

Association of pre-pregnancy body mass index with adverse pregnancy outcome among first-time mothers

Li Li¹ Equal first author, 1, 2, 3, Yanhong Chen² Equal first author, 2, 4, Zhifeng Lin⁵, Weiyan Lin⁵, Yangqi Liu⁵, Weilin Ou⁵, Chengli Zeng⁵, Li Ke^{Corresp. 2, 3, 5}

¹ Center for Reproductive Medicine, The Third Affiliated Hospital of Guangzhou Medical University, Guangzhou, Guangdong, China

² Key Laboratory for Major Obstetric Diseases of Guangdong Provinces, Guangzhou, Guangdong, China

³ Key Laboratory of Reproduction and Genetics of Guangdong Higher Education Institutes, Guangzhou, Guangdong, China

⁴ Department of Obstetrics and Gynecology, The Third Affiliated Hospital of Guangzhou Medical University, Guangzhou, Guangdong, China

⁵ Department of Medical Record, The Third Affiliated Hospital of Guangzhou Medical University, Guangzhou, Guangdong, China

Corresponding Author: Li Ke
Email address: keli1221@126.com

Background: Studies have reported an increased risk of adverse pregnancy outcome associated with pre-pregnancy body mass index (BMI). However, the data on such associations in urban areas of southern Chinese women is limited, which drive us to clarify the associations of pre-pregnancy BMI and the risks of adverse pregnancy outcomes (preterm birth (PTB) and low birth weight (LBW)) and maternal health outcomes (gestational hypertension and cesarean delivery). **Methods:** We performed a hospital-based case-control study including 3,864 Southern Chinese women who gave first birth to a live singleton infant from January 2015 to December 2015. PTB was stratified into three subgroups according to gestational age (extremely PTB, very PTB and moderate PTB). Besides, we combined birth weight and gestational age to dichotomise as being small for gestational age (SGA, less than the tenth percentile of weight for gestation) and non-small for gestational age (NSGA, large than the tenth percentile of weight for gestation), gestational week was also classified into categories of term, 34-36 week and below 34 week.. We then divided newborns into six groups: (1) term and NSGA; (2) 34-36 week gestation and NSGA; (3) below 34 week gestation and NSGA; (4) term and SAG; (5) 34-36 week gestation and SAG; (6) below 34 week gestation and SAG. Adjusted logistic regression models was used to estimate the odds ratios of adverse outcomes. **Results:** Underweight women were more likely to give LBW (AOR=1.44, 95% CI 1.11 to 1.89), the similar result was seen in term and SAG as compare with term and NSAG (AOR=1.78, 95% CI 1.45-2.17). Whereas underweight was significantly associated with a lower risk of gestational hypertension (AOR=0.45, 95% CI 0.25-0.82) and caesarean delivery (AOR=0.74, 95% CI 0.62-0.90). The risk of extremely PTB is relatively higher among overweight and obese mothers in a subgroup analysis of PTB (AOR=8.12, 95% CI=1.11 to

59.44; AOR=15.06, 95% CI=1.32 to 172.13, respectively). Both maternal overweight and obesity were associated with a greater risk of gestational hypertension (AOR=1.71, 95% CI=1.06 to 2.77; AOR=5.54, 95% CI=3.02 to 10.17, respectively) and caesarean delivery (AOR=1.91, 95% CI=1.53 to 2.38; AOR=1.85, 95% CI=1.21 to 2.82, respectively).

Conclusions: Our study suggested that maternal overweight and obesity were associated with a significantly higher risk of gestational hypertension, caesarean delivery and extremely PTB. Underweight was correlated with an increased risk of LBW and conferred a protective effect regarding the risk for gestational hypertension and caesarean delivery for the first-time mothers among Southern Chinese.

Association of Pre-Pregnancy Body Mass Index with adverse pregnancy outcome among first-time mothers

Li Li^{1,2,3*}, Yanhong Chen^{2,4*}, Zhifeng Lin⁵, Weiyan Lin⁵, Yangqi Liu⁵, Weilin Ou⁵, Chengli Zeng, Li Ke^{2,3,5#}

¹Center for Reproductive Medicine, the Third Affiliated Hospital of Guangzhou Medical University, Guangzhou, China

²Key Laboratory for Major Obstetric Diseases of Guangdong Provinces, Guangzhou, China

³Key Laboratory of Reproduction and Genetics of Guangdong Higher Education Institutes, Guangzhou, China

⁴Department of Obstetrics and Gynecology, the Third Affiliated Hospital of Guangzhou Medical University, Guangzhou, China

⁵Department of Medical Record, the Third Affiliated Hospital of Guangzhou Medical University, Guangzhou, China

*These authors have contributed equally to this work

#Corresponding authors:

Li Ke, Department of Medical Record,, the Third Affiliated Hospital of Guangzhou Medical University, Guangzhou 510310, China. Phone: 86-20-81292138; FAX: 86-20-81292908; E-mail: keli1221@126.com.

Abstract

Background: Studies have reported an increased risk of adverse pregnancy outcome associated with pre-pregnancy body mass index (BMI). However, the data on such associations in urban areas of southern Chinese women is limited, which drive us to clarify the associations of pre-pregnancy BMI and the risks of adverse pregnancy outcomes (preterm birth (PTB) and low birth weight (LBW)) and maternal health outcomes (gestational hypertension and cesarean delivery).

Methods: We performed a hospital-based case-control study including 3,864 Southern Chinese women who gave first birth to a live singleton infant from January 2015 to December 2015. PTB was stratified into three subgroups according to gestational age (extremely PTB, very PTB and moderate PTB). Besides, we combined birth weight and gestational age to dichotomise as being small for gestational age (SGA, less than the tenth percentile of weight for gestation) and non-small for gestational age (NSGA, large than the tenth percentile of weight for gestation), gestational week was also classified into categories of term, 34-36 week and below 34 week.. We then divided newborns into six groups: (1) term and NSGA; (2) 34–36 week gestation and NSGA; (3) below 34 week gestation and NSGA; (4) term and SAG; (5) 34–36 week gestation and SAG; (6) below 34 week gestation and SAG. Adjusted logistic regression models was used to estimate the odds ratios of adverse outcomes.

