ORIGINAL ARTICLE

Title: Relationship between sleep-disordered breathing and sleeping position at the 37th

week of pregnancy: an observational cross-sectional study

Authors' full names: Midori Ura, MPH¹, Keisaku Fujimoto, MD, PhD²

Authors' affiliations:

¹Department of Medical Laboratory Science, Faculty of Health Sciences, Junshin

Gakuen University

Address: 1-1-1, Chikushigaoka 815-8510 Fukuoka, Japan.

²Department of Clinical Laboratory Sciences, Shinshu University School of Health

Sciences

Address: 3-1-1, Asahi 390-8621 Matsumoto, Nagano, Japan.

Corresponding author full contact details:

Name: Midori Ura

E-mail: midori ura@shinshu-u.ac.jp

ura.m@junshin-u.ac.jp

Tel: +81-92-554-1255

ORCID: 0000-0003-4602-1870

Compliance with ethical standards:

Ethical Committee Permission

All research protocols were approved by the Ethics Committee of Shinshu University, School of Medicine (2728).

(注)

Research Involving Human Participants and/or Animals

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (Shinshu University) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent

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

Conflicts of Interest

The authors declare that they have no conflicts of interest.

ABSTRACT

Purpose: Sleeping in the lateral position during pregnancy can potentially reduce the severity of sleep-disordered breathing (SDB). However, this hypothesis has not been formally investigated in pregnant women. Unlike previous studies that have relied largely on self-reported measures of sleeping position, we investigated the relationship between SDB and sleeping position during late pregnancy using objective measurements.

Methods: Thirty pregnant women at the 37th gestational week and 30 non-pregnant women (n-Pr) participated in the present study. The pregnant women were divided into 2 groups: those with body mass index (BMI) ≥30 kg/m² (with obesity, p-Ob), and those with BMI <30 kg/m² (without obesity, p-nOb). Data were collected using a portable screening device to detect SDB indicated by the respiratory disturbance index (RDI), as well as sleeping position.

Results: The occurrence of the lateral sleeping position was higher in pregnant women than in n-Pr (P < .05). The total RDI significantly differed among the 3 groups [P < .01; p-Ob, 10.7 (3.1); p-nOb, 7.0 (3.0); n-Pr, 4.3 (2.9)]. The p-Ob group showed significantly lower RDI in the lateral position than in the supine position (P = .04). Moreover, there was a significant difference in RDI between p-Ob and p-nOb for the supine position (P = .001), but there was no between-group difference for the lateral position.

Conclusions: Sleeping in the lateral position is likely to mitigate existing SDB in pregnant women with obesity in late pregnancy and may be an effective precaution against undiagnosed SDB and associated complications.

Keywords:

Pregnancy, Sleep-disordered Breathing, Obstetric Complications, Sleep Position, Screening Tests, Public Health

INTRODUCTION:

Pregnant women are at increased risk of sleep-disordered breathing (SDB), partly because of the drastic changes they undergo, including weight gain [1], airflow limitation [2], mucosal oedema [3], nasal congestion [1,3], and snoring [1-7]. Obesity may further increase the risk of SDB in pregnant women [5,6,8-10], and pre-existing SDB can be exacerbated by pregnancy. Obstructive sleep apnoea (OSA), a severe type of SDB, adversely affects maternal and foetal health [7] and is related to various complications, including pregnancy-induced hypertension (PIH) [1,11,12], pre-eclampsia [1,7], gestational diabetes mellitus [12,13], stillbirth [14], and foetal growth restriction [1]. Thus, the early diagnosis and treatment of SDB in pregnant women are essential to reduce the risk of complications. Unfortunately, SDB is difficult to diagnose because of a lack of clear objective symptoms, and SDB in pregnancy remains underdiagnosed [5,6]. Furthermore, a screening test for SDB in the pregnant population has not yet been well established [6]. Therefore, a comprehensive, large scale study is warranted to investigate SDB in high-risk pregnancies, including in pregnant women with obesity, in order to facilitate the early diagnosis and management of this condition.

