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Risk Factors and Glycemic Control in Small for Gestational Age Infants Born to Mothers with Gestational Diabetes Mellitus: A Case-Control Study Utilizing Propensity Score Matching Based on a Large Population

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TITLE PAGE

Title

Risk Factors and Glycemic Control in Small for Gestational Age Infants Born to Mothers with Gestational Diabetes Mellitus: A Case-Control Study Utilizing Propensity Score Matching Based on a Large Population

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30 **Risk Factors and Glycemic Control in Small for Gestational Age Infants Born to**
31 **Mothers with Gestational Diabetes Mellitus: A Case-Control Study Utilizing Propensity**
32 **Score Matching Based on a Large Population**

33 **Abstract**

34 **Background:** Small for gestational age (SGA) poses a significant concern for newborns, being
35 linked to neonatal complications and potential metabolic disorders in adulthood, especially
36 when born to mothers with gestational diabetes, elevating their risk of complications and
37 mortality. However, the pregnancy risk factors and glycemic control associated with SGA
38 infants born to mothers with gestational diabetes mellitus (GDM) remain unclear.

39 **Aims:** To identify the pregnancy risk factors and glycemic control associated with SGA infants
40 born to mothers with GDM.

41 **Method:** This case-control study was conducted in Fujian among 1910 women with GDM.
42 Data were collected by the integrated electronic medical record system. Using 1:4 propensity
43 scores matching analysis to adjust gestational age as confounder. Univariate and multivariate
44 analyses were performed to identify risk factors.

45 **Results:** Risk factors for SGA born to mothers with GDM included a history of low birth weight,
46 gestational hypertension, oligohydramnios, short maternal height, underweight pre-pregnancy
47 BMI, and inadequate weight growth. While SGA was protected by weakly positive ketonuria
48 levels in the first trimester, multiparous, anemia, and previous uterine scar were protective
49 factors for SGA. Moreover, 2h postprandial glucose in the third trimester, as well as the 0 h and
50 2 h 75g Oral Glucose Tolerance Test (OGTT) were linked to a decreased risk of SGA.

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4 51 **Conclusions:** SGA infants are the result of multifactorial interactions among GDM pregnant
5
6 52 women. Notably, OGTT and glycemic control levels were associated with SGA. There is a
7
8 53 need for enhanced perinatal monitoring and antenatal care to reduce SGA.

11 54 **Strengths and limitations of this study**

- 13 55 ● Propensity score matching effectively controlled for confounding variables and reduced
14
15 56 bias, enhancing the study's result validity. This approach provided credible insights into
16
17 57 risk factors and glycemic control for SGA infants born to mothers with GDM.
- 18
19 58 ● A large population size increases statistical power, enabling the detection of subtle
20
21 59 associations and providing more generalizable findings.
- 22
23 60 ● As a case-control study relying on retrospective data from medical records, there might be
24
25 61 incomplete or missing information that could influence the study outcomes.
- 26
27 62 ● The findings may primarily apply to the specific population from which the data was
28
29 63 collected, limiting their generalizability to other regions or diverse populations.
- 30
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37 64 **Keywords:** Gestational diabetes mellitus; Small for gestational age; Pregnancy risk factors;
38
39 65 Glycemic control

41 66 42 67 **Background**

43
44
45 68 Gestational diabetes mellitus (GDM) is a glucose intolerance that develops or first
46
47 69 becomes detectable during pregnancy [1], which has the most common metabolic disease and
48
49 70 affected up to 25% of pregnant women [2]. GDM is becoming more common in China, with
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51 71 14.8% of pregnant women suffering from the disease [3]. It causes a slew of short-term and
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53 72 long-term maternal and fetal health issues, particularly associated with accelerated growth

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4 73 velocity. Fetuses receive increased amounts of glucose through maternal hyperglycemia, which
5
6 74 promotes insulin secretion and increases fetal growth [4]. Furthermore, hyperglycemia causes
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9 75 placental vascular dysfunction, reducing the supply of oxygen and nutrients to the fetus [5].
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11
12 76 There is still 2.7% GDM pregnant women deliver children that have fetal growth restrictions
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14 77 (FGR) [6]. The incidence of small for gestational age (SGA) infants whose mothers had GDM
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17 78 was 6.45% in China [7], but it is little research is known about SGA infants born to Chinese
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19
20 79 women with GDM.

21
22 80 SGA infants are commonly defined as having birth weight below the 10th percentile for a
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24 81 given gestational age and sex [8], including constitutionally small infants without pathological
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27 82 growth restriction. In China, the total number of SGA births is the fifth highest in the world [9],
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30 83 which imposes a tremendous medical and socioeconomic burden. SGA infants have an
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33 84 increased risk of adverse perinatal outcomes: stillbirth, asphyxia, or birth defects. Additionally,
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36 85 compared to infants of appropriate for gestational age (AGA), SGA infants are prone to have
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39 86 poor cognitive or psychological outcomes as well as metabolic diseases, such as type 2 diabetes,
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42 87 insulin resistance, and arterial hypertension in adulthood [10], [11]. In addition, GDM has been
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45 88 linked to delayed development and stunted fetal growth [12], which may exacerbate the adverse
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48 89 health outcomes of SGA. Epidemiological studies have shown that SGA infants born to mothers
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51 90 with GDM have higher rates of neonatal complications or death [13], [14]. They are also at
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54 91 higher risk of developing long-term cardiovascular offspring hospitalization [15]. Given the
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57 92 seriousness of the consequences, identifying its potential influencing factors is of great
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60 93 significance for the screening and prevention of SGA births among GDM pregnant women.

94 Maternal glycemia is well known to be associated with perinatal outcomes, including

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4 95 influencing offspring' birthweight [16]. According to Hyperglycemia and Adverse Pregnancy
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6 96 outcomes (HAPO), women with higher glucose levels are considered to be at greater risk.
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9 97 Currently, the goals of prenatal treatment are still tight glucose monitoring and strict glucose
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11 98 control [17], [18]. As a result, the portion of women who experience hypoglycemia is generally
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14 99 deemed to be at low risk for antenatal care. Several investigations have reported an association
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17 100 between maternal hypoglycemia and FGR or SGA [19]–[22]. Particularly, Asian women with
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20 101 low glucose levels are vulnerable to delivering infants with FGR [6]. Whereas other researchers
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23 102 haven't reached a similar conclusion [23]. Presently, the related pregnancy factors for SGA
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26 103 born to women with GDM remain unclear. Moreover, few studies have examined the maternal
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29 104 glycemic level associated with SGA infants born to mothers with GDM. After the diagnosis of
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32 105 GDM, timely recognition of glycemic abnormalities is critical for normal fetal growth and
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35 106 development. Consequently, the purpose of this study was to explore the influencing factors
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38 107 during pregnancy associated with SGA infants born to mothers with GDM in China.

108 **Method**

109 **Study design and population**

110 This case-control study included pregnancies affected by GDM who delivered between
111 January 2019 and December 2020 from a tertiary Maternal and Child Health Hospital in Fuzhou
112 City, Fujian Province. All pregnant women followed a routine prenatal care protocol and
113 scheduled frequent visits to the health system to identify risk factors and initiate preventive care
114 measures [24].

115 Eligible participants were pregnant women diagnosed with GDM based on 75 grams oral
116 glucose tolerance test (OGTT) between 24–32 weeks' gestation according to the modified

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4 117 International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria [25],
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6 118 when one or more of the following glucose levels were elevated: fasting plasma glucose level
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9 119 ≥ 5.1 mmol/L, 1 h plasma glucose level ≥ 10.0 mmol/L, and 2 h plasma glucose level ≥ 8.5
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11 120 mmol/L [25]. The pregnant women with multiple gestations, a clinical diagnosis of
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14 121 pregestational diabetes mellitus (PGDM), or overt diabetes (fasting plasma glucose (FBG) \geq
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17 122 7.0 mmol/L or 2-h ≥ 11.0 mmol/L) were excluded. A total of 6,839 participants were enrolled,
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20 123 all of whom had complete demographic and clinical data.

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22 124 All participants included in this study were divided into the SGA group (case group, <10th
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24 125 percentile), AGA group (controlling group, between 10 and 90th percentile), and LGA group
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27 126 (>90th percentile) according to the association between gestational age and birth weight.
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30 127 Finally, for each SGA infant, four gestation age-matched AGA infants were randomly selected
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33 128 using PSM analysis with gestation age-matched (Figure 1).

34 35 129 **Data collection and study outcomes**

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37 130 Maternal demographic characteristics, pregnancy characteristics and pregnancy
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40 131 complications, and outcomes were collected retrospectively by one researcher from the
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43 132 electronic medical record database of the one hospital in our study. In addition, we collected
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46 133 glycemic levels including 75g OGTT glycemia, FPG in the 3rd trimester, and 2-h postprandial
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49 134 glucose in the 3rd trimester. Based on the number of abnormal OGTT values, women with
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52 135 GDM were stratified into 1, 2, or 3 items of abnormal OGTT values, respectively
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54 136 (Supplementary material 1).

