

## ORIGINAL ARTICLE

# Relationships between pregnancy outcomes, biochemical markers and pre-pregnancy body mass index

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**Objective:** We examined the relationships between pre-pregnancy maternal body mass index (BMI), pregnancy outcomes and biochemical markers.

**Design:** This study was conducted as a cross-sectional analysis.

**Subjects:** Korean women in their second and third trimesters of pregnancy were recruited at two hospitals in the metropolitan Seoul area. Pre-pregnancy BMI was categorized in four groups according to the Asia-Pacific standard.

**Measurements:** Fasting blood samples were obtained and analyzed for serum levels of homocysteine, folate and high-sensitivity C-reactive protein (hs-CRP). Concentrations of fetal fibronectin were assessed in the cervix and vagina, and cervical length was measured.

**Results:** Obese subjects had a lower education level and a lower income level than subjects of normal weight. The level of maternal stress was positively associated with pre-pregnancy BMI. Normal weight subjects were more likely to eat breakfast and consume meals of appropriate size than the rest of our sample. In overweight and obese subjects, weight gain during pregnancy was significantly lower than in the underweight and normal subjects. High pre-pregnancy maternal BMI increased the risks of preterm delivery (odds ratio (OR) = 2.85, confidence interval (CI) = 1.20–6.74), low-birth-weight (LBW) infants (overweight subjects: OR = 5.07, CI = 1.76–14.63; obese subjects: OR = 4.49, CI = 1.54–13.13) and macrosomia. In obese subjects, the average serum folate level was significantly lower than in the underweight subjects. In obese subjects, the average serum hs-CRP level was significantly higher than in the rest of our sample.

**Conclusion:** Pregnancy outcomes are influenced by pre-pregnancy BMI. These findings suggest that women can minimize their risks of preterm delivery, LBW and macrosomia by maintaining normal pre-pregnancy BMI.

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**Keywords:** pre-pregnancy BMI; preterm delivery; low birth weight; macrosomia

### Introduction

Women with low pre-pregnancy body mass index (BMI) ( $<19.8 \text{ kg m}^{-2}$ ) experience high risk of delivering low-birth-weight (LBW) newborns, whereas women with high pre-pregnancy BMI ( $>29.0 \text{ kg m}^{-2}$ ) experience increased risk of macrosomia.<sup>1</sup> LBW increases the risks of infant mortality and impaired development.<sup>2</sup> In Korea, the number

of LBW infants increased from 18 532 in 1993 to 22 725 in 2008.<sup>3</sup>

A preterm birth is defined as delivery before 37 completed weeks gestation.<sup>4</sup> Preterm infants experience significant perinatal mortality.<sup>5</sup> The number of preterm infants born in Korea, increased from 40 114 in 1996 to 62 869 in 2008.<sup>3</sup> Studies suggest increased risks of preterm delivery for underweight women, whereas obese women experience significantly lower rates of preterm delivery.<sup>6,7</sup>

Several biochemical markers are considered to be associated with LBW and preterm delivery. Elevated total homocysteine concentrations in plasma or serum are associated with preeclampsia, intrauterine growth retardation, perinatal death, preterm birth and LBW.<sup>8–10</sup> Low-serum folate is significantly correlated with increased risks of neural

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tube defects, preterm birth and LBW.<sup>11</sup> Elevated levels of C-reactive protein (CRP) are associated with increased risks of preterm delivery and increasing BMI of mother.<sup>12</sup> Finally, the levels of fetal fibronectin (fFN) in the cervix and vagina measured between 22 and 37 weeks gestation are considered potential markers of preterm delivery<sup>13</sup> and short cervical length is associated with an increased risk of preterm delivery.<sup>14</sup>

The available data on pregnancy outcomes associated with pre-pregnancy maternal BMI are inconsistent. Some studies<sup>6,7</sup> report increased risk of preterm delivery among underweight women, whereas others<sup>15</sup> report increased risk of preterm delivery among obese women. Previous studies have only rarely investigated the relationships between biochemical markers such as homocysteine, folate, high sensitivity CRP, fFN or cervical length and pre-pregnancy BMI. In this study, we examined the relationships between pre-pregnancy maternal BMI, pregnancy outcomes and biochemical markers.

## Subjects and methods

### Subjects

Subjects were recruited at MizMedi Hospital and Ewha Womans University Hospital, Seoul, Korea between April 2006 and April 2009. A total of 830 pregnant women in their second and third trimesters (19–39 weeks) participated in this study. After excluding subjects with incomplete height and weight records, 608 subjects were included in this analyses. General and obstetric characteristics, anthropometric measurements, and information regarding health habits and nutrient intake were obtained through interviews using a standardized questionnaire. The general and obstetric questions addressed age, educational level, income level, occupation status, number of family members, gestational period at baseline, total number of pregnancies and morning sickness. Weight gain during pregnancy was calculated by subtracting the pre-pregnancy weight from weight just before delivery. Pre-pregnancy BMI was calculated using self reported height and pre-pregnancy weight. We collected information on health habits, including smoking, alcohol drinking, coffee drinking, stress, weight reduction attempts, physical activity and exercise status. The stress levels of the subjects were measured using a questionnaire developed by Holmes *et al.*<sup>16</sup> and classified as low (scores <12) or high (scores ≥12) out of a possible total score of 41.<sup>17</sup> The subjects' dietary habits were assessed by assessing meal frequency, frequency of eating breakfast, regularity of mealtimes, amount consumed at each meal and frequency of eating out. Data regarding weight before delivery, gestational age, neonate weight and neonate height were collected from hospital records after delivery. Pre-pregnancy BMI was categorized in four groups according to the Asia-Pacific standard: the underweight group