Sleeping in the lateral position is recommended for the management of position-dependent OSA in the general population [15]. This 'positional therapy' prevents airway collapse caused by sleeping in a supine position and has also been recommended for obstetric patients with OSA [5]. However, no study to date has used objective measurements to evaluate the effect of sleeping in the lateral position on SDB severity in pregnant women, with most previous studies employing subjective measurements such as self-reports [16-18]. In general, studies using self-reports are affected by recall bias, and the reliability of self-reported results during sleep is questionable. Furthermore, most previous reports have considered women of different gestational ages within the

third trimester as one group [14-19], despite the fact that the severity of SDB increases as gestation progresses [5,10,17]. Studying participants at the same gestational age may provide more accurate and reliable data on the influence of gestational stage on SDB severity.

The present study investigated the relationship between SDB and sleeping position at the 37th gestational week using an objective method to assess sleeping position. The primary aim was to clarify whether the severity of SDB is reduced by sleeping in the lateral position and to investigate whether pregnancy increases the severity of SDB.

MATERIALS AND METHODS:

Study participants

Thirty-four pregnant women aged 20 to 40 years were recruited via flyers and oral invitations during their visits to the Obstetrics and Gynecology department at our hospital owing to their pregnancy. Thirty non-pregnant women aged 20 to 43 years also participated and comprised the control group.

Participants were excluded if they had multiple pregnancies, were diagnosed with sleep apnoea-hypopnea syndrome (SAS) or cardiovascular diseases such as congenital heart disease or atrial fibrillation, or if they were taking medications such as sleeping pills or tranquilizers.

Study design

This was an observational cross-sectional and case-control study conducted in Japanese women. Pregnant women were divided into groups depending on their prepregnancy body mass index (BMI: kg/m²), as defined by the 'BMI classification' [20]. This resulted in a total of 3 groups: pregnant women with obesity (BMI ≥30 kg/m²; p-

Ob; n = 15), pregnant women without obesity (BMI <30 kg/m²; p-nOb; n = 15), and non-pregnant women with a normal BMI (n-Pr; n = 30). The 3 groups were matched for age and height, and in pregnant women, examinations were conducted between the 37^{th} and early 38^{th} gestational weeks. In addition, both weight and BMI before pregnancy in the p-nOb group were matched with those of the n-Pr group. We chose to match p-nOb with n-Pr in weight and BMI before pregnancy to investigate the relationship between pregnancy and sleep variables [13].

Protocol

The 'Sleep EYE®' (GD700; GAC Co., Nagano, Japan), a non-restrictive portable screening device, was used to measure total recording time (TRT), time spent in bed (TIB), and body position (supine or back/right or left side), and to detect SDB indicated by the respiratory disturbance index (RDI). The Sleep EYE® (width, 812 mm; depth, 555 mm; height, 33 mm; and weight, 1.6 kg) is a sheet containing 99 membrane-type pressure-sensitive sensors to detect gravitational alterations. The automatic scoring of respiratory events derived from the Sleep EYE® was performed using analytical software and was followed by manual scoring to confirm the validity of the automatic scoring. The details of the principle of the Sleep EYE® have been previously reported [21-24]. Takasaki *et al.* [21] demonstrated a significant correlation between the RDI obtained from the SD-101 (a larger-sized variant of the Sleep EYE®) and the apnoeahypopnea index (AHI) from polysomnography (PSG) data of apnoeahypopnea episodes in the supine and lateral positions in women with suspected SAS (all r > .95). We defined SDB as an RDI greater than or equal to 5 events per hour (RDI was the average number of respiratory events per hour during TIB).

Data collection

Participants slept on the Sleep EYE® at home or in the hospital (if they were hospitalized). They were asked to conduct recordings for 2 nights during their 37th gestational week to prevent missing or faulty recordings, and non-pregnant participants recorded sleep for one night.

