**Maternal night-time eating and sleep duration in relation to length of gestation and preterm birth**

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**Abbreviations:** BMI, body mass index; GDM, gestational diabetes mellitus; GUSTO, Growing Up in Singapore Towards healthy Outcomes; MET, metabolic equivalent; PTB, preterm birth; STAI, State-Trait Anxiety Inventory

**Background & Aims:** Maternal metabolic disturbance arising from inappropriate meal timing or sleep deprivation may disrupt circadian rhythm, potentially inducing pregnancy complications. We examined the associations of maternal night-time eating and sleep duration during pregnancy with gestation length and preterm birth.

**Methods:** We studied 673 pregnant women from the Growing Up in Singapore Towards healthy Outcomes (GUSTO) cohort. Maternal energy intake by time of day and nightly sleep duration were assessed at 26-28 weeks’ gestation. Based on 24-h dietary recall, night-eating was defined as consuming >50% of total energy intake from 1900-0659h. Short sleep duration was defined as <6 h night sleep. Night-eating and short sleep were simultaneously analyzed to examine for associations with a) gestation length using multiple linear regression, and b) preterm birth (<37 weeks’ gestation) using logistic regression.

**Results:** Overall, 15.6% women engaged in night-eating, 12.3% had short sleep and 6.8% delivered preterm. Adjusting for confounding factors, night-eating was associated with 0.45 weeks shortening of gestation length (95% CI -0.75, -0.16) and 2.19-fold higher odds of delivering preterm (1.01, 4.72). Short sleep was associated with 0.33 weeks shortening of gestation length (-0.66, -0.01), but its association with preterm birth did not reach statistical significance (1.81; 0.76, 4.30).

**Conclusions:** During pregnancy, women with higher energy consumption at night than during the day had shorter gestation and greater likelihood of delivering preterm. Misalignment of eating time with day-night cycles may be a contributing factor to preterm birth. This points to a potential target for intervention to reduce the risk of preterm birth. Observations for nightly sleep deprivation in relation to gestation length and PTB warrant further confirmation.

**Keywords:** Circadian rhythm; Meal timing; Gestation length; Pregnancy; Preterm birth; Sleep duration

**Introduction**

Preterm birth (PTB) affects 11% of pregnancies worldwide [1]. It is not only a leading cause of neonatal mortality, but it is also linked with adverse short- and long-term health outcomes [2]. PTB occurs for a variety of reasons, but it can also happen spontaneously for unknown reasons [2]. Observations that humans have evolved to give birth predominantly at particular times of day (i.e. between late night and early morning hours) and after at least 28 weeks of gestation [3] indicate that parturition is controlled by the body's circadian timing system (circadian rhythm) [4]. Emerging evidence suggests that the disruption of normal circadian rhythm may be a contributor factor to PTB [4].

Maternal shift-work has been related to adverse birth outcomes, including PTB [4,5]. It has been proposed that shift-work interferes with patterns of eating-fasting, sleep-activity and light-dark exposure, leading to desynchronization of circadian clocks controlling the timing of birth via neuroendocrine changes [4,5]. In today’s society, more and more individuals are exposed to conditions similar to those of night workers [6]. A recent trend has been observed towards increased energy intake in the late evening/ at night [7]. In parallel, nightly sleep duration has also declined over recent years, with more women reporting sleep deprivation than men [8]. Both of these phenomena are postulated to cause alterations of circadian rhythms [9,10]. During pregnancy, this may potentially disrupt the circadian systems regulating physiological process and reproductive function [4,11], consequently affecting successful pregnancy.

Previous studies showed that women consuming higher energy intakes in the late evening/ at night were more likely to have impaired glucose tolerance during pregnancy [12,13]. With regards to birth outcomes, to our knowledge no studies have explored whether higher energy intake at night during pregnancy is associated with PTB. Despite the potential adverse effect of sleep deprivation on maternal-fetal health [8], few studies have been conducted to examine sleep duration and PTB risk [14]. Based on a pregnancy cohort, we aimed to study associations of maternal night-time eating and sleep duration with gestation length and PTB. We hypothesized that consuming energy predominantly at night and having insufficient night sleep during pregnancy were independently associated with shorter gestation and greater likelihood of delivering preterm.

**Materials and methods**

**Study design and participants**

Data were drawn from a prospective mother-offspring cohort study in Singapore, the Growing Up in Singapore Towards healthy Outcomes (GUSTO) (clinicaltrials.gov, NCT01174875) [15]. This study was conducted according to the Helsinki Declaration, and all procedures were approved by the Singapore National Health Care Group Domain Specific Review Board (reference D/09/021) and the SingHealth Centralised Institutional Review Board (reference 2009/280/D).

Pregnant women attending antenatal care in their first trimester of pregnancy, from June 2009 to September 2010, at the KK Women’s and Children’s Hospital and National University Hospital in Singapore were recruited. These women were aged ≥18 years and had homogeneous parental ethnic groups (Chinese, Malay or Indian). Those receiving chemotherapy or psychotropic drugs and those with type 1 diabetes mellitus were excluded. All women provided informed written consent upon recruitment.