(<18.5 kg m<sup>-2</sup>), normal weight group (18.5–22.9 kg m<sup>-2</sup>), overweight group (23.0–24.9 kg m<sup>-2</sup>) and obese group (≥25 kg m<sup>-2</sup>).<sup>18</sup>

### Methods

Fasting blood samples were obtained from subjects during the second and third trimesters (19–39 weeks) of pregnancy, and the serum levels of homocysteine, folate and hs-CRP were measured. The samples were collected into a serum separating tube (plain tube). Serum were separated by centrifugation at 3000 r.p.m. for 15 min and stored at -70 °C until analysis. Serum homocysteine concentration levels was determined by fluorescent polarization immunoanalysis using an automatic analyzer (Hitachi 7180, Daiichi, Japan) with a Liquid Stable 2-Part Homocysteine Reagent Kit (Catch, Bothell, WA, USA). The upper limit of homocysteine reference values was taken as 15.0 μmol l<sup>-1</sup>.<sup>19</sup> Serum folate levels were measured by radioimmunoassay<sup>20</sup> with a vitamin B12/folate dual radioassay kit (MP Biomedicals, Huntsville, AL, USA). The normal range for this assay is 3–16 ng ml<sup>-1</sup>.<sup>21</sup> Serum hs-CRP levels were measured by a latex immunoturbidimetric assay<sup>22</sup> that uses latex particles with monoclonal anti-CRP antibody, and performed on automatic analyzers (Hitachi 7080). The interassay and intraassay coefficients of variation were both <10%.<sup>23</sup> Concentrations of fFN in vaginal secretions were measured by enzyme-linked immunosorbent assay<sup>24</sup> using a human fFN PTD check (Adeza Biomedical, Sunnyvale, CA, USA), with concentrations greater than or equal to 50 ng ml<sup>-1</sup> considered as positive. Cervical length was measured by 3D ultrasonography (Accuvix XQ, Seoul, Korea). Cervical length was measured by tracing from the internal os to the external os in cervix cannal. The cutoff value for cervical length is 25 mm. This is cutoff value of below the tenth percentile at 24 weeks of gestation for prediction of preterm delivery.<sup>25</sup>

### Statistical analyses

Statistical analyses were performed with SPSS for Windows, version 17.0. The statistical differences among the four groups were analyzed by ANOVA with *post-hoc* analysis via Tukey's test. The values are presented as mean ± s.d. The  $\chi^2$  test was used to identify significant differences between groups. The risks of preterm delivery, LBW and macrosomia are presented as adjusted odds ratios (ORs) with the 95% confidence interval (CI) computed by binary logistic analysis. Results were considered significant when  $P < 0.05$ .

## Results

The results of general and obstetric maternal characteristics according to pre-pregnancy BMI are reported in Table 1. The maternal age was significantly lower in the underweight

**Table 1** General and obstetric characteristics of mothers according to pre-pregnancy BMI

|                                       | Pre-pregnancy BMI       |                         |                         |                         | P-value             |
|---------------------------------------|-------------------------|-------------------------|-------------------------|-------------------------|---------------------|
|                                       | Underweight (n = 111)   | Normal weight (n = 363) | Overweight (n = 67)     | Obese (n = 67)          |                     |
| Gestational period at baseline (week) | 27.8 ± 4.6 <sup>a</sup> | 26.3 ± 4.2              | 26.1 ± 3.7              | 27.3 ± 5.0              | 0.060 <sup>b</sup>  |
| Age (years)                           | 30.7 ± 3.6 <sup>a</sup> | 32.3 ± 4.0 <sup>b</sup> | 32.8 ± 3.7 <sup>b</sup> | 32.9 ± 3.8 <sup>b</sup> | <0.001              |
| <i>Educational years</i>              |                         |                         |                         |                         |                     |
| ≤12                                   | 17 (17.0) <sup>c</sup>  | 56 (17.3)               | 16 (25.8)               | 30 (50.8)               | <0.001 <sup>d</sup> |
| >12                                   | 83 (83.0)               | 268 (82.7)              | 46 (74.2)               | 29 (49.2)               |                     |
| <i>Monthly income level (\$)</i>      |                         |                         |                         |                         |                     |
| ≤1800                                 | 14 (14.1)               | 41 (12.8)               | 11 (17.7)               | 19 (32.8)               | 0.002               |
| >1800                                 | 85 (85.9)               | 279 (87.2)              | 51 (82.3)               | 39 (67.2)               |                     |
| <i>Employment status</i>              |                         |                         |                         |                         |                     |
| Yes                                   | 33 (32.4)               | 126 (39.7)              | 28 (45.2)               | 11 (20.0)               | 0.014               |
| No                                    | 69 (67.6)               | 191 (60.3)              | 34 (54.8)               | 44 (80.0)               |                     |
| Number of family members (person)     | 2.7 ± 1.0               | 2.7 ± 0.9               | 3.0 ± 1.1               | 3.0 ± 1.3               | 0.076               |
| Total number of pregnancies           | 1.9 ± 1.1 <sup>a</sup>  | 2.2 ± 1.2 <sup>ab</sup> | 2.0 ± 1.0 <sup>ab</sup> | 2.4 ± 1.3 <sup>b</sup>  | 0.025               |
| <i>Morning sickness</i>               |                         |                         |                         |                         |                     |
| Yes                                   | 45 (50.0)               | 119 (40.8)              | 36 (62.1)               | 21 (42.0)               | 0.018               |
| No                                    | 45 (50.0)               | 173 (59.2)              | 22 (37.9)               | 29 (58.0)               |                     |

Abbreviation: BMI, body mass index. BMI ( $\text{kg m}^{-2}$ ) categories according to the Asia-Pacific standard: underweight (<18.5), normal weight (18.5–22.9), overweight (23.0–24.9), obese ( $\geq 25$ ). <sup>a</sup>Mean ± s.d. <sup>b</sup>P-value by analysis of variance. <sup>c</sup>N (%). <sup>d</sup>P-value by  $\chi^2$ -test. Values followed by different alphabets within the same row are significantly different at  $P < 0.05$  by Tukey's test.