55
56 137 The primary outcome of this study was SGA babies born to women with GDM.
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59 138 Gestational age was determined by subtracting the date of last menstrual period (LMP) reported
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4 139 by the mother or by the first ultrasound scan (USS) from the date of birth. SGA was defined as
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6 140 birth weight below the 10th percentile for gestational age and sex, based on birth weight curves
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9 141 in Chinese [26], [27].
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11 142 **Statistical analysis**

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14 143 All statistical analyses were performed using IBM SPSS, version 27.0, and R, version
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16
17 144 4.1.3. We applied a 1:4 nearest-neighbor matching with a caliper of 0.01, a preset value for
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20 145 propensity score matching (PSM), to lessen the potential selection bias and obtain matched data.
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22 146 The outcomes were compared between the SGA group and the AGA group among GDM
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25 147 pregnant women. Continuous variables were presented as mean \pm standard deviation (SD) or as
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27 148 medians (interquartile range [IQR] 25th percentile–75th percentile), compared by using
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30 149 independent *t*-test or the Mann–Whitney test. Categorical variables were presented as the
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33 150 frequency with percentages and analyzed by the Chi-square test or Fisher’s exact test.
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35 151 We examined the risk factors associated with SGA infants born to mothers with GDM
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38 152 using the Binary logistic regression model. Variables were carefully chosen to ensure
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41 153 parsimony of the final model (forward LR, entry 0.05, removal 0.10). Further, to explore the
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44 154 association between maternal glycemc levels and SGA, adjusted for parity, previous uterine
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47 155 scar, history of low birth weight, gestational hypertensive disorder, oligohydramnios, anemia,
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50 156 pre-pregnancy BMI, height, GWG rate, and ketonuria in 1st trimester. A two-sided p-value of
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53 157 <0.05 was considered statistically significant in all analyses.

54 158 **Ethics approval**

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56 159 This study was approved by the Ethics Committee (No.2019-161). Given all maternal and
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59 160 neonatal data were extracted from the hospital EMR system by a unique identifier with no
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4 161 participant involved in the design, the written informed consent was waived.

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6 162 **3 Results**

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9 163 **3.1 Selection of GDM pregnant women**

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11 164 A total of 6,839 GDM pregnant women were enrolled in the study according to eligible
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14 165 and exclusion criteria, including 382 SGA infants, 964 LGA infants, and 5,493 AGA infants.

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17 166 After the 1:4 PSM analysis, 382 SGA infants were selected and 1,528 AGA infants were
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19 167 randomly matched with the SGA group according to the gestational age at birth (Figure 1).

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22 168 After propensity analysis, the mean (*SD*) gestational age at birth was 38.6 (*SD* = 1.61) weeks
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24 169 in the AGA group and 38.59 (*SD* = 1.62) weeks in the SGA group, there was no evidence of
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27 170 differences in the gestational age between the two groups (*P* = 0.983).

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30 171 **3.2 Characteristics and univariate analysis of AGA and SGA**

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32 172 The average age of the participants was 31.67 (*SD* = 4.36) years old. Among all women,
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35 173 Han Chinese accounts for 97.91%. Approximately 50% of the participants in both groups had
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37 174 a college or university education. More than 50% of the women in the SGA group were
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40 175 nulliparous, which was slightly more than the percentage of women in the AGA group (35.3%)
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42
43 176 who were nulliparous (*P* < 0.001). The previous uterine scar was shown statistically significant
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45 177 (*P* < 0.05).

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48 178 Regarding the pregnancy history, there was no statistically significant evidence of
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51 179 differences in the history of abortion or miscarriage, history of preterm delivery, history of fetal
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53 180 distress, and history of GDM. While statistically significant evidence of differences in history
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56 181 of macrosomia (*P* = 0.012) and history of low birth weight (*P* = 0.04), differences in
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58 182 oligohydramnios (*P* < 0.001) and anemia (*P* = 0.034) were statistically significant in terms of the

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4 183 pregnancy complications.

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6 184 In addition, height, pre-pregnancy BMI, and GWG rate were shown statistically significant
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9 185 (all $P < 0.05$). Regarding the glycemic level, 75g OGTT 0 h and 2 h glycemia, ketonuria in 1st
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11 186 trimester, fasting glucose, and 2-h postprandial glucose in the 3rd trimester were shown
12
13 187 statistically significant ($P < 0.05$). The characteristics of the SGA group and AGA group are
14
15 188 presented in Table 1.

19 189 **3.3 Multivariable logistic regression analysis for the factors of SGA**

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22 190 The multivariable analysis indicated that history of low birth weight (OR=5.01, 95%CI
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24 191 1.21-20.72, $P=0.026$) was an independent risk factor for SGA. Mothers with gestational
25
26 192 hypertensive disorder were more likely to have SGA (Gestational hypertension: OR=2.78,
27
28 193 95%CI 1.68-4.59, $P < 0.001$; preeclampsia and eclampsia: OR=6.31, 95%CI 3.35-11.91, $P <$
29
30 194 0.001). The risk of SGA was fourfold greater in pregnant women with oligohydramnios than in
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32 195 women with normal amniotic fluid (OR=4.22, 95%CI 2.5-7.12, $P < 0.001$). Mothers with lower
33
34 196 height had a higher risk of SGA (150–154.9 cm: OR=2.02, 95% CI 1.46-2.79, $P < 0.001$; 145–
35
36 197 149.9 cm: OR=1.95, 95%CI 1.21-3.14, $P=0.006$; < 145 cm: OR =7.42, 95%CI 1.76-31.25,
37
38 198 $P=0.006$) compared with >155 cm height. Underweight pre-pregnancy had a 64% more chance
39
40 199 of SGA (OR = 1.64, 95%CI 1.17-2.3, $P = 0.004$) than normal. Also, mothers who had
41
42 200 inadequate weight gain during pregnancy had a 37% more chance of SGA than appropriate gain
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44 201 (OR=1.37, 95%CI 1.05-1.8, $P = 0.023$).

45
46 202 However, the multivariate analysis also revealed that multiparous was a protective factor
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48 203 (OR=0.55, 95%CI 0.43-0.71, $P < 0.001$) compared to nulliparity. The SGA risk was reduced
49
50 204 by previous uterine scar experience (OR=0.57, 95%CI 0.39-0.83, $P=0.004$). Anemia was

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4 205 associated with a decreased incidence of SGA (OR=0.71, 95%CI 0.53-0.96, $P=0.027$). Two or
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6 206 three items with elevated blood glucose values on OGTT showed a lower probability of SGA
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9 207 (OR=0.67, 95%CI 0.52-0.86, $P=0.002$; OR=0.32, 95%CI 0.18-0.55, $P < 0.001$) than one
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11 208 elevated item. Ketonuria levels ranging from 0.5 to 3.9 mmol/l in the 1st trimester had a lower
12
13 209 risk of SGA than < 0.5 mmol/l. (OR=0.59, 95%CI 0.42-0.81, $P=0.001$). The forest map of
14
15 210 multivariate logistic regression analysis is shown in Figure 2.

211 3.4 Association between Blood glucose level and the risk of SGA

212 We further explored the relationship between OGTT, glycemic control level in 3rd
213 trimester and SGA. Specifically, multivariate analysis revealed that when adjusted for parity,
214 previous uterine scar, history of low birth weight, gestational hypertensive disorder,
215 oligohydramnios, anemia, pre-pregnancy BMI, height, GWG rate, and ketonuria in 1st trimester.
216 75g OGTT 0 h glycemia, 75g OGTT 2 h glycemia, and 2-h postprandial glucose in 3rd trimester
217 were associated with a decreased risk for SGA (OR=0.44, 95% CI 0.32-0.6, $P < 0.001$;
218 OR=0.89, 95% CI 0.82-0.96, $P=0.003$; OR = 0.84, 95% CI 0.76-0.93, $P < 0.001$). Nevertheless,
219 75g OGTT 0 h glycemia had a stronger association with SGA outcomes than 2-h OGTT and
220 2-h postprandial glucose in 3rd trimester did. While there were no significant associations
221 between 75g OGTT 1 h glycemia, FPG in 3rd trimester and SGA (Table 2).

222 4 Discussion

223 In this retrospective study, some key maternal demographic characteristics (height, BMI,
224 and GWG rate), pregnancy characteristics (parity, previous uterine scar, and history of LBW),
225 pregnancy complications (hypertensive disorders, oligohydramnios, and anemia), OGTT (0h,

226 2h) and glycemic control level (2-h postprandial glucose in the 3rd trimester) were identified
227 as risk factors for SGA in GDM.