Statistical analysis

Data are expressed as the mean [standard deviation (SD)]. The Shapiro-Wilk test was used to clarify whether the data (participant characteristics and sleeping conditions, positions, and RDI) showed a normal distribution, followed by unpaired *t*-tests that were used to compare differences between the p-Ob and p-nOb groups and between the p-nOb and n-Pr groups. Spearman's rank correlation coefficient was used to analyse the association between BMI at recording time and total RDI. A paired *t*-test was performed to compare differences between the supine and the lateral positions within the same participants. All tests were 2-tailed, and *P*-values under .05 were considered statistically significant. All data were analysed using IBM SPSS Statistics (version 24, IBM Corporation, Armonk, NY, USA).

RESULTS:

Nineteen pregnant women with obesity, 15 pregnant women with normal BMI, and 30 non-pregnant women agreed to participate in the study. Of 19 pregnant women with obesity, one was excluded from analysis due to treatment with inhaled oxygen while in the hospital, and 3 dropped out after agreeing to participate due to the development of pregnancy-induced hypertension at 37 and 34 weeks gestation (n = 2), or onset of labour pains on the date of examination (n = 1).

A total of 60 women participated in this study (p-Ob = 15, p-nOb = 15, n-Pr = 30). Eight of the 30 pregnant women (p-Ob = 7, p-nOb = 1) underwent the study in the hospital due to pregnancy complications. Five of these hospitalized pregnant women underwent recordings for one night only for the following reasons: birth on the next day (n = 2); discomfort due to anxiety (n = 1), discomfort due to room temperature (n = 1); 24-hour urine collection (n = 1). All other participants underwent the study at home. In the p-Ob group, there were no significant differences between home- and hospital-based recordings regarding sleeping conditions, positions, and RDI (unpaired t-tests).

Table 1 shows subject demographics and clinical characteristics. As expected, there were differences in weight and BMI both pre-pregnancy and at the time of recording between the p-Ob and p-nOb groups (all P < .001). Sleeping conditions, positions, and RDI results are shown in Table 2. The proportion of time spent in the lateral position of the TIB was significantly greater in the pregnant women, regardless of BMI, than in the n-Pr group (P < .05).

Fig. 1 illustrates a strong correlation between BMI at recording time and total RDI (r = .648, P < .001). Predictably, Table 2 shows significant between-group differences in the total RDI values (p-Ob vs p-nOb, P = .003; p-nOb vs n-Pr, P = .006). In particular, RDI values in the p-Ob group were significantly greater than those in the p-nOb group for the supine position (P = .001); however, there was no significant difference in RDI for the lateral position between p-Ob and p-nOb (P = .40) (Table 2).

Fig. 2 demonstrates comparisons of the same subjects between the supine and the lateral positions. The p-Ob (A) group showed significantly lower RDI in the lateral position than in the supine position (P = .04), whereas there was no significant difference in the RDI values in supine and lateral positions between the p-nOb (B) and n-Pr (C) groups. Furthermore, in the p-Ob group (A), all participants who showed RDI

values in the supine position of 11.4 or greater (n = 10) showed lower RDI values for the lateral position (P = .01).

DISCUSSION:

The major findings of the present study include the following: 1) in p-Ob the severity of SDB was decreased by sleeping in the lateral position; 2) pregnancy is likely to increase the severity of SDB; and 3) pregnant women tend to sleep more frequently in the lateral position than do non-pregnant women.

The benefits of the lateral position have previously been demonstrated in women with position-dependent OSA among the general population [15]. However, although an effect has been hypothesized [5], our study is one of the first to demonstrate that there is a relationship between SDB and sleeping position in the late-pregnancy population with obesity. These results are supported by anatomical evidence. Izci *et al.* [25] demonstrated that the upper airways in pregnant females were smaller in the third trimester of pregnancy than those in non-pregnant women. They also reported posture-dependent size differences in the upper airways, supine yielding the narrowest airways, followed by the lateral and seated positions. This suggests that a common type of SDB in pregnant women with obesity in our study may be position-dependent, although not all the cases in the present study were classified according to Cartwright's criteria for position-dependent OSA [15].

