Research: Pregnancy

Sleep duration and quality, and risk of gestational diabetes mellitus in pregnant Chinese women

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Abstract

Aims To examine the association between sleep disturbances during pregnancy and risk of gestational diabetes mellitus.

Methods From 2010 to 2012, 12 506 women in Tianjin, China, were screened using a 50-g 1-h glucose challenge test at 24–28 weeks' gestation. Those with glucose challenge test values of ≥ 7.8 mmol/l were invited to further undergo a 75-g 2-h oral glucose tolerance test. Gestational diabetes was determined according to the International Association of Diabetes and Pregnancy Study Group's definition. Self-reported sleep duration and sleep quality during pregnancy was documented using a modified questionnaire. Logistic regression was used to obtain odds ratios and 95% CIs.

Results A total of 919 women (7.3%) had gestational diabetes. Sleep duration was found to have an approximate J-shaped association with gestational diabetes risk after adjusting for covariates. Compared with a sleep duration of 7–9 h/day (43% of 12 506 women), the adjusted odds ratios for sleep duration of ≥ 9 h/day (55%) and < 7 h/day (2%) for gestational diabetes were 1.21 (95% CI 1.03–1.42) and 1.36 (95% CI 0.87–2.14), respectively. Compared with good sleep quality (37.9% of 12 506 women), the adjusted odds ratios of moderate (59.9%) and poor sleep quality (2.2%) for gestational diabetes were 1.19 (95% CI 1.01–1.41) and 1.61 (95% CI 1.04–2.50), respectively.

Conclusion In pregnant Chinese women, poor sleep quality, and shorter and longer duration of sleep during pregnancy were independently associated with an increased risk of gestational diabetes.

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Introduction

The prevalence of gestational diabetes mellitus (GDM) is increasing worldwide, with adverse short-term and long-term suboptimum health outcomes in both mothers and their offspring. In particular, women with gestational diabetes have a high risk of developing Type 2 diabetes and cardiovascular disease in later life and their offspring are more prone to developing childhood obesity, impaired glucose tolerance and increased prevalence of cardiovascular risk factors during adolescence and early adulthood [1,2]. Given that gestational diabetes is likely to be multi-causal in its aetiology, it is important to identify novel risk factors in order to design better prevention strategies for gestational diabetes before or during pregnancy.

Sleep disturbances, especially extreme sleep duration, poor sleep quality and sleep-disordered breathing, are common during pregnancy because of pregnancy-related hormonal changes, anxiety and physical discomfort. Emerging evidence suggests that sleep disturbances during pregnancy might be associated with adverse pregnancy outcomes such as preeclampsia, longer labour times, higher cesarean section rates, intrauterine growth restriction and preterm birth [3–5]. A large body of literature comprising epidemiological studies suggests that sleep disturbances in non-pregnant populations may elevate the risk of impaired glucose metabolism, insulin resistance and Type 2 diabetes [6–10]. In a meta-analysis of 9795 pregnant women, sleep-disordered breathing was found to be associated with an increased risk of gestational diabetes [pooled BMI adjusted odds ratio (OR) 3.06 (95% CI 1.89–4.96)] [11]. However, the risk associations of gestational diabetes and other
What’s new?

- Sleep disturbances increase the risk of Type 2 diabetes mellitus but it is uncertain whether they also increase the risk of gestational diabetes mellitus.
- Using a large prospective population-based study of Chinese pregnant women, this study is the first to report that suboptimum sleep quality as well as shorter and longer sleep duration during pregnancy were associated with increased risk of gestational diabetes, the latter being presented by an approximately J-shaped risk relationship.

features of sleep disturbances, such as sleep duration and quality of sleep, remain conflicting and inconclusive [5,12–15]. There is therefore a need to investigate the association between sleep disturbances, especially extreme sleep duration and poor sleep quality, and the risk of gestational diabetes to better understand its aetiology and identify women who are at high risk of gestational diabetes so as to prevent and reduce the risk of its occurrence.

We established a large cohort of pregnant women and their children for the period 2010 to 2012 in Tianjin, China [16]. Using data from this cohort, the aim of the present analysis was to examine the association between self-reported sleep duration and sleep quality during pregnancy and the risk of gestational diabetes among Chinese women.

