Body mass index and hemoglobin concentration have an additive effect on blood pressure among pregnant women in Guangxi, China

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Abstract

**Background:** Body mass index (BMI) and hemoglobin (Hb) are positively associated with hypertensive disorders in pregnancy. The aim of this study was to estimate a potential interaction between high BMI and high Hb concentrations on systolic blood pressure (SBP) and diastolic blood pressure (DBP) among pregnant women.

**Methods:** We recruited 4497 single-birth women aged 18–43 years who received routine antenatal care from three hospitals of Guigang, Guangxi, China. Relevant data were derived from medical records of each woman. Multivariable linear regression was used to evaluate the association of high BMI and high Hb concentrations with SBP and DBP by trimesters of pregnancy.

**Results:** In multivariable analyses, BMI was positively associated with SBP throughout all trimesters, and higher Hb concentrations was associated with increased SBP only in the first trimester (all \( P \) for trend <0.05). BMI and Hb concentrations were positively associated with DBP in the first and third trimesters (all \( P \) for trend <0.05). The average differences in SBP and DBP comparing women with high BMI and high Hb concentrations to those with non-high BMI and non-high Hb were 1.6 mmHg (95% CI: -0.3 to 3.5 mmHg) and 2.4 mmHg (95% CI: -0.1 to 4.8 mmHg) in the first trimester, 1.4 mmHg (95% CI: -1.4 to 4.2 mmHg) and 1.0 mmHg (95% CI: -1.7 to 3.7 mmHg) in the second trimester, and 2.9 mmHg (95% CI: 0.3 to 5.4 mmHg) and 3.5 mmHg (95% CI: 1.0 to 5.9 mmHg) in the third trimester, respectively.

**Conclusion:** Our findings suggest that high BMI and high Hb concentrations may have interactions of additive effects on increased SBP and DBP in late stages of pregnancy.
Keywords: body mass index; hemoglobin; blood pressure; systolic; diastolic
Background

High blood pressure during pregnancy contributes to the risks of not only adverse neonatal outcomes but also maternal deaths [1, 2]. Although the etiology of hypertensive disorders during pregnancy is not yet completely clear, maternal anthropometric measure such as high body mass index (BMI) in pregnancy has been reported to increase the risk of pregnancy-induced hypertension (PIH) or preeclampsia [3-6]. Similarly, several studies have shown that maternal hemoglobin (Hb) levels were positively associated with PIH [7-9]. Moreover, a review suggests that higher than normal hemoglobin concentrations should be regarded as an indicator of possible pregnancy complications [10]. Some of the above findings [4, 5, 7], however, may be limited because of small-size sample size or insufficient gestational weeks.

The mechanisms underlying the positive association of Hb levels with pregnancy blood pressure are incompletely understood, but previous evidences suggested that elevated Hb levels might impact hypertensive disorders in pregnant [7, 10, 11] as well as non-pregnant women [12] via hemoconcentration or increased blood viscosity, which is generally associated with both overall adiposity and abdominal adiposity [13]. Further, a population-based study, particularly on the association between Hb levels and BMI during pregnancy, showed that Hb levels were significantly associated with BMI in 561 pregnant women [14]. However, less is known about the combined effect of BMI and Hb levels on blood pressure in pregnancy. Thus, in this large sample study, we fully evaluated the potential interaction between high BMI and high Hb concentrations on systolic blood pressure (SBP) and diastolic blood pressure (DBP) in all
trimesters of pregnancy.

Methods

Study population

The present study was embedded in the antenatal care from three hospitals of Guigang, Guangxi Zhuang Autonomous Region, China during December 2007 to January 2011. The three hospitals were randomly selected from three stratifications including primary, secondary, and tertiary hospitals, respectively. A total of 5701 healthy women aged ≥18 years with singleton pregnancies who attended their first antenatal care at gestational weeks 10 to 16 were accumulatively enrolled, we excluded 41 in vitro fertilization and 1163 with incomplete data. Finally, 4497 eligible women aged 18–43 years were left to follow up with the routine antenatal visits. Gestational age was based on the first day of the last menstrual period, for 1169 women (26%) with neither a known first day of the last menstrual period nor a regular menstrual cycle, the ultrasound estimate was used at the first antenatal visit. Pregnancy was classified into the first, second, and third trimesters using gestational age: <14, 14–27, and 28–42 weeks, respectively.