**Table 2** Maternal anthropometric characteristics according to pre-pregnancy BMI

|  | Pre-pregnancy BMI        |                           |                          |                          | P-value            |
|--|--------------------------|---------------------------|--------------------------|--------------------------|--------------------|
|  | Underweight (n = 111)    | Normal weight (n = 363)   | Overweight (n = 67)      | Obese (n = 67)           |                    |
| Height (cm)                              | 162.8 ± 4.6 <sup>b</sup> | 161.3 ± 4.7 <sup>ab</sup> | 161.0 ± 4.2 <sup>a</sup> | 160.1 ± 4.8 <sup>a</sup> | 0.002 <sup>b</sup> |
| Pre-pregnancy weight (kg)                | 46.8 ± 3.2 <sup>a</sup>  | 53.2 ± 4.1 <sup>b</sup>   | 61.7 ± 3.6 <sup>c</sup>  | 71.1 ± 8.1 <sup>d</sup>  | <0.001             |
| Pre-pregnancy BMI ( $\text{kg m}^{-2}$ ) | 17.6 ± 0.7 <sup>a</sup>  | 20.4 ± 1.2 <sup>b</sup>   | 23.8 ± 0.5 <sup>c</sup>  | 27.7 ± 2.5 <sup>d</sup>  | <0.001             |
| Body weight at delivery (kg)             | 60.5 ± 6.0 <sup>a</sup>  | 66.9 ± 6.5 <sup>b</sup>   | 73.4 ± 6.2 <sup>c</sup>  | 81.7 ± 9.3 <sup>d</sup>  | <0.001             |

Abbreviation: BMI, body mass index. BMI ( $\text{kg m}^{-2}$ ) categories according to the Asia-Pacific standard: see Table 1. <sup>a</sup>Mean ± s.d. <sup>b</sup>P-value by analysis of variance. Values followed by different alphabets within the same row are significantly different at  $P < 0.05$  by Tukey test.

group than the other groups ( $P < 0.001$ ). The percentage of subjects with less than 12 years of education was significantly higher in the obese group than in the other groups. The percentage of subjects with monthly income below \$1800 was significantly higher in the obese group than in the other groups. Furthermore, the obese group had a higher rate of unemployment than the other groups ( $P < 0.05$ ). Therefore, the obese group had an overall lower education level ( $P < 0.001$ ), lower income level and higher rate of unemployment ( $P < 0.05$ ).

The risk of obesity increased with increasing total number of pregnancies. The percentage of women experiencing morning sickness was significantly higher in the overweight group than in the other groups ( $P < 0.05$ ).

The results of maternal anthropometric characteristics according to pre-pregnancy BMI are reported in Table 2. Maternal height in the underweight group was significantly ( $P < 0.05$ ) taller than the overweight and obese groups.

Pre-pregnancy weights and BMIs were significantly ( $< 0.001$ ) different among the groups.

The results of maternal health-related habits with regard to pre-pregnancy BMI are reported in Table 3. Most of the pregnant women quit smoking and drinking alcohol when they recognized their pregnancy. No significant differences were found in frequency of coffee consumption among the groups. The frequency of pre-pregnancy weight reduction attempts was significantly high in the obese group ( $P < 0.05$ ) than in the other groups. The percentages of subjects who reported high stress levels were significantly higher in the overweight and obese groups than in the underweight and normal weight groups ( $P < 0.001$ ).

The results of maternal dietary habits according to pre-pregnancy BMI are reported in Table 4. The normal weight group showed higher frequencies of breakfast consumption and proper meal size than the other groups ( $P < 0.05$ ). No significant differences were found in meal frequency,