Results: Underweight women were more likely to give LBW (AOR=1.44, 95% CI 1.11 to 1.89), the similar result was seen in term and SAG as compare with term and NSAG (AOR=1.78, 95% CI 1.45–2.17). Whereas underweight was significantly associated with a lower risk of gestational hypertension (AOR=0.45, 95% CI 0.25–0.82) and caesarean delivery (AOR=0.74, 95% CI 0.62–

0.90). The risk of extremely PTB is relatively higher among overweight and obese mothers in a subgroup analysis of PTB (AOR=8.12, 95% CI=1.11 to 59.44; AOR=15.06, 95% CI=1.32 to 172.13, respectively). Both maternal overweight and obesity were associated with a greater risk of gestational hypertension (AOR=1.71, 95% CI=1.06 to 2.77; AOR=5.54, 95% CI=3.02 to 10.17, respectively) and caesarean delivery (AOR=1.91, 95% CI=1.53 to 2.38; AOR=1.85, 95% CI=1.21 to 2.82, respectively).

Conclusions: Our study suggested that maternal overweight and obesity were associated with a significantly higher risk of gestational hypertension, caesarean delivery and extremely PTB. Underweight was correlated with an increased risk of LBW and conferred a protective effect regarding the risk for gestational hypertension and caesarean delivery for the first-time mothers among Southern Chinese.

Keyword: Pregnancy outcome; BMI; Preterm birth; Low birth weight; gestational hypertension; caesarean delivery

Introduction

Preterm birth (PTB) is an important adverse pregnancy outcome with a significant impact on infant mortality and morbidity (Boghossian et al. 2016). The incidence of PTB worldwide is expected to be 11.1%, and China has more than 1.1 million PTB each year, which ranks second in the world (Blencowe et al. 2012). In spite of high-level advancement in healthcare services, the rate of PTB still seems to be climbing. According to statistics, perinatal mortality is as high as 70% in low birth weight (LBW) with neonatal weight below 2500 grams (Hack et al. 1994; Rutter 1995), most of them are born preterm. Growing evidence has shown that the incidence and development of PTB is a complex process that is influenced by a variety of environmental and genetic factors (He et al. 2017; Liu et al. 2017; Qiu et al. 2017; Xiao et al. 2016). Therefore, it is helpful to develop approaches of effective prevention and treatment of neonatal morbidity and mortality by elucidating etiological factors contributing to PTB or LBW.

Recent results provide support to pre-pregnancy maternal body mass index (BMI) is one of the potential risk factors for PTB (Hendler et al. 2005; Lynch et al. 2014; Shaw et al. 2014) and LBW (Han et al. 2011; Liu et al. 2016). In recent decades, the prevalence of obesity and overweight among women in many countries has increased at an alarming rate, especially in developing countries. Different countries, regions and incomes have different patterns of overweight and obesity that is more common among women in developing countries and men in developed countries (Ng et al. 2014). Moreover, epidemiological studies have been suggested that maternal overweight and obesity have been shown to be association with PTB (Lynch et al. 2014; Shaw et al. 2014; Su et al. 2020), LBW (Rahman et al. 2015) and adverse maternal health

outcomes, such as gestational hypertension (Santos et al. 2019) and cesarean delivery (Paidas Teefey et al. 2020; Rahman et al. 2015). Similarly, several observational studies show that underweight women in pre-pregnancy is the major risk factor for LBW and PTB (Ehrenberg et al. 2003; Madzia et al. 2020; Qu et al. 2019). However, the conclusions of various studies on the correlation between pre-pregnancy BMI and PTB appear to be paradoxical. It was reported that the risk of PTB in women with pre-pregnancy high BMI was significantly increased (Baeten et al. 2001; Chen et al. 2020; Cnattingius et al. 1998; Cnattingius et al. 2013; Weiss et al. 2004; Zhou et al. 2019), whereas other studies contradicted this result, suggesting that women with a high pre-pregnancy BMI could have a protective impact on PTB (Chen et al. 2013; Khashan & Kenny 2009; Sebire et al. 2001). Furthermore, similar results have also been reported on association between pre-pregnancy BMI and LBW (Li et al. 2020; Ronnenberg et al. 2003a; Wu et al. 2020). However, there are relatively few studies of the effects of pre-pregnancy BMI on subsequent pregnancies for first-time mothers among Southern Chinese women. Although several researchers (Liu et al. 2019; Pan et al. 2016; Ronnenberg et al. 2003b) have conducted relevant research in domestic, these previous papers are mainly limited to earlier data or pregnant women in rural areas. Thus, studies on the role of pre-pregnancy BMI in adverse pregnancy outcomes for first-time mothers in urban areas of Southern China remain scarce.

Given above controversial results, we conducted a hospital-based case-control study to determine whether there is a higher risk of adverse outcome in women with abnormal BMI as compared with normal BMI women among first-time mothers in urban areas of southern China.

Methods

Study subjects

This was a hospital-based, case-control study conducted in The Third Affiliated Hospital of Guangzhou Medical University, Guangdong, China. Pregnant women who gave birth for the first time were included between January 2015 and December 2015. A total of 322 women with PTB and 3,362 women with term delivery controls were enrolled. These people also could be divided into 317 cases of LBW and 3,367 controls of normal birth weight. This study was approved by the institutional review board of The Third Affiliated Hospital of Guangzhou Medical University, Guangdong, China (Medical Ethics Hearing [2020]No.036). And Institutional Review Board waived the need for consent.

