

## Original

## Status of Pregnant Women's Mental and Physical Stress and Influences of Work

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### Abstract

To investigate and clarify stress levels of pregnant women and the impact of employment on pregnancy and child's health both objectively and scientifically by the stages of pregnancy using the GHQ-28, which has reliability and validity, and using an oxidative stress marker (urinary 8-OHdG), which can accurately measure oxidative stress levels of workers. The subjects were 145 women during natural and single pregnancy. The survey was conducted by a Questionnaire to clarify their general background, daily activities, working status, mental stress (GHQ28) and measurement of oxidative stress urinary 8-hydroxydeoxy guanosine (8-OHdG) in early (12–16 w), in middle (22–26 w) and in late (32–36 w) pregnancy.

The results of their mental and physical stress levels were higher during the early stages of pregnancy, and they then decreased with the advancement of pregnancy in both the working and the non-working women. The results also revealed high levels of mental stress in the primiparous working women. It is necessary for industrial physicians and other occupational health care staff to provide support to working women in their early stages of pregnancy, and it is particularly important to provide working primiparous women with emotional support during maternal health consultation.

This study was Japan Environment & Children's Adjunct study.

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### —Key words—

pregnancy, working, urinary 8-OHdG

### Introduction

Women now play essential roles in Japanese society, since their labor force participation accounts for 41.0% of the entire workforce. However, they have other social roles that men cannot perform, such as pregnancy, childbirth, and raising children; therefore, establishing a social environment in which women can continue their work while being pregnant and raising children is an important subject in industrial medicine and occupational health. Many studies that investigated the impact of employment on pregnancy, delivery, and child's health in working women have reported that it significantly increases the risk of threatened abortion/preterm delivery or low birth weight; however, their mechanism has not been clarified<sup>1)</sup>.

The GHQ, which was developed by Goldberg *et al.*<sup>2)</sup> in England, is a widely used questionnaire to diagnose, assess, and identify psychiatric disorders. This was translated into Japanese by Nakagawa *et al.*<sup>3)</sup>, and used as the short Japanese version of the GHQ-28. This scale has good reliability and validity, and is used to measure

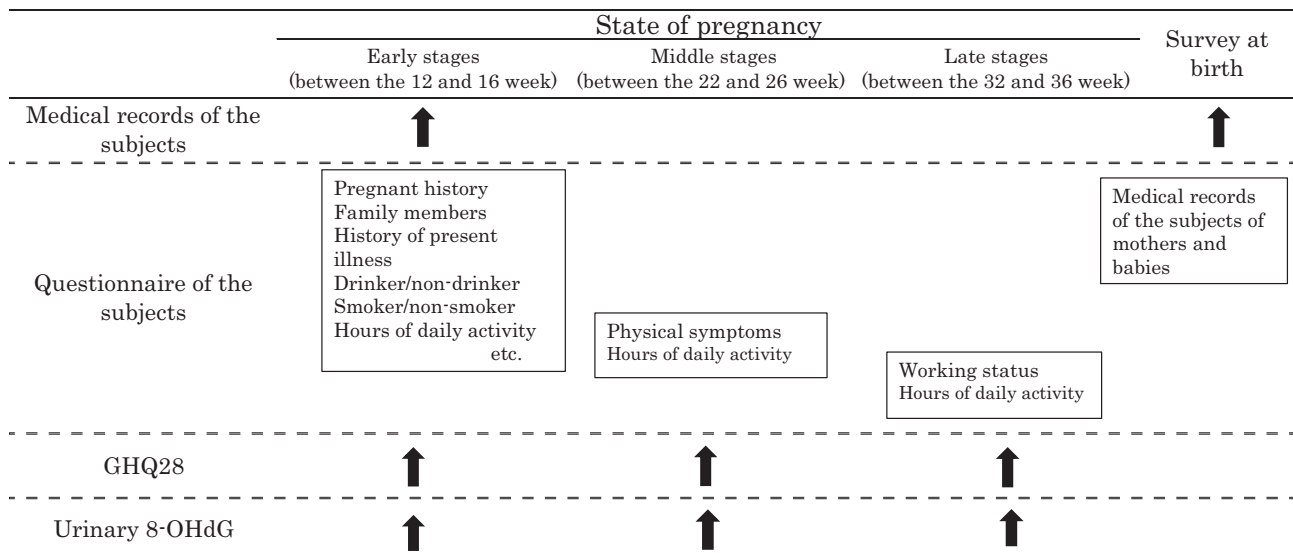


Fig. 1 Study protocol

total score and 4 subscales, namely, Somatic symptoms, Anxiety and Insomnia, Social Dysfunction, and Severe Depression. The total possible score ranges from 0 to 28, with higher scores indicating a greater probability of psychiatric distress. The cut-off point of the GHQ-28 score to detect psychological distress is 5/6.