The pregnant women spent significantly greater time in the lateral position. Takasaki et al. [21] mentioned a weak correlation between SD-101 and PSG in the reported duration of postures. Although the accuracy of positioning in Sleep EYE® remains uncertain, previous research [5,6,13,16] may also support this finding. Thus, our finding

could be interpreted to indicate that there is a tendency for pregnant women to sleep more frequently in the lateral position than do non-pregnant women.

Additionally, an enlarged uterus and abdominal pressure cause an elevation of the diaphragm, and as a result, functional residual capacity is reduced in pregnant women [26]. Because of these anatomical changes, pregnant women are at risk of hypoxemia and sleep-related hypoventilation during sleep in the supine position [25]. This suggests that pregnant women face risks of hypoxemia and sleep-related hypoventilation. In addition to positional OSA, these symptoms are likely to be reduced by sleeping in the lateral position.

Focusing on the RDI value, the increased RDI in p-nOb, which was presumed to be caused by pregnancy, was not decreased in the lateral position (Table 2). That is, the SDB was not a type of positional OSA. As mentioned in the Introduction, mucosal oedema [3], nasal congestion [1,3], and rhinitis [5] are common in pregnant women. These changes may cause or worsen SDB, but they are not always decreased by sleeping in lateral position because they are induced by oestrogen [5].

On the other hand, interestingly, in the p-Ob group the effect of sleeping in the lateral position on RDI reduction seemed particularly remarkable in women who had RDI values of more than 11.4 in the supine position (Fig. 2A). In 2014, The American Academy of Sleep Medicine [27] accepted SDB diagnosis in adults by using the RDI values of portable monitoring, considering the RDI as equivalent to the AHI values obtained from PSG. However, the standard RDI value used in the present study is debatable, because when we applied this reference value to the RDI obtained from the Sleep EYE®, the prevalence of SDB in these groups far exceeded published results (p-Ob, 15/15 [100%]; p-nOb, 11/15 [73%]; n-Pr, 9/30 [30%]) [10,19,28].

Indeed, previous studies have investigated the correlation between data from PSG and the SD-101. In 2 studies, RDI ≥11.5 [21] and RDI ≥12.4 [22] were stated to correspond to an AHI ≥5 on PSG. If we apply these cut-off values to the data from the present study, the prevalence of SDB seems more reasonable: p-Ob, 5/15 [33.3%]; p-nOb, 1 to 2/15 [6.7–13.3%], n-Pr: 1/30 [3.3%]. Even so, a relatively high prevalence of SDB was observed in our participants in the p-Ob group, and this might be due to the timing of measurement—the women in our study were in later stages of pregnancy than those enrolled in other studies [10,19,28-30]. Therefore, more pregnant women might have developed SDB, reflecting the influence of the precise timing of examination at the 37th week of pregnancy.

The current study also found a significant difference in the total RDI between the p-nOb and n-Pr groups, suggesting that the severity of SDB worsened during pregnancy (Table. 2). In addition, pregnant women with higher BMI were more likely to develop SDB (Fig. 1, Table 2). These facts have previously been reported using PSG [6,7,9,10]. The present study, however, demonstrated a similar trend to PSG data using a portable device. Although PSG is a gold standard to diagnose SDB, since it requires the use of many electrodes, tight bands on the chest and abdomen, and hospitalization, this measurement can worsen sleep quality for pregnant participants. In comparison, the device used in our study only required to be switched on and the participants could sleep on a sheet at home, which imposed little physical and psychological burden on the participant and therefore hardly disturbed participants' usual sleep. Thus, the device used in this study was suitable for use as a screening test in pregnant women.

The present study demonstrated using objective measurements that women in the late stages of pregnancy tended to sleep in the lateral position than non-pregnant women (Table 2). This finding suggests that SDB caused or exacerbated by pregnancy might be

relieved by spending more time in the lateral position. Since pregnant women in general, and especially those with obesity, represent a group at high risk for SDB, we recommend sleeping in the lateral position as a means to reduce the risk of SDB and possible complications.

