

# Maternal sleep duration and neonatal birth weight: The Japan Environment and Children's Study

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## Abstract

**Objective:** To evaluate the effect of maternal sleep duration (MSD) on low birth weight infants (LBW), small for gestational age infants (SGA), and macrosomia. **Design:** Prospective cohort study **Setting:** The Japan Environment and Children's Study (JECS) **Population:** Participants enrolled in JECS, with singleton pregnancies after 22 weeks, who gave birth between 2011 and 2014. **Methods:** Participants were categorized into five groups according to MSD during pregnancy: G1 (MSD <6.0 h), G2 (6.0–7.9 h), G3 (8.0–8.9 h), G4 (9.0–9.9 h), and G5 (10.0–12.0 h). **Main outcome measures:** The effect of MSD on the risk of LBW (<2,500 g and <1,500 g), SGA, and macrosomia (>4,000 g) with G2 as the reference, while adjusting for gestational excessive body weight gain (BWG). Analysis was also performed after stratification by gestational BWG. **Results:** We analyzed 82,171 participants. The adjusted odds ratios (aORs) of LBW <2,500 g in G4 and G5 and of SGA in G4 were 0.90 (95% confidence interval [CI], 0.83-0.99), 0.86 (95% CI, 0.76-0.99), and 0.91 (95% CI, 0.82-0.99), respectively, before adjusting for excessive gestational BWG. No significant association was observed between MSD and these outcomes after adjusting for excessive gestational BWG. Among women with appropriate gestational BWG, the aORs of LBW <2,500 g and SGA in G4 were 0.88 (95% CI, 0.80-0.97) and 0.87 (95% CI, 0.78-0.97), respectively. **Conclusion:** This study revealed that 9.0–9.9 h of MSD significantly decreased LBW <2,500 g and SGA in pregnant women with appropriate gestational BWG, relative to 6.0–7.9 h of MSD.

## Introduction

Neonatal birth weight, which is related to perinatal morbidity and mortality,<sup>1–4</sup> is affected by several obstetric complications, including preterm births (PTB), fetal growth restriction (FGR), and preeclampsia.<sup>5,6</sup> Specifically, birth weight <1,500 g, defined as very low birth weight, is affected by severe prematurity and leads to increased mortality.<sup>7</sup> Additionally, small for gestational age (SGA) infants have also been associated with neonatal and post-neonatal mortality.<sup>4,8,9</sup> Further, LBW and SGA are associated with increased risk of coronary artery disease, diabetes mellitus, and arterial hypertension in adult life, as described in the Baker hypothesis,<sup>10</sup> which has been revised to the concept of developmental origins of health and disease (DOHaD).<sup>11</sup> Conversely, macrosomia, defined as birth weight >4,000 g, is also associated with a risk of morbidity in infants.<sup>2,12</sup>

Several modifiable factors, including maternal pre-pregnancy body weight, gestational maternal body weight gain (BWG), and diet, have a major impact on the neonatal birth weight.<sup>5,12–14</sup> Similarly, maternal sleep duration (MSD) during pregnancy also affects obstetric outcomes.<sup>15–17</sup> However, the association between MSD and neonatal birth weight remains unclear.<sup>15,18</sup> Previous studies have reported reduced MSD as a risk factor for SGA,<sup>19,20</sup> but Morokuma et al. reported no association between MSD and SGA in a study including

8,631 participants.<sup>21</sup> Moreover, the appropriate MSD required to prevent LBW, SGA, and macrosomia has not been elucidated. As sleep is often disturbed in pregnant women,<sup>15</sup> appropriate MSD would be a great concern for pregnant women.

The present study evaluated the effect of MSD on neonatal birth weight using the data from a nationwide Japanese prospective birth cohort study.

## Methods

### *Study design*

In this study, we used the data from the Japan Environment and Children's Study (JECS), which is a nationwide, government-funded, prospective birth cohort study that was started in January 2011 to investigate the effects of environmental factors on children's health.<sup>22,23</sup> Briefly, JECS is funded directly by Japan's Ministry of the Environment and involves collaboration between the Programme Office (National Institute for Environmental Studies), the Medical Support Centre (National Centre for Child Health and Development), and 15 Regional Centres (Hokkaido, Miyagi, Fukushima, Chiba, Kanagawa, Koshin, Toyama, Aichi, Kyoto, Osaka, Hyogo, Tottori, Kochi, Fukuoka, and South Kyushu / Okinawa).<sup>23</sup> The eligibility criteria for expectant mothers to participate in JECS were as follows: (1) residing in the study areas at the time of recruitment and expected to continually reside in Japan for the foreseeable future; (2) an expected delivery date between August 01, 2011 and mid-2014; and (3) capable of participating in the study without difficulty (i.e., able to comprehend the Japanese language and complete the self-administered questionnaires).