**Dietary assessment**

At 26–28 weeks’ gestation, clinic staff trained by an experienced dietician administered a 24-h dietary recall using a 5-stage, multiple-pass interviewing technique [16]. Women were asked about the time, type, description and amount of food and beverages consumed throughout the day. Standardized household measuring utensils and food pictures of various portion sizes were shown to assist women in quantifying their food and drink intakes. Total energy intake was assessed using nutrient analysis software (Dietplan, version 7, Forestfield Software, UK) containing a local food composition database, with modifications made for inaccuracies found.

Maternal dietary intake was also assessed using a 3-day food diary among a small subset of women (n=196). We have previously shown that dietary information and circadian eating pattern derived from the 24-h recall were valid in comparison with the 3-day food diary data [17,18]. To retain consistency with analysis methods used in our previous publications [13,18] and to increase statistical power, we therefore present results based on the 24-h recall data in this study.

We determined daytime and night-time periods according to the local time of sunrise and sunset which occur at ~0700h and ~1900h, respectively, throughout the year in equatorial Singapore (1.352o N). Night-eating was defined as consuming >50% of total daily energy intake during 1900–0659h; while day-eating which served as the reference category was defined as consuming >50% of total daily energy intake during 0700-1859h [13]. One woman with equal proportions of total daily energy intake between day and night was excluded from the analysis. Number of eating episodes were defined as events that provided ≥210 kJ (~50 kcal) with time intervals between eating episodes of ≥15 min [19].

**Sleep assessment**

At 26–28 weeks’ gestation, only a subset of women (n=682) was asked for sleep related questions. Women were assessed for their nightly sleep duration based on the following question: “During the past month, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spend in bed)” [20]. According to the United States National Sleep Foundation, <6 h of sleep was considered insufficient in adults aged 18–64 years [21]. Our previous study demonstrated that women who slept <6 h per night were more likely to have gestational diabetes mellitus (GDM) [22]. We therefore define short sleep as <6 h in this study and sleep duration ≥6 h served as the reference category.

**Gestation duration and preterm birth**

Gestation duration was determined based on an ultrasound scan in the first trimester, a gold standard for gestational age assessment [2]. PTB was defined as birth before 37 completed weeks of gestation [23].

**Covariates**

Clinic staff recorded women’s characteristics (e.g., date of birth, ethnicity, education, household income, employment status) and lifestyle behaviors (e.g., physical activity and anxiety level) during the recruitment visit and at 26-28 weeks’ gestation. Duration and frequency of physical activity were ascertained to derive metabolic equivalent (MET-min/week) scores [24]. Women self-administered the State-Trait Anxiety Inventory (STAI-state) questionnaire to assess anxiety levels [25]. Height was measured with a SECA 213 stadiometer (SECA Corp., Hamburg, Germany) and used to compute early pregnancy body mass index (BMI) based on the formula: weight at ≤14 weeks’ gestation (kg)/ height (m2). BMI status was categorized as <23 versus ≥23 kg/m2 based on cut-off points for Asian populations [26]. We also recorded women self-reported pre-pregnancy weight. However, since maternal measured weight at the first antenatal visit (≤14 weeks’ gestation) was strongly correlated with reported pre-pregnancy weight (r = 0.96; *p*<0.001) and not subjected to recall bias, it was used for analysis in this study. Women performed an oral glucose tolerance test to evaluate fasting and 2-h post-load plasma glucose for GDM diagnosis, as defined by World Health Organization 1999 criteria [27]. Infant sex was retrieved from hospital medical notes.

**Statistical analysis**

Statistical analyses were performed using IBM SPSS statistics, version 19, or Stata-Corp Stata Statistical Software, release 13. Independent Student *t*-tests and Fisher’s exact tests were used to compare continuous and categorical maternal characteristics between groups of women with day-eating vs. night-eating, and between those reporting sufficient sleep vs. short sleep. Night-eating and short sleep duration were simultaneously analyzed to examine for associations with a) gestation length using multiple linear regression, and b) PTB using logistic regression, with adjustment for confounders. Where applicable, results were expressed as β coefficients or odds ratios (OR), with associated 95% confidence intervals (CI).

Confounders were determined based on clinical judgement, literature review [2,18,22,28] and by using a directed acyclic graph. Multivariable models were adjusted for maternal age (years, continuous), ethnicity (Chinese, Malay, Indian), education (none/ primary/ secondary, post-secondary, tertiary), monthly household income (≤1999, 2000–5999 and ≥6000 Singapore dollars), employment (unemployed, employed), night shift (no, yes), physical activity (<600, 600-3000 and >3000 MET-min/week), early pregnancy BMI (<23, ≥23 kg/m2), anxiety (STAI-state) score (continuous), total eating episodes (continuous), total energy intake (kJ, continuous) and infant sex (boys, girls).

