in regulation of glucose [30, 31]. Those mechanisms may also have an influence on glucose metabolism among pregnant population.

Additionally, our findings are consistent with prior study on the association of sleep quality and risk of GDM. Cai et al. [34] observed that women with poor

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**Fig. 4** Association of sleep quality with the risk of GDM by maternal age

| Subgroup        | N   | GDM | OR (95%CI) |
|-----------------|-----|-----|------------|
| All participants| 220 | 55  | 2.33 (1.14–4.98) |
| Age             |     |     |            |
| <35             | 176 | 44  | 2.72 (1.22–6.43) |
| ≥35             | 44  | 11  | 1.03 (0.14–8.06) |
sleep quality during pregnancy had a higher risk of GDM (adjusted OR 1.75; 95% CI 1.11–2.76), which was similar to our finding. They also found sleeping < 6 h per night during pregnancy had the same effect and this association was of statistical significance (adjusted OR 1.96; 95% CI 1.05–3.66). However, we did not observe that sleep duration could significantly increase the risk of GDM. One plausible explanation is our participants were at a different period of pregnancy. We conducted a questionnaire survey < 20 weeks of pregnancy, while Cai et al. assessed their sleep quality at 26–28 weeks of pregnancy together with the OGTT. Since evidence has shown greater gestational age was associated with higher PSQI scores in women [25], we may not able to observe that association in early pregnancy. In addition, the study design, and statistical methods in our two studies were different, which may contribute to the diverse results.

Strengths and limitations

Our study is the first research that has been conducted to estimate the association between poor sleep quality and the risk of developing GDM in China and fills a gap in the research on early pregnancy. We performed a nested case–control study design and selected a PS matching model to study the relationship between sleep quality and the risk of developing GDM. PS matching is analogous to randomization procedures in randomized control studies. It improves the methodological quality of our study, and thus strengthens causal explanations of our results [35, 36, 37].

Several limitations need to be addressed when interpreting our findings. First, we used subjective methods to assess women’s sleep quality. Future research should consider both subjective and objective measures of sleep behaviors and compare their effect on the risk of developing GDM. Second, some researchers recommend that higher PSQI global score cut-off points (7+) are more appropriate among the pregnancy population [38, 39]. Third, due to the COVID-19 pandemic, the cohort in our study was constructed for only 1 year, so the sample size was lower than expected. Although our new findings suggested younger pregnant women (< 35 years old) with poor sleep quality had higher risk of GDM, cohorts with larger sample size are needed to verify our results. Fourth, we assessed sleep quality only once in early pregnancy. In future studies, it may be advisable to collect data of sleep quality (both subjective and objective) at multiple time points across pregnancy in larger cohorts to assess the causal relationship between sleep quality and the risk of developing GDM.

Conclusion

In summary, we found that women with poor sleep quality in early pregnancy had a higher risk of developing GDM. Future studies should examine the relationship between specific sleep problems and each health outcome during/after pregnancy by assessing sleep quality at multiple time points across pregnancy. To improve expectant mothers’ sleep quality and their pregnancy outcomes, the significance of healthy sleep habits should be emphasized during prenatal visits in the early stage.

Author contribution All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Xu Zhou, Xiang Hong, and Kaiping Huang. The first draft of the manuscript was written by Xu Zhou and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data availability The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Zhongda Hospital affiliated to Southeast University (No. 2018ZDSYLL116-P01).

Consent to participate Informed consent was obtained from all individual participants included in the study.

Competing interests The authors declare no competing interests.

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