**Table 3** Maternal health-related habits according to pre-pregnancy BMI

|  | Pre-pregnancy BMI      |                         |                     |                | P-value <sup>a</sup> |
|--|------------------------|-------------------------|---------------------|----------------|----------------------|
|  | Underweight (n = 111)  | Normal weight (n = 363) | Overweight (n = 67) | Obese (n = 67) |                      |
| <i>Smoking</i>                                   |                        |                         |                     |                |                      |
| Non-smoker                                       | 88 (86.3) <sup>b</sup> | 287 (91.1)              | 56 (90.3)           | 48 (82.8)      | 0.197                |
| Ex-smoker  | 14 (13.7)              | 28 (8.9)                | 6 (9.7)             | 10 (17.2)      |                      |
| Current smoker                                   | 0 (0.0)                | 0 (0.0)                 | 0 (0.0)             | 0 (0.0)        |                      |
| <i>Alcohol drinking</i>                          |                        |                         |                     |                |                      |
| Non-drinker                                      | 67 (65.7)              | 202 (63.9)              | 34 (54.0)           | 34 (58.6)      | 0.698                |
| Ex-drinker                                       | 35 (34.3)              | 113 (35.8)              | 29 (46.0)           | 24 (41.4)      |                      |
| Current drinker                                  | 0 (0.0)                | 1 (0.3)                 | 0 (0.0)             | 0 (0.0)        |                      |
| <i>Frequency of coffee drinking</i>              |                        |                         |                     |                |                      |
| No   | 42 (41.6)              | 133 (41.4)              | 25 (40.3)           | 19 (32.2)      | 0.553                |
| 1–2 per week                                     | 35 (34.7)              | 87 (27.1)               | 16 (25.8)           | 15 (25.4)      |                      |
| 3–4 per week                                     | 15 (14.9)              | 70 (21.8)               | 14 (22.6)           | 16 (27.1)      |                      |
| > 5 per week                                     | 9 (8.9)                | 31 (9.7)                | 7 (11.3)            | 9 (15.3)       |                      |
| <i>Stress<sup>c</sup></i>                        |                        |                         |                     |                |                      |
| Low  | 84 (83.2)              | 269 (83.5)              | 40 (64.5)           | 38 (64.4)      | <0.001               |
| High   | 17 (16.8)              | 53 (16.5)               | 22 (35.5)           | 21 (35.6)      |                      |
| <i>Pre-pregnancy weight reduction attempt</i>    |                        |                         |                     |                |                      |
| Yes  | 7 (8.0)                | 69 (23.8)               | 18 (31.0)           | 23 (46.9)      | <0.001               |
| No   | 80 (92.0)              | 221 (76.2)              | 40 (69.0)           | 26 (53.1)      |                      |
| <i>Weight reduction attempt during pregnancy</i> |                        |                         |                     |                |                      |
| Yes  | 4 (4.6)                | 9 (3.1)                 | 3 (5.2)             | 3 (6.0)        | 0.714                |
| No   | 83 (95.4)              | 277 (96.9)              | 55 (94.8)           | 47 (94.0)      |                      |
| <i>Physical activity<sup>d</sup></i>             |                        |                         |                     |                |                      |
| Light  | 62 (69.7)              | 185 (65.4)              | 39 (67.2)           | 33 (68.8)      | 0.641                |
| Moderate   | 21 (23.6)              | 88 (31.1)               | 18 (31.0)           | 13 (27.1)      |                      |
| Heavy  | 6 (6.7)                | 10 (3.5)                | 1 (1.7)             | 2 (4.2)        |                      |
| <i>Regular exercise</i>                          |                        |                         |                     |                |                      |
| ≥ 3 times per week                               | 16 (18.0)              | 64 (22.5)               | 9 (15.8)            | 15 (31.3)      | 0.206                |
| < 2 times per week                               | 73 (82.0)              | 221 (77.5)              | 48 (84.2)           | 33 (68.8)      |                      |

Abbreviation: BMI, body mass index. BMI (kg m<sup>-2</sup>) categories according to the Asia-Pacific standard: see Table 1. <sup>a</sup>P-value by  $\chi^2$ -test. <sup>b</sup>N (%). <sup>c</sup>low < 12, high ≥ 12. <sup>d</sup>Light: walk and stand a day less than 2 h, office job and housework; moderate: walk and stand a day for 2–4 h, marketer and teacher; heavy: walk and stand a day for 4–6 h, construction industry and tennis.

regularity of mealtimes or frequency of eating out among the groups.

The pregnancy outcomes of mothers and neonates for all pre-pregnancy BMI categories are reported in Table 5. In the overweight and obese groups, the amount of weight gained during pregnancy was significantly ( $P < 0.001$ ) less than the underweight and normal weight groups. In the overweight and obese groups, gestational age was significantly shorter than in the underweight and normal weight groups ( $P < 0.001$ ). The percentage of women delivering preterm was significantly higher in the overweight and obese groups ( $P < 0.006$ ) than in the underweight and normal weight groups. The frequencies of LBW (< 2.5 kg) and macrosomia (≥ 4 kg) were significantly higher in the overweight and obese groups ( $P < 0.001$ ) than in the other groups. The neonates born to obese mothers were significantly shorter (cm) than those born to mothers of normal weight ( $P < 0.02$ ).

In the normal group (mean birth weight; 3.29 kg), birth weight was significantly ( $P < 0.001$ ) higher than in the preterm group (mean 2.13 kg), and the gestational age of LBW neonates (33.29 weeks) was significantly ( $P < 0.001$ ) shorter than in the normal (38.80 weeks) and macrosomic (39.71 weeks) neonates (data not shown).

The results of biochemical markers and cervical length according to pre-pregnancy BMI category are reported in Table 6. In the obese group, serum folate levels were significantly lower than in the underweight group ( $P < 0.05$ ). In the obese group, serum hs-CRP levels were significantly higher than in the other groups ( $P < 0.001$ ), but serum homocysteine levels, cervical lengths and fFN levels did not significantly differ between groups.

The results of ORs and 95% CI for preterm delivery, LBW and macrosomia according to pre-pregnancy BMI are reported in Table 7. The risk of delivering a preterm was