The preterm group was defined to deliver within 37 weeks of conception without congenital abnormalities or neurological damage. The control group between 37 and 42 weeks of gestation without congenital abnormalities or neurological damage was matched with the case in the residential area for one week at the same hospital. For both groups, we excluded women with a multiple pregnancy, stillbirth, prior deliveries, embryo transfer and in vitro fertilization.

All data for this study was collected from women who gave their first birth during hospitalization, including maternal age, education, gravidity, occupation, health insurance, height and weight before of pregnancy. Gestational hypertension, caesarean delivery, birth weight and gestational week at delivery were obtained from the medical records. Pre-pregnancy BMI defined as the body weight in kilograms divided by the square of the height in metres (kg/m^2). BMI is classified as underweight ($<18.5 \text{ kg/m}^2$), normal weight ($18.5\text{--}23.9 \text{ kg/m}^2$), overweight

(24.0–27.9 kg/m²), and obesity (≥ 28.0 kg/m²) according to the weight standard of Chinese adults (Zhou & Cooperative Meta-Analysis Group of the Working Group on Obesity in 2002). In this study, child birth weight below 2500 grams was considered LBW. Once the two occasions systolic blood pressure (BP) or diastolic BP values of pregnant women measured at intervals of 24 hours exceed 140 mmHg or 90 mmHg respectively, they are diagnosed as gestational hypertension.

Statistical analysis

t test (for continuous variables) or χ^2 test (for categorical variables) was used to assess the difference in demographic characteristics between two groups. Adjusted odds ratios (OR) with 95% confidence intervals obtained from logistic regression model were used to quantify associations between pre-pregnancy BMI and adverse outcomes, adjusting for age, occupation, health insurance and education. We also further divided gestational age into four subtypes: extremely PTB (<28 gestational week), very PTB (28–31 gestational week), moderate PTB (32–36 gestational week) and normal (≥ 37 gestational week). Besides, we referred to the method provided by Tanya Marchant et al (Marchant et al. 2012) apply to weight for gestational age, details were described as below: we combined birth weight and gestational age to dichotomise as being small for gestational age (SGA, less than the tenth percentile of weight for gestation) (Oken et al. 2003) and non-small for gestational age (NSGA, large than the tenth percentile of weight for gestation). As in previous studies, gestational week was classified into categories of term, 34–36 week and below 34 week. We then divided newborns into six groups: (1) term and

138 NSGA; (2) 34–36 week gestation and NSGA; (3) below 34 week gestation and NSGA; (4) term
 139 and SAG; (5) 34–36 week gestation and SAG; (6) below 34 week gestation and SAG. A two-
 140 sided p-value of 0.05 or less was accepted to be statistically significant. Data were analyzed
 141 using Statistical Analysis Software 9.4. (SAS Institute, Cary, NC).

142

Results

Characteristics of the study subjects

The baseline maternal characteristics are shown in table 1. Of the 3,684 live births, 8.7% (n=322) were PTBs, and the remaining 91.3% (n=3362) were term births. The proportions of underweight, normal weight, overweight, and obesity women were 23.29%, 63.36%, 10.72%, and 2.63%, respectively. There were significant differences between PTB group and terms group with respect to age, health insurance, occupation and education (all $P<0.01$). There were no significant differences between the two groups with regard to gravidity ($P>0.05$). The variables in the normal and the LBW group were basically the same as those in the term and preterm groups.

Association analysis between pre-pregnancy BMI and adverse outcomes

The association between pre-pregnancy BMI and the risk of adverse outcomes are considered in table 2 and table 3. Underweight, overweight and obesity did not increase the risk of PTB as compare with normal weight (AOR=1.01, 95% CI=0.76 to 1.34; AOR=1.25, 95% CI=0.87 to 1.80; and AOR=1.27, 95% CI=0.65 to 2.51, respectively). However, When PTB was stratified into three subgroups, both maternal overweight and obesity increased the risks of extremely PTB (AOR=8.12, 95% CI=1.11 to 59.44; AOR=15.06, 95% CI=1.32 to 172.13, respectively).

Pre-pregnancy underweight was significantly associated with the increased risk for LBW. In comparison with women who had normal pre-pregnancy BMI, women with low BMI category was more likely to deliver a LBW infant (crude OR=1.48, 95% CI=1.14 to 1.93). After the

164 adjustment for potential confounding factors, the AOR associated with the risk for giving birth to
 165 a LBW infant were 1.44 (95% CI=1.11 to 1.89), the similar result was seen in table 4 as
 166 compared with term and NSAG (AOR=1.78, 95% CI=1.45 to 2.17). Underweight was also
 167 significantly associated with a lower risk of gestational hypertension (AOR=0.45, 95% CI=0.25
 168 to 0.82) and caesarean delivery (AOR=0.74, 95% CI=0.62 to 0.90). Both maternal overweight
 169 and obesity were found to be a risk factor for gestational hypertension (AOR=1.71, 95% CI=1.06
 170 to 2.77; AOR=5.54, 95% CI=3.02 to 10.17, respectively) and caesarean delivery (AOR=1.91, 95%
 171 CI=1.53 to 2.38; AOR=1.85, 95% CI=1.21 to 2.82, respectively).

172

Discussion

Our study demonstrated that maternal underweight prior to pregnancy, as compared with normal weight women, significantly elevated the risk for LBW for the first-time mothers among Southern Chinese. Maternal underweight were also found to be at lower risk of gestational hypertension and caesarean delivery. In women who had a high pre-pregnancy BMI, our study showed a significantly higher risk of gestational hypertension, caesarean delivery and extremely PTB.