As women with night-eating tended to have a later sleeping time, which was associated with shorter sleep, we further controlled for bedtime (continuous) in the multivariable model to examine its potential effects on the associations between night-eating/ sleep duration and gestation length/ PTB. Our previous studies showed that maternal night-eating and short sleep duration were associated with higher plasma glucose during pregnancy [13,22], which has been reported as the risk factor of PTB. We therefore separately controlled for GDM (no, yes), fasting plasma glucose and 2-h post-load plasma glucose to examine for any potential mediating effect on the pathway between night-eating/ sleep duration and gestation length/ PTB. In a previous study, short (≤6 h) and long sleep (≥9 h) were reported to increase the odds of PTB [29]. We explored the possibility of this U-shaped relationship by examining PTB distribution across sub-categories of sleep duration, i.e. <6, 6-6.99, 7-7.99, 8-8.99 and ≥9 h [22].

Missing values for covariates were imputed 20 times using multiple imputation analyses by chained equations [30]. These included maternal education (n=6), monthly household income (n=40), physical activity (n=3), early pregnancy BMI (n=12), anxiety score (n=2), bedtime (n=3), fasting plasma glucose (n=27) and 2-h post-load plasma glucose (n=27). The number of imputations was determined based on efficiency consideration and percentage of missing values [31]. The results of the 20 analyses were pooled using Rubin’s rule [32].

Two sensitivity analyses were performed. First, we included only women with a complete dataset for confounders (n=617). Second, we conducted principal component analysis to reduce the number of confounders in the model in order to avoid overfitting issue [33]. For the principal component analysis, first four components which contributed to eigenvalues ≥1.0 were selected and adjusted in the regression model. Components 1 to 4 were mainly represented by education, anxiety score, age and early pregnancy BMI, respectively. Therefore, we also performed additional analysis by adjusting only these four confounders in the model.

In the present analysis, we did not perform any adjustment for multiple comparisons. This study focused on examination of an a priori hypothesis relating to specific exposures and outcomes, based on emerging literature on the health importance of chrononutrition and chronobiology. Correction of these analyses for multiple testing would therefore not be appropriate [34,35].

**Results**

Of 1152 enrolled GUSTO women who conceived natural singleton pregnancies, 1080 completed a 24-h dietary recall at 26-28 weeks’ gestation, but 13 had reported implausible total energy intakes of <500 kcal/d (n=3) or >3500 kcal/d (n=10) and they were excluded, as in previous studies [13,18]. We further excluded 1 woman with equal proportions of total energy intake between day and night. From the remaining 1066 women, a subset of them (n=682) were assessed for sleep duration. At delivery, 9 women had withdrawn from the study. A final sample of 673 women was included in this study (Figure 1). Excluded women were similar to those included with respect to maternal age, ethnicity, night shift status, early pregnancy BMI, STAI-state score and GDM diagnosis, but had lower education attainment (25.1% vs 37.3% with tertiary level), lower household income (16.9% vs. 34.2% with household income ≥6000 Singapore dollars), and were more likely to be unemployed (37.8% vs 29.0%) and to be physically active (22.1% vs 16.8% with >3000 MET-min/week) (Supplementary Table 1).

Recruited 1152 pregnant women

1080 completed dietary assessment

1067 with plausible total energy intake

682 completed sleep questionnaire

673 included for main analysis

Implausible total daily energy intake

* >3500 kcal (n=10)
* <500 kcal (n=3)

1066 assessed for night-eating

Consumption of equal proportions of total energy intake during day and night (n=1)

Without sleep duration data (n=384)

Dropped out at delivery stage (n=9)

617 included for sensitivity analysis

Missing potential covariates

* Education (n=6)
* Monthly household income (n=40)
* Physical activity (n=3)
* Early pregnancy body mass index (n=12)
* Anxiety score (n=2)
* Bedtime (n=3)
* Fasting and 2-h post-load plasma glucose (n=27)

**Figure 1** Flowchart of participants included for analysis from the Growing Up in Singapore Towards healthy Outcomes (GUSTO) study

Characteristics of the women by day-night eating and sleep duration are presented in Table 1. 15.6% (n=105) engaged in night-eating and 12.3% (n=83) had short sleep. In comparison to women with day-eating, those with night-eating had higher anxiety levels (37.4 vs. 33.7), higher fasting plasma glucose (4.4 vs. 4.3 mmol/l), less frequent daily eating episodes (3.6 vs. 4.2 times) and later bedtime (2336 vs. 2307h). Women with short sleep were older (32.4 vs. 30.7 years), more likely to be ethnically Malay (41.0% vs. 27.1%) or Indian (24.1% vs. 18.7%), be physically active (25.3% vs. 15.4% with >3000 MET-min/week), had higher anxiety levels (36.9 vs. 33.9) and fasting plasma glucose (4.4 vs. 4.3 mmol/l), and later bedtime (2336 vs. 2308h) as compared to women with sufficient sleep. Overall, 6.8% (n=46) delivered before 37 weeks’ gestation. Of those delivered preterm, 91.3% (n=42) were late preterm (34-36 weeks’ gestation); while 65.2% (n=30) were spontaneous and 34.8% (n=16) were medically indicated. The main medical indications of PTB were fetal distress, maternal distress, pre-eclampsia and diabetes.