8-OHdG is marker of oxidative DNA damage in whose structure guanine has been oxidized by reactive oxygen<sup>4</sup>. Since urinary 8-OHdG can reflect oxidative stress non-invasively, it is now widely used as an oxidative stress marker. It was reported that urinary 8-OHdG levels of female shift workers were significantly higher than those of female part-time workers<sup>5</sup>. Moreover, the urinary 8-OHdG of male shift workers was reported to increase compared with male day-time workers<sup>6</sup>. Urinary 8-OHdG is widely used as an oxidative stress marker to study the influence of working, but no report has yet been done concerning pregnant women.

We investigated the difference in GHQ28 and urinary 8-OHdG between working and non-working pregnant women, GHQ28 and 8-OHdG levels were measured at 2 stages of pregnancy; early and late, in 2012<sup>7</sup>. GHQ28 and urinary 8-OHdG were higher during the early stages of pregnancy but then decreased with the advancement of pregnancy in both the working and non-working women. Urinary 8-OHdG levels in working pregnant women were lower than that in non-working pregnant women during early pregnancy. Therefore, working in early pregnancy did not adversely influence pregnancy with respect to the oxidative stress marker 8-OHdG. In addition to the survey items of a previous study<sup>7</sup>, we added a middle-stage pregnancy survey, and changed the method of measuring urinary 8-OHdG from enzyme-linked immunosorbent assay (ELISA) to 2-step high-performance liquid chromatography (HPLC).

This study was conducted as an Adjunct Study outlined in the JECS protocol paper<sup>8</sup>. The study protocol was approved by the Ministry of the Environment.

## Subject and Methods

This study involved pregnant women who consulted one of three medical institutions in K City and agreed to participate in this study. Their informed consent was obtained through the cooperation of nurses from each institution. Data obtained from working and non-working pregnant women were compared.

### 1. Survey protocol (Fig. 1)

#### ① Survey during the early stages of pregnancy (between around 12 and 16 weeks)

Medical records of the subjects, Questionnaire survey (general background/medical history/history of present illness, hours of daily activity) + GHQ-28 + collection of biological samples (maternal urine)

#### ② Survey during the middle stages of pregnancy (between around 22 and 26 weeks)

Questionnaire survey (Physical symptoms, hours of daily activity) + GHQ-28 + collection of biological samples (maternal urine)

③ Survey during the late stages of pregnancy (between around 32 and 36 weeks)

Questionnaire survey (work status, hours of daily activity) + GHQ-28 + collection of biological samples (maternal urine)

④ Survey shortly after giving birth (during hospitalization)

Medical records of the subjects of mothers and babies

## 2. Survey period

The survey was performed between October 2012 and March 2013, and 180 pregnant women agreed to participate in this study. Biological samples were collected by October 2013, and an analysis of the obtained data and measurement of urinary 8-OHdG were initiated from November of the same year.

Consent was newly obtained from pregnant females recruited for JECS, which had been conducted at the Sub-unit Center, University of Occupational and Environmental Health, Japan.

## 3. Methods of collection and analysis of urine samples

The remainder of urine samples collected and used for general antenatal check-up was divided into aliquots of 1 mL in tubes and stored in a  $-80^{\circ}\text{C}$  freezer. After centrifuging the urine samples to remove sediment, urinary 8-OHdG was separated using coupled-column HPLC, and measured using an electrochemical detector (ECD)<sup>9</sup>. Since the urine used in this study involved spot samples, urinary creatinine concentration was measured to correct the amount of urinary 8-OHdG.

## 4. Ethical considerations

This study was conducted with the approval of the conflict of interest committee (Approval No. 240519) and ethics committee (Approval No. H24-099) of the University of Occupational and Environmental Health, Japan.