The proportions of overweight and obesity were lower than underweight in our study, which were similar to previously reported data from other Chinese studies (Pan et al. 2016). Our finding showed that underweight women increase the risk of LBW in subsequent pregnancy, which is consistent with the result of a review study by Liu et al. (Liu et al. 2016). The study, including 60 studies covering 1,392,799 women, showed that infants had a higher risk of having a LBW when their mothers were underweight (OR, 1.67, 95%CI, 1.39–2.02) as compare to women with normal weight. Previous studies have demonstrated that maternal nutrition during pregnancy has great influence on providing the essential nutrients for fetal growth (Nnam 2015) and pregnant women who are undernourished tend to have LBW infant (Allen 2001). Maternal nutritional imbalance may be a key factor in the reduction of surface area and placental weight. In the lower surface area and placental weight, nutrient and waste transfer between the maternal and fetal circulation is reduced and other normal processes, such as fetal development and growth, are also restricted (Lechtig et al. 1975). Thus, maternal malnutrition may lead to LBW infant. Moreover, the finding in our study on association between underweight and LBW was also in line with

previous literature (Li et al. 2013; Liu et al. 2012).

Previous literature has revealed that maternal overweight and obesity were associated with the increased risk for gestational hypertension and caesarian delivery (Lewandowska et al. 2020; Machado et al. 2020; Vince et al. 2020). Our study also confirmed these findings. However, the risk of gestational hypertension and caesarean delivery were reduced among underweight mothers. Although mechanism by which obesity responsible for the increased risk of gestational hypertension or caesarean delivery is unclear, maternal obesity lead to an increase in the number and size of adipocytes or pelvic malacia. A significant amount of adipocytes has been proposed as a cause of excessive inflammatory reaction, pregnant female possibly experienced obstructive dystocia due to pelvic malacia lead to a relatively narrow birth canal. Therefore, both gestational hypertension and caesarean delivery were affected by obesity in obese mothers (Kriketos et al. 2004; Young & Woodmansee 2002).

In our study, the risk of PTB is relatively higher among overweight and obese mothers but the association was not statistically significant (table 2). However, this association has dramatically changed in a subgroup analysis of gestational age (table 3). Our result regarding extremely PTB is consistent with a previous study (Su et al. 2020). Overweight and obesity are generally considered to be the risk factors for PTB due to the effects of placental insufficiency (Lassance et al. 2015; Pereira et al. 2015), inflammatory state (Gaillard et al. 2016), insulin sensitivity (Catalano et al. 1999) and cellular oxidative stress (Ballesteros-Guzman et al. 2019). However, conclusions on the relationship between pre-pregnancy BMI and PTB seem to be paradoxical among different studies. The differences emerged between studies could be

attributed to study design or power, recall bias, multiple comparisons, eating habits and different ethnicities. Additionally, the category of BMI was different among the studies.

Although some confounding factors had been controlled, alcohol consumption and maternal smoking were not adjusted as only one woman claimed to have a history of alcohol consumption and smoking in our data. So we did not adjust for these two variables.

However, there are a number of potential limitations of this study that merit consideration. One limitation of the current study is that it is difficult to distinguish between spontaneous and iatrogenic PTB, which we could not assess the association between special types of PTB and pre-pregnancy BMI. Additionally, the BMI we obtained in our study derived from weight and height information by women self-reported, which could lead to bias risk estimates of PTB (Michels et al. 1998).

In conclusion, our study suggested that maternal overweight and obesity were associated with a significantly higher risk of gestational hypertension, caesarean delivery and extremely PTB. Underweight was correlated with an increased risk of LBW and conferred a protective effect regarding the risk for gestational hypertension and caesarean delivery for the first-time mothers among Southern Chinese.

233 **Acknowledgements**

234 The authors are grateful to all subjects who participated in this study.

235

236 **Funding**

237 The authors received no specific funding for this work.

238

239 **Competing interests**

240 The authors declare that they have no competing interests.

241

242

243

244

245

246

247

248

249

250

251

252

253

254

References

- 256 Allen LH. 2001. Biological mechanisms that might underlie iron's effects on fetal growth and preterm birth. *J Nutr*
257 131:581S-589S.
- 258 Baeten JM, Bukusi EA, and Lambe M. 2001. Pregnancy complications and outcomes among overweight and obese
259 nulliparous women. *Am J Public Health* 91:436-440.
- 260 Ballesteros-Guzman AK, Carrasco-Legleu CE, Levorio-Carrillo M, Chavez-Corral DV, Sanchez-Ramirez B,
261 Marinelarena-Carrillo EO, Guerrero-Salgado F, and Reza-Lopez SA. 2019. Prepregnancy Obesity, Maternal
262 Dietary Intake, and Oxidative Stress Biomarkers in the Fetomaternal Unit. *Biomed Res Int* 2019:5070453.
- 263 Blencowe H, Cousens S, Oestergaard MZ, Chou D, Moller AB, Narwal R, Adler A, Vera Garcia C, Rohde S, Say L, and
264 Lawn JE. 2012. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with
265 time trends since 1990 for selected countries: a systematic analysis and implications. *Lancet* 379:2162-
266 2172.
- 267 Boghossian NS, McDonald SA, Bell EF, Carlo WA, Brumbaugh JE, Stoll BJ, Laptook AR, Shankaran S, Walsh MC, Das A,
268 Higgins RD, Eunice Kennedy Shriver National Institute of Child H, and Human Development Neonatal
269 Research N. 2016. Association of Antenatal Corticosteroids With Mortality, Morbidity, and
270 Neurodevelopmental Outcomes in Extremely Preterm Multiple Gestation Infants. *JAMA Pediatr* 170:593-
271 601.
- 272 Catalano PM, Huston L, Amini SB, and Kalhan SC. 1999. Longitudinal changes in glucose metabolism during
273 pregnancy in obese women with normal glucose tolerance and gestational diabetes mellitus. *Am J Obstet*
274 *Gynecol* 180:903-916.
- 275 Chen CN, Chen HS, and Hsu HC. 2020. Maternal Prepregnancy Body Mass Index, Gestational Weight Gain, and Risk
276 of Adverse Perinatal Outcomes in Taiwan: A Population-Based Birth Cohort Study. *Int J Environ Res Public*
277 *Health* 17.
- 278 Chen Y, Li G, Ruan Y, Zou L, Wang X, and Zhang W. 2013. An epidemiological survey on low birth weight infants in
279 China and analysis of outcomes of full-term low birth weight infants. *BMC Pregnancy Childbirth* 13:242.
- 280 Cnattingius S, Bergstrom R, Lipworth L, and Kramer MS. 1998. Prepregnancy weight and the risk of adverse
281 pregnancy outcomes. *N Engl J Med* 338:147-152.
- 282 Cnattingius S, Villamor E, Johansson S, Edstedt Bonamy AK, Persson M, Wikstrom AK, and Granath F. 2013.
283 Maternal obesity and risk of preterm delivery. *JAMA* 309:2362-2370.
- 284 Ehrenberg HM, Dierker L, Milluzzi C, and Mercer BM. 2003. Low maternal weight, failure to thrive in pregnancy,
285 and adverse pregnancy outcomes. *Am J Obstet Gynecol* 189:1726-1730.
- 286 Gaillard R, Rifas-Shiman SL, Perng W, Oken E, and Gillman MW. 2016. Maternal inflammation during pregnancy
287 and childhood adiposity. *Obesity (Silver Spring)* 24:1320-1327.
- 288 Hack M, Taylor HG, Klein N, Eiben R, Schatschneider C, and Mercuri-Minich N. 1994. School-age outcomes in
289 children with birth weights under 750 g. *N Engl J Med* 331:753-759.
- 290 Han Z, Mulla S, Beyene J, Liao G, McDonald SD, and Knowledge Synthesis G. 2011. Maternal underweight and the
291 risk of preterm birth and low birth weight: a systematic review and meta-analyses. *Int J Epidemiol* 40:65-
292 101.