**Table 1** Descriptive characteristics of participants from the GUSTO study

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Variable | Total(n=673) | Day-eating (n=568; 84.4%) | Night-eating (n=105; 15.6%) | *P*a | Sufficient sleep (n=590; 87.7%) | Short sleep (n=83; 12.3%) | *P*b |
| Maternal age, years | 30.9 + 5.0 | 31.0 + 5.0 | 30.2 + 5.3 | 0.143 | 30.7 + 4.9 | 32.4 + 5.6 | 0.004 |
| Ethnicity, n (%) |  |  |  | 0.919 |  |  | 0.003 |
|  Chinese | 349 (51.9) | 296 (52.1) | 53 (50.5) |  | 320 (54.2) | 29 (34.9) |  |
|  Malay | 194 (28.8) | 162 (28.5) | 32 (30.5) |  | 160 (27.1) | 34 (41.0) |  |
|  Indian | 130 (19.3) | 110 (19.4) | 20 (19.0) |  | 110 (18.7) | 20 (24.1) |  |
| Education, n (%) |  |  |  | 0.086 |  |  | 0.561 |
|  None/ Primary/ Secondary | 175 (26.0) | 140 (24.6) | 35 (33.3) |  | 149 (25.2) | 26 (31.3) |  |
|  Post-secondary | 247 (36.7) | 207 (36.5) | 40 (38.1) |  | 219 (37.2) | 28 (33.8) |  |
|  Tertiary | 251 (37.3) | 221 (38.9) | 30 (28.6) |  | 222 (37.6) | 29 (34.9) |  |
| Monthly household income, n (%) |  |  |  | 0.330 |  |  | 0.598 |
|  ≤SGD 1999 | 92 (13.7) | 73 (12.9) | 19 (18.1) |  | 79 (13.4) | 13 (15.7) |  |
|  SGD 2000-5999 | 351 (52.2) | 296 (52.1) | 55 (52.4) |  | 305 (51.7) | 46 (55.4) |  |
|  ≥SGD 6000 | 230 (34.2) | 199 (35.0) | 31 (29.5) |  | 206 (34.9) | 24 (28.9) |  |
| Employment status, n (%) |  |  |  | 0.079 |  |  | 0.441 |
|  Unemployed | 195 (29.0) | 158 (27.8) | 37 (35.2) |  | 168 (28.5) | 27 (32.5) |  |
|  Employed | 478 (71.0) | 410 (72.2) | 68 (64.8) |  | 422 (71.5) | 56 (67.5) |  |
| Night shift, n (%) |  |  |  | 0.109 |  |  | 0.976 |
|  No | 641 (95.2) | 544 (95.8) | 97 (92.4) |  | 562 (95.3) | 79 (95.2) |  |
|  Yes | 32 (4.8) | 24 (4.2) | 8 (7.6) |  | 28 (4.7) | 4 (4.8) |  |
| Physical activity, n (%) |  |  |  | 0.779 |  |  | 0.038 |
|  <600 MET-min/week | 245 (36.4) | 210 (37.0) | 35 (33.3) |  | 223 (37.8) | 22 (26.5) |  |
|  600-3000 MET-min/week | 316 (47.0) | 265 (46.6) | 51 (48.6) |  | 276 (46.8) | 40 (48.2) |  |
|  >3000 MET-min/week | 112 (16.6) | 93 (16.4) | 19 (18.1) |  | 91 (15.4) | 21 (25.3) |  |
| BMI at ≤14 weeks’ gestation, n (%) |  |  |  | 0.255 |  |  | 0.163 |
|  <23 kg/m2 | 358 (53.2) | 297 (52.3) | 61 (58.1) |  | 320 (54.2) | 38 (45.8) |  |
|  ≥23 kg/m2 | 315 (46.8) | 271 (47.4) | 44 (41.9) |  | 270 (45.8) | 45 (54.2) |  |
| STAI-state score | 34.3 + 10.1 | 33.7 + 10.0 | 37.4 + 9.9 | 0.001 | 33.9 + 9.9 | 36.9 + 11.2 | 0.013 |
| Gestational diabetes, n (%) |  |  |  | 0.379 |  |  | 0.260 |
|  No | 538 (79.9) | 458 (80.6) | 80 (76.2) |  | 476 (80.7) | 62 (74.7) |  |
|  Yes | 135 (20.1) | 110 (19.4) | 25 (23.8) |  | 114 (19.3) | 21 (25.3) |  |
| Fasting plasma glucose, mmol/l | 4.3 + 0.4 | 4.3 + 0.4 | 4.4 + 0.5 | 0.023 | 4.3 + 0.4 | 4.4 + 0.5 | 0.044 |
| 2-h post-load plasma glucose, mmol/l | 6.5 + 1.5 | 6.5 + 1.5 | 6.4 + 1.7 | 0.344 | 6.5 + 1.5 | 6.7 + 1.6 | 0.265 |
| Total energy intake, kJ (1 kcal=4.186 kJ) | 7715 + 2401 | 7778 + 2376 | 7374 + 2515 | 0.113 | 7736 + 2400 | 7568 + 2417 | 0.551 |
| Daily eating episodes, times | 4.1 + 1.3 | 4.2 + 1.3 | 3.6 + 1.1 | <0.001 | 4.2 + 1.3 | 4.0 + 1.4 | 0.261 |
| Bedtime, 24h | 2311 + 0143 | 2307 + 0133 | 2336 + 0222 | 0.043 | 2308 + 0140 | 2336 + 0203 | 0.020 |
| Infant sex, n (%) |  |  |  | 0.525 |  |  | 0.923 |
|  Boy | 352 (52.3) | 294 (51.8) | 58 (55.2) |  | 309 (52.4) | 43 (51.8) |  |
|  Girl | 321 (47.7) | 274 (48.2) | 47 (44.8) |  | 281 (47.6) | 40 (48.2) |  |
| Gestation age at birth, weeks | 38.8 + 1.4 | 38.9 + 1.4 | 38.5 + 1.6 | 0.005 | 38.9 + 1.3 | 38.5 + 1.7 | 0.031 |
| Preterm birth (<37 weeks’ gestation), n (%) |  |  |  | 0.137 |  |  | 0.253 |
|  No | 627 (93.2) | 533 (93.8) | 94 (89.5) |  | 552 (93.6) | 75 (90.4) |  |
|  Yes | 46 (6.8) | 35 (6.2) | 11 (10.5) |  | 38 (6.4) | 8 (9.6) |  |