The follow-up of study participants throughout pregnancy is shown in Figure 1. Of 4497 participants at study entry, 3472 women were in the first trimester, 1025 women were in the second trimester. With following up, 2986 women and 2261 women were left at the end of gestational weeks 24 and 36, respectively. All eligible participants provided written informed consent, the Guangxi Medical University Institutional Review Board approved the present
Data collection and laboratory measures

The three hospitals performed the same antenatal examination, laboratory procedure, and quality control. At the first antenatal visit, baseline information on maternal age, ethnicity, education, family income, residence, gestational age, parity, smoking, alcohol use, and folic acid supplement was based on interview questionnaires, anthropometric measures (e.g. body weight and height) and blood pressure were recorded through physical examinations. Blood pressure readings and body weight were prospectively recorded from the first to the last antenatal visit. Blood pressure was measured with Omron HEM 907 IntelliSense professional digital blood pressure monitor (Omron Healthcare Ltd., Dalian, China) using an averaging mode in a sitting position. After at least 5 minutes of rest, an appropriately sized upper arm cuff was applied to the right arm, the mean value of two blood pressure readings with a pause of 60 seconds between each measurement was recorded.

Fasting blood was repeatedly collected at the first antenatal visit, around gestational weeks 20, 24, 32, and 36. All samples were performed using the standard protocol for clinical laboratory tests. Hb concentration and hematocrit value in whole blood were performed with Beckman Coulter AcT 5 Diff hematology analyzer (Beckman Coulter Inc., Fullerton, USA), and were determined via cyanmethemoglobin method and micro-hematocrit method, respectively. The interassay coefficients of variation for Hb concentrations ranged from 3.1% to 8.9% throughout the study period. Serum total cholesterol, serum triglycerides, and plasma
glucose were measured using Hitachi 7170A or 7020 full-automatic biochemical analyzer (Hitachi Ltd., Tokyo, Japan).

**Definitions of variables**

BMI was calculated by dividing weight in kilograms by standing height that was measured at enrollment in meters squared (kg/m$^2$). BMI was divided into quartiles, high BMI was defined as being more than or equal to the highest quartile cutoff of BMI. High Hb concentration was defined as an Hb level of $\geq 13.0$ g/dL [15]. Diabetes mellitus was defined as a fasting glucose $\geq 126$ mg/dL, a non-fasting glucose $\geq 200$ mg/dL, or a self-report physician diagnosis, or current medication use.

Family income was the total combined family income including wages, salaries, self-employment, and the other source during the last 12 months. Urban residence was defined as urban districts, central or fringe areas of city or town with a population density higher than 1500/km$^2$. Parity was the numbers of times woman has given birth including stillbirths. Never smokers were defined as women who reported having smoked <100 cigarettes before the first antenatal visit. Current smokers were defined as women who had smoked $\geq 100$ cigarettes and reported that they were smoking now. Former smokers were defined as women who had smoked $\geq 100$ cigarettes but were not current smokers. Alcohol use was defined as women once consumed alcohol regardless of quantify and frequency from the first day of the last menstrual period to the first antenatal visit. Folic acid supplement was defined as women took a daily supplement of folic acid during 3 months before pregnancy to the first antenatal visit.
**Statistical analysis**

We evaluated separately the effects of BMI and Hb concentrations on blood pressure by trimesters of pregnancy. With respect to the statistical analyses of BMI, Hb concentrations, SBP, and DBP, the first measurements at study entry were used in the first trimester; the averages of two measurements around gestational weeks 20 and 24 were used in the second trimester; the averages of two measurements around gestational weeks 32 and 36 were used in the third trimester. All analyses were performed using Stata, version 12 (StataCorp LP, College Station, Texas).