# Results

## 1. Subjects

Of the 180 pregnant women who agreed to participate in this study, a total of 145 women were used as study subjects after excluding 35 women due to the following 6 reasons.

① Withdrawal from the survey (miscarriage, transfer to another medical institution, retraction of consent) (7 women)

② Twin pregnancy (4 women)

③ Administration of drugs due to pregnancy complications that required medical care (autoimmune disease, mental disorders, kidney disease) (7 women)

④ Not all the questionnaires were returned (7 women)

⑤ Deficiency in the amount of and problems with biological samples collected (8 women)

⑥ Urinary level of 8-OHdG was below the detection limit (2 women)

## 2. Age of the subjects and primiparous, multiparous

The mean ages of the subjects and their partners were  $31.3 \pm 5.4$  (ranging from 17 to 43 years) and  $32.6 \pm 6.3$  years (ranging from 17 to 53 years), respectively. The numbers of primiparous and multiparous women were 57 and 88, and their mean ages were  $31.0 \pm 6.3$  and  $31.5 \pm 4.8$  years, respectively.

## 3. Work status

1) Work status during the early to late stages of pregnancy

The numbers of subjects who were employed and not employed during the early, middle, and late stages of pregnancy were 94 (64.8%) and 51 (35.2%), 76 (52.4%) and 69 (47.6%), and 35 (24.1%) and 110 (75.9%), respectively (Table 1).

2) Number of subjects by employment status and Job-leaving status

Of the 94 women working during the early stages of pregnancy, 18 women had left their jobs by the time the survey was conducted in the middle stages of pregnancy. Of the 76 remaining women, 11 women had left their job by the time the survey was conducted in the late stages of pregnancy. The job-leaving rate of all working subjects was 30.9% (n=29). Out of 65 employed subjects at late stage, 30 were on maternity leave and 35 were actively working.

**Table 1** Stages of pregnancy and work status Number (%)

	Early stage	Middle stage	Late stage
Working	94 (64.8)	76 (52.4)	35 (24.1)
Non-working	51 (35.2)	69 (47.6)	110 (75.9)
Total	145 (100)	145 (100)	145 (100)

**Table 2** Numbers of pregnancy complications

	Number
Threatened abortion/preterm delivery	38
Mild pregnancy-induced hypertension	3
Gestational diabetes	1
Intrauterine growth restriction	3
total	45

### 3) Reasons for leaving one's job

The following statements (1–4) were observed as reasons for leaving one's job among 18 women who left their jobs by the middle stages of pregnancy.

- ① Severe morning sickness (8 subjects)
- ② Poor physical condition (5 subjects)
- ③ Bleeding (1 subject)
- ④ Domestic reasons, such as parenting (2 subjects)
- ⑤ Not stated (2 subjects)

The following statements (1–4) were observed as reasons for leaving one's job among 11 women who left their jobs by the middle to late stages of pregnancy.

- ① Contract or fixed-term employees were not allowed to take maternity and parenting leave (4 subjects)
- ② Resignation due to pregnancy has been predetermined by the company (1 subject)
- ③ Domestic reasons, such as moving house (2 subjects)
- ④ No particular reasons (2 subjects)
- ⑤ Not stated (2 subjects)

## 4. Incidence of pregnancy complications

1) As shown below, 45 subjects (31.0%) developed pregnancy complications (Table 2). No subjects were admitted to hospital for the treatment of pregnancy complications.

2) Incidence of pregnancy complications in the working and non-working women

Of the 38 women who had experienced threatened abortion/preterm delivery, 19 were employed and the other 19 were not employed during the early stages of pregnancy. Only 1 working woman left her job due to "bleeding" during the early stages of pregnancy. Two out of 3 subjects diagnosed with mild pregnancy-induced hypertension had been employed until the middle stages, and 1 woman continued her job until the late stages of pregnancy. One woman who was diagnosed with gestational diabetes mellitus had not been employed from the early stages of pregnancy. One out of 3 subjects diagnosed with intrauterine growth restriction continued her job until the middle stages, but the other 2 subjects had not been employed from the early stages of pregnancy.

The survey results did not show the significant impact of employment on pregnancy complications.

## 5. Child's health status

1) All subjects gave birth to full-term infants (37 weeks and 0 days–41 weeks and 5 days). The mean birth weight of infants was  $3,037 \pm 376$  g. One baby who was born in a state of apparent death had undergone appropriate treatment, therefore no health problems were noted during the neonatal period.