To validate the present results, we would ideally conduct a screening test for SDB by enrolling the entire pregnant population. However, that is not realistic because women at a reproductive age are less likely to have SDB [28]. On the other hand, Fig. 1 may suggest one possible cut-off point to effectively reduce SDB: a BMI over approximately 35 kg/m² (RDI: nearly equal to 10 from the Sleep EYE® data). This value is simply a statistically suggested point. Hence, in pregnant women, even mild SDB or obesity may be related to some pregnancy-related complications [10,19], and therefore, it might be better to consider a BMI of 30 kg/m² (RDI = 8.0 of the Sleep EYE®) as an indicator of possible complications.

Limitations

First, the Sleep EYE® cannot discriminate between the supine and prone positions, or between the right and left lateral positions. Therefore, the occurrence of the supine position might have been overestimated in non-pregnant women. This overestimation is, however, less likely to have occurred in pregnant women, because it is hard to sleep in a prone position in late pregnancy. Second, the Sleep EYE® cannot score sleep stages; thus, careful interpretation of the findings associated with TIB is needed because 'time spent in bed' was less accurate than 'total sleep time' measured by EEG. Third, this was a cross-sectional study with a small sample size, and we did not recruit a group of non-pregnant participants with obesity. Thus, it is unknown when the pregnant women with obesity developed SDB and when they started frequently sleeping in the lateral position; these could have been present before pregnancy. However, obesity is not highly

prevalent amongst non-pregnant Japanese women without co-morbidities such as diabetes mellitus and hypertension. These co-morbidities may affect results, and thus affect the analysis. Thus, recruitment of non-pregnant Japanese women without co-morbidities was difficult. Regardless, further studies need to be conducted to overcome this limitation.

Conclusions

To overcome the limitations of previous studies, the present study objectively investigated the relationship between SDB and sleeping position in pregnant women in late-stage pregnancy. The current study suggests that the increased RDI induced by pregnancy observed in non-pregnant obese women is not likely to be reduced by sleeping in the lateral position. This suggests the existence of various causes of hypoxemia in pregnancy. On the other hand, pregnant women with obesity have a higher risk of SDB. Our findings suggest that sleeping in the lateral position could mitigate the severity of SDB in pregnant women with obesity; as a result, this sleep strategy may potentially prevent pregnancy-related complications, particularly in the late stage of pregnancy.

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Table 1. Demographics and clinical characteristics of study participants

	Pregnant		Non-pregnant	P-value	
	BMI ≥ 30 (n =	BMI < 30 (n	BMI < 30 (n	p-Ob vs	p-nOb vs
	15)	= 15)	= 30)	p-nOb	n-Pr
Age (years)	32.0 (4.5)	32.9 (5.7)	29.1 (7.1)	.62	.07
Height (cm)	159.6 (5.6)	159.9 (4.0)	159.1 (6.6)	.88	.69
Pre-pregnancy weight (kg)	91.1 (9.2)	53.6 (6.7)	52.8 (5.9)	<.001	.68
Pre-pregnancy BMI (kg/m²)	36.0 (3.9)	21.0 (2.2)	20.9 (1.9)	<.001	.87
Pregnancy weight (kg) ^a	96.0 (10.2)	61.6 (7.1)	N/A	<.001	N/A
Pregnancy BMI (kg/m²) ^a	37.7 (4.0)	24.1 (2.4)	N/A	< .001	N/A
Gestational week	37.0 (0.4)	37.1 (0.3)	N/A	.58	N/A

Data are expressed as mean (SD).

Significant P-values (under .05) are written in bold.

BMI: body mass index (kg/m²); p-Ob: pregnant women with obesity (BMI \geq 30 kg/m²); p-nOb: pregnant women without obesity (BMI <30 kg/m²); n-Pr: non-pregnant women; N/A: not applicable.

^aAt the time of recording.

Table 2. Comparison of sleeping conditions, positions, and respiratory disturbance index during the 37th gestational week in pregnant women with and without obesity and in non-pregnant women.