BMI and Hb concentrations were categories into quartiles. First, we used multivariable linear regression to calculate the differences in SBP and DBP comparing quartiles 2-4 of BMI or Hb to the lowest quartile. Second, we evaluated the additive effects between high BMI and high Hb concentrations on SBP and DBP using multivariable linear regression. Third, using multivariable linear regression, we further estimated the multiplicative effects between BMI and Hb concentrations on SBP and DBP by including BMI, Hb concentrations, and BMI times Hb concentrations as continuous variables in models.

For the above multivariable regression, we used 3 levels of adjustment. Model 1 was adjusted for age (continuous) and ethnicity (Han, Zhuang, other). Model 2 was further adjusted for education (<12 years, ≥12 years), family income <US$ 3000 (yes, no), urban residence (yes, no), parity (0, 1, >1), smoking (never, former, current), alcohol use (yes, no), and folic acid supplement (yes, no). Model 3 was further adjusted for hematocrit (continuous), serum total
cholesterol (continuous), serum triglycerides (continuous), and diabetes mellitus (yes, no). Tests for linear trend were obtained by including the medians for each quartile of BMI and Hb as continuous variables in the regression models. We performed Wald tests to evaluate linear trend for the interaction using the *testparm* commands.

**Results**

The main characteristics of the study population by trimester are shown in Table 1. On average, the mean age of women by trimester ranged from 25.2 to 26.3 years. The means of BMI, Hb concentrations, SBP and DBP by trimester ranged from 22.9 to 26.5 kg/m$^2$, 11.7 to 12.5 g/dL, 107.0 to 112.8 mmHg and 66.4 to 73.8 mmHg, respectively. BMI increased progressively during pregnancy, however, Hb concentrations, SBP and DBP in the second trimester were lower than in the first and third trimesters.

The highest quartile cutoffs of BMI were 24.9 kg/m$^2$, 26.4 kg/m$^2$, and 28.7 kg/m$^2$ in the first, second, and third trimesters, respectively. In the first trimester, BMI and Hb were positively associated with both SBP and DBP (Figure 2). After adjustment for age and ethnicity, women with high BMI and high Hb had significantly increased differences for SBP (the average difference=2.0 mmHg, 95% CI: 0.3 to 3.8 mmHg) and DBP (the average difference=3.1 mmHg, 95% CI: 0.8 to 5.4 mmHg), compared to women with non-high BMI and non-high Hb (Table 2, model 1). In last multivariable-adjusted models, however, the differences in SBP and DBP became non-significant ($P$ for trend $>$0.05) (Table 2, model 3).

Only BMI was positively associated with SBP in the second trimester (Figure 2). We did
not further find significant differences in SBP or DBP depending on the interaction between high BMI and high Hb regardless of multivariable-adjusted models (Table 3, models 1-3). The average differences in SBP and DBP, comparing women with high BMI and high Hb to those with non-high BMI and non-high Hb, were 1.4 mmHg (95% CI: -1.4 to 4.2 mmHg) and 1.0 mmHg (95% CI: -1.7 to 3.7 mmHg), respectively (Table 3, model 3).

In the third trimester, BMI was positively with both SBP and DBP, but higher Hb was only associated with higher DBP (Figure 2). After adjustment for age and ethnicity, there was a progressive increase in the difference for SBP or DBP across categories of BMI and Hb (Table 4, models 1-3). Full adjustment for confounding did not materially affect this association. The average differences in SBP and DBP, comparing women with high BMI and high Hb to those with non-high BMI and non-high Hb, were 2.9 mmHg (95% CI: 0.3 to 5.4 mmHg) and 3.5 mmHg (95% CI: 1.0 to 5.9 mmHg), respectively (Table 4, model 3).

For the multiplicative effects, no interactions between BMI and Hb concentrations on SBP and DBP were statistically significant in 3 trimesters of pregnancy regardless of multivariable-adjusted models.

**Discussion**

In this study, differences in the associations of BMI and Hb with SBP or DBP were present throughout pregnancy. BMI was positively associated with SBP across 3 trimesters, but with DBP in the first and third trimesters; higher Hb concentrations were associated with increased SBP only in the first trimester, but with increased DBP in the first and third trimesters.
Furthermore, we found significant interactions of additive effects between high BMI and high Hb on increased SBP and DBP only in the third trimester.