He JR, Lai YM, Liu HH, Liu GJ, Li WD, Fan XJ, Wei XL, Xia XY, Kuang YS, Liu XD, Chen NN, Lu JH, Chen QZ, Mai WB, Xia HM, and Qiu X. 2017. Maternal IGF1 and IGF1R polymorphisms and the risk of spontaneous preterm birth. *J Clin Lab Anal* 31.

Hendler I, Goldenberg RL, Mercer BM, Iams JD, Meis PJ, Moawad AH, MacPherson CA, Caritis SN, Miodovnik M, Menard KM, Thurnau GR, and Sorokin Y. 2005. The Preterm Prediction Study: association between maternal body mass index and spontaneous and indicated preterm birth. *Am J Obstet Gynecol* 192:882-886.

Khashan AS, and Kenny LC. 2009. The effects of maternal body mass index on pregnancy outcome. *Eur J Epidemiol* 24:697-705.

Kriketos AD, Greenfield JR, Peake PW, Furler SM, Denyer GS, Charlesworth JA, and Campbell LV. 2004. Inflammation, insulin resistance, and adiposity: a study of first-degree relatives of type 2 diabetic subjects. *Diabetes Care* 27:2033-2040.

Lassance L, Haghiac M, Leahy P, Basu S, Minium J, Zhou J, Reider M, Catalano PM, and Hauguel-de Mouzon S. 2015. Identification of early transcriptome signatures in placenta exposed to insulin and obesity. *Am J Obstet Gynecol* 212:647 e641-611.

Lechtig A, Yarbrough C, Delgado H, Martorell R, Klein RE, and Behar M. 1975. Effect of moderate maternal malnutrition on the placenta. *Am J Obstet Gynecol* 123:191-201.

Lewandowska M, Wieckowska B, and Sajdak S. 2020. Pre-Pregnancy Obesity, Excessive Gestational Weight Gain, and the Risk of Pregnancy-Induced Hypertension and Gestational Diabetes Mellitus. *J Clin Med* 9.

Li N, Liu E, Guo J, Pan L, Li B, Wang P, Liu J, Wang Y, Liu G, Baccarelli AA, Hou L, and Hu G. 2013. Maternal prepregnancy body mass index and gestational weight gain on pregnancy outcomes. *PLoS One* 8:e82310.

Li X, Gao R, Dai X, Liu H, Zhang J, Liu X, Si D, Deng T, and Xia W. 2020. The association between symptoms of depression during pregnancy and low birth weight: a prospective study. *BMC Pregnancy Childbirth* 20:147.

Liu GJ, He JR, Kuang YS, Fan XJ, Li WD, Lu JH, Xia XY, Liu XD, Chen NN, Mai WB, Xia HM, and Qiu X. 2017. Associations of maternal PLA2G4C and PLA2G4D polymorphisms with the risk of spontaneous preterm birth in a Chinese population. *Mol Med Rep* 15:3607-3614.

Liu L, Ma YN, Wang NN, Lin WJ, Liu Y, and Wen DL. 2019. Maternal body mass index and risk of neonatal adverse outcomes in China: a systematic review and meta-analysis. *BMC Pregnancy Childbirth* 19.

Liu P, Xu L, Wang Y, Zhang Y, Du Y, Sun Y, and Wang Z. 2016. Association between perinatal outcomes and maternal pre-pregnancy body mass index. *Obes Rev* 17:1091-1102.

Liu Y, Dai W, Dai X, and Li Z. 2012. Prepregnancy body mass index and gestational weight gain with the outcome of pregnancy: a 13-year study of 292,568 cases in China. *Arch Gynecol Obstet* 286:905-911.

Lynch AM, Hart JE, Agwu OC, Fisher BM, West NA, and Gibbs RS. 2014. Association of extremes of prepregnancy BMI with the clinical presentations of preterm birth. *Am J Obstet Gynecol* 210:428 e421-429.

Machado C, Monteiro S, Oliveira MJ, and Grupo de Estudo de Diabetes e Gravidez da Sociedade Portuguesa de D. 2020. Impact of overweight and obesity on pregnancy outcomes in women with gestational diabetes - results from a retrospective multicenter study. *Arch Endocrinol Metab* 64:45-51.

Madzia J, McKinney D, Kelly E, and DeFranco E. 2020. Influence of Gestational Weight Gain on the Risk of Preterm Birth for Underweight Women Living in Food Deserts. *Am J Perinatol*.