**Table 4** Maternal dietary habits according to pre-pregnancy BMI

|   | Pre-pregnancy BMI     |                         |                     |                | P-value <sup>a</sup> |
|---|-----------------------|-------------------------|---------------------|----------------|----------------------|
|   | Underweight (n = 111) | Normal weight (n = 363) | Overweight (n = 67) | Obese (n = 67) |                      |
| <i>Meal frequency (times per day)</i>                       |                       |                         |                     |                |                      |
| Once  | 0 (0.0) <sup>b</sup>  | 1 (0.3)                 | 1 (1.7)             | 0 (0.0)        | 0.693                |
| Twice   | 29 (29.9)             | 68 (22.0)               | 17 (28.8)           | 12 (23.1)      |                      |
| Three   | 59 (60.8)             | 216 (69.9)              | 37 (62.7)           | 34 (65.4)      |                      |
| Four  | 3 (3.1)               | 9 (2.9)                 | 1 (1.7)             | 1 (1.9)        |                      |
| Irregular   | 6 (6.2)               | 15 (4.9)                | 3 (5.1)             | 5 (9.6)        |                      |
| <i>Breakfast frequency (days per week)</i>                  |                       |                         |                     |                |                      |
| 0–1   | 20 (22.2)             | 32 (11.0)               | 11 (19.0)           | 10 (20.0)      | 0.013                |
| 2–3   | 11 (12.2)             | 29 (9.9)                | 13 (22.4)           | 3 (6.0)        |                      |
| 4–5   | 12 (13.3)             | 64 (21.9)               | 10 (17.2)           | 9 (18.0)       |                      |
| ≥6  | 47 (52.2)             | 167 (57.2)              | 24 (41.4)           | 28 (56.0)      |                      |
| <i>Regularity of meal time (three meals a day per week)</i> |                       |                         |                     |                |                      |
| > 6   | 31 (34.4)             | 103 (35.6)              | 15 (25.9)           | 20 (40.8)      | 0.750                |
| 4–5   | 47 (52.2)             | 148 (51.2)              | 36 (62.1)           | 24 (49.0)      |                      |
| < 2–3   | 12 (13.3)             | 38 (13.1)               | 7 (12.1)            | 5 (10.2)       |                      |
| <i>Amount of meal<sup>c</sup></i>                           |                       |                         |                     |                |                      |
| Overeat   | 20 (22.2)             | 56 (19.2)               | 11 (19.0)           | 10 (20.0)      | 0.048                |
| Proper  | 68 (75.5)             | 230 (79.0)              | 41 (70.6)           | 36 (72.0)      |                      |
| A little  | 2 (2.2)               | 5 (1.7)                 | 6 (10.3)            | 4 (8.0)        |                      |
| <i>Eating out</i>   |                       |                         |                     |                |                      |
| ≥2 per day  | 2 (2.2)               | 12 (4.2)                | 1 (1.8)             | 1 (2.1)        | 0.487                |
| 1 per day   | 12 (13.3)             | 48 (16.8)               | 9 (15.8)            | 4 (8.5)        |                      |
| > 1 per week  | 67 (74.4)             | 174 (60.8)              | 40 (70.2)           | 31 (66.0)      |                      |
| > 1 per month   | 6 (6.7)               | 32 (11.2)               | 5 (8.8)             | 8 (17.0)       |                      |

Abbreviation: BMI, body mass index. BMI ( $\text{kg m}^{-2}$ ) categories according to the Asia-Pacific standard: see Table 1. <sup>a</sup>P-value by  $\chi^2$ -test. <sup>b</sup>N (%). <sup>c</sup>Amount of meal size was measured by self report.

**Table 5** Pregnancy outcomes of mothers and neonates according to pre-pregnancy BMI

|  | Pre-pregnancy BMI          |                         |                     |                | P-value            |
|--|----------------------------|-------------------------|---------------------|----------------|--------------------|
|  | Underweight (n = 111)      | Normal weight (n = 363) | Overweight (n = 67) | Obese (n = 67) |                    |
| Maternal weight gain during pregnancy (kg) | 13.72 ± 4.52b <sup>a</sup> | 13.71 ± 4.83b           | 11.59 ± 5.04a       | 10.36 ± 4.83a  | <0.001b            |
| <i>Gestational age (weeks)</i>             |                            |                         |                     |                |                    |
| < 37                                       | 38.60 ± 2.35c              | 38.29 ± 2.75bc          | 37.18 ± 3.82ab      | 36.88 ± 3.73a  | <0.001             |
| ≥ 37                                       | 17 (17.0) <sup>c</sup>     | 59 (18.4)               | 18 (31.6)           | 22 (33.8)      | 0.006 <sup>d</sup> |
| Neonates weight (kg)                       | 3.05 ± 0.53                | 3.09 ± 0.60             | 2.94 ± 0.84         | 2.93 ± 0.77    | 0.170              |
| < 2.5                                      | 10 (10.0)                  | 44 (13.9)               | 16 (28.6)           | 17 (26.6)      | <0.001             |
| 2.5–3.99                                   | 89 (89.0)                  | 265 (83.6)              | 37 (66.1)           | 42 (65.6)      |                    |
| ≥ 4  | 1 (1.0)                    | 8 (2.5)                 | 3 (5.4)             | 5 (7.8)        |                    |
| Length (cm)                                | 48.96 ± 3.08ab             | 49.09 ± 3.60b           | 48.34 ± 4.99ab      | 47.46 ± 5.48a  | 0.020              |

Abbreviation: BMI, body mass index. BMI ( $\text{kg m}^{-2}$ ) categories according to the Asia-Pacific standard: see Table 1. <sup>a</sup>Mean ± s.d. <sup>b</sup>P-value by analysis of variance. <sup>c</sup>N (%). <sup>d</sup>P-value by  $\chi^2$ -test. Values followed by different alphabets within the same row are significantly different at  $P < 0.05$  by Tukey test.

increased in the overweight group (OR = 2.85, CI = 1.20–6.74) and the risk of delivering a LBW infant was increased in the overweight (OR = 5.07, CI = 1.76–14.63) and obese groups (OR = 4.49, CI = 1.54–13.13). The risk of delivering a macrosomia was increased with increasing pre-pregnancy BMI ( $P$  for trend = 0.010).