Some observational studies have consistently shown a positive association between maternal BMI and blood pressure, whether in pregnancy [3-6] or prepregnancy [16-19], although these associations were concluded by different statistical models. However, a recent system review including 13 trials indicates that dietary intervention appears effective to reduce total and weekly gestational weight gain, but no significant effect on preventing preeclampsia and gestational diabetes [20]. For Hb, several observational studies found significantly increased Hb concentrations in women who developed PIH in the second or third trimester [7-9]. Also, a recent study showed that Hb level was positively associated with both SBP and DBP in a large cohort of healthy individuals [21]. We excluded women with PIH or preeclampsia mainly owing to antihypertensive medication, in contrast to the previous studies that defined outcomes as PIH or preeclampsia, our study thus focused on the effects of BMI and Hb on SBP and DBP in the whole range of trimesters of pregnancy. As a whole, our findings suggest that BMI may have a stronger effect than Hb concentrations on SBP, especially in the second and third trimesters.

This is the first analysis to our knowledge of the potential interaction between high BMI and high Hb concentrations on SBP and DBP in pregnancy. Our main finding is that both SBP and DBP are significantly elevated in pregnant women with high BMI and high Hb in the third trimester, but not in the first and second trimesters. The combination of high BMI and high Hb indicated an additive effect, even although SBP and DBP increased only 2.9 mmHg and 3.5
mmHg with the addictive effect, respectively, perhaps we cannot rule out the possible effect on adverse pregnancy outcomes. Randomized controlled trial data have shown that lowering SBP of 3 mmHg may result in a 16% reduction of cardiovascular events and a 22% reduction of fatal and nonfatal strokes [22]. For pregnant women, the possible effect of increased SBP and DBP by around 3 mmHg thus needs to be confirmed in further studies. Moreover, the tendency of blood pressure in women with high BMI and high Hb concentrations may need to be monitored with care during the antenatal care.

The mechanisms for increased BMI or Hb concentrations with elevated blood pressure in pregnancy have been postulated. For maternal BMI, the associations of gestational adiposity with dyslipidaemia, hyperglycaemia, and insulin resistance are well recognized [4, 23-25]. These risk patterns lead to oxidative stress and lipoprotein oxidation contributing to endothelial dysfunction [26] that is characterized by the pathogenesis of preeclampsia [27]. Additionally, several functional changes associated with maternal obesity, including lipid alternations, sleep apnea, and increased cardiac output and oxygen consumption, are involved in hypertensive disorders in pregnancy [28-30]. For Hb, the mechanisms that contribute to hypertensive disorders of pregnancy may be related with blood viscosity, which can be induced by elevation of hematocrit and Hb levels, since it has been suggested that increased blood viscosity may worsen cardiovascular function partly through an effect on blood pressure [31]. Given this finding regarding blood viscosity, it might probably explain the previous studies [7-9] that the positive associations between increased Hb and PIH were in agreement with elevated blood viscosity during pregnancy. Furthermore, free Hb is a scavenger of nitric oxide (NO), which
can relax the muscle cells, increased free Hb levels may thus bind to NO and contribute to vasoconstriction and hypertension [32, 33]. With so many potential mechanisms involved, perhaps it is not surprised by the differences in the associations of increased BMI and Hb concentrations with SBP or DBP throughout pregnancy.

The mechanisms underlying the interaction between high BMI and high Hb concentrations on increased blood pressure are unclear. Based on the association of elevated blood viscosity with adiposity or increased Hb levels [7, 10-13], the present study partly supports our hypothesis that high BMI and high Hb concentrations may have a combined effect on increased blood pressure via elevated blood viscosity during normal pregnancy. However, we do not have a good explanation for the interaction in the third trimester, but not in the first and second trimesters. Generally in normal pregnancy, blood volume, stroke volume, and cardiac output increase progressively from the first trimester until term [34], whereas blood viscosity has a drop until 29 weeks gestation, followed by a small increase toward term [35]. In our study, although hematocrit seemed to be similar with the change in blood viscosity above-mentioned, we cannot determine the change in hemodynamics owing to lack of measuring blood viscosity using viscometer. Further studies thus need to systematically evaluate the role of blood viscosity in the associations of increased BMI or Hb concentrations with blood pressure in pregnancy.