Marchant T, Willey B, Katz J, Clarke S, Kariuki S, ter Kuile F, Lusingu J, Ndyomugenyi R, Schmiegelow C, Watson-Jones D, and Armstrong Schellenberg J. 2012. Neonatal mortality risk associated with preterm birth in East

Africa, adjusted by weight for gestational age: individual participant level meta-analysis. *PLoS Med* 9:e1001292.

Michels KB, Greenland S, and Rosner BA. 1998. Does body mass index adequately capture the relation of body composition and body size to health outcomes? *Am J Epidemiol* 147:167-172.

Ng M, Fleming T, Robinson M, Thomson B, Graetz N, Margono C, Mullany EC, Biryukov S, Abbafati C, Abera SF, Abraham JP, Abu-Rmeileh NM, Achoki T, AlBuhairan FS, Alemu ZA, Alfonso R, Ali MK, Ali R, Guzman NA, Ammar W, Anwar P, Banerjee A, Barquera S, Basu S, Bennett DA, Bhutta Z, Blore J, Cabral N, Nonato IC, Chang JC, Chowdhury R, Courville KJ, Criqui MH, Cundiff DK, Dabhadkar KC, Dandona L, Davis A, Dayama A, Dharmaratne SD, Ding EL, Durrani AM, Esteghamati A, Farzadfar F, Fay DF, Feigin VL, Flaxman A, Forouzanfar MH, Goto A, Green MA, Gupta R, Hafezi-Nejad N, Hankey GJ, Harewood HC, Havmoeller R, Hay S, Hernandez L, Hussein A, Idrisov BT, Ikeda N, Islami F, Jahangir E, Jassal SK, Jee SH, Jeffreys M, Jonas JB, Kabagambe EK, Khalifa SE, Kengne AP, Khader YS, Khang YH, Kim D, Kimokoti RW, Kinge JM, Kokubo Y, Kosen S, Kwan G, Lai T, Leinsalu M, Li Y, Liang X, Liu S, Logroscino G, Lotufo PA, Lu Y, Ma J, Mainoo NK, Mensah GA, Merriman TR, Mokdad AH, Moschandreas J, Naghavi M, Naheed A, Nand D, Narayan KM, Nelson EL, Neuhauser ML, Nisar MI, Ohkubo T, Oti SO, Pedroza A, Prabhakaran D, Roy N, Sampson U, Seo H, Sepanlou SG, Shibuya K, Shiri R, Shiue I, Singh GM, Singh JA, Skirbekk V, Stapelberg NJ, Sturua L, Sykes BL, Tobias M, Tran BX, Trasande L, Toyoshima H, van de Vijver S, Vasankari TJ, Veerman JL, Velasquez-Melendez G, Vlassov VV, Vollset SE, Vos T, Wang C, Wang X, Weiderpass E, Werdecker A, Wright JL, Yang YC, Yatsuya H, Yoon J, Yoon SJ, Zhao Y, Zhou M, Zhu S, Lopez AD, Murray CJ, and Gakidou E. 2014. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 384:766-781.

Nnam NM. 2015. Improving maternal nutrition for better pregnancy outcomes. *Proc Nutr Soc* 74:454-459.

Oken E, Kleinman KP, Rich-Edwards J, and Gillman MW. 2003. A nearly continuous measure of birth weight for gestational age using a United States national reference. *BMC Pediatr* 3:6.

Paidas Teefey C, Reforma L, Koelper NC, Sammel MD, Srinivas SK, Levine LD, and Durnwald CP. 2020. Risk Factors Associated With Cesarean Delivery After Induction of Labor in Women With Class III Obesity. *Obstet Gynecol* 135:542-549.

Pan Y, Zhang S, Wang Q, Shen H, Zhang Y, Li Y, Yan D, and Sun L. 2016. Investigating the association between prepregnancy body mass index and adverse pregnancy outcomes: a large cohort study of 536 098 Chinese pregnant women in rural China. *BMJ Open* 6:e011227.

Pereira RD, De Long NE, Wang RC, Yazdi FT, Holloway AC, and Raha S. 2015. Angiogenesis in the placenta: the role of reactive oxygen species signaling. *Biomed Res Int* 2015:814543.

Qiu X, Gao F, Qiu Y, Bao J, Gu X, Long Y, Liu F, Cai M, and Liu H. 2017. Association of maternal serum homocysteine concentration levels in late stage of pregnancy with preterm births: a nested case-control study. *J Matern Fetal Neonatal Med*:1-5.

Qu P, Liu F, Zhao D, Wang Y, Wang M, Wang L, Dang S, Wang D, Shi J, and Shi W. 2019. A propensity-matched study of the association between pre-pregnancy maternal underweight and perinatal outcomes of singletons conceived through assisted reproductive technology. *Reprod Biomed Online* 39:674-684.

Rahman MM, Abe SK, Kanda M, Narita S, Rahman MS, Bilano V, Ota E, Gilmour S, and Shibuya K. 2015. Maternal body mass index and risk of birth and maternal health outcomes in low- and middle-income countries: a systematic review and meta-analysis. *Obes Rev* 16:758-770.