Values are means + SDs or n (%). GUSTO, Growing Up in Singapore Towards healthy Outcomes; SGD, Singapore dollar; MET, metabolic equivalent; BMI, body mass index; STAI, State-Trait Anxiety Inventory

aBased on independent t-test for continuous variables or Fisher’s exact test for categorical variables

Associations of night-eating and short sleep duration during pregnancy with gestation length are shown in Table 2. After adjustment for confounders (Model 1), night-eating was associated with 0.45 weeks (95% CI -0.75, -0.16) shortening of gestation; while short sleep at night was associated with 0.33 weeks (-0.66, -0.01) shortening of gestation. Further inclusion of bedtime (Model 2) and GDM (Model 3) did not alter the associations of night-eating and short sleep with gestation age at birth. Similar findings were observed with adjustment for fasting and 2-h post-load plasma glucose (Supplementary Table 2).

**Table 2** Associations of night-eating and short sleep duration during pregnancy with gestation length (n=673)

|  |  |
| --- | --- |
|  | Gestation age at birth (weeks) |
| Variables | Model 1 |  | Model 2 |  | Model 3 |
|  | β (95% CI) |  | β (95% CI) |  | β (95% CI) |
| Day-night eating |  |  |  |  |  |
|  Day-eating | 1.00 |  | 1.00 |  | 1.00 |
|  Night-eating | -0.45 (-0.75, -0.16) |  | -0.45 (-0.75, -0.15) |  | -0.44 (-0.74, -0.14) |
|  |  |  |  |  |  |
| Sleep duration |  |  |  |  |  |
|  Sufficient sleep ≥6 hours | 1.00 |  | 1.00 |  | 1.00 |
|  Short sleep <6 hours | -0.33 (-0.66, -0.01) |  | -0.33 (-0.66, 0.01) |  | -0.32 (-0.65, 0.01) |

Analysis was performed using multivariable linear regression model. CI, confidence interval.

Model 1: Adjusted for age, ethnicity, education, monthly household income, employment status, night-shift, physical activity, early pregnancy body mass index, anxiety score, total eating episodes, total energy intake and infant sex

Model 2: Adjusted for Model 1 + bedtime

Model 3: Adjusted for Model 1 + gestational diabetes mellitus

Associations of night-eating and short sleep duration during pregnancy with PTB are presented in Table 3. After adjustment for confounders (Model 1), women with night-eating had a 2.19-fold (95% CI 1.01, 4.72) higher odds of PTB. Additional adjustment for bedtime (Model 2), GDM (Model 3), fasting and 2-h post-load plasma glucose (Supplementary Table 2) did not alter the ORs substantially. The association between short sleep at night and PTB did not reach statistical significance across models. Based on PTB distribution across sub-categories of sleep duration, the proportion of PTB was highest in women who reported sleeping <6 h per night (9.6%) and lowest in those with ≥9 h of sleep per night (4.0%) (Figure 2).

**Table 3** Associations of night-eating and short sleep duration during pregnancy with preterm birth (n=673)

|  |  |
| --- | --- |
|  | Preterm birth <37 weeks of gestation |
| Variables | Model 1 |  | Model 2 |  | Model 3 |
|  | OR (95% CI) |  | OR (95% CI) |  | OR (95% CI) |
| Day-night eating |  |  |  |  |  |
|  Day-eating | 1.00 |  | 1.00 |  | 1.00 |
|  Night-eating | 2.19 (1.01, 4.72) |  | 2.08 (0.95, 4.53) |  | 2.14 (0.99, 4.66) |
|  |  |  |  |  |  |
| Sleep duration |  |  |  |  |  |
|  Sufficient sleep ≥6 hours | 1.00 |  | 1.00 |  | 1.00 |
|  Short sleep <6 hours | 1.81 (0.76, 4.30) |  | 1.70 (0.71, 4.08) |  | 1.78 (0.75, 4.25) |

Analysis was performed using multivariable binary logistic regression model. OR, odds ratio; CI, confidence interval.