The present study has some limitations. First, owing to our cross-sectional analysis, we cannot determine the causality between increased BMI or Hb concentration and elevated blood pressure. Second, the physiological adaptations in maternal BMI, Hb concentration, and blood
pressure are dynamic throughout pregnancy. We cannot collect blood samples at every antenatal visit due to the schedule in routine antenatal care, hence this probably weakened the representation of 3 trimesters of pregnancy only using the measurement at study entry, around gestational weeks 20 and 24, 32 and 36. Finally, we accumulatively lost 943 (21%) and 417 (14%) participants with the follow-up in two subsequent trimesters, respectively. Based on our analysis, the characteristics of participants lost to follow up were not significantly different with the original participants except for family income and urban residence. Moreover, the regression coefficient in each trimester did not significantly change after adjustment for the two variables, our results thus did not substantially be influenced by loss to follow up.

Conclusions

BMI and Hb concentrations appear to have different associations with blood pressure throughout pregnancy. Even more important, our findings indicate interactions of addictive effects between high BMI and high Hb on both SBP and DBP in the third trimester of pregnancy. Further prospective research is needed to identify the precise mechanisms of the interaction, and evaluate its clinical and biological role in pregnancy.

Competing interests

All authors have no competing interests.

Authors’ contributions
QZ, JX and XQ designed the research and wrote the manuscript. QZ and YD analyzed the data. YL contributed in the program development and participated in the program protocol. JH and XL collaborated in the data interpretation and assisted in data analysis. All authors reviewed and edited manuscript. The final manuscript was read and approved by all authors.

Acknowledgments

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References


22. Staessen JA, Birkenhager WH: Evidence that new antihypertensives are superior to


Figure Legends

**Figure 1 Flow diagram of study participants throughout pregnancy.** 3472, 2986, and 2261 at each time point represent the number of women with complete data including body mass index (BMI), blood pressure, and blood samples as well as basic characteristics in the first, second and third trimesters, respectively.

**Figure 2 Differences (95% CIs) in SBP and DBP with BMI and Hb by trimester.** Differences were adjusted for age (continuous), ethnicity (Han, Zhuang, other), education (<12 years, ≥12 years), family income <US$ 3000 (yes, no), urban residence (yes, no), parity (0, 1, >1), smoking (never, former, current), alcohol use (yes, no), folic acid supplement (yes, no), hematocrit (continuous), total cholesterol (continuous), triglycerides (continuous), and diabetes mellitus (yes, no). Comparing the highest to the lowest quartile: *P* for trend <0.05, **P** for trend <0.001.
Table 1 Baseline characteristics of the study population by trimester†