228 Maternal height exerts the most significant effect. Our results also confirmed maternal
229 stature <145cm is a strong indicator for SGA, which was similar to previous studies [28]. This
230 may contribute to inadequate self-nutrition in GDM pregnant women who were short stature,
231 while the shift to a sugar-controlled diet may have a significant impact on the adequate supply
232 of nutrients for fetal growth. Further, GWG and BMI both reflect maternal nutritional status.
233 This study found that inadequate weight gain and underweight BMI were associated with an
234 increased risk of SGA in women with GDM, similar to previous findings. [29]. This may be
235 due to pregnant women who were inadequate weight gain or were underweight may have
236 chronic malnutrition, which is harmful to fetal growth and development. Thus, health
237 education, pregnancy nutrition monitoring, and personalized nutrition therapy should be
238 provided to women diagnosed with GDM by the hospital.

239 Nulliparous pregnant women with GDM were associated with an increased risk of SGA
240 birth outcomes in this study. A retrospective study in Chinese suggested that nulliparity was
241 associated with an increased risk of SGA [30]. This could be explained by multiparous women
242 having higher uteroplacental blood flow, allowing the fetus to access more energy, and a larger
243 uterine cavity creating favorable conditions for fetal growth [30]. While nulliparous women
244 with a higher pulsatility index of uterine artery (UtA-PI) and higher blood impedance than
245 multiparous women, resulting in less uteroplacental perfusion, blood flow and SGA [31], [32].
246 Apart from physiological reasons, first-time mothers with GDM have even less experience in
247 managing the demands of dietary change and glycemic control. Cesarean sections are preferred

248 by Chinese women. In 2018, the rate of Chinese maternal cesarean section was 36.7%, the
249 highest in Asia [33]. In this research, having a history of previous uterine scar reduced the risk
250 of giving birth to SGA among GDM pregnant women. The reason could be concluded that the
251 previous uterine scar may be the established association between the multiparous and high rate
252 of cesarean section in China.

253 Women with GDM are also at an increased risk for Hypertensive disorders (HD) due to
254 insulin resistance and underlying pathology of the metabolic syndrome [34]. HD is closely
255 associated with birth weight [35], and GDM combined with HD increases the risk of adverse
256 outcomes. This corresponds with our findings that gestational hypertension as well as
257 preeclampsia and eclampsia are risk factors for delivering SGA in pregnant women with GDM.
258 HD can cause maternal umbilical blood vessel spasms and systemic small arterial spasms,
259 which affect maternal-fetal circulation and insufficient oxygen supply, thus affecting the
260 intrauterine growth and development of the fetus [36]. With hypertensive disorders, the
261 decrease of serum vascular endothelial growth factor (VEGF) and placental growth factor
262 (PlGF) levels and the increase of soluble fms-like tyrosine kinase-1 (sFLT-1) levels may reflect
263 underlying placental dysfunction and are related to fetal growth and development inhibition
264 [37], [38]. Oligohydramnios may be accompanied by complicated pregnancy, such as
265 hypertensive disorders [39]. This could be a sign of chronic suboptimal placental function [40],
266 which might reduce fetal resources and are associated with SGA. Thus, maternal blood pressure
267 should be closely monitored and regular ultrasound examinations should be performed to assess
268 changes in her condition.

269 Contrary to earlier research, this study discovered that maternal anemia during pregnancy

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4 270 reduces the incidence of SGA [41]. The reason could be that women with GDM pay close
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6 271 attention to their diet, including supplementation recommended by their obstetrician to correct
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9 272 anemia. As a result, they may be able to reduce the risk of SGA with appropriate nutritional
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11 273 supplementation. Besides, the effect of anemia on pregnancy outcomes varies between
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13
14 274 gestational periods. Therefore, further research is needed to investigate the effect of hemoglobin
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17 275 concentration on SGA at different gestational ages.

18
19 276 There is no doubt that maternal glycemic parameter levels influence fetal growth [42].
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21
22 277 Compared with GDM women having only one hyperglycemic value in OGTT, those with 2 or
23
24 278 3 elevated glucose values may decrease the risk of SGA. This may contribute to a more severe
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27 279 disturbance in glucose metabolism and insulin sensitivity. Blood glucose passes through the
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30 280 placental circulation to the fetus, and extra glucose in the fetus is stored as body fat [43]. Besides,
31
32 281 OGTT-0h and OGTT-2h were found to be significant predictors of SGA when the glucose
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35 282 values were analyzed as continuous variables. Therefore, for GDM women with high fasting
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38 283 glucose and 2h OGTT are less likely to deliver SGA infants and therefore need to be aware of
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41 284 their potential to deliver high birth weight newborns. In addition, GDM women with low 0h
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43 285 and 2h OGTT do not need for excessively rigorous strict glucose control throughout pregnancy,
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46 286 but should be concerned about the occurrence of FGR. It is therefore important to adjust their
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49 287 dietary, exercise and insulin management strategies according to their glycaemic status. As a
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51 288 result, their nutritional measures, exercise, and insulin administration must be tailored to their
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53 289 glycemic condition.

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56 290 The results of the multifactorial analysis showed that 2-h postprandial glucose in the 3rd
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58 291 trimester was associated with delivering SGA in pregnant women with GDM. 2-h postprandial

292 glucose after GDM diagnosis can reflect the appropriateness of a diet modification plan [44].

293 In clinical practice, pregnant women are advised to control their glycemic levels when

294 diagnosed with GDM. However, due to fear of insulin and lack of knowledge about GDM

295 treatment options, some women may follow an overly strict diet. Consequently, maternal

296 glucose regulation is inadequate, which can lead to fetal undergrowth [20]. Hence, pregnant

297 women diagnosed with GDM should be warned of the potential risk of SGA if they are found

298 to have low glucose values. Besides, more attention should be paid to glucose status in the

299 practice of maternal and child health care. Understanding the glycemic status is an important

300 step in adjusting the diet and exercise plan, ideally to ensure normal fetal development and

301 avoid SGA.

302 **Limitation**

303 There are a few limitations to our analysis. Firstly, data regarding women's history of

304 smoking and drinking was not recorded. Although the incidence of smoking and drinking

305 among pregnant women is low due to Chinese customs, smoking and drinking experience may

306 be potential contributors to SGA. Secondly, data was collected from a single hospital and may

307 not be representative of other areas. Thirdly, this study is a **case-control** study even though a

308 PSM analysis was conducted to minimize the bias.

309 **Conclusion**

310 SGA infants born to women with GDM are the result of a multifactorial interaction,

311 including maternal demographic characteristics, pregnancy characteristics, pregnancy

312 complications and clinical and laboratory parameters. Notably, SGA was correlated with OGTT

313 and glycemic control levels. It is difficult to reverse once SGA has occurred, perinatal

314 monitoring and antenatal care are crucial for identifying risk factors that can help predict and
315 prevent SGA.

316

317 **DECLARATION**

318 **Ethics approval and consent to participate**

319 This study was performed in accordance with the Declaration of Helsinki. The study was
320 approved by the Ethical Committee of Fujian Maternal and Child Health Hospital, affiliated
321 hospital of Fujian Medical University, China (No: 2019-161). As this was a retrospective case-
322 control study involving review of medical records, informed consent from individual
323 participants was not obtained. However, all data collected were treated confidentially and used
324 solely for the purpose of this study. Measures were taken to ensure the privacy and anonymity
325 of the patients' information.

326 **Consent for publication**

327 Not applicable.

328 **Availability of data and materials**

329 The dataset supporting the conclusions is available from the corresponding author on
330 reasonable request.

331 **Conflict of interest**

332 No conflict of interest has been declared by the authors.

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336 Author contributions

337 Jianing Li and Yuqing Pan: Writing- Original draft preparation, Writing- Reviewing and
338 Editing, Visualization. Xiumin Jiang: Supervision, Conceptualization. Qingxiang Zheng and
339 Xiaoqian Chen: Methodology, Validation. Yu Zhu, Rulin Liu and Ling Huang: Investigation,
340 Data curation.