Patients and methods

We established a universal screening and management system for gestational diabetes in the three-tier antenatal care system of the urban districts of Tianjin, China in 1999 [17]. For the period October 2010 to August 2012, we had detailed documentation of the clinical and biochemical profiles of a cohort of pregnant women and their infants from their first antenatal visit to delivery. The study population and data collection methods have been described in detail previously [16]. Briefly, 19 669 pregnant women within the first 12 weeks of gestation were registered for pregnancy and attended their first antenatal care at a primary care hospital. Between 24 and 28 weeks’ gestation, all these women were screened for gestational diabetes using a 50-g glucose challenge test. Of 19 669 pregnant women, 1080 (5.5%) did not undergo a glucose challenge test. Of the remaining 18 589 women, 2953 (15.9%) were found to have glucose challenge test values of $\geq 7.8$ mmol/l and were referred to Tianjin Women and Children’s Health Centre for a 75-g oral glucose tolerance test (OGTT) [16]. In the OGTT, fasting, 1-h and 2-h plasma glucose levels were measured after overnight fasting of at least 8 h. Gestational diabetes was defined based on the International Association of Diabetes and Pregnancy Study Group thresholds: fasting plasma glucose $\geq 5.1$ mmol/l or 1-h plasma glucose $\geq 10.0$ mmol/l or 2-h plasma glucose $\geq 8.5$ mmol/l [18].

Maternal age, first-degree family history of diabetes, parity, ethnicity, education attainment, smoking and alcohol consumption before and during pregnancy were collected using questionnaires at the first antenatal care visit or at the time of the glucose challenge test. Sleep items were included in the questionnaire at the time of the glucose challenge test. The Pittsburg Sleep Quality Index (PSQI) is a well-validated scale for measurement of self-reported sleep duration and sleep quality [19]. However, because of the busy clinical settings and multiple purposes of our survey, we selected only two items to measure global performance of sleep, i.e. actual sleep hours and quality of sleep, with modification of sleep hours to also include duration in the day time. The two questions were: ‘How many hours of sleep did you get every day during the index pregnancy, including both day and night time?’ and ‘How did you feel about your sleep quality during the index pregnancy: good, moderate or poor?’

Height, weight and blood pressure were measured using a standardized protocol at first antenatal care visit. Height was measured without shoes to the nearest 0.5 cm. Weight was measured without shoes and in light clothing to the nearest 0.1 kg at first antenatal care visit and re-measured at the time of glucose challenge test. BMI was calculated as weight in kg divided by body height in m². Sitting blood pressure was measured using a calibrated mercury sphygmomanometer after at least 10 min of rest.

We sequentially excluded 1080 women (5.5%) who did not have glucose challenge test results, 781 women (4.0%) who had a positive glucose challenge test but did not undergo an OGTT and 5302 women (27.0%) with missing sleep information. Finally, 12 506 women (63.6%) were included in the analysis (Fig. 1). Written informed consent was obtained before data collection. The study was approved by the Ethics Committee for Clinical Research of Tianjin Women and Children’s Health Centre.

Statistical analyses

All analyses were performed using IBM SPSS Statistics 20.0 (IBM SPSS, Chicago, IL, USA), unless specified. P values of $<0.05$ (two-tailed) were taken to indicate statistical significance. To capture possible non-linear associations of sleep duration with the risk of gestational diabetes, SAS software (release 9.10) was used to perform restricted cubic spline analysis in binary logistic regression to plot OR curves of gestational diabetes against sleep duration (SAS Institute, Cary, NC, USA) [20]. A detailed description of the restricted cubic spline analysis is available in Appendix S1. We visually checked the linearity of the OR curve. Because sleep duration was associated with gestational diabetes in a approximately J-shaped curve, we further stratified duration of sleep into
three groups at identified thresholds by visual checking, i.e. < 7 h/day, 7–9 h/day (used as the reference group) and ≥ 9 h/day. Sleep quality was classified into three categories according to self-reported subjective feeling: good (used as the reference group); moderate; and poor.

Clinical and biochemical variables of women according to gestational diabetes diagnosis status were compared using Student’s t-test, a Mann–Whitney U-test, the chi-squared test or Fisher’s exact test, as appropriate. We used univariable and multivariable binary logistic regression models to obtain ORs and their 95% CIs for sleep duration and sleep quality for gestational diabetes. In multivariable analysis, covariates included maternal age, height, pre-pregnancy BMI, family history of diabetes, parity, education, Han ethnicity, systolic/diastolic blood pressure at first antenatal care visit, multiple pregnancies, habitual smoking before/during pregnancy, alcohol consumption before/during pregnancy, and weight gain from first antenatal care visit to glucose challenge test time. The Ryan–Holm step-down Bonferroni procedure was used to adjust P values and 95% CIs for multiple comparisons [21].

We also compared the distributions of clinical and biochemical characteristics of excluded (n = 7163) and included (n = 12 506) women to estimate potential impacts of exclusion of the 7163 women from the main analysis.