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>1st trimester (N = 3472)</th>
<th>2nd trimester (N = 2986)</th>
<th>3rd trimester (N = 2261)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age, year</td>
<td>26.0 (0.8)</td>
<td>26.3 (0.5)</td>
<td>25.2 (0.6)</td>
</tr>
<tr>
<td>The Han, n (%)</td>
<td>2226 (64.1)</td>
<td>1965 (65.8)</td>
<td>1526 (67.5)</td>
</tr>
<tr>
<td>Education (≥12 years), n (%)</td>
<td>1476 (42.5)</td>
<td>1170 (39.2)</td>
<td>1011 (44.7)</td>
</tr>
<tr>
<td>Family income (&lt;$ 3000), n (%)</td>
<td>736 (21.2)</td>
<td>582 (19.5)</td>
<td>355 (15.7)</td>
</tr>
<tr>
<td>Urban residence, n (%)</td>
<td>1628 (46.9)</td>
<td>1582 (53.0)</td>
<td>1302 (57.6)</td>
</tr>
<tr>
<td>Parity (nulliparous), n (%)</td>
<td>2170 (62.5)</td>
<td>1765 (59.1)</td>
<td>1490 (65.9)</td>
</tr>
<tr>
<td>Current smoker, n (%)</td>
<td>21 (0.6)</td>
<td>6 (0.2)</td>
<td>11 (0.5)</td>
</tr>
<tr>
<td>Alcohol use, n (%)</td>
<td>281 (8.1)</td>
<td>290 (9.7)</td>
<td>274 (12.1)</td>
</tr>
<tr>
<td>Folic acid supplement, n (%)</td>
<td>1430 (41.2)</td>
<td>1135 (38.0)</td>
<td>988 (43.7)</td>
</tr>
<tr>
<td>Hematocrit, %</td>
<td>37.1 (0.3)</td>
<td>34.3 (0.4)</td>
<td>36.5 (0.3)</td>
</tr>
<tr>
<td>Serum total cholesterol, mg/dL</td>
<td>181.6 (1.1)</td>
<td>221.5 (0.7)</td>
<td>243.6 (0.8)</td>
</tr>
<tr>
<td>Serum triglyceride, mg/dL</td>
<td>124.9 (0.9)</td>
<td>177.1 (1.1)</td>
<td>256.8 (1.3)</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>69 (2.0)</td>
<td>66 (2.2)</td>
<td>133 (5.9)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>22.9 (0.2)</td>
<td>24.1 (0.2)</td>
<td>26.5 (0.3)</td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
<td>12.5 (0.2)</td>
<td>11.7 (0.1)</td>
<td>11.8 (0.1)</td>
</tr>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>110.5 (1.3)</td>
<td>107.0 (1.1)</td>
<td>112.8 (1.0)</td>
</tr>
<tr>
<td>Diastolic blood pressure, mmHg</td>
<td>68.4 (0.6)</td>
<td>66.4 (0.5)</td>
<td>73.8 (0.7)</td>
</tr>
</tbody>
</table>

†Values are means (standard error) or number (percentage) unless otherwise noted.
Table 2 Difference (95% CI) in blood pressure by categories of BMI and Hb levels in first trimester

<table>
<thead>
<tr>
<th></th>
<th>Non-High BMI $^{a}$</th>
<th></th>
<th>High BMI $^{a}$</th>
<th></th>
<th>$P$ for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hb &lt;13.0 g/dL</td>
<td>Hb ≥13.0 g/dL</td>
<td>Hb &lt;13.0 g/dL</td>
<td>Hb ≥13.0 g/dL</td>
<td></td>
</tr>
<tr>
<td>Number</td>
<td>1549</td>
<td>1018</td>
<td>549</td>
<td>356</td>
<td></td>
</tr>
<tr>
<td>SBP (mmHg)$^{b}$</td>
<td>110.6</td>
<td>111.0</td>
<td>113.6</td>
<td>112.2</td>
<td></td>
</tr>
<tr>
<td>Model 1$^{c}$</td>
<td>0.0 (reference)</td>
<td>0.3 (-1.3, 1.8)</td>
<td>3.5 (1.2, 5.8)</td>
<td>2.0 (0.3, 3.8)</td>
<td>0.02</td>
</tr>
<tr>
<td>Model 2$^{d}$</td>
<td>0.0 (reference)</td>
<td>0.3 (-1.3, 1.9)</td>
<td>3.4 (1.1, 5.7)</td>
<td>1.9 (0.1, 3.6)</td>
<td>0.08</td>
</tr>
<tr>
<td>Model 3$^{e}$</td>
<td>0.0 (reference)</td>
<td>-0.5 (-2.1, 1.0)</td>
<td>2.8 (0.7, 4.9)</td>
<td>1.6 (-0.3, 3.5)</td>
<td>0.19</td>
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<tr>
<td>DBP (mmHg)$^{b}$</td>
<td>67.2</td>
<td>68.5</td>
<td>69.2</td>
<td>70.3</td>
<td></td>
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<tr>
<td>Model 1$^{c}$</td>
<td>0.0 (reference)</td>
<td>1.2 (-0.8, 3.3)</td>
<td>2.8 (0.3, 5.3)</td>
<td>3.1 (0.8, 5.4)</td>
<td>0.003</td>
</tr>
<tr>
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<td>0.0 (reference)</td>
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<td>Model 3$^{e}$</td>
<td>0.0 (reference)</td>
<td>0.4 (-1.6, 2.5)</td>
<td>2.1 (-0.4, 4.7)</td>
<td>2.4 (-0.1, 4.8)</td>
<td>0.07</td>
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</table>

CI, confidence interval; SBP, systolic blood pressure; DBP, diastolic blood pressure; Hb, Hemoglobin.