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344 Reference

- 345 [1] L. Reitzle *et al.*, ‘Gestational diabetes in Germany: Development of screening
346 participation and prevalence’, Robert Koch-Institut, report, Jun. 2021. doi:
347 10.25646/8325.
- 348 [2] A. A. Choudhury and V. Devi Rajeswari, ‘Gestational diabetes mellitus - A metabolic
349 and reproductive disorder’, *Biomedicine & Pharmacotherapy*, vol. 143, p. 112183, Nov.
350 2021, doi: 10.1016/j.biopha.2021.112183.
- 351 [3] C. Gao, X. Sun, L. Lu, F. Liu, and J. Yuan, ‘Prevalence of gestational diabetes mellitus
352 in mainland China: A systematic review and meta-analysis’, *J Diabetes Investig*, vol. 10,
353 no. 1, pp. 154–162, Jan. 2019, doi: 10.1111/jdi.12854.
- 354 [4] J. Pedersen, ‘Weight and Length at Birth of Infants of Diabetic Mothers’, *Acta*
355 *Endocrinologica (Norway)*, vol. 16, no. 4, pp. 330–342, Aug. 1954, doi:
356 10.1530/acta.0.0160330.
- 357 [5] I. M. Langmia *et al.*, ‘Cardiovascular Programming During and After Diabetic Pregnancy:
358 Role of Placental Dysfunction and IUGR’, *Front Endocrinol (Lausanne)*, vol. 10, p. 215,
359 Apr. 2019, doi: 10.3389/fendo.2019.00215.
- 360 [6] A. U. Nayak, A. M. A. Vijay, R. Indusekhar, S. Kalidindi, V. M. Katreddy, and L.
361 Varadhan, ‘Association of hypoglycaemia in screening oral glucose tolerance test in
362 pregnancy with low birth weight fetus’, *World J Diabetes*, vol. 10, no. 5, pp. 304–310,
363 May 2019, doi: 10.4239/wjd.v10.i5.304.
- 364 [7] J. Chen *et al.*, ‘Demographic and Clinical Features of Small-for-Gestational-Age Infants
365 Born to Mothers With Gestational Diabetes Mellitus’, *Frontiers in Pediatrics*, vol. 9,
366 2021, Accessed: Nov. 19, 2022. [Online]. Available:
367 <https://www.frontiersin.org/articles/10.3389/fped.2021.741793>
- 368 [8] R. A. Pilliod, Y. W. Cheng, J. M. Snowden, A. E. Doss, and A. B. Caughey, ‘The risk of
369 intrauterine fetal death in the small-for-gestational-age fetus’, *Am J Obstet Gynecol*, vol.

- 370 207, no. 4, p. 318.e1–6, Oct. 2012, doi: 10.1016/j.ajog.2012.06.039.
- 371 [9] A. C. C. Lee *et al.*, ‘National and regional estimates of term and preterm babies born small
372 for gestational age in 138 low-income and middle-income countries in 2010’, *Lancet Glob
373 Health*, vol. 1, no. 1, pp. e26–36, Jul. 2013, doi: 10.1016/S2214-109X(13)70006-8.
- 374 [10] R. P. Anne *et al.*, ‘Propensity-Matched Comparison of Very Preterm Small- and
375 Appropriate-for-Gestational-Age Neonates’, *Indian J Pediatr*, vol. 89, no. 1, pp. 59–66,
376 Jan. 2022, doi: 10.1007/s12098-021-03878-3.
- 377 [11] Q. Chen *et al.*, ‘Association between maternal blood lipids levels during pregnancy and
378 risk of small-for-gestational-age infants’, *Sci Rep*, vol. 10, p. 19865, Nov. 2020, doi:
379 10.1038/s41598-020-76845-1.
- 380 [12] A. Yuste Gómez, M. del P. Ramos Álvarez, and J. L. Bartha, ‘Influence of Diet and
381 Lifestyle on the Development of Gestational Diabetes Mellitus and on Perinatal Results’,
382 *Nutrients*, vol. 14, no. 14, p. 2954, Jul. 2022, doi: 10.3390/nu14142954.
- 383 [13] B. Barquiel, L. Herranz, N. Martínez-Sánchez, C. Montes, N. Hillman, and J. L. Bartha,
384 ‘Increased risk of neonatal complications or death among neonates born small for
385 gestational age to mothers with gestational diabetes’, *Diabetes Research and Clinical
386 Practice*, vol. 159, p. 107971, Jan. 2020, doi: 10.1016/j.diabres.2019.107971.
- 387 [14] T. F. Esakoff, A. Guillet, and A. B. Caughey, ‘Does small for gestational age worsen
388 outcomes in gestational diabetics?’, *The Journal of Maternal-Fetal & Neonatal Medicine*,
389 vol. 30, no. 8, pp. 890–893, Apr. 2017, doi: 10.1080/14767058.2016.1193142.
- 390 [15] E. Neimark, T. Wainstock, E. Sheiner, L. Fischer, and G. Pariente, ‘Long-term
391 cardiovascular hospitalizations of small for gestational age (SGA) offspring born to
392 women with and without gestational diabetes mellitus (GDM) ‡’, *Gynecol Endocrinol*,
393 vol. 35, no. 6, pp. 518–524, Jun. 2019, doi: 10.1080/09513590.2018.1541233.
- 394 [16] L. N. R. Alves *et al.*, ‘Investigation of maternal polymorphisms in genes related to glucose
395 homeostasis and the influence on birth weight: a cohort study’, *J Pediatr (Rio J)*, vol. 98,
396 no. 3, pp. 296–302, Sep. 2021, doi: 10.1016/j.jpmed.2021.06.007.
- 397 [17] X. Cao *et al.*, ‘Comprehensive intensive therapy for Chinese gestational diabetes benefits
398 both newborns and mothers’, *Diabetes Technol Ther*, vol. 14, no. 11, pp. 1002–1007, Nov.
399 2012, doi: 10.1089/dia.2012.0142.
- 400 [18] S. Morampudi, G. Balasubramanian, A. Gowda, B. Zomorodi, and A. S. Patil, ‘The
401 Challenges and Recommendations for Gestational Diabetes Mellitus Care in India: A
402 Review’, *Front Endocrinol (Lausanne)*, vol. 8, p. 56, Mar. 2017, doi:
403 10.3389/fendo.2017.00056.
- 404 [19] T. Dassios, A. Greenough, S. Leontiadi, A. Hickey, and N. A. Kametas, ‘Admissions for
405 hypoglycaemia after 35 weeks of gestation: perinatal predictors of cost of stay’, *J Matern
406 Fetal Neonatal Med*, vol. 32, no. 3, pp. 448–454, Feb. 2019, doi:
407 10.1080/14767058.2017.1381905.
- 408 [20] J. Leng *et al.*, ‘Small-for-gestational age and its association with maternal blood glucose,
409 body mass index and stature: a perinatal cohort study among Chinese women’, *BMJ Open*,
410 vol. 6, no. 9, p. e010984, Sep. 2016, doi: 10.1136/bmjopen-2015-010984.
- 411 [21] I. B. Delibas, S. Tanriverdi, and B. Cakmak, ‘Does reactive hypoglycemia during the 100
412 g oral glucose tolerance test adversely affect perinatal outcomes?’, *Ginekol Pol*, vol. 89,