Either or both of the following recruitment protocols were applied: (1) recruitment at the time of the first prenatal examination at the cooperating obstetric facilities; and (2) recruitment at local government offices issuing a pregnancy journal, called the Maternal and Child Health Handbook, that is given to all expecting mothers in Japan before they receive municipal services for pregnancy, delivery, and childcare. We contacted pregnant women through cooperating health care providers and/or local government offices issuing Maternal and Child Health Handbooks and registered those willing to participate. Self-administered questionnaires, which were completed by the women during the first trimester and second/third trimester, were used to collect information on demographic factors, medical and obstetric history, physical and mental health, lifestyle, occupation, environmental exposure at home and in the workplace, housing conditions, and socioeconomic status.<sup>23</sup>

The JECS protocol was reviewed and approved by the Ministry of the Environment Institutional Review Board on Epidemiological Studies on March 23, 2010 (No. 15000141)<sup>22,23</sup> and by the Ethics Committees of all participating institutions. The JECS was conducted in accordance with the principles of the Declaration of Helsinki and other national regulations and guidelines. Written informed consent was obtained from all participating women.

### *Data collection*

The current analysis used the data set released in June 2016 (data set: jecs-ag-20160424). Specifically, we used three types of data: (1) M-T1, obtained from a self-reported questionnaire that was collected during the first trimester (the first questionnaire) and included questions regarding maternal medical background; (2) M-T2, obtained from a self-reported questionnaire that was collected during the second or third trimester (second questionnaire) and included questions regarding lifestyle and socioeconomic status; and (3) Dr-0m, collected from the medical records' transcripts provided by each participant's institution and that included obstetrical outcomes such as gestational age, birth weight, neonatal sex, and maternal body weight. The participants with singleton pregnancies after 22 weeks were included in the present study. The women with missing information were excluded from the analysis.

### *Exposure variables*

MSD was calculated using the data of questionnaire in M-T2.<sup>24</sup> The participants were categorized into five groups according to MSD during pregnancy: G1 (MSD < 6.0 h), G2 (MSD 6.0–7.9 h), G3 (MSD 8.0–8.9

h), G4 (MSD 9.0–9.9 h), and G5 (MSD 10.0–12.0 h) based on the report of Ministry of Health, Labour and Welfare, Japan,<sup>25</sup> which suggests 6.0–7.9 h of sleep as the appropriate sleep duration for general adults to prevent several health problems. The participants who reported MSD >12.0 h were excluded from the present study because these participants were considered to have reported inaccurate MSD.

### *Obstetric outcomes and confounding factors*

LBW was classified into two categories: LBW < 2,500 g and LBW < 1,500 g.<sup>1</sup> SGA was defined as a birth weight below 1.5 standard deviations, corrected for gestational age and sex, according to “New Japanese neonatal anthropometric charts for gestational age at birth”.<sup>8</sup> Macrosomia was defined as neonatal birth weight >4,000 g.<sup>12</sup>

The following parameters were considered as potential confounding factors: maternal age, body mass index (BMI) before pregnancy, parity, maternal smoking status, maternal alcohol consumption status, maternal educational status, annual household income, PTB before 37 weeks, and gestational BWG. Maternal age was categorized into three age groups: <20 years, 20–29 years, and [?]30 years based on a previous study that showed that maternal age was related to certain obstetric outcomes, such as PTB, LBW, and SGA.<sup>26</sup> BMI before pregnancy was categorized into three groups (<18.5 kg/m<sup>2</sup>, 18.5–25.0 kg/m<sup>2</sup>, and >25.0 kg/m<sup>2</sup>).<sup>27,28</sup> Parity was categorized into two groups (nulliparous and multiparous). Maternal participants were requested to provide information about their smoking status by choosing one of the following: “Yes, I still smoke”; “Never”; “Previously did but quit before recognizing current pregnancy”; and “Previously did but quit after learning of current pregnancy.” The maternal participants who chose “Yes, I still smoke” comprised the smoking category, whereas the other participants comprised the non-smoking category. Maternal participants were requested to provide information about their alcohol consumption status by choosing one of the following: “never drank,” “quit drinking before pregnancy,” “quit drinking during early pregnancy,” and “kept drinking during pregnancy.”<sup>29</sup> The maternal participants who chose “kept drinking during pregnancy” comprised the drinking category, while the other participants comprised the non-drinking category. The educational status of the mother was categorized into four groups on the basis of the number of years of education (junior high school, <10 years; high school, 10–12 years; professional school or university, 13–16 years; and graduate school, [?]17 years). Annual household income was categorized into four groups (<2,000,000 JPY, 2,000,000–5,999,999 JPY, 6,000,000–9,999,999 JPY, and [?]10,000,000 JPY). PTB was defined as the birth before 37 weeks of gestation, the record of which was collected from Dr-0m data. The data for gestational BWG were obtained from Dr-0m data, which included information about body weight before pregnancy (kg) and body weight just before delivery (kg). Gestational BWG was defined as body weight just before delivery minus body weight before pregnancy (kg). We defined appropriate BWG as less than 12 kg and excessive BWG as more than 12 kg, according to the criteria aimed at appropriate birth weight, described by Ministry of Health, Labour and Welfare, Japan.<sup>27,28</sup> These confounding factors were chosen on the basis of the clinical importance.<sup>5,13,14</sup>