2) Birth weight of infants according to mothers' work status

We compared the birth weight of infants of mothers who worked and did not work during the early stages of pregnancy; however, no difference was observed. Similarly, work status during the middle and late stages of pregnancy did not affect the birth weight of infants.

## 6. Comparisons by the stages of pregnancy

1) GHQ-28 scores during the early, middle, and late stages of pregnancy

The total GHQ-28 scores and those for each subscale measured during the early, middle, and late stages of pregnancy were analyzed using ANOVA and Tukey-Kramer test. In terms of the results, the total score and scores for Somatic Symptoms, Anxiety and Insomnia, Social Dysfunction, and Severe Depression were highest

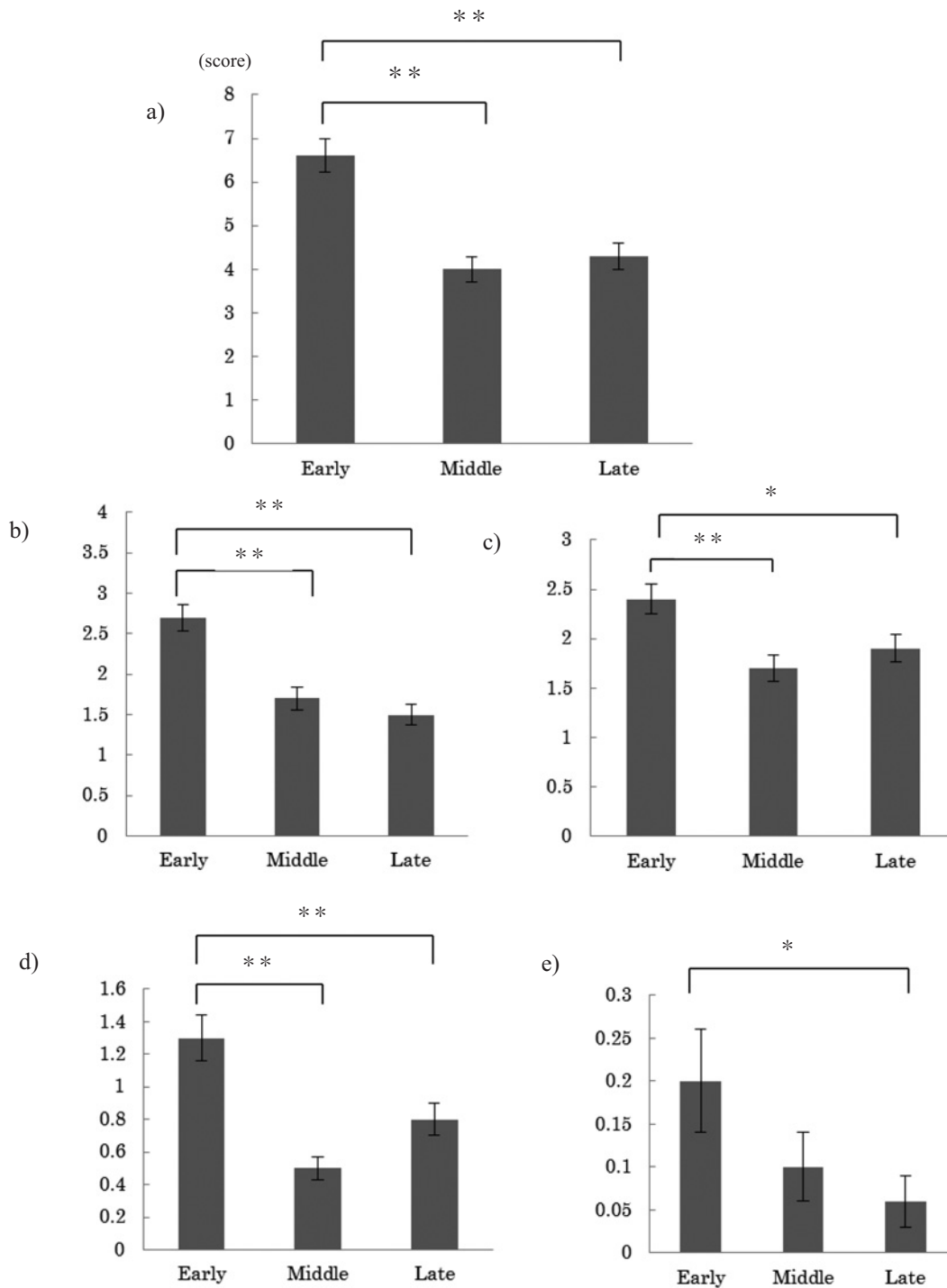
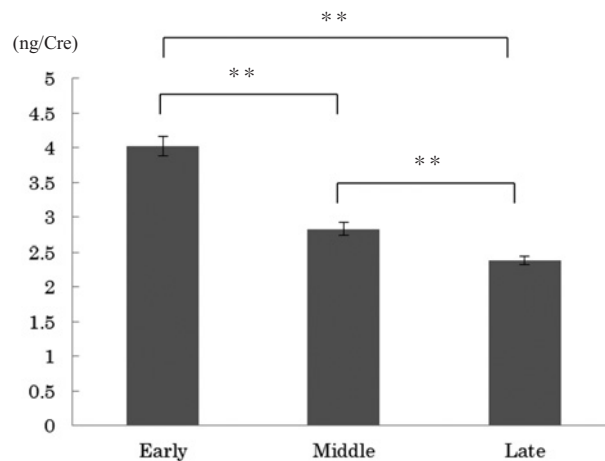