- 1
2
3 413 no. 1, pp. 25–29, 2018, doi: 10.5603/GP.a2018.0005.
- 4 414 [22] S. Shinohara, Y. Uchida, M. Hirai, S. Hirata, and K. Suzuki, ‘Relationship between
5 415 maternal hypoglycaemia and small-for-gestational-age infants according to maternal
6 416 weight status: a retrospective cohort study in two hospitals’, *BMJ Open*, vol. 6, no. 12, p.
7 417 e013749, Dec. 2016, doi: 10.1136/bmjopen-2016-013749.
- 8 418 [23] M. Morikawa *et al.*, ‘Glycemic control and fetal growth of women with diabetes mellitus
9 419 and subsequent hypertensive disorders of pregnancy’, *PLOS ONE*, vol. 15, no. 3, p.
10 420 e0230488, Mar. 2020, doi: 10.1371/journal.pone.0230488.
- 11 421 [24] W. Hu, H. Hu, W. Zhao, A. Huang, Q. Yang, and J. Di, ‘Current status of antenatal care
12 422 of pregnant women-8 provinces in China, 2018’, *BMC Public Health*, vol. 21, no. 1, p.
13 423 1135, Jun. 2021, doi: 10.1186/s12889-021-11154-4.
- 14 424 [25] International Association of Diabetes and Pregnancy Study Groups Consensus Panel *et*
15 425 *al.*, ‘International association of diabetes and pregnancy study groups recommendations
16 426 on the diagnosis and classification of hyperglycemia in pregnancy’, *Diabetes Care*, vol.
17 427 33, no. 3, pp. 676–682, Mar. 2010, doi: 10.2337/dc09-1848.
- 18 428 [26] L. Dai *et al.*, ‘Population-based birth weight reference percentiles for Chinese twins’, *Ann*
19 429 *Med*, vol. 49, no. 6, pp. 470–478, Sep. 2017, doi: 10.1080/07853890.2017.1294258.
- 20 430 [27] B. Zhang *et al.*, ‘Birthweight percentiles for twin birth neonates by gestational age in
21 431 China’, *Sci Rep*, vol. 6, p. 31290, Aug. 2016, doi: 10.1038/srep31290.
- 22 432 [28] R. Khanam *et al.*, ‘Maternal short stature and under-weight status are independent risk
23 433 factors for preterm birth and small for gestational age in rural Bangladesh’, *Eur J Clin*
24 434 *Nutr*, vol. 73, no. 5, pp. 733–742, May 2019, doi: 10.1038/s41430-018-0237-4.
- 25 435 [29] Q.-X. Zheng *et al.*, ‘Prepregnancy body mass index and gestational weight gain are
26 436 associated with maternal and infant adverse outcomes in Chinese women with gestational
27 437 diabetes’, *Sci Rep*, vol. 12, no. 1, p. 2749, Feb. 2022, doi: 10.1038/s41598-022-06733-3.
- 28 438 [30] L. Lin, C. Lu, W. Chen, C. Li, and V. Y. Guo, ‘Parity and the risks of adverse birth
29 439 outcomes: a retrospective study among Chinese’, *BMC Pregnancy Childbirth*, vol. 21, p.
30 440 257, Mar. 2021, doi: 10.1186/s12884-021-03718-4.
- 31 441 [31] F. Prefumo, A. Bhide, S. Sairam, L. Penna, B. Hollis, and B. Thilaganathan, ‘Effect of
32 442 parity on second-trimester uterine artery Doppler flow velocity and waveforms’,
33 443 *Ultrasound Obstet Gynecol*, vol. 23, no. 1, pp. 46–49, Jan. 2004, doi: 10.1002/uog.908.
- 34 444 [32] I. Derwig *et al.*, ‘Association of placental perfusion, as assessed by magnetic resonance
35 445 imaging and uterine artery Doppler ultrasound, and its relationship to pregnancy
36 446 outcome’, *Placenta*, vol. 34, no. 10, pp. 885–891, Oct. 2013, doi:
37 447 10.1016/j.placenta.2013.07.006.
- 38 448 [33] J. Qiao *et al.*, ‘A Lancet Commission on 70 years of women’s reproductive, maternal,
39 449 newborn, child, and adolescent health in China’, *Lancet*, vol. 397, no. 10293, pp. 2497–
40 450 2536, Jun. 2021, doi: 10.1016/S0140-6736(20)32708-2.
- 41 451 [34] Y. Baumfeld *et al.*, ‘Pre-Conception Dyslipidemia Is Associated with Development of
42 452 Preeclampsia and Gestational Diabetes Mellitus’, *PLoS One*, vol. 10, no. 10, p. e0139164,
43 453 Oct. 2015, doi: 10.1371/journal.pone.0139164.
- 44 454 [35] N. Li *et al.*, ‘Preconception Blood Pressure and Risk of Low Birth Weight and Small for
45 455 Gestational Age: A Large Cohort Study in China’, *Hypertension*, vol. 68, no. 4, pp. 873–

- 1
2
3 456 879, Oct. 2016, doi: 10.1161/HYPERTENSIONAHA.116.07838.
- 4 457 [36] V. A. Luyckx *et al.*, ‘Effect of fetal and child health on kidney development and long-
5 458 term risk of hypertension and kidney disease’, *Lancet*, vol. 382, no. 9888, pp. 273–283,
6 459 Jul. 2013, doi: 10.1016/S0140-6736(13)60311-6.
- 7 460 [37] Y. Tang, W. Ye, X. Liu, Y. Lv, C. Yao, and J. Wei, ‘VEGF and sFLT-1 in serum of PIH
8 461 patients and effects on the foetus’, *Exp Ther Med*, vol. 17, no. 3, pp. 2123–2128, Mar.
9 462 2019, doi: 10.3892/etm.2019.7184.
- 10 463 [38] M. Badagonis, T. N. Sergentanis, P. Pervanidou, E. Kalampokas, N. Vlahos, and M.
11 464 Eleftheriades, ‘Preeclampsia and Cerebral Palsy in Offspring’, *Children (Basel)*, vol. 9,
12 465 no. 3, p. 385, Mar. 2022, doi: 10.3390/children9030385.
- 13 466 [39] N. Rabie, E. Magann, S. Steelman, and S. Ounpraseuth, ‘Oligohydramnios in complicated
14 467 and uncomplicated pregnancy: a systematic review and meta-analysis’, *Ultrasound*
15 468 *Obstet Gynecol*, vol. 49, no. 4, pp. 442–449, Apr. 2017, doi: 10.1002/uog.15929.
- 16 469 [40] M. Vahid Dastjerdi, A. Ghahghaei-Nezamabadi, A. Tehranian, and M. Mesgaran, ‘The
17 470 Effect of Sildenafil on Pregnancy Outcomes in Pregnant Women With Idiopathic
18 471 Borderline Oligohydramnios: A Randomized Controlled Trial’, *J Family Reprod Health*,
19 472 vol. 16, no. 2, pp. 124–131, Jun. 2022, doi: 10.18502/jfrh.v16i2.9482.
- 20 473 [41] D. Liu *et al.*, ‘Maternal Hemoglobin Concentrations and Birth Weight, Low Birth Weight
21 474 (LBW), and Small for Gestational Age (SGA): Findings from a Prospective Study in
22 475 Northwest China’, *Nutrients*, vol. 14, no. 4, p. 858, Feb. 2022, doi: 10.3390/nu14040858.
- 23 476 [42] Z. He *et al.*, ‘Late-Pregnancy Dysglycemia After Negative Testing for Gestational
24 477 Diabetes and Risk of the Large-for-Gestational-Age Newborns: A Nest Case-Control
25 478 Study Based on the Xi’an Longitudinal Mother-Child Cohort Study’, *Front Pediatr*, vol.
26 479 10, p. 829706, May 2022, doi: 10.3389/fped.2022.829706.
- 27 480 [43] H. D. McIntyre, J. Fuglsang, U. Kampmann, S. Knorr, and P. Ovesen, ‘Hyperglycemia
28 481 in Pregnancy and Women’s Health in the 21st Century’, *International Journal of*
29 482 *Environmental Research and Public Health*, vol. 19, no. 24, Dec. 2022, doi:
30 483 10.3390/ijerph192416827.
- 31 484 [44] L. Monnier and C. Colette, ‘Target for Glycemic Control’, *Diabetes Care*, vol. 32, no.
32 485 Suppl 2, pp. S199–S204, Nov. 2009, doi: 10.2337/dc09-S310.
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4 488 **Figure 1 Flow diagram of selection of GDM pregnant women in this study**

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6 489 **Abv:** GDM: gestational diabetes mellitus; PSM: propensity score matching; AGA: appropriate
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9 490 for gestational age; LGA: Large for gestational age; SGA: small for gestational age.

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14 492 **Figure 2** Forest plot of the risk factors of SGA (Binary logistic regression analysis).

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Table 1 Characteristics of AGA group and SGA group matched according to 1:4 PSM analysis.

Variables	AGA group (n=1528)	SGA group (n=382)	$\chi^2/t/Z$	<i>P</i>
Maternal Age				
18~35	1220(79.8)	305(79.8)	0.063 ^a	0.969
36~45	305(20)	76(19.9)		
≥46	3(0.2)	1(0.3)		
Nationality				
The Han	1498(98)	372(97.4)	0.638 ^a	0.424
Minority nationality	30(2)	10(2.6)		
Residence				
Urban	825(54)	196(51.3)	0.884 ^a	0.347
Rural	703(46)	186(48.7)		
Education				
Elementary and below	528(34.6)	126(33)	3.476 ^a	0.324
Secondary / Highschool	223(14.6)	45(11.8)		
College / University	770(50.4)	210(55)		
Postgraduate or above	7(0.5)	1(0.3)		
Occupation				
Manual worker	284(18.6)	69(18.1)	2.074 ^a	0.557
Mental worker	708(46.3)	192(50.3)		
Unemployed	381(24.9)	86(22.5)		
Freelance	155(10.1)	35(9.2)		
Marital status				
Unmarried	27(1.8)	8(2.1)	1.179 ^a	0.555
Married	1497(98)	374(97.9)		
Divorced or widowed	4(0.3)	0(0)		
Parity				
Nulliparous	539(35.3)	195(51)	32.130 ^a	<0.001
Multiparous	989(64.7)	187(49)		
Assisted reproductive technology (ART)				
No	1446(94.6)	362(94.8)	.010 ^a	0.919
Yes	82(5.4)	20(5.2)		
Previous uterine scar				
No	1196(78.3)	337(88.2)	19.089 ^a	<0.001
Yes	332(21.7)	45(11.8)		
Family history				
No	1367(89.5)	336(88)	2.809 ^a	0.422
Hypertension	76(5)	26(6.8)		
Diabetes	46(3)	13(3.4)		