Results

Characteristics of the study population

The clinical and biochemical characteristics of subjects are shown in Table 1. Of 12 506 pregnant women, 7.3% (919 women) had gestational diabetes. The median (interquartile range) sleep duration was 9 (8–10) h, 2.0% of women (n = 250) reported a shorter sleep duration, i.e. < 7 h/day and 55.0% of women (n = 6881) reported a longer sleep duration, i.e. ≥ 9 h/day. At the same time, 37.9, 59.9 and 2.2% of women reported good, moderate and poor sleep quality, respectively. Women with gestational diabetes were older, shorter, had a higher BMI and higher systolic/diastolic blood pressure at first antenatal care visit, were more likely to be habitual smokers and drinkers before pregnancy, had multiple pregnancies and a first-degree family history of diabetes than those without gestational diabetes (Table 1). Women with gestational diabetes were more likely to sleep for a shorter or longer duration, and had worse sleep quality compared with those without.

Risk associations of sleep duration and sleep quality with gestational diabetes

Sleep duration during pregnancy was associated with gestational diabetes risk in an approximately J-shaped manner after adjusting for possible covariates, with a nadir at 7.5 h of sleep duration (Fig. 2). In women who slept ≥ 9 h/day and in those who slept ≤ 7 h/day, sleep duration was associated with gestational diabetes in a linear manner, although the slope was less steep in women with short sleep duration.

In univariable analysis and using sleep duration of 7–9 h/day as the reference, the ORs for sleep duration ≥ 9 h/day and < 7 h/day for gestational diabetes were 1.21 (95% CI 1.03–1.42) and 1.36 (95% CI 0.87–2.14), respectively (Table 2). Compared with women with good sleep quality, women with moderate and poor sleep quality were at increased risk of gestational diabetes [OR for moderate-quality sleep: 1.62 (95% CI 1.20–2.17); OR for poor-quality sleep: 1.77 (95% CI 1.26–2.48)].

After adjusting for covariates, the OR for sleep duration ≥ 9 h/day for gestational diabetes was slightly enhanced [1.29 (95% CI 1.09–1.52)], while the ORs for gestational diabetes for those with moderate and poor sleep quality were attenuated [1.19 (95% CI 1.01–1.41); 1.61 (95% CI 1.04–2.50)].

Comparison of population characteristics between women included and excluded

Compared with women included in the analysis (n = 12 506), women excluded (n = 7163) were older,
had a higher BMI at first antenatal care visit, a higher rate of multipara and multi-pregnancy, and higher weight gain from first antenatal care visit to glucose challenge test time, but were less likely to be habitual smokers during pregnancy and alcohol drinkers before or during pregnancy (Table S1).

**Discussion**

In the present large prospective population-based study in Chinese pregnant women, we observed a roughly J-shaped relationship between self-reported sleep duration and the risk of gestational diabetes. Thereby, women with longer sleep duration (≥ 9 h/day) had an increased risk of gestational diabetes as compared with those with sleep duration of 7–9 h/day, although the positive association between shorter sleep duration (<7 h/day) and gestational diabetes risk did not reach statistical significance. More importantly, suboptimum sleep quality, i.e. moderate and poor sleep quality, was associated with increased risk of gestational diabetes in a more robust way, highlighting the importance of not only maintaining a normal length of sleep but also good-quality sleep to reduce the risk of gestational diabetes during pregnancy.

Both shorter and longer sleep durations were suggested to be associated with impaired glucose metabolism in the general population [6–10]. Short sleep duration was also found to be associated with abnormal glucose metabolism in pregnant...
women [5,12,13,15]. Qiu et al. [15] analysed the data on 1290 pregnant US women and reported that women who slept ≤ 4 h/night during early pregnancy had a significantly higher risk of gestational diabetes compared with those sleeping 9 h/night [Relative Risk 5.56 (95% CI 1.31–23.69)]. The authors of a small study in 169 women with a singleton pregnancy observed an inverse correlation between self-reported sleep duration and 1-h glucose level for a 50-g OGTT (r = −0.121, P < 0.01) and the OR of sleep duration < 7 h/night vs ≥ 7 h/night was 2.4 (95% CI 1.0–5.9) [5]. Another small study of 189 nulliparas women also found that self-reported sleep duration < 7 h/night was independently associated with the increased risk of gestational diabetes [adjusted OR 11.7 (95% CI 1.2–114.5)] [12]. More recently, in a small prospective observational study, 63 women were asked to wear an actigraph wristwatch for 7 days and nights before 1-h OGTT in mid-pregnancy [13]. The results showed that the objectively measured night-time sleep duration was inversely proportional to 1-h OGTT levels (r = −0.28, P = 0.03) and the shorter night-time sleep duration led to an increased risk of hyperglycaemia (defined as 1-h OGTT levels ≥ 130 mg/dl). There are many different definitions of reduced sleep duration. In the present study, we used < 7 h/day as a threshold and only 2% of Chinese women (n = 250) had short sleep duration, which may explain its non-significant association with gestational diabetes.