Fig. 2 Comparison of GHQ-28 scores during the early, middle, and late stages of pregnancy.  
 a) Total Scores b) Somatic Symptoms c) Anxiety and Insomnia  
 d) Social Dysfunction e) Severe Depression N = 145  
 ANOVA and Tukey-Kramer test \*\*p<0.01, \*p<0.05

during the early stages of pregnancy, showing that mental health of the subjects was most impaired during the early stages of pregnancy, which were the same results as in a previous study (Fig. 2).

2) Comparison of urinary 8-OHdG levels during the early, middle, and late stages of pregnancy

The level of creatinine-adjusted urinary 8-OHdG was highest during the early stages, and it significantly declined over time in the middle and late stages of pregnancy (p<0.01) (Fig. 3). As with the results of the GHQ-28, stress level was also highest during the early stages of pregnancy, showing the same result as in a previous



**Fig. 3** Comparison of Urinary 8-OHdG levels (with creatinine correction) during the early, middle, and late stages of pregnancy. N = 145  
ANOVA and Tukey-Kramer test \*\*p<0.01

study<sup>7</sup> that compared the early and late stages of pregnancy.

The above results show that emotional and physical stress levels were highest during the early stages of pregnancy, regardless of work status.

### 7. Comparison of GHQ-28 and Urinary 8-OHdG based on stages of pregnancy between working versus non-working women

#### 1) GHQ28

The total score of the GHQ and score for “anxiety/insomnia” measured during the early stages of pregnancy were significantly higher in the working than in the non-working women ( $P<0.05$ ) (Table 3). The results of comparison between primiparous and multiparous women who worked during the early stages of pregnancy showed that “anxiety and insomnia” score was significantly higher in the former than in the latter group ( $P<0.05$ ), indicating poorer mental health in the working primiparous women. No significant difference was observed in the total score of the GHQ-28 measured during the middle and late stages of pregnancy between the working and non-working women.

#### 2) Urinary 8-OHdG

No difference was observed in the urinary 8-OHdG and physical stress levels between the working and non-working women in all stages of pregnancy.

### 8. Factors affecting urinary 8-OHdG levels

Since the urinary 8-OHdG level had a log-normal distribution, the data were log-transformed prior to multiple regression analysis.

The urinary 8-OHdG level was used as a dependent variable, and parity, work status, age, pre-pregnancy BMI, the number of children and family members, sleeping hours, hours of housekeeping activities, resting hours, and smoking status were used as independent variables. In terms of the results of the analysis, the subjects with a habit of smoking showed significantly higher urinary 8-OHdG levels in all stages of pregnancy than nonsmokers ( $P<0.05$ )<sup>10,11</sup>. No correlation was observed between the urinary 8-OHdG level and other variables in all stages of pregnancy.