## Discussion

In this study, obese mothers were characterized by low educational levels and income levels, and were more likely to be unemployed. Another group of researchers<sup>26</sup> reported that repeated exposure to the negative environments

**Table 6** Biochemical markers and cervical length according to pre-pregnancy BMI

|   | Pre-pregnancy BMI             |                                |                                |                              | P-value            |
|---|-------------------------------|--------------------------------|--------------------------------|------------------------------|--------------------|
|   | Underweight (n = 111)         | Normal weight (n = 363)        | Overweight (n = 67)            | Obese (n = 67)               |                    |
| Homocysteine ( $\mu\text{mol l}^{-1}$ ) | 4.98 $\pm$ 1.58 <sup>a</sup>  | 4.80 $\pm$ 1.65                | 5.03 $\pm$ 1.90                | 5.02 $\pm$ 2.06              | 0.681 <sup>b</sup> |
| Folate ( $\text{ng ml}^{-1}$ )          | 12.01 $\pm$ 6.19 <sup>b</sup> | 10.36 $\pm$ 5.72 <sup>ab</sup> | 10.38 $\pm$ 5.21 <sup>ab</sup> | 8.09 $\pm$ 4.57 <sup>a</sup> | 0.008              |
| Hs-CRP ( $\text{mg dl}^{-1}$ )          | 0.28 $\pm$ 0.65 <sup>a</sup>  | 0.29 $\pm$ 0.45 <sup>a</sup>   | 0.33 $\pm$ 0.27 <sup>a</sup>   | 0.65 $\pm$ 0.80 <sup>b</sup> | 0.001              |
| Cervical length (cm)                    | 3.67 $\pm$ 0.87               | 3.87 $\pm$ 0.79                | 3.96 $\pm$ 0.84                | 3.73 $\pm$ 1.01              | 0.126              |
| <i>Fetal fibronectin</i>                |                               |                                |                                |                              |                    |
| Negative                                | 50 (96.2) <sup>d</sup>        | 189 (95.0)                     | 35 (92.1)                      | 31 (88.6)                    | 0.410 <sup>d</sup> |
| Positive                                | 2 (3.8)                       | 10 (5.0)                       | 3 (7.9)                        | 4 (11.4)                     |                    |

Abbreviations: BMI, body mass index; Hs-CRP, high sensitivity C-reactive protein. BMI ( $\text{kg m}^{-2}$ ) categories according to the Asia-Pacific standard: see Table 1. <sup>a</sup>Mean  $\pm$  s.d. <sup>b</sup>P-value by analysis of variance. <sup>c</sup>N (%). <sup>d</sup>P-value by  $\chi^2$ -test. Values followed by different alphabets within the same row are significantly different at  $p < 0.05$  by Tukey test.

**Table 7** ORs and 95% CIs for preterm delivery, LBW and macrosomia according to pre-pregnancy BMI

|   | Pre-pregnancy BMI |                   |                   |                   | P-value            |
|---|-------------------|-------------------|-------------------|-------------------|--------------------|
|   | Underweight       | Normal-weight     | Overweight        | Obese             |                    |
| <i>Preterm delivery (&lt; 37 weeks)</i> |                   |                   |                   |                   |                    |
| No. of cases per controls               | 17/83             | 59/261            | 18/39             | 22/43             | 0.002 <sup>a</sup> |
| OR (95% CI) <sup>b</sup>                | 1                 | 0.91 (0.45–1.87)  | 2.85 (1.20–6.74)  | 2.29 (0.97–5.42)  |                    |
| <i>LBW (&lt; 2.5 kg)</i>                |                   |                   |                   |                   |                    |
| No. of cases per controls               | 10/89             | 44/265            | 16/37             | 17/42             | <0.001             |
| OR (95% CI) <sup>c</sup>                | 1                 | 1.61 (0.64–4.07)  | 5.07 (1.76–14.63) | 4.49 (1.54–13.13) |                    |
| <i>Macrosomia (&gt; 4 kg)</i>           |                   |                   |                   |                   |                    |
| No. of cases per controls               | 1/89              | 8/265             | 3/37              | 5/42              | 0.010              |
| OR (95% CI) <sup>c</sup>                | 1                 | 1.97 (0.23–16.61) | 4.20 (0.36–48.46) | 7.82 (0.85–71.51) |                    |

Abbreviations: BMI, body mass index; CI, confidence interval; LBW, low-birth weight; OR, odds ratio. Pre-pregnancy BMI cutoff categories according to the Asia-Pacific standard: 1 = underweight group (< 18.5), 2 = normal-weight group (18.5–22.9), 3 = overweight group (23.0–24.9), 4 = obese group ( $\geq 25$ ). <sup>a</sup>P-value for linear trend test. <sup>b</sup>ORs and 95% CI were analyzed by logistic regression. OR was adjusted for maternal age, stress. <sup>c</sup>Models adjusted for maternal age, pregnancy experiences.

associated with low educational level and poor socioeconomic status leads to worse health outcomes. People of low socioeconomic status may be at increased risk of obesity because of the higher frequencies of unhealthy behaviors.

We found that total number of pregnancies was positively correlated with pre-pregnancy BMI. Other studies<sup>27,28</sup> also reported an increased maternal body weight with parity and suggested a strong relationship between parity and weight gain in women.

The percentage of mothers who had morning sickness was higher in the overweight group than in the normal weight group. Other researchers have also reported that the risk of morning sickness increases with the increasing body weight.<sup>29</sup>

In our study, stress levels were significantly higher in the overweight and obese mothers than in the mothers who were underweight or normal weight. A previous study of mothers of African descent<sup>30</sup> reported that higher stress levels were associated with greater weight gain. These results

indicate that women who have higher pre-pregnancy BMI may be expected to experience higher levels of pregnancy-related stress.

Women with unhealthy dietary habits are more likely to be obese.<sup>31</sup> In this study, subjects of normal weight were more likely to eat breakfast and to consume meals of appropriate size than subjects in the other groups; therefore, normal weight subjects exhibited more desirable dietary habits than underweight, overweight or obese subjects.

We found that weight gain during pregnancy in the overweight and obese groups was significantly lower than in the underweight and normal groups. This result is in agreement with a previous study which reported that weight gain during pregnancy decreased with increasing BMI.<sup>32</sup> In this study, we found that the average length of neonates delivered by obese mothers was significantly shorter than the average length of neonates delivered by mothers of normal weight, because of the high rates of preterm and LBW delivery in the obese group.