There are some consistent findings regarding associations between longer duration of sleep and the risk of Type 2 diabetes in several populations [6–8]. Between 1982 and 1992, researchers from the First National Health and Nutrition Examination Survey reported in 8992 US subjects that those with sleep duration ≥ 9 h/night were more likely to have incident diabetes over an 8- to 10-year follow-up period, even after adjusting for confounders [OR 1.52 (95% CI 1.06–2.18)] [8]. Data from the Quebec Family Study suggested that, in addition to short sleep duration (5–6 h/day), long sleep duration (9–10 h/day) was also associated with the presence of Type 2 diabetes or impaired glucose tolerance in adults [7]. A perspective study of 70 026 women enrolled in the Nurses Health Study found that long sleep duration (≥ 9 h/day) was positive associated with diabetes incidence, and this association persisted after controlling for covariates including BMI [6]. Conversely, there are currently no studies in the literature reporting associations between longer duration of sleep and gestational diabetes. In the present study, we found that longer duration of sleep (≥ 9 h/day) may also increase the risk of gestational diabetes in pregnant Chinese women. Poor sleep quality has also been reported to be associated with increased risk of Type 2 diabetes in multiple studies [9,10]. A significant association between unsatisfactory overall sleep quality and an elevated diabetes risk has been reported in a study of 3570 Japanese workers with no family history of diabetes, in which sleep quality was assessed using the Athens Insomnia Scale [9]. Difficulty in maintaining sleep was also associated with an increased incidence of diabetes in men aged 45–65 years in
mid-Sweden [10]. In support of these findings, the present study also found that self-reported suboptimum sleep quality, either moderate or poor, was associated with an increased risk of gestational diabetes in pregnant Chinese women, in addition to sleep duration. In the majority of studies, sleep disturbance and gestational diabetes were associated with poor socio-economic status [22,23], which could confound the risk association of gestational diabetes with sleep disturbance. In the present study, the risk association of gestational diabetes with sleep duration and quality remained significant after adjustment for household income, education attainment and occupation.

The biological mechanism underlying the link between sleep disturbances and gestational diabetes, including short or long duration of sleep and poor sleep quality, is not well understood. Sleep disturbances have been linked to increased inflammatory response and elevated oxidative stress [24–26], which are biomarkers of endothelial dysfunction. Evidence suggests that endothelial dysfunction may be implicated in the pathogenesis of insulin resistance in Type 2 diabetes [27]. In addition, sympathetic overactivity, dysregulation of the hypothalamic–pituitary axis, with elevations in serum cortisol levels, and peripheral vasoconstriction are also proposed mechanisms [28,29]. The mechanisms by which long sleep duration may elevate gestational diabetes risk are even more elusive. Women with longer sleep duration may spend less time taking part in physical activity, and physical inactivity directly or indirectly affects glucose regulation [7]. Another possibility is that some co-existing confounders, such as obstructive sleep apnoea, may be responsible for the observed association between long sleep duration and impaired glucose metabolism [6].

Identification of the association between sleep disturbances during pregnancy and the risk of gestational diabetes has clinical implications. Sleep disturbances, such as extreme sleep duration and poor sleep quality, are modifiable factors. Early screening and maintaining an optimum sleep duration may be useful for prevention of gestational diabetes and, potentially, improvement of pregnancy outcomes and long-term health outcomes in the mother and children. This requires further investigation in different populations of pregnant women.

The major strength of the present study is that it was a prospective population-based study with a large sample size and nearly all traditional risk factors for gestational diabetes were available and adjusted for. The study also had some limitations. First, its cross-sectional nature means that its results can only be hypothesis-generating and more external replications and randomized controlled trials are needed to confirm the potential causal associations between sleep disturbances during pregnancy and gestational diabetes. Second, a high proportion of women were not included in the analysis because of missing sleeping information. Notably, women excluded from the analysis were more likely to have traditional risk factors for gestational diabetes, including being older and having a higher BMI at first antenatal care visit, a higher rate of multipara and multi-pregnancy, and higher weight gain from first antenatal care visit to glucose challenge test time. The observed effect sizes might therefore depart from the true values. Third, sleep duration and sleep quality were measured by two self-reported questions modified from the well-validated PSQI for administrative ease. In the PSQI validation study, self-reported sleep hours were found to be longer than objectively measured sleep hours in pregnant women [30]. Thus, a further study is recommended to validate the thresholds selected in the present study, which might be higher than the real values.

In conclusion, we observed a J-shaped association between sleep duration during pregnancy and the risk of gestational diabetes in Chinese pregnant women. Short and long sleep duration were all associated with increased risk of gestational diabetes. Poor sleep quality was also associated with increased risk of gestational diabetes. Because of their potential modifiable nature, further studies, especially with objective sleep measures, are needed to confirm these associations in Chinese and other populations of pregnant women.

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**Competing interests**

None declared.

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**References**


Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Restricted cubic spline analysis.

Table S1. Clinical and biochemical characteristics of subjects according to inclusion or exclusion in analysis.