$^{a}$ High BMI indicated BMI ≥24.9 kg/m$^2$; non-high BMI indicated BMI <24.9 kg/m$^2$.

$^{b}$ Mean SBP; mean DBP.

$^{c}$ Model 1: Adjusted for age (continuous) and ethnicity (Han, Zhuang, other).

$^{d}$ Model 2: Further adjusted for education (<12 years, ≥12 years), family income <US$ 3000 (yes, no), urban residence (yes, no), parity (0, 1, >1), smoking (never, former, current), alcohol use (yes, no), and folic acid supplement (yes, no).

$^{e}$ Model 3: Further adjusted for hematocrit (continuous), total cholesterol (continuous), triglycerides (continuous), and diabetes mellitus (yes, no).
Table 3 Difference (95% CI) in blood pressure by categories of BMI and Hb levels in second trimester

<table>
<thead>
<tr>
<th></th>
<th>Non-High BMI</th>
<th>High BMI</th>
<th>P for trend</th>
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<tr>
<td></td>
<td>Hb &lt;13.0 g/dL</td>
<td>Hb ≥13.0 g/dL</td>
<td></td>
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<tr>
<td>Number</td>
<td>1472</td>
<td>644</td>
<td></td>
</tr>
<tr>
<td>SBP (mmHg)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>105.9</td>
<td>107.4</td>
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<tr>
<td>Model 1&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0.0 (reference)</td>
<td>1.3 (-0.9, 3.4)</td>
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<tr>
<td>Model 2&lt;sup&gt;d&lt;/sup&gt;</td>
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<td>DBP (mmHg)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>65.9</td>
<td>66.8</td>
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<td>Model 2&lt;sup&gt;d&lt;/sup&gt;</td>
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<td>0.8 (-1.5, 3.0)</td>
<td>0.42</td>
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<td>Model 3&lt;sup&gt;e&lt;/sup&gt;</td>
<td>0.0 (reference)</td>
<td>0.6 (-1.6, 2.8)</td>
<td>0.59</td>
</tr>
</tbody>
</table>

CI, confidence interval; SBP, systolic blood pressure; DBP, diastolic blood pressure; Hb, Hemoglobin.

<sup>a</sup> High BMI indicated BMI ≥26.4 kg/m²; non-high BMI indicated BMI <26.4 kg/m².

<sup>b</sup> Mean SBP; mean DBP.

<sup>c</sup> Model 1: Adjusted for age (continuous) and ethnicity (Han, Zhuang, other).

<sup>d</sup> Model 2: Further adjusted for education (<12 years, ≥12 years), family income <US$ 3000 (yes, no), urban residence (yes, no), parity (0, 1, >1), smoking (never, former, current), alcohol use (yes, no), and folic acid supplement (yes, no).