In this study, serum folate levels were significantly lower in the obese group than in the underweight group, and serum hs-CRP levels were significantly higher in the obese group than in the other groups. Other study have demonstrated that pregnant women delivering preterm infants tend to have lower concentration of folate in serum,<sup>33</sup> and that obese women are at increased risk of delivering infants with neural tube defects.<sup>34</sup> Dietary folate supplementation (400 mcg daily) is associated with a 35% decrease in the risk of preterm birth among women of childbearing age, especially those who are obese.<sup>35</sup> Obese women of childbearing age should be encouraged to take a folate supplement daily and should receive education regarding the prevention of neural tube defects. It is known that serum CRP levels increase with increasing BMI,<sup>36</sup> and that an elevated concentration of maternal serum CRP in early pregnancy is associated with an increased risk of preterm delivery.<sup>15</sup>

In this study, high pre-pregnancy BMI increased the risk of preterm delivery, LBW delivery and macrosomia. Khashan and Kenny<sup>6</sup> reported that the risk of preterm delivery was reduced by almost 10% for overweight (RR=0.89, CI=0.83–0.95) and obese women (RR=0.90, CI=0.84–0.97), but was increased in underweight women (RR=1.33, CI=1.16–1.53). Frederick *et al.*<sup>1</sup> reported that the risk of delivering LBW infants in the underweight group was increased by 51 percent (RR=1.51, CI=1.02–2.25) and that increased BMI is related to an increased risk of macrosomia. These results conflict with our own; however, our results indicate that the concentration of serum folate was significantly lower in the obese group and that the concentration of hs-CRP was significantly higher in the obese group. The relationships that we detected between low folate status and preterm delivery<sup>33</sup> and low folate status and LBW infant delivery<sup>37</sup> have been reported previously. Elevated concentrations of maternal serum CRP are associated with increased risk of preterm delivery (OR=2.15, CI=0.85–5.42), and the percentage of preterm deliveries are significantly higher in obese mothers than in mothers of normal weight.<sup>15</sup> Therefore, the increased risk of preterm delivery and the risk of delivering a LBW infant in the obese group that we observed may be explained by low-serum folate and high-hs-CRP levels in our results.

In conclusion, pregnancy outcomes are influenced by pre-pregnancy BMI. Maintaining normal pre-pregnancy BMI reduces the risk of delivering preterm, LBW and macrosomic infants. Women of childbearing age should try to access education, such as books or web-based material, about healthy eating and exercising to maintain a normal weight before becoming pregnant or between pregnancies. Therefore women of childbearing age need to attend to their health and well-being before pregnancy for the health of their infant. Also, obese women of childbearing age who plan to have children should be encouraged to take a folate supplement daily.

## Conflict of interest

The authors declare no conflict of interest.

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## References

- 1 Frederick IO, Williams MA, Sales AE, Martin DP, Killien M. Pre-pregnancy body mass index, gestational weight gain, and other maternal characteristics in relation to infant birth weight. *Matern Child Health J* 2008; **12**: 557–567.
- 2 Godfrey KM, Barker DJ. Fetal nutrition and adult disease. *Am J Clin Nutr* 2000; **71**: 1344s–1352s.
- 3 Korean Statistical Information Service. *Population Trend Survey* Seoul 2008; www.kosis.kr.
- 4 World Health Organization. WHO: recommended definitions, terminology and format for statistical tables related to the perinatal period and use of a new certificate for cause of perinatal deaths. Modifications recommended by FIGO as amended October 14, 1976. *Acta Obstet Gynecol Scand* 1977; **56**: 247–253.
- 5 Johnson JW. Obstetric aspects of preterm delivery. *Clin Obstet Gynecol* 1980; **23**: 15–16.
- 6 Khashan AS, Kenny LC. The effects of maternal body mass index on pregnancy outcome. *Eur J Epidemiol* 2009; **24**: 697–705.
- 7 Johnson TS, Rottier KJ, Luellwitz A, Kirby RS. Maternal prepregnancy body mass index and delivery of a preterm infant in Missouri 1998–2000. *Public Health Nurs* 2009; **26**: 3–13.
- 8 Burke G, Robinson K, Refsum H, Stuart B, Drumm J, Graham I. Intrauterine growth retardation, perinatal death, and maternal homocysteine levels. *N Engl J Med* 1992; **326**: 69–70.
- 9 Vollset SE, Refsum H, Irgens LM, Emblem BM, Tverdal A, Gjessing HK *et al.* Plasma total homocysteine, pregnancy complications, and adverse pregnancy outcomes: the Hordaland Homocysteine Study. *Am J Clin Nutr* 2000; **71**: 962–968.
- 10 Leeda M, Riyazi N, de Vries JI, Jakobs C, van Geijn HP, Dekker GA. Effects of folic acid and vitamin B6 supplementation on women with hyperhomocysteinemia and a history of preeclampsia or fetal growth restriction. *Am J Obstet Gynecol* 1998; **179**: 135–139.
- 11 Refsum H. Folate, vitamin B12 and homocysteine in relation to birth defects and pregnancy outcome. *Br J Nutr* 2001; **85** (Suppl 2): S109–S113.
- 12 Pannacciulli N, Cantatore FP, Minenna A, Bellacicco M, Giorgino R, De Pergola G. C-reactive protein is independently associated with total body fat, central fat, and insulin resistance in adult women. *Int J Obes Relat Metab Disord* 2001; **25**: 1416–1420.
- 13 Morrison JC, Allbert JR, McLaughlin BN, Whitworth NS, Roberts WE, Martin RW. Oncofetal fibronectin in patients with false labor as a predictor of preterm delivery. *Am J Obstet Gynecol* 1993; **168**: 538–542.
- 14 Murakawa H, Utumi T, Hasegawa I, Tanaka K, Fuzimori R. Evaluation of threatened preterm delivery by transvaginal ultrasonographic measurement of cervical length. *Obstet Gynecol* 1993; **82**: 829–832.
- 15 Lohsoonthorn V, Qiu C, Williams MA. Maternal serum C-reactive protein concentrations in early pregnancy and subsequent risk of preterm delivery. *Clin Biochem* 2007; **40**: 330–335.
- 16 Holesmes T, Rache R. The Social readjustment rating scale. *J Psychosom Reprod Med* 1967; **11**: 213–218.