Model 1: Adjusted for age, ethnicity, education, monthly household income, employment status, night-shift, physical activity, early pregnancy body mass index, anxiety score, total eating episodes, total energy intake and infant sex

Model 2: Adjusted for Model 1 + bedtime

Model 3: Adjusted for Model 1 + gestational diabetes mellitus

**Figure 2** Distribution of preterm birth across sub-categories of sleep duration

In the sensitivity analysis based on women with complete data (n=617), the results remained similar, with night-eating during pregnancy being associated with shorter gestation (-0.50 weeks; -0.80, -0.19) and higher odds of PTB (2.56; 1.15, 5.70). Similarly, short sleep at night was associated with shorter gestation (-0.35 weeks; -0.70, -0.02), but its relation with PTB did not reach significance (2.12; 0.87, 5.19) (Supplementary Table 3). When model adjustment was performed using reduced number of covariates, similar findings were observed (Supplementary Table 4).

**Discussion**

In this Asian cohort study, we assessed predominant eating period and night sleep duration of women during their late-second trimester of pregnancy, and associations with gestation length and PTB. We observed that women with a higher proportion of total daily energy intake during night-time relative to day-time had a shorter gestation length and higher odds of PTB, after adjustment for socio-demographic characteristics and lifestyle factors. Bedtime and glycemic measures did not seem to substantially influence the association between night-eating and PTB. Short sleep at night was associated with shorter gestation, but its association with PTB did not reach statistical significance.

To date, studies investigating the effect of time of food intake has mostly focused on metabolic outcomes [10,36]. The extent to which eating time can influence reproductive health is a new area of research. The present study suggests that night-time energy intake plays a role in early childbirth. This finding is supported by the report from the Nurses’ Health Study showing elevated risk for early PTB among night-shift nurses [37]. Although food intake was not directly assessed by Lawson et al. [37], it has been suggested that increased consumption during the night that occurs in night-shift workers can be a risk factor for circadian disruption [6] which contributes to PTB [4], and our results provide more evidence for this association. We demonstrated that both the amount and the time at which food is consumed relative to day-night cycles during pregnancy were associated with PTB.

There are biologically plausible reasons for an association between night-eating and PTB. The time of food intake has been shown to be a powerful signal for the circadian system [6,10]. When eating time does not coincide with day-night cycles (circadian rhythms), food creates a circadian conflict which can affect the functions of various organs [6]. Consuming food during the night, which is the rest phase of the body, may induce circadian misalignment [6] and suppress melatonin secretion [11], resulting in dysregulation of uterine contractility and birth timing [4]. Melatonin suppression can also lead to increased oxidative stress, cause damage to cellular components and trigger premature placental ageing which is likely to increase PTB risk [38]. Emerging evidence suggests that increased energy intake at night elevates inflammation [39] and glucose levels [12,13], which have been linked with uterine activation and PTB [40,41]. Adjustment for measures of glycemia, however, did not substantially alter the association between night-eating and PTB, suggesting night-eating may impact gestational length through different mechanisms.

Although short sleep duration <6 h was associated with shorter gestation, the effect estimate could be too small to translate into a significant increase in PTB risk. Our results are consistent with some [42,43] but not all [29,44] prior studies that have assessed maternal sleep duration and PTB. A Ghanaian study showed that short sleep ≤6 h in the third trimester was not associated with PTB [43]. Similarly, a study of Californian women also found no association between sleep duration (<7h or >8 h) in the second trimester and PTB [42]. More recently, a longitudinal study reported a higher risk of PTB among Chinese women with sleep deprivation (<7 h sleep) in the third trimester, but not in the first or second trimester [44]. This is in line with our findings as we measured sleep duration only in the second trimester of pregnancy. In contrast in a Peruvian study, both short (≤6 h) and long sleep durations (≥9 h) in the first six months of pregnancy were associated with spontaneous PTB [29]. We did not observe any evidence of a U-shaped relationship between sleep duration and PTB; however, spontaneous and medically indicated PTB were not differentiated in our analysis due to the small sample size.

There are multiple limitations that should be acknowledged when interpreting our results. First, our PTB outcome did not distinguish between spontaneous and medically indicated PTB. Additional to constraint of the small numbers in our study, their risk factors may partly overlap [23] and the underlying mechanisms influencing PTB risk are unclear. Second, the present findings may not be applicable to other ethnicities and the general population since this study was restricted to group of Asian pregnant women who volunteered to participate in a cohort study and delivered in two hospitals in Singapore. Moreover, differences in characteristics (i.e. education, household income, employment status and physical activity) were noted between included and excluded women, which could affect generalizability of findings. Although we controlled for these variables in the analysis, replication of the study in a more diverse sample is required. Third, dietary data was derived from a single day 24-hour recall and may not represent usual intake. Nonetheless, the 24-h recall was previously validated against a 3-day food diary for eating patterns in a subsample of women [17,18]. We did not perform further analyses to validate the present results using 3-day food diaries due to the small available sample size (n=196) in this study. Fourth, sleep duration was based on recalled usual night sleep hours in the past one month, which may have been misreported and thereby attenuated our results. However, a strong correlation has been shown between self-reported usual night sleep duration and diary-derived night sleep duration [45]. Nevertheless, the use of an objective measure such as polysomnography or multiple actigraphs could improve data accuracy. Fifth, both diet and sleep measures were evaluated at a single time-point during the second trimester, which restricted our ability to evaluate the trimester-specific effects of maternal eating time and sleep duration on PTB. A strong design for future studies of maternal habitual nightly eating habit, sleep duration and pregnancy outcomes should include serial assessments to thoroughly describe diet and sleep across the entire pregnancy. Finally, the observed relationships could be partly affected by unmeasured or residual confounding such as light exposure.