*	Pregnant		Non-pregnant	P-value	
	BMI ≥ 30 (n =	BMI < 30 (n	BMI < 30 (n	p-Ob vs	p-nOb vs
	15)	= 15)	= 30)	p-nOb	n-Pr
Sleep conditions					
TRT (min)	448.2 (124.2)	436.3 (104.1)	376.2 (56.1)	.78	.01
TIB (min)	432.3 (116.5)	429.3 (103.4)	373.5 (55.3)	.94	.02
Sleeping positions					
Supine (min)	240.1 (144.4)	273.0 (140.3)	279.2 (66.1)	.54	.83
% Supine in TIB (%)	55.5 (29.0)	63.6 (25.1)	74.8 (16.0)	.53	.03
Lateral (min)	192.2 (136.3)	156.1 (102.2)	94.1 (63.3)	.42	.02
% Lateral in TIB (%)	44.5 (29.0)	36.4 (25.1)	25.2 (16.0)	.52	.03
RDI (times/hour)					
Total	10.7 (3.1)	7.0 (3.0)	4.3 (2.9)	.003	.006
in Supine position	12.4 (6.3)	6.0 (3.0)	4.4 (3.1)	.001	.13
in Lateral position	8.0 (4.5)	6.6 (4.4)	3.4 (3.2)	.40	.008

Data are expressed as mean (SD).

Significant P-values (under .05) are written in bold.

BMI: body mass index (kg/m²); p-Ob: pregnant women with obesity (BMI \geq 30 kg/m²); p-nOb: pregnant women without obesity (BMI <30 kg/m²); n-Pr: non-pregnant women; TRT: total recording time; TIB: time spent in bed; RDI: respiratory disturbance index.

Figures and figure legends

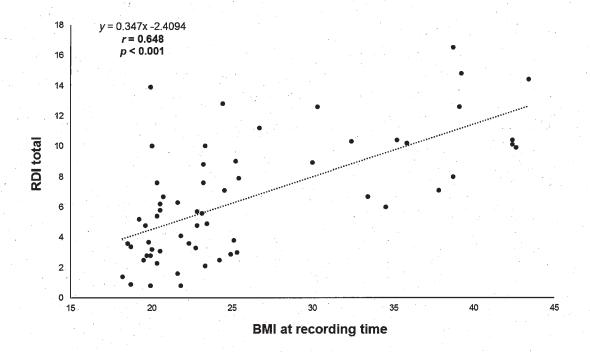


Fig. 1 Correlation between BMI at recording time and total RDI. Spearman's coefficient showed a strong correlation between BMI at the recording time (x-axis) and RDI total (y-axis) (N=60)

BMI: body mass index (kg/m²); RDI: respiratory disturbance index

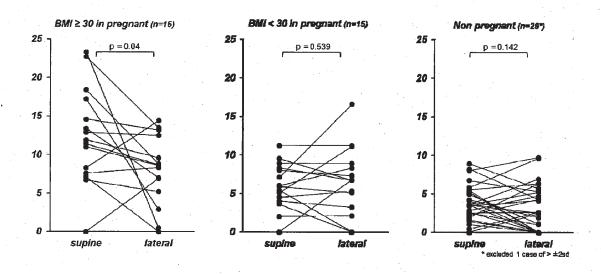


Fig. 2 Comparison of RDI values between the supine position and the lateral position among the 3 groups. Analysis performed using paired t-tests showed that the pregnant women with obesity (A) showed significantly lower RDI in the lateral position than in the supine position, and if the RDI values in the supine position were 11.4 or greater (n = 10), all of them showed lower RDI values for the lateral position. On the other hand, there were no significant differences in the RDI values between supine and lateral positions for the groups of pregnant women without obesity (B) and for non-pregnant women (C)

* One case in the non-pregnant (C) group was excluded from the statistical analysis because it was an outlier (more than mean (2 SD): total RDI, 13.9; in supine, 14.4; in lateral, 6.9)

BMI: body mass index (kg/m²); RDI: respiratory disturbance index