- 17 Kim YJ, Lee SS. The relation of maternal stress with nutrients intake and pregnancy outcome in pregnant women. *Korean J Nutr* 2008; **41**: 776–785.
- 18 Wen CP, Cheng TYD, Tsai SP, Chan HT, Hsu HL, Hsu CC *et al*. Are Asians at greater mortality risks for being overweight than Caucasians? Redefining obesity for Asians. *Public Health Nutr* 2009; **12**: 497–506.
- 19 Varis K, Sipponen P, Laxén F, Samloff IM, Huttunen JK, Taylor PR *et al*. Implications of serum pepsinogen I in early endoscopic diagnosis of gastric cancer and dysplasia. *Scand J Gastroenterol* 2000; **35**: 950–956.
- 20 Sauberlich HE. *Laboratory tests for the assessment of nutritional status*. 2nd ed. CRC Press: Boca Raton, FL, USA, 1999; p115: p345–348.
- 21 Zeitlin A, Frishman WH, Chang CJ. The association of vitamin B12 and folate blood levels with mortality and cardiovascular morbidity incidence in the old old: the Bronx aging study. *Am J Ther* 1997; **4**: 275–281.
- 22 Otsuji S, Shibata H, Ueda M. Turbidimetric immunoassay of serum C-reactive protein. *Clin Chem* 1982; **28**: 2121–2124.
- 23 Roberts WL, Moulton L, Law TC, Farrow G, Cooper-Anderson M, Savory J *et al*. Evaluation of nine automated high-sensitivity C-reactive protein methods: implications for clinical and epidemiological applications. Part 2. *Clin Chem* 2001; **47**: 418–425.
- 24 Jeon KS, Lee TH, Koh MH, Won SY, Lee HW, Lee DH *et al*. Clinical efficacy of cervicovaginal fetal fibronectin in induction of labor. *Korean J Obstet Gynecol* 2002; **45**: 220–225.
- 25 Iams JD, Goldenberg RL, Meis PJ, Mercer BM, Moawad A, Das A *et al*. The length of the cervix and the risk of spontaneous premature delivery. *N Engl J Med* 1996; **334**: 567–572.
- 26 Zhang Q, Wang Y. Trends in the association between obesity and socioeconomic status in U.S. adult: 1971 to 2000. *Obes Res* 2004; **12**: 1622–1632.
- 27 Rossner S, Ohlin A. Pregnancy as a risk factor for obesity: lessons from the Stockholm Pregnancy and Weight Development Study. *Obes Res* 1995; **3**: 267s–275s.
- 28 Ohlin A, Rossner S. Factors related to body weight changes during and after pregnancy: The Stockholm Pregnancy Weight Development Study. *Obes Res* 1996; **4**: 271–276.
- 29 Depue RH, Bernstein L, Ross RK, Judd HL, Henderson BE. Hyperemesis gravidarum in relation to estradiol levels, pregnancy outcome, and other maternal factors: a seroepidemiologic study. *Am J Obstet Gynecol* 1987; **156**: 1137–1141.
- 30 Fowler-Brown AG, Bennett GG, Goodman MS, Wee CC, Corbie-Smith GM, James SA. Psychosocial stress and 13-year BMI change among blacks: the Pitt County Study. *Obesity* 2009; **17**: 2106–2109.
- 31 Ko GT, Chan JC, Tong SD, Chan AW, Wong PT, Hui SS *et al*. Associations between dietary habits and risk factors for cardiovascular diseases in a Hong Kong Chinese working population the Better Health for Better Hong Kong health promotion campaign. *Asia Pac J Clin Nutr* 2007; **16**: 757–765.
- 32 Chu SY, Callaghan WM, Bish CL, D'Angelo D. Gestational weight gain by body mass index among US women delivering live births, 2004–2005: fueling future obesity. *Am J Obstet Gynecol* 2009; **200**: 271–277.
- 33 Siega-Riz AM, Savitz DA, Zeisel SH, Thorp JM, Herring A. Second trimester folate status and preterm birth. *Am J Obstet Gynecol* 2004; **191**: 1851–1857.
- 34 Shaw GM, Velie EM, Schaffer D. Increased risk for neural tube defects among offspring of obese women. *JAMA* 1996; **275**: 1093–1096.
- 35 Case AP, Ramadhani TA, Canfield MA, Beverly L, Wood R. Folic acid supplementation among diabetic, overweight, or obese women of childbearing age. *J Obstet Gynecol Neonatal Nurs* 2007; **36**: 335–341.
- 36 Madan JC, Davis JM, Craig WY, Collins M, Allan W, Quinn R *et al*. Maternal obesity and markers of inflammation in pregnancy. *Cytokine* 2009; **47**: 61–64.
- 37 Scholl TO, Hediger ML, Schall JI, Khoo CS, Fischer RL. Dietary and serum folate: their influence on the outcome of pregnancy. *Am J Clin Nutr* 1996; **63**: 520–525.



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