In summary, we found that women with higher energy consumption at night during the late-second trimester of pregnancy had shorter gestation and a higher rate of PTB. The study suggests that misalignment of eating time with day-night cycles may be a risk factor for PTB. Although reduction in gestation length was modest and late preterm (34-36 weeks’ gestation) accounted for 91% of PTB cases in this study, the child health consequences are of clinical and public health importance. Increased risks for infant morbidity and childhood disabilities have been shown for infants with modest decrease in gestation across a broad spectrum, for both term and PTBs [46,47]. Moreover, late preterm birth is also strongly associated with a number of components of the metabolic syndrome and cardiovascular disease in adult life [48]. Our current findings thus call for increased clinical attention to maternal time of food intake, and the study of potential intervention strategies based on circadian eating approach which are feasible and culturally appropriate, with the aim of reducing risk of PTB. Observations for nightly sleep deprivation in relation to gestation length and PTB warrant further confirmation.

**Statement of authorship**

YSC, KMG, LPS and KHT contributed in the conception and design of the GUSTO study. SLL and FY conceptualized and designed the present study. SLL, SC and MTC organized and cleaned the data. YBC advised on the statistical analysis. SLL performed data analysis and wrote the first draft. SLL, YBC, SC, KMG, MFFC, FY and JKYC interpreted the findings and revised drafts of the paper. All authors read and approved the final manuscript.

**Conflict of interest**

KMG, YSC and FY have received reimbursement to speak at conferences sponsored by companies selling nutritional products. KMG and YSC are part of an academic consortium that has received research funding from Abbott, Nutrition, Nestle and Danone. Other authors declare that they have no conflict of interest.

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**Supplementary Table 1** Women’s baseline characteristics according to their inclusion status in the present analysis from the GUSTO study (n=1152)

|  |  |  |  |
| --- | --- | --- | --- |
| Variable | Included (n=673) | Excluded (n=479) | *P*a |
| Maternal age, years | 30.9 + 5.0 | 30.9 + 5.8 | 0.942 |
| Ethnicity, n (%) |  |  | 0.136 |
|  Chinese | 349 (51.9) | 277 (57.8) |  |
|  Malay | 194 (28.8) | 121 (25.3) |  |
|  Indian | 130 (19.3) | 81 (16.9) |  |
| Education, n (%) |  |  | <0.001 |
|  None/ Primary/ Secondary | 175 (26.0) | 199 (41.5) |  |
|  Post-secondary | 247 (36.7) | 160 (33.4) |  |
|  Tertiary | 251 (37.3) | 120 (25.1) |  |
| Monthly household income, n (%) |  |  | <0.001 |
|  <SGD 2000 | 93 (13.8) | 97 (20.3) |  |
|  SGD 2000-5999 | 350 (52.0) | 301 (62.8) |  |
|  ≥SGD 6000 | 230 (34.2) | 81 (16.9) |  |
| Employment status, n (%) |  |  | 0.003 |
|  Unemployed | 195 (29.0) | 181 (37.8) |  |
|  Employed | 478 (71.0) | 298 (62.2) |  |
| Night shift, n (%) |  |  |  |
|  No | 641 (95.2) | 459 (95.8) | 0.704 |
|  Yes | 32 (4.8) | 20 (4.2) |  |
| Physical activity, n (%) |  |  | 0.005 |
|  <600 MET-min/week | 245 (36.4) | 134 (28.0) |  |
|  600-3000 MET-min/week | 315 (46.8) | 239 (49.9) |  |
|  >3000 MET-min/week | 113 (16.8) | 106 (22.1) |  |
| BMI at ≤14 weeks’ gestation, n (%) |  |  | 0.599 |
|  <23 kg/m2 | 358 (53.2) | 254 (53.0) |  |
|  ≥23 kg/m2 | 315 (46.8) | 225 (47.0) |  |
| STAI-state score | 34.3 + 10.1 | 34.0 + 11.1 | 0.628 |
| Gestational diabetes, n (%) |  |  | 0.506 |
|  No | 537 (79.8) | 375 (78.3) |  |
|  Yes | 136 (20.2) | 104 (21.7) |  |

Values are means + SDs or n (%). GUSTO, Growing Up in Singapore Towards healthy Outcomes; SGD, Singapore dollar; MET, metabolic equivalent; BMI, body mass index; STAI, State-Trait Anxiety Inventory

aBased on independent t-test for continuous variables or Fisher’s exact test for categorical variables