### *Statistical analyses*

Participant characteristics were summarized according to the maternal sleeping status. All variables were found to follow a normal distribution based on the Shapiro-Wilk test. One-way analysis of variance was used to compare continuous variables among different MSD groups, and the chi-square test was used to compare categorical variables.

Initially, adjusted odds ratios (aORs) and 95% confidence intervals (CIs) for LBW <2,500 g, LBW <1,500 g, SGA, and macrosomia were calculated using a multiple logistic regression model, with women in G2 as the reference. In Model 1, aOR for LBW was adjusted for maternal age, BMI before pregnancy, parity, maternal smoking status, maternal alcohol consumption status, maternal educational status, annual household income, and PTB before 37 weeks. aOR for SGA was adjusted for maternal age, BMI before pregnancy, maternal smoking status, maternal alcohol consumption status, maternal educational status, and annual household income. aOR for macrosomia was adjusted for maternal age, BMI before pregnancy, parity, maternal smoking status, maternal alcohol consumption status, maternal educational status, and annual household income. In

Model 2, excessive gestational BWG was added as a confounding factor (in addition to those of Model 1) to calculate aORs for these outcomes.

Further, we stratified the participants on the basis of gestational BWG, and aORs for LBW <2,500 g and SGA were calculated using a multiple logistic regression model, with women in G2 as the reference, using the comparable confounding factors in Model 1.

SPSS version 26 (IBM Corp., Armonk, NY, USA) was used for statistical analyses. Differences with p-values <0.05 were considered statistically significant.

## Results

The total number of fetal records during 2011–2014 was 104,102. After applying our inclusion criteria, 82,171 participants were eligible for this study (Figure 1). Among 82,171 participants, 3,958 (4.8%) were in G1, 37,944 (46.2%) in G2, 23,769 (28.9%) in G3, 11,976 (14.6%) in G4, and 4,524 (5.5%) in G5.

Table 1 summarizes the maternal background and obstetric outcomes based on the MSD groups. All maternal background characteristics were significantly affected by MSD. Birth weight increased significantly, and the incidence of LBW < 2,500 g was significantly lower in G4 and G5. No significant differences were observed in the incidence of PTB, LBW < 1,500 g, SGA, and macrosomia among the groups.

Table 2 shows the aORs of LBW < 2,500 g, LBW < 1,500 g, SGA, and macrosomia among all groups with G2 as a reference. No significant association was observed between MSD and these outcomes after adjusting for excessive gestational BWG in model 2. Additionally, there was no significant association between MSD and LBW < 1,500 g and macrosomia.

Table 3 shows the aORs of LBW < 2,500 g and SGA among all groups with G2 as a reference, after stratification by gestational BWG. No significant association was observed between MSD and these outcomes in women with excessive gestational BWG.

## Discussion

### *Main findings*

The present study suggests that >9 h of MSD decreased the incidence of LBW < 2,500 g and SGA but did not affect the outcome after adjusting for excessive gestational BWG, which implies that both long MSD and excessive gestational BWG had great impact on decreasing the risk of LBW and SGA. Additionally, 9 to <10 h of MSD significantly decreased the risk of LBW <2,500 g and SGA in women with appropriate gestational BWG.