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3	Both	39(2.6)	7(1.8)		
4					
5	History of abortion or miscarriage				
6	No	896(58.6)	251(65.7)	6.393 ^a	0.041
7	Spontaneous miscarriage	348(22.8)	71(18.6)		
8	Induced abortions	284(18.6)	60(15.7)		
9					
10	History of preterm delivery				
11	No	1467(96)	368(96.3)	.087 ^a	0.768
12	Yes	61(4)	14(3.7)		
13					
14	History of macrosomia				
15	No	1481(96.9)	379(99.2)	6.290 ^a	0.012
16	Yes	47(3.1)	3(0.8)		
17					
18	History of GDM				
19	No	1523(99.7)	382(100)	1.253 ^a	0.263
20	Yes	5(0.3)	0(0)		
21					
22	History of fetal distress				
23	No	1512(99)	380(99.5)	.897 ^a	0.343
24	Yes	16(1)	2(0.5)		
25					
26	History of low birth weight				
27	No	1523(99.7)	376(98.4)	8.252 ^a	0.004
28	Yes	5(0.3)	6(1.6)		
29					
30	Intrahepatic cholestasis of pregnancy (ICP)				
31	No	1508(98.7)	377(98.7)	.000 ^a	1.000
32	Yes	20(1.3)	5(1.3)		
33					
34	Gestational hypertensive disorder				
35	No	1431(93.7)	324(84.8)	34.867 ^a	<0.001
36	Gestational hypertension	62(4.1)	31(8.1)		
37	Preeclampsia and eclampsia	27(1.8)	22(5.8)		
38	Chronic hypertension with superimposed preeclampsia	4(0.3)	3(0.8)		
39	Chronic hypertension (of any cause)	4(0.3)	2(0.5)		
40					
41	Hyperthyroid				
42	No	1487(97.3)	376(98.4)	1.576 ^a	0.209
43	Yes	41(2.7)	6(1.6)		
44					
45	Hypothyroid				
46	No	1434(93.8)	349(91.4)	3.045 ^a	0.081
47	Yes	94(6.2)	33(8.6)		
48					
49	Anemia				
50	No	1149(75.2)	307(80.4)	4.508 ^a	0.034
51	Yes	379(24.8)	75(19.6)		
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53	Polyhydramnios				
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3	No	1517(99.3)	381(99.7)	1.027 ^a	0.311
4	Yes	11(0.7)	1(0.3)		
5					
6	Oligohydramnios				
7	No	1490(97.5)	349(91.4)	32.314 ^a	<0.001
8	Yes	38(2.5)	33(8.6)		
9					
10	Height (cm)				
11	≥155	1248(81.7)	275(72)	22.232 ^a	<0.001
12	150–154.9	197(12.9)	73(19.1)		
13	145–149.9	79(5.2)	29(7.6)		
14					
15	< 145	4(0.3)	5(1.3)		
16					
17					
18	Pre-pregnancy BMI (kg/m²)				
19	Normal	1130(74)	271(70.9)	9.175 ^a	0.01
20	Underweight	172(11.3)	64(16.8)		
21	Overweight / Obese	226(14.8)	47(12.3)		
22					
23	GWG rate				
24	Inadequate gain	690(45.2)	199(52.1)	6.107 ^a	0.047
25	Appropriate gain	539(35.3)	121(31.7)		
26	Excessive gain	299(19.6)	62(16.2)		
27					
28					
29	Ketonuria in 1st trimester(mmol/l)				
30	< 0.5	1049(68.7)	275(72)	9.963 ^a	0.007
31	0.5-3.9	336(22)	59(15.4)		
32	≥4	143(9.4)	48(12.6)		
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36	Ketonuria in 2nd trimester (mmol/l)				
37	< 0.5	1090(71.3)	293(76.7)	4.903 ^a	0.086
38	0.5-3.9	308(20.2)	59(15.4)		
39	≥4	130(8.5)	30(7.9)		
40					
41					
42	Elevated blood glucose in OGTT				
43	One item	482(31.5)	161(42.1)	24.605 ^a	<0.001
44	Two items	878(57.5)	204(53.4)		
45	Three items	168(11.0)	17(4.5)		
46	75g OGTT 0 h glycemia (mmol/l)	4.83±0.48	4.64±0.44	7.187	<0.001
47	75g OGTT 1 h glycemia (mmol/l)	9.84±1.41	9.89±1.36	-0.585	0.559
48	75g OGTT 2 h glycemia (mmol/l)	8.06±1.59	7.83±1.58	2.586	0.01
49	FPG in the 3rd trimester (mmol/l)	4.48(5.52-5.15)	4.69(4.40-5.01)	-4.7	<0.001
50	2-h postprandial glucose in 3rd trimester (mmol/l)	5.09±1.30	5.7±1.14	5.825	<0.001
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56 494 **Abv:** SGA: small-for-gestational-age; AGA: appropriate-weight-for-gestational-age; OGTT:
 57 495 Oral Glucose Tolerance Test; FPG: fasting plasma glucose; the first trimester of pregnancy:7–
 58 496 10 gestational weeks; the second trimester of pregnancy: 21–24 gestational weeks; the third

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497 trimester of pregnancy: 33–37 gestational weeks.

498 Bold values indicate statistically significant ($P < 0.05$)

499 Data are presented as n (%), mean \pm SD, or median (interquartile range) as appropriate.

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Table 2 Logistic regression analysis for SGA based on maternal glycemc parameters

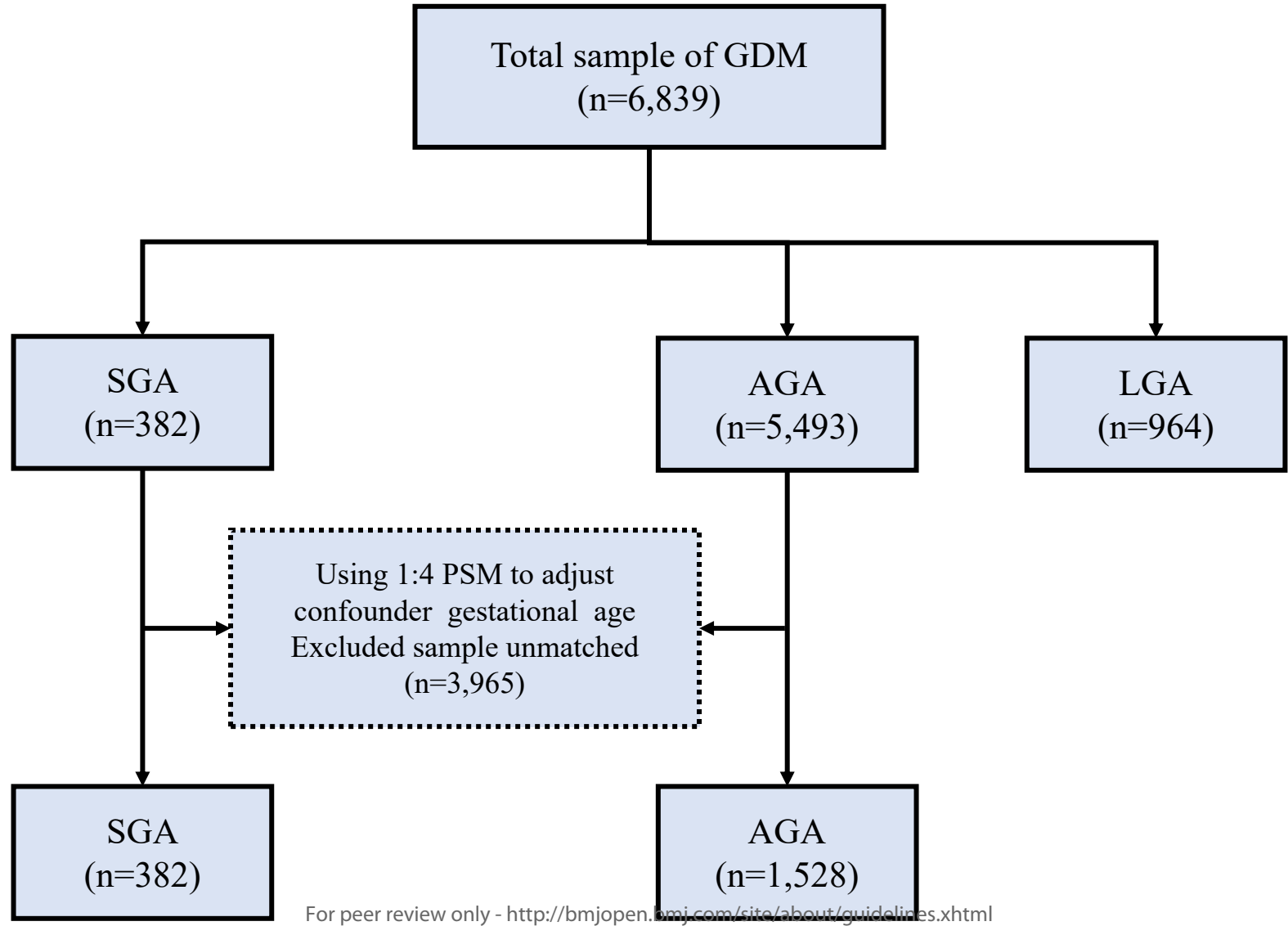
Variables	Crude OR (95% CI)	<i>P</i>	Adjusted† OR (95% CI)	<i>P</i>
75g OGTT 0 h glycemia	0.40(0.31-0.52)	< 0.001	0.44(0.32-0.6)	< 0.001
75g OGTT 1 h glycemia	1.02(0.95-1.11)	0.558	1.04(0.95-1.14)	0.378
75g OGTT 2 h glycemia	0.91(0.85-0.98)	0.010	0.89(0.82-0.96)	0.003
FPG in 3rd trimester	0.59(0.46-0.75)	< 0.001	0.89(0.68-1.15)	0.370
2-h postprandial glucose in 3rd trimester	0.76(0.68-0.84)	< 0.001	0.84(0.76-0.93)	0.001