**Supplementary Table 2** Associations of night-eating and short sleep duration during pregnancy with gestation age at delivery and preterm birth, with additional plasma glucose adjustment (n=673)

|  |  |  |  |
| --- | --- | --- | --- |
|  | Gestation age at birth (weeks)a |  | Preterm birth <37 weeks of gestationb |
|  | β (95% CI) |  | OR (95% CI) |
| **Model 1** |  |  |  |
|  Day-night eating |  |  |  |
|  Day-eating | 1.00 |  | 1.00 |
|  Night-eating | -0.41 (-0.71, -0.11) |  | 2.14 (0.99, 4.67) |
|  |  |  |  |
|  Sleep duration |  |  |  |
|  Sufficient sleep ≥6 hours | 1.00 |  | 1.00 |
|  Short sleep <6 hours | -0.30 (-0.63, 0.02) |  | 1.79 (0.75, 4.26) |
|  |  |  |  |
| **Model 2** |  |  |  |
|  Day-night eating |  |  |  |
|  Day-eating | 1.00 |  | 1.00 |
|  Night-eating | -0.45 (-0.75, -0.15) |  | 2.12 (0.98, 4.60) |
|  |  |  |  |
|  Sleep duration |  |  |  |
|  Sufficient sleep ≥6 hours | 1.00 |  | 1.00 |
|  Short sleep <6 hours | -0.32 (-0.64, 0.01) |  | 1.76 (0.74, 4.19) |

Model 1: Adjusted for age, ethnicity, education, monthly household income, employment status, night-shift, physical activity, early pregnancy body mass index, anxiety score, total eating episodes, total energy intake, infant sex, fasting plasma glucose

Model 2: Adjusted for age, ethnicity, education, monthly household income, employment status, night-shift, physical activity, early pregnancy body mass index, anxiety score, total eating episodes, total energy intake, infant sex, 2-h post-load plasma glucose

aAnalysis was performed using multivariable linear regression model. CI, confidence interval

bAnalysis was performed using multivariable binary logistic regression model. OR, odds ratio; CI, confidence interval

**Supplementary Table 3** Associations of night-eating and short sleep duration during pregnancy with gestation age at delivery and preterm birth based on complete case analysis (n=617)

|  |  |  |  |
| --- | --- | --- | --- |
|  | Gestation age at birth (weeks)a |  | Preterm birth <37 weeks of gestationb |
|  | β (95% CI) |  | OR (95% CI) |
| Day-night eating |  |  |  |
|  Day-eating | 1.00 |  | 1.00 |
|  Night-eating | -0.50 (-0.80, -0.19) |  | 2.56 (1.15, 5.70) |
|  |  |  |  |
| Sleep duration |  |  |  |
|  Sufficient sleep ≥6 hours | 1.00 |  | 1.00 |
|  Short sleep <6 hours | -0.35 (-0.70, -0.02) |  | 2.12 (0.87, 5.19) |

Adjusted for age, ethnicity, education, monthly household income, employment status, night-shift, physical activity, early pregnancy body mass index, anxiety score, total eating episodes, total energy intake and infant sex

aAnalysis was performed using multivariable linear regression model. CI, confidence interval

bAnalysis was performed using multivariable binary logistic regression model. OR, odds ratio; CI, confidence interval

**Supplementary Table 4** Associations of night-eating and short sleep duration during pregnancy with gestation age at delivery and preterm birth based on complete case analysis, adjusting for reduced number of covariates (n=617)

|  |  |  |  |
| --- | --- | --- | --- |
|  | Gestation age at birth (weeks)a |  | Preterm birth <37 weeks of gestationb |
|  | β (95% CI) |  | OR (95% CI) |
| **Model 1** |  |  |  |
|  Day-night eating |  |  |  |
|  Day-eating |  |  |  |
|  Night-eating | -0.48 (-0.78, -0.18) |  | 2.27 (1.08, 4.80) |
|  |  |  |  |
|  Sleep duration |  |  |  |
|  Sufficient sleep ≥6 hours |  |  |  |
|  Short sleep <6 hours | -0.35 (-0.68, -0.01) |  | 1.77 (0.77, 4.09) |
|  |  |  |  |
| **Model 2** |  |  |  |
|  Day-night eating |  |  |  |
|  Day-eating |  |  |  |
|  Night-eating | -0.46 (-0.77, -0.16) |  | 2.18 (1.03, 4.61) |
|  |  |  |  |
|  Sleep duration |  |  |  |
|  Sufficient sleep ≥6 hours |  |  |  |
|  Short sleep <6 hours | -0.34 (-0.68, -0.01) |  | 1.71 (0.74, 3.93) |

Model 1: Adjusted for component 1 (education), component 2 (anxiety score), component 3 (age) and component 4 (early pregnancy body mass index), as derived from principal component analysis

Model 2: Adjusted for education, anxiety score, age and early pregnancy body mass index

aAnalysis was performed using multivariable linear regression model. CI, confidence interval

bAnalysis was performed using multivariable binary logistic regression model. OR, odds ratio; CI, confidence interval