### *Interpretation*

The present study, using a large prospective cohort, showed that both MSD and gestational BWG affected neonatal birth weight. Previous studies with relatively small sample sizes have shown a conflicting relationship between MSD and neonatal birth weight.<sup>15,19–21</sup> On the basis of the findings of the present study, we speculate that long MSD, along with gestational BWG, decreases the incidence of LBW and SGA.<sup>14</sup> Although the effect of MSD on gestational BWG is not clearly defined,<sup>30,31</sup> recent studies have reported that excessive sleep duration increased obesity in non-pregnant adults.<sup>32,33</sup> The fetuses in mothers with excessive gestational BWG may receive more nutrients and fetal growth through increased plasma volume, which may increase cardiac output and utero-placental blood flow compared to those in mothers with insufficient gestational BWG.<sup>34,35</sup> Therefore, sufficient BWG by proper diet and sufficient MSD is required to prevent LBW and SGA; however, the concerns about disadvantages of maternal obesity prevail.<sup>36,37</sup>

Conversely, the direct effect of MSD on obstetric outcomes in the appropriate gestational BWG group has not been yet reported. As well as maternal inflammatory stress has been reported to be related to several obstetric outcomes such as PTB, FGR, and preeclampsia,<sup>38–40</sup> previous studies have also reported that disturbed maternal sleep may cause adverse obstetric outcomes, with augmentation of maternal inflammatory response.<sup>15,41</sup> Increased inflammation may interfere with the remodeling of spiral arteries in the placenta,

thereby leading to PTB, FGR, and preeclampsia.<sup>42–44</sup> Thus, preventing reduced MSD may reduce maternal inflammation and prevent these adverse obstetric outcomes. Further, maternal inflammatory stress is also affected by lifestyle, including dietary habits and exercises<sup>45,46</sup>; and comprehensive modification of these lifestyles may help in reducing inflammatory stress.

However, >10 h of MSD did not decrease the incidence of LBW and SGA in women with appropriate gestational BWG, which implies that >10 h of MSD did not affect neonatal birth weight. This may be because >10 h of MSD might be affected by maternal diseases, conditions, and behaviors, such as depression, excessive mental stress, and use of sleeping pills,<sup>24,47,48</sup> which may potentially decrease the neonatal birth weight.<sup>49–51</sup> Moreover, because too long MSD may have other unfavorable effects including excessive BWG,<sup>32,33</sup> we do not suggest that pregnant women should have >10 h of sleep.

### *Strengths and limitations*

The strength of the present study is that the aORs of LBW and SGA provide clear information for perinatal counseling. Owing to the large study population, including >80,000 participants, our results must be reliable. Since pregnant women have more sleep problems, affected by gestational age and hormonal changes,<sup>24</sup> than their non-pregnant counterparts, the effect of MSD on fetal and neonatal health may be a great concern for pregnant women. There is no consensus on appropriate MSD required to prevent adverse obstetric outcomes. Therefore, the present study may help to suggest adequate MSD required to prevent LBW and SGA.

The present study has several limitations. First, MSD in the present study is based on self-reported questionnaire data, which might have resulted in an inaccurate calculation of actual MSD. In addition, MSD is a volatile index because it varies daily in the individuals and may vary with gestational age.<sup>24</sup> Careful interpretation is needed regarding these instabilities of MSD. Further study with polysomnography and unified gestational age may preclude this limitation. Second, we did not account for the quality of sleep by evaluating factors such as time zone, division, where to sleep, and with whom to sleep. We evaluated MSD as a simple quantitative measurement of maternal sleep. Careful interpretation of the results is needed because the quality of maternal sleep, in addition to MSD, may also affect obstetric outcomes.

### **Conclusion**

This study revealed that both >9 h of MSD and excessive gestational BWG had great impact on the incidence of LBW and SGA, and 9 to <10 h of MSD decreased the risk of LBW and SGA in women with appropriate gestational BWG. It is important for care providers to provide the latest data for proper counseling regarding the association between MSD and neonatal birth weight and suggest comprehensive modifications in lifestyles of pregnant women, including sufficient MSD, to prevent LBW and SGA. Furthermore, because JECS is a prospective cohort study, future elucidation of long-term childhood outcomes on the basis of MSD and neonatal birthweight would strengthen the conclusion of this study.

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S.M., K.H., H.N., and K.F. contributed to the study design. K.S., A.S., and Y.O. collected the data. T.M. analyzed the data and wrote the manuscript. M.H., S.Y., K.H., K.S., A.S., Y.O., H.N., K.F., and the JECS group reviewed the manuscript and provided critical advice. All authors approved the final manuscript.

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## Table legends

**Table 1.** Maternal medical background and obstetric outcomes of participants according to maternal sleep duration status

**Table 2.** Crude odds ratios (cORs), adjusted odds ratios (aORs), and 95% confidence interval (CI) of obstetric complications stratified by maternal sleep duration

**Table 3.** Crude odds ratios (cORs), adjusted odds ratios (aORs), and 95% confidence interval (CI) of low birth weight infants < 2,500 g and small for gestational age infants in women with appropriate and excessive gestational body weight gain

## Figure legends

**Figure 1.** Flowchart depicting enrollment of the participants in the study

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