† Adjusted for parity, previous uterine scar, history of low birth weight, gestational hypertensive disorder, oligohydramnios, anemia, pre-pregnancy BMI, height, GWG rate, and ketonuria in 1st trimester.

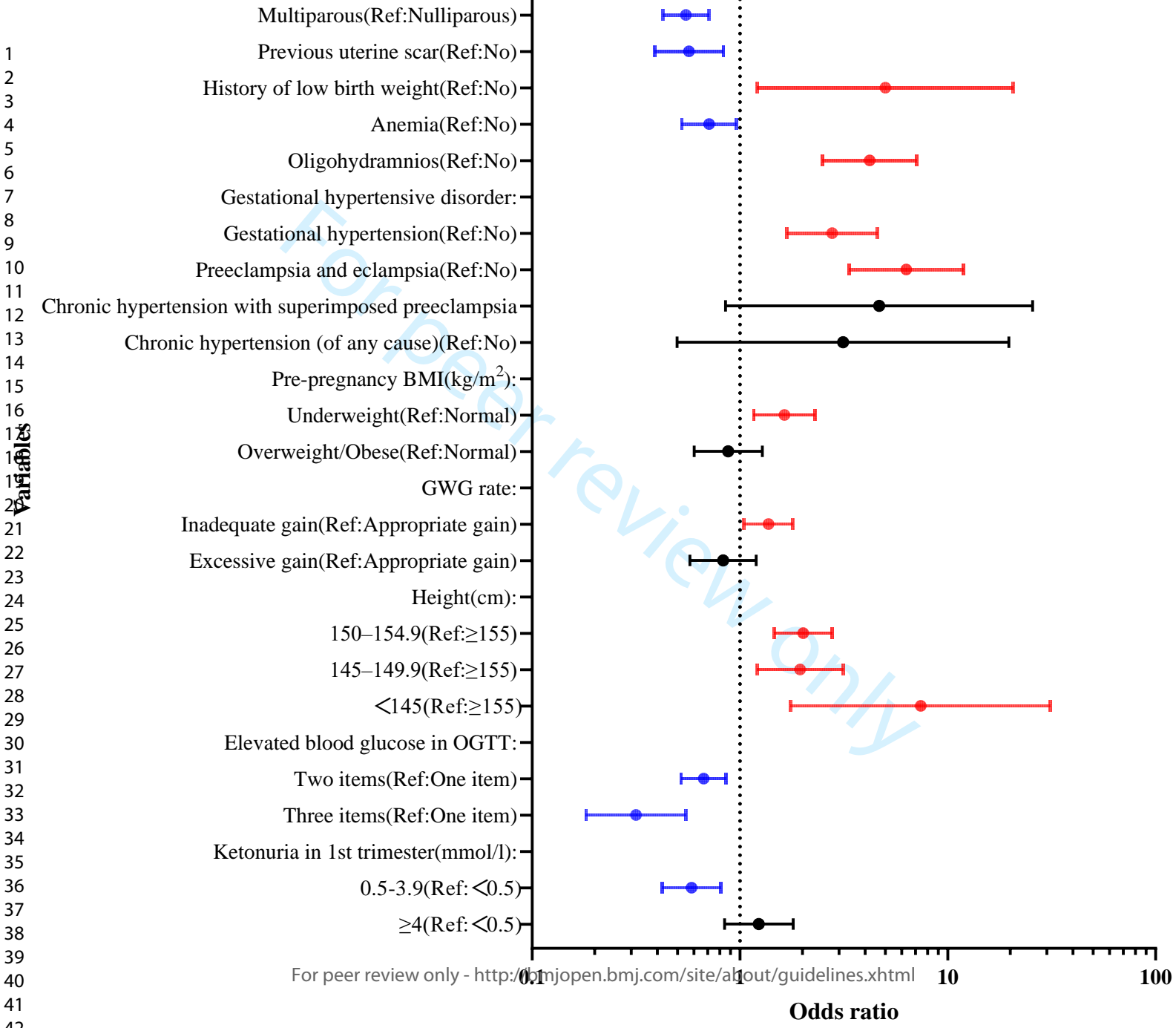
Abv: OGTT: Oral Glucose Tolerance Test; FPG: fasting plasma glucose; the third trimester of pregnancy: 33–37 gestational weeks.

OR: odd ratios, CI: confidence interval.

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Supplementary material 1

1 Maternal demographic characteristic

Maternal characteristics collected included maternal age, ethnicity, educational level, occupation, marital status, place of residence, stature, pre-pregnancy Body mass index, and GWG rate.

Height: women were classified into four categories based on height < 145 cm, 145-149.9 cm, 150-154.9 cm, and ≥ 155 cm. Body mass index (BMI): BMI was calculated as weight (kg)/ [height (m)]². Using BMI, women were classified as underweight (BMI<18.5 kg/m²), normal weight (18.5–24.9 kg/m²), overweight (25–29.9 kg/m²), or obese (≥ 30 kg/m²). Gestational weight gain rate (GWG rate): To assess the adequacy of GWG among the study population, the GWG rate of each participant, which was calculated by dividing the total GWG by gestational age in weeks, was compared with the minimum recommended GWG rate. According to the IOM 2009 guidelines, The GWG of all included participants was categorized as inadequate weight gain, normal weight gain, and excessive weight gain.

2 Pregnancy characteristics

Pregnancy characteristics collected included parity, assisted reproductive technology-conceived pregnancy (ART), previous uterine scar (previous cesarean section or myomectomy), family history of hypertension or diabetes, pregnancy history (history of miscarriage, history of GDM, history of preterm labor, history of fetal distress, history of LBW).

3 Pregnancy complications

Pregnancy complications collected included intrahepatic cholestasis of pregnancy (ICP), pregnancy-associated hypertensive disorders, hyperthyroid, hypothyroid, anemia (defined by

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4 hemoglobin < 11 g/dL before delivery) (Goonewardene, Shehata, and Hamad 2012), and
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7 pathology of amniotic fluid (oligohydramnios and polyhydramnios)

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9 The gestational hypertensive disorder was classified into four categories: gestational
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11 hypertension, preeclampsia, and eclampsia, chronic hypertension with superimposed
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13 preeclampsia, preeclampsia and eclampsia chronic hypertension (of any cause), which was
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15 diagnosed using standard criteria (Anon 2013).
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18 19 **Reference**

20
21
22 Anon. 2013. 'Hypertension in Pregnancy: Executive Summary'. *Obstetrics & Gynecology*
23
24 122(5):1122–31. doi: 10.1097/01.AOG.0000437382.03963.88.
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27 Goonewardene, Malik, Mishkat Shehata, and Asma Hamad. 2012. 'Anaemia in Pregnancy'.
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29 *Best Practice & Research. Clinical Obstetrics & Gynaecology* 26(1):3–24. doi:
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31 10.1016/j.bpobgyn.2011.10.010.
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Reporting checklist for case-control study.

Based on the STROBE case-control guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the STROBE case-control reporting guidelines, and cite them as:

von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies.

			Page Number
Title and abstract			
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	2
Abstract	#1b	Provide in the abstract an informative and balanced summary	2-3

of what was done and what was found

Introduction

Background / [#2](#) Explain the scientific background and rationale for the 3-5
 rationale investigation being reported

Objectives [#3](#) State specific objectives, including any prespecified 5
 hypotheses

Methods

Study design [#4](#) Present key elements of study design early in the paper 5-6

Setting [#5](#) Describe the setting, locations, and relevant dates, including 5-7
 periods of recruitment, exposure, follow-up, and data collection

Eligibility criteria [#6a](#) Give the eligibility criteria, and the sources and methods of 5-6
 case ascertainment and control selection. Give the rationale
 for the choice of cases and controls. For matched studies, give
 matching criteria and the number of controls per case

Eligibility criteria [#6b](#) For matched studies, give matching criteria and the number of 7
 controls per case

[#7](#) Clearly define all outcomes, exposures, predictors, potential 5-6
 confounders, and effect modifiers. Give diagnostic criteria, if
 applicable

Data sources / [#8](#) For each variable of interest give sources of data and details of 8
 measurement methods of assessment (measurement). Describe
 comparability of assessment methods if there is more than one

group. Give information separately for cases and controls.