<sup>e</sup> Model 3: Further adjusted for hematocrit (continuous), total cholesterol (continuous), triglycerides (continuous), and diabetes mellitus (yes, no).
<table>
<thead>
<tr>
<th></th>
<th>Non-High BMI $^a$</th>
<th></th>
<th>High BMI $^a$</th>
<th></th>
<th>P for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hb &lt;13.0 g/dL</td>
<td>Hb ≥13.0 g/dL</td>
<td>Hb &lt;13.0 g/dL</td>
<td>Hb ≥13.0 g/dL</td>
<td></td>
</tr>
<tr>
<td>Number</td>
<td>991</td>
<td>536</td>
<td>510</td>
<td>224</td>
<td></td>
</tr>
<tr>
<td>SBP (mmHg) $^b$</td>
<td>111.6</td>
<td>112.9</td>
<td>113.5</td>
<td>115.1</td>
<td></td>
</tr>
<tr>
<td>Model 1$^c$</td>
<td>0.0 (reference)</td>
<td>1.4 (-0.7, 3.6)</td>
<td>2.0 (0.4, 3.7)</td>
<td>3.6 (1.2, 6.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>Model 2$^d$</td>
<td>0.0 (reference)</td>
<td>1.2 (-0.8, 3.3)</td>
<td>2.0 (0.2, 3.8)</td>
<td>3.4 (1.0, 5.8)</td>
<td>0.005</td>
</tr>
<tr>
<td>Model 3$^e$</td>
<td>0.0 (reference)</td>
<td>1.0 (-1.3, 3.2)</td>
<td>1.8 (-0.3, 3.9)</td>
<td>2.9 (0.3, 5.4)</td>
<td>0.01</td>
</tr>
<tr>
<td>DBP (mmHg) $^b$</td>
<td>70.4</td>
<td>71.5</td>
<td>73.1</td>
<td>74.3</td>
<td></td>
</tr>
<tr>
<td>Model 1$^c$</td>
<td>0.0 (reference)</td>
<td>1.7 (-0.6, 4.1)</td>
<td>2.8 (0.8, 4.7)</td>
<td>4.8 (2.3, 7.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Model 2$^d$</td>
<td>0.0 (reference)</td>
<td>1.4 (-1.0, 3.8)</td>
<td>2.4 (0.4, 4.4)</td>
<td>4.0 (1.6, 6.4)</td>
<td>0.001</td>
</tr>
<tr>
<td>Model 3$^e$</td>
<td>0.0 (reference)</td>
<td>1.0 (-1.3, 3.4)</td>
<td>2.3 (0.2, 4.3)</td>
<td>3.5 (1.0, 5.9)</td>
<td>0.008</td>
</tr>
</tbody>
</table>

CI, confidence interval; SBP, systolic blood pressure; DBP, diastolic blood pressure; Hb, Hemoglobin.

$^a$ High BMI indicated BMI ≥28.7 kg/m$^2$; non-high BMI indicated BMI <28.7 kg/m$^2$.

$^b$ Mean SBP; mean DBP.

$^c$ Model 1: Adjusted for age (continuous) and ethnicity (Han, Zhuang, other).

$^d$ Model 2: Further adjusted for education (<12 years, ≥12 years), family income <US$ 3000 (yes, no), urban residence (yes, no), parity (0, 1, >1), smoking (never, former, current), alcohol use (yes, no), and folic acid supplement (yes, no).

$^e$ Model 3: Further adjusted for hematocrit (continuous), total cholesterol (continuous), triglycerides (continuous), and diabetes mellitus (yes, no).
5701 healthy women with singleton pregnancies enrolled at gestational weeks 10 to 16

4497 eligible women (3472 in the first trimester and 1025 in the second trimester) included with follow-up

2986 included at the end of gestational age 24 weeks

2261 included at the end of gestational age 36 weeks

1204 excluded: 41 vitro fertilization
1163 incomplete data

1511 excluded: 252 miscarriage or stillbirth
81 use of antihypertensive drugs
235 blood sample unavailable
943 loss to follow-up

725 excluded: 24 stillbirth
199 use of antihypertensive drugs
85 blood sample unavailable
417 loss to follow-up

1204 excluded: 41 vitro fertilization
1163 incomplete data

1511 excluded: 252 miscarriage or stillbirth
81 use of antihypertensive drugs
235 blood sample unavailable
943 loss to follow-up
Figure 2

The figure shows the difference in blood pressure (SBP and DBP) between BMI and hemoglobin levels across the 1st, 2nd, and 3rd trimesters of pregnancy. The data is presented as mean difference with 95% confidence intervals (CI), measured in mmHg. Statistically significant differences are indicated by asterisks (*) above the data points. The graph indicates a trend of increasing differences in blood pressure between BMI and hemoglobin levels across the trimesters.