- Ronnenberg AG, Wang X, Xing H, Chen C, Chen D, Guang W, Guang A, Wang L, Ryan L, and Xu X. 2003a. Low preconception body mass index is associated with birth outcome in a prospective cohort of Chinese women. *Journal Of Nutrition* 133:3449-3455.
- Ronnenberg AG, Wang XB, Xing HX, Chen CZ, Chen DF, Guang WW, Guang AQ, Wang LH, Ryan L, and Xu XP. 2003b. Low preconception body mass index is associated with birth outcome in a prospective cohort of Chinese women. *Journal Of Nutrition* 133:3449-3455.
- Rutter N. 1995. The extremely preterm infant. *Br J Obstet Gynaecol* 102:682-687.
- Santos S, Voerman E, Amiano P, Barros H, Beilin LJ, Bergstrom A, Charles MA, Chatzi L, Chevrier C, Chrousos GP, Corpeleijn E, Costa O, Costet N, Crozier S, Devereux G, Doyon M, Eggesbo M, Fantini MP, Farchi S, Forastiere F, Georgiu V, Godfrey KM, Gori D, Grote V, Hanke W, Hertz-Picciotto I, Heude B, Hivert MF, Hryhorczuk D, Huang RC, Inskip H, Karvonen AM, Kenny LC, Koletzko B, Kupers LK, Lagstrom H, Lehmann I, Magnus P, Majewska R, Makela J, Manios Y, McAuliffe FM, McDonald SW, Mehegan J, Melen E, Mommers M, Morgen CS, Moschonis G, Murray D, Ni Chaoimh C, Nohr EA, Nybo Andersen AM, Oken E, Oostvogels A, Pac A, Papadopoulou E, Pekkanen J, Pizzi C, Polanska K, Porta D, Richiardi L, Rifas-Shiman SL, Roeleveld N, Ronfani L, Santos AC, Standl M, Stigum H, Stoltenberg C, Thiering E, Thijs C, Torrent M, Tough SC, Trnovec T, Turner S, van Gelder M, van Rossem L, von Berg A, Vrijheid M, Vrijkotte T, West J, Wijga AH, Wright J, Zvinchuk O, Sorensen T, Lawlor DA, Gaillard R, and Jaddoe V. 2019. Impact of maternal body mass index and gestational weight gain on pregnancy complications: an individual participant data meta-analysis of European, North American and Australian cohorts. *BJOG* 126:984-995.
- Sebire NJ, Jolly M, Harris JP, Wadsworth J, Joffe M, Beard RW, Regan L, and Robinson S. 2001. Maternal obesity and pregnancy outcome: a study of 287,213 pregnancies in London. *Int J Obes Relat Metab Disord* 25:1175-1182.
- Shaw GM, Wise PH, Mayo J, Carmichael SL, Ley C, Lyell DJ, Shachar BZ, Melsop K, Phibbs CS, Stevenson DK, Parsonnet J, Gould JB, and March of Dimes Prematurity Research Center at Stanford University School of M. 2014. Maternal prepregnancy body mass index and risk of spontaneous preterm birth. *Paediatr Perinat Epidemiol* 28:302-311.
- Su XJ, Huang SJ, Li X, and Du QL. 2020. Prepregnancy Overweight and Obesity Are Associated with an Increased Risk of Preterm Birth in Chinese Women. *Obes Facts* 13:237-244.
- Vince K, Brkic M, Poljicanin T, and Matijevic R. 2020. Prevalence and impact of pre-pregnancy body mass index on pregnancy outcome: a cross-sectional study in Croatia. *J Obstet Gynaecol*:1-5.
- Weiss JL, Malone FD, Emig D, Ball RH, Nyberg DA, Comstock CH, Saade G, Eddleman K, Carter SM, Craigo SD, Carr SR, D'Alton ME, and Consortium FR. 2004. Obesity, obstetric complications and cesarean delivery rate--a population-based screening study. *Am J Obstet Gynecol* 190:1091-1097.
- Wu J, Yang X, Huang J, Kuang Y, Chen Q, and Wang Y. 2020. Effect of maternal body mass index on neonatal outcomes in women with endometriosis undergoing IVF. *Reprod Biomed Online* 40:559-567.
- Xiao Q, Cui YY, Lu J, Zhang GZ, and Zeng FL. 2016. Risk for Gestational Diabetes Mellitus and Adverse Birth Outcomes in Chinese Women with Polycystic Ovary Syndrome. *Int J Endocrinol* 2016:5787104.
- Young TK, and Woodmansee B. 2002. Factors that are associated with cesarean delivery in a large private practice: the importance of prepregnancy body mass index and weight gain. *Am J Obstet Gynecol* 187:312-318; discussion 318-320.
- Zhou BF, and Cooperative Meta-Analysis Group of the Working Group on Obesity in C. 2002. Predictive values of

416 body mass index and waist circumference for risk factors of certain related diseases in Chinese adults--
 417 study on optimal cut-off points of body mass index and waist circumference in Chinese adults. *Biomed*
 418 *Environ Sci* 15:83-96.
 419 Zhou Y, Li H, Zhang Y, Zhang L, Liu J, and Liu J. 2019. Association of Maternal Obesity in Early Pregnancy with
 420 Adverse Pregnancy Outcomes: A Chinese Prospective Cohort Analysis. *Obesity (Silver Spring)* 27:1030-
 421 1036.
 422

Table 1 (on next page)

Baseline maternal characteristics of the first-time mothers between two groups

Table 1

1 Table 1:

2 Baseline maternal characteristics of the first-time mothers between two groups

variable	Terms (N=3362)	PTB (N=322)	<i>P</i>	Normal (N=3367)	LBW (N=317)	<i>P</i>
Age			<0.001			<0.001
< 25	421 (12.52)	55 (17.08)		418 (12.41)	58 (18.30)	
25-34	2628 (78.17)	220 (68.32)		2630 (78.11)	218 (68.77)	
≥ 35	313 (9.31)	47 (14.60)		319 (9.48)	41 (12.93)	
Health insurance			<0.001			<0.001
Care for urban employees	2269 (67.49)	161 (50.00)		2261 (67.15)	169 (53.31)	
Free medical service	87 (2.59)	6 (1.86)		90 (2.67)	3 (0.95)	
Full-cost	1006 (29.92)	155 (47.14)		1016 (30.18)	145 (45.74)	
Occupation			0.004			0.007
Professional	1534 (45.63)	119 (36.96)		1532 (45.50)	121 (38.17)	
Business	355 (10.56)	28 (8.70)		358 (10.63)	25 (7.89)	
Housewife	389 (11.57)	46 (14.29)		388 (11.52)	47 (14.83)	
Others	1084 (32.24)	129 (40.06)		1089 (32.35)	124 (39.12)	
Gravidity			0.214			0.875
< 2	2245 (66.78)	204 (63.35)		2237 (66.44)	212 (66.88)	
≥ 2	1117 (33.22)	118 (36.65)		1130 (33.56)	105 (33.12)	
Education			<0.001			<0.001
Less than high school	439 (13.06)	86 (26.71)		444 (13.19)	81 (25.55)	
High school	444 (13.21)	38 (11.80)		443 (13.16)	39 (12.30)	
College	2479 (73.73)	198 (61.49)		2480 (73.65)	197 (62.15)	