## Discussion

### 1. Work status and job-leaving rate in the pregnant women

More than half of the subjects ( $n=94$ , 64.8%) worked during the early stages of pregnancy (12–16 weeks), showing a similar result to that in a previous study (66.1%). This result is also similar to that of “The 14th Annual Population and Social Security Survey (a national survey on marriage)”<sup>12</sup> conducted by the National Institute of Population and Social Security Research in 2010, which reported that the “employment rate of married

**Table 3** Comparison of GHQ-28 during the early stages of pregnancy between working versus non-working women

		Mean ± SD		
Total Scores				
working	(n = 94)	7.23 ± 4.58	□	*
non-working	(n = 51)	5.53 ± 4.39		
Somatic Symptoms				
working		2.88 ± 1.81	□	n.s
non-working		2.31 ± 2.02		
Anxiety and Insomnia				
working		2.67 ± 1.78	□	*
non-working		1.96 ± 1.60		
Social Dysfunction				
working		1.47 ± 1.79	□	n.s
non-working		1.00 ± 1.51		
Severe Depression				
working		0.20 ± 0.81	□	n.s
non-working		0.27 ± 0.77		

independent t-test \*p&lt;0.05

women” was approximately 60%. In this study, however, 29 pregnant women (30.9%) left their jobs for physical reasons, such as “severe morning sickness” and “poor physical condition,” during the early stages of pregnancy or for social reasons, such as “not being allowed to take maternity and parental leave” and “resignation due to pregnancy had been predetermined by the company” during the middle to late stages of pregnancy. Although the job-leaving rate of pregnant women had decreased compared with that in a previous study (39.0%), it still exceeded 30% in this study.

As measures to support the maternal health of working women, the “Labor Standards Act” and the “Equal Employment Opportunity Law” stipulate that pregnant women have the opportunity to take maternity and parental leave, to be transferred to light duties, and to receive support to reduce the stress of commuting<sup>13)</sup>. However, maternity leave during the early stages of pregnancy is not stipulated by law, so women are only allowed to take it when they are diagnosed with pregnancy complications, such as hyperemesis gravidarum or threatened abortion. The use of a “Maternal Health Management Card” under the “Equal Employment Opportunity Law” is advised for all employers; however, the percentage of companies whose employees applied for this card remained at 1.9% in 2004<sup>13)</sup>. During the early stages of pregnancy, various factors that are particular to this stage, such as the pregnancy not being easily noticed by co-workers, a work and social environment in which pregnant women feel difficulty announcing their pregnancy, and uncomfortable feelings arising after announcing their pregnancy, are considered to be complexly intertwined and affect their separation from work. Furthermore, it is expected that there are many small-sized companies that lack sufficient knowledge about maternity or parental leave, and maintain a conventional rule to terminate the employment of pregnant women. To create a work environment in which women can continue working safely and healthily, there is an urgent need to establish related systems, promote understanding at workplaces and in society, and develop a cooperative system between medical institutions and workplaces under the initiative of industrial physicians and other occupational health care staff<sup>4)</sup>.

## 2. Examination by the stages of pregnancy

In this study, the results of both the GHQ-28, which is used to measure the psychological aspects of quality of life, and urinary 8-OHdG, which is used to measure physical stress, verified that mental and physical stress levels were higher during the early than the late stages of pregnancy, showing similar results to those in a previous study. We have hypothesized that mental and physical stress levels of pregnant women are higher during the late stages of pregnancy because symptoms associated with an enlarged uterus develop during the late

stages of pregnancy (lower back pain, breathing problems associated with the elevation of the diaphragm, edema due to the compression of the veins, constipation, mobility problems due to weight gain); however, this was once again rejected in this study, as in the previous one.

As factors most strongly affecting high mental and physical stress levels during the early stages of pregnancy, symptoms associated with hyperemesis gravidarum occurring during this stage are considered<sup>15</sup>. Although the exact cause of hyperemesis gravidarum remains unknown, approximately 50–80% of pregnant women are reported to experience nausea and vomiting<sup>16</sup>. In addition, during this stage, pregnant women often develop ambivalent emotions, such as the joy of being pregnant, confusion and lack of confidence about becoming a parent, and anxiety about whether or not they can manage to continue working<sup>17</sup>.

Mental and physical stress levels were highest during the early stages of pregnancy in this study. This result is significantly beneficial to providing maternal health consultation to not only working pregnant women but also to all pregnant women. Medical providers who are engaged in obstetric care must consider this to provide sensible care and support to them. In this study, 8 and 5 subjects stated “severe morning sickness” and “poor physical condition” as reasons for leaving their jobs, respectively. Considering cases of pregnant women who successfully managed to continue their work by taking short breaks during work when suffering from morning sickness in the early stages of pregnancy or obtaining short-term leave, medical providers and bosses at workplaces must proactively provide care and support to them without waiting for requests from pregnant women<sup>18</sup>. Industrial physicians and other occupational health care staff who provide employers with safety and health services must also provide support to working pregnant women, especially during the early stages of pregnancy, and promote understanding of employees towards their occupational environment.

### 3. Comparison between the working and non-working pregnant women

The total score on the GHQ-28 and the score for “anxiety/insomnia” measured during the early stages of pregnancy were significantly higher in the working than in the non-working pregnant women ( $P < 0.05$ ). The results of comparison between the primiparous and multiparous women who worked during the early stages of pregnancy showed that “anxiety/insomnia” score was significantly higher in the former than in the latter group, indicating poorer mental health in the working primiparous women.

On the other hand, no difference was observed in the urinary 8-OHdG level between the working and non-working women in all stages of pregnancy, showing no impact of work status on physical stress. As we mentioned above, pregnant women are expected to experience various emotions during the early stages of pregnancy, such as anxiety and confusion. Mental stress level was higher in the working primiparous women, possibly because they were bothered by work-related factors, such as “anxiety over whether or not they can continue working”, and emotional factors, such as “anxiety and confusion about becoming a parent” at the same time<sup>19–21</sup>. Medical providers and other occupational health care staff who are engaged in obstetric care must focus on providing emotional support to working primiparous women.

We compared the presence or absence of pregnancy complications and birth weight of infants between the working and non-working women, but no difference was observed, showing no evidence of a negative impact of employment on pregnancy. The results suggest the possibility that pregnant women could continue their work safely by providing protections when they suffer from severe morning sickness, allowing them to take short-term leave if needed, and providing emotional support, especially to working primiparous women.

### Conclusions

Mental and physical stress levels were higher during the early stages of pregnancy, and they then decreased with the advancement of pregnancy in both the working and the non-working women. The results also revealed high levels of mental stress in the primiparous working women. No significant difference was observed in the incidence of pregnancy complications, birth weight of infants, and physical stress level between the working and non-working pregnant women, showing no evidence of a negative impact of employment on pregnancy.

Medical providers who are engaged in obstetric care must take account of high levels of mental and physical stress during the early stages of pregnancy, when providing care and support to them. It is also necessary



for industrial physicians and other occupational health care staff to provide support to working women in their early stages of pregnancy, and it is particularly important to provide working primiparous women with emotional support during maternal health consultation. In order to establish a pregnancy-friendly work environment, the dissemination of the existing systems and promotion of understanding at the workplace are needed through implementing enlightenment activities.

This study was Japan Environment & Children's Adjunct Study.

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## 妊婦の精神的・身体的ストレス状況と労働による影響の調査

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### —キーワード—

妊娠, 労働, 尿中 8-OHdG

本研究は妊婦のストレス状況と労働による妊娠・出生児への影響を, 信頼性・妥当性が検証されている精神的ストレス尺度 (GHQ28), ならびに労働者の酸化的ストレスレベルの測定指標として精度が実証されている酸化ストレスマーカー (尿中 8-OHdG) をもちいて妊娠時期別に追跡調査を行い科学的に解明することを目的とした. 対象者は自然単胎妊娠の 145 名であり, 妊娠初期 (妊娠 12~16 週) 妊娠中期 (妊娠 22~26 週) および妊娠後期 (妊娠 32~36 週) に生活状況や就業状況, 精神的ストレス状況 (GHQ28) を質問票を用いて調査し, さらに尿中酸化ストレス (8-OHdG) を測定した.

その結果, 就労・非就労を問わず妊婦は妊娠初期の精神的・身体的ストレスが最も高く, 妊娠後期になるにつれて低下することが明らかになった. また初産婦である就労妊婦の精神的ストレスが高いことが明らかになった. 産業医や産業保健スタッフが妊婦保健指導を行う際は, 妊娠初期の就労妊婦への支援を行う必要性や, 特に初産婦である就労妊婦への心理的支援を行うことが重要である.

本調査は環境省の子どもの健康と環境に関する全国調査における追加調査で行った.

利益相反: 利益相反基準に該当無し

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