3 Abbreviation: PTB, preterm birth; LBW, low birth weight.

Table 2(on next page)

Crude and AOR for the association between pre-pregnancy BMI and adverse outcomes

Table 2

1 Table 2:

2 Crude and AOR for the association between pre-pregnancy BMI and adverse outcomes

Outcomes	BMI status	Case	Control	OR (95% CI)	P	AOR* (95% CI)	P
PTB	Underweight	75 (23.29)	783 (23.29)	1.04 (0.79-1.37)	0.787	1.01 (0.76-1.34)	0.943
		197	2137	1.00			
	Normal weight	(61.18)	(63.56)	(reference)		1.00 (reference)	
	Overweight	40 (12.42)	355 (10.56)	1.22 (0.86-1.75)	0.272	1.25 (0.87-1.80)	0.224
LBW	Obesity	10 (3.11)	87 (2.59)	1.25 (0.64-2.44)	0.519	1.27 (0.65-2.51)	0.486
	Underweight	94 (29.65)	764 (22.69)	1.48 (1.14-1.93)	0.003	1.44 (1.11-1.89)	0.007
		179	2155	1.00			
	Normal weight	(56.47)	(64.00)	(reference)		1.00 (reference)	
Gestational hypertension	Overweight	34 (10.73)	361 (10.73)	1.13 (0.77-1.66)	0.521	1.17 (0.80-1.73)	0.423
	Obesity	10 (3.15)	87 (2.58)	1.38 (0.71-2.71)	0.343	1.41 (0.72-2.78)	0.322
	Underweight	13 (9.92)	845 (23.78)	0.43 (0.24-0.78)	0.006	0.45 (0.25-0.82)	0.009
			2254	1.00			
Cesarean delivery	Normal weight	80 (61.07)	(63.44)	(reference)		1.00 (reference)	
	Overweight	23 (17.56)	372 (10.47)	1.74 (1.08-2.81)	0.022	1.71 (1.06-2.77)	0.03
	Obesity	15 (11.45)	82 (2.31)	5.15 (2.85-9.33)	<0.001	5.54 (3.02-10.17)	<0.001
		194		0.70 (0.59-0.84)	<0.001	0.74 (0.62-0.90)	0.002
Cesarean delivery	Underweight	(17.60)	664 (25.72)	1.00			
		686	1684	(reference)		1.00 (reference)	
	Normal weight	(62.25)	(63.83)	2.01 (1.62-2.50)	<0.001	1.91 (1.53-2.38)	<0.001
	Overweight	(16.33)	215 (8.33)				

**1.84 (1.22-
2.77)**

0.004

1.85 (1.21-2.82)

0.004

Obesity

42 (3.81)

55 (2.13)

3 Abbreviations: OR, odds ratio; CI, confidence interval; AOR, adjusted odds ratio; PTB, preterm birth; LBW, low birth weight.

4 *Adjusted OR and 95% CI were calculated by the logistic regression model after adjusting for age, health insurance, occupation and education.

Table 3(on next page)

Adjusted* a relative risk for the associations between pre-pregnancy BMI and PTB by gestational age

Table 3

1 Table 3:

2 Adjusted* a relative risk for the associations between pre-pregnancy BMI and PTB by gestational age

Gestational age	Underweight	Normal weight	Overweight	Obesity
Term	-	1.00 (reference)	-	-
Moderately PTB	0.97 (0.71-1.33)	1.00 (reference)	1.18 (0.79-1.77)	1.23 (0.58-2.59)
Very PTB	1.05 (0.54-2.02)	1.00 (reference)	1.28 (0.55-2.96)	0.77 (0.10-5.77)
Extremely PTB	3.22 (0.53-19.59)	1.00 (reference)	8.12 (1.11-59.44)	15.06 (1.32-172.13)

3 Abbreviations: PTB, preterm birth.

4 *Adjusted OR and 95% CI were calculated by the logistic regression model after adjusting for age, health insurance, occupation and education.

5

Table 4(on next page)

Adjusted* a relative risk for the associations between pre-pregnancy BMI and weight for gestational age

Table 4

1 Table 4:

2 Adjusted* a relative risk for the associations between pre-pregnancy BMI and weight for gestational age

Weight for gestational age	Underweight	Normal weight	Overweight	Obesity
NSAG				
Term	-	1.00 (reference)	-	-
34–36 week	0.88 (0.58-1.34)	1.00 (reference)	1.29 (0.80-2.06)	1.40 (0.59-3.29)
<34 week	1.52 (0.94-2.47)	1.00 (reference)	1.48 (0.77-2.84)	0.97 (0.23-4.11)
SAG				
Term	1.78 (1.45-2.17)	1.00 (reference)	0.88 (0.63-1.21)	1.89 (0.48-1.66)
34–36 week	1.49 (0.79-2.81)	1.00 (reference)	0.43 (0.10-1.82)	0.86 (0.12-6.41)
<34 week	0.73 (0.20-2.63)	1.00 (reference)	1.62 (0.44-5.89)	2.23 (0.28-17.91)

3 Abbreviations: NSAG, non-small for gestational age; SAG, small for gestational age.

4 *Adjusted OR and 95% CI were calculated by the logistic regression model after adjusting for age, health insurance, occupation and education.

5