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4	Bias	#9	Describe any efforts to address potential sources of bias 7
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7	Study size	#10	Explain how the study size was arrived at n/a
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10	Quantitative	#11	Explain how quantitative variables were handled in the 5-6
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12	variables		analyses. If applicable, describe which groupings were
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14			chosen, and why
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17	Statistical	#12a	Describe all statistical methods, including those used to control 5-7
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19	methods		for confounding
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23	Statistical	#12b	Describe any methods used to examine subgroups and n/a
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25	methods		interactions
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28	Statistical	#12c	Explain how missing data were addressed
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30	methods		
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33	Statistical	#12d	If applicable, explain how matching of cases and controls was 7
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35	methods		addressed
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39	Statistical	#12e	Describe any sensitivity analyses n/a
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41	methods		
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44	Results		
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47	Participants	#13a	Report numbers of individuals at each stage of study—eg 8
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49			numbers potentially eligible, examined for eligibility, confirmed
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51			eligible, included in the study, completing follow-up, and
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57	Participants	#13b	Give reasons for non-participation at each stage 8
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1	Participants	#13c	Consider use of a flow diagram	Figure 1
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4	Descriptive data	#14a	Give characteristics of study participants (eg demographic,	8
5			clinical, social) and information on exposures and potential	
6			confounders. Give information separately for cases and	
7			controls	
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14	Descriptive data	#14b	Indicate number of participants with missing data for each	8
15			variable of interest	
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19	Outcome data	#15	Report numbers in each exposure category, or summary	8
20			measures of exposure. Give information separately for cases	
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27	Main results	#16a	Give unadjusted estimates and, if applicable, confounder-	8-9
28			adjusted estimates and their precision (eg, 95% confidence	
29			interval). Make clear which confounders were adjusted for and	
30			why they were included	
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37	Main results	#16b	Report category boundaries when continuous variables were	8-9
38			categorized	
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42	Main results	#16c	If relevant, consider translating estimates of relative risk into	n/a
43			absolute risk for a meaningful time period	
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48	Other analyses	#17	Report other analyses done—e.g., analyses of subgroups and	n/a
49			interactions, and sensitivity analyses	
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53	Discussion			
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56	Key results	#18	Summarise key results with reference to study objectives	10-11
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1	Limitations	#19	Discuss limitations of the study, taking into account sources of	14
2			potential bias or imprecision. Discuss both direction and	
3			magnitude of any potential bias.	
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9	Interpretation	#20	Give a cautious overall interpretation considering objectives,	14
10			limitations, multiplicity of analyses, results from similar studies,	
11			and other relevant evidence.	
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16	Generalisability	#21	Discuss the generalisability (external validity) of the study	11-14
17			results	
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22	Other Information			
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25	Funding	#22	Give the source of funding and the role of the funders for the	15
26			present study and, if applicable, for the original study on which	
27			the present article is based	
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BMJ Open

Risk Factors and Glycemic Control in Small for Gestational Age Infants Born to Mothers with Gestational Diabetes Mellitus: A Case-Control Study Utilizing Propensity Score Matching Based on a Large Population

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Primary Subject Heading:	Paediatrics
Secondary Subject Heading:	Obstetrics and gynaecology
Keywords:	Risk Factors, Diabetes in pregnancy < DIABETES & ENDOCRINOLOGY, Child protection < PAEDIATRICS

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TITLE PAGE**Title**

Risk Factors and Glycemic Control in Small for Gestational Age Infants Born to Mothers with Gestational Diabetes Mellitus: A Case-Control Study Utilizing Propensity Score Matching Based on a Large Population

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4 29 **Risk Factors and Glycemic Control in Small for Gestational Age Infants Born to**
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6 30 **Mothers with Gestational Diabetes Mellitus: A Case-Control Study Utilizing Propensity**
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9 31 **Score Matching Based on a Large Population**
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11 32 **Abstract**

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14 33 **Background:** Small for gestational age (SGA) poses a significant concern for newborns, being
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17 34 linked to neonatal complications and potential metabolic disorders in adulthood, especially
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20 35 when born to mothers with gestational diabetes mellitus (GDM), elevating their risk of
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22 36 complications and mortality. However, the pregnancy risk factors and glycemic control
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25 37 associated with SGA infants born to mothers with GDM remain unclear.

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27 38 **Aims:** To identify the pregnancy risk factors and glycemic control associated with SGA infants
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30 39 born to mothers with GDM.

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32 40 **Method:** This case-control study was conducted among 1910 women with GDM in China. Data
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35 41 were collected by the integrated electronic medical record system. Using 1:4 propensity scores
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38 42 matching analysis to adjust gestational age as confounder. Univariate and multivariate analyses
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41 43 were performed to identify risk factors.

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43 44 **Results:** Risk factors for SGA born to mothers with GDM included a history of low birth weight,
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46 45 gestational hypertension, oligohydramnios, short maternal height, underweight pre-pregnancy
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49 46 BMI, and inadequate weight growth. While SGA was protected by weakly positive ketonuria
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52 47 levels in the first trimester, multiparous, anemia, and previous uterine scar were protective
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54 48 factors for SGA. Moreover, 2-h postprandial glucose and hemoglobin A1c (HbA1c) in the 2nd
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56 49 trimester, as well as the 0-h and 2-h 75g Oral Glucose Tolerance Test (OGTT) were linked to

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4 50 risk of SGA.
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7 51 **Conclusions:** SGA infants are the result of multifactorial interactions among GDM pregnant
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9 52 women. Notably, OGTT and glyceemic control levels were associated with SGA. There is a
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11 53 need for enhanced perinatal monitoring and antenatal care to reduce SGA.
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14 **Strengths and limitations of this study**

- 15
16 55 ● Propensity score matching effectively controlled for confounding variables and reduced
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18 56 bias, enhancing the study's result validity. This approach provided credible insights into
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20 57 risk factors and glyceemic control for SGA infants born to mothers with GDM.
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24 58 ● A large population size increases statistical power, enabling the detection of subtle
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26 59 associations and providing more generalizable findings.
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29 60 ● As a case-control study relying on retrospective data from medical records, there might be
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31 61 incomplete or missing information that could influence the study outcomes.
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34 62 ● The findings may primarily apply to the specific population from which the data was
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36 63 collected, limiting their generalizability to other regions or diverse populations.
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40 64 **Keywords:** Gestational diabetes mellitus; Glyceemic control; Pregnancy risk factors; Small for
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42 65 gestational age
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47 **Background**

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50 68 Gestational diabetes mellitus (GDM) is a glucose intolerance that develops or first
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52 69 becomes detectable during pregnancy [1], which has the most common metabolic disease and
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54 70 affected up to 25% of pregnant women [2]. In China, the prevalence of GDM has been
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4 71 increasing, with 14.8% of pregnant women now affected [3]. This condition gives rise to a
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6 72 range of short-term and long-term maternal and fetal health issues, particularly associated with
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9 73 increased pace of fetal growth. Fetuses receive increased amounts of glucose through maternal
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11 74 hyperglycemia, which promotes insulin secretion and increases fetal growth [4]. Furthermore,
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14 75 hyperglycemia causes placental vascular dysfunction, reducing the supply of oxygen and
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17 76 nutrients to the fetus [5]. There is still 2.7% GDM pregnant women deliver children that have
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20 77 fetal growth restrictions (FGR) [6]. Additionally, the incidence of small for gestational age
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22 78 (SGA) infants born to mothers with GDM was 6.45% in China [7]. However, limited research
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25 79 is available on SGA infants born to Chinese women with GDM.

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27 80 SGA infants are commonly defined as having birth weight below the 10th percentile for a
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30 81 given gestational age and sex [8], including infants who are naturally small without pathological
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33 82 growth restriction. In China, the total number of SGA births is the fifth highest in the world [9],
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36 83 imposing a tremendous medical and socioeconomic burden. SGA infants have an increased risk
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39 84 of adverse perinatal outcomes, such as stillbirth, asphyxia, or birth defects. Additionally,
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42 85 compared to appropriate for gestational age (AGA) infants, SGA infants are prone to have poor
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45 86 cognitive or psychological outcomes as well as metabolic diseases, such as type 2 diabetes,
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48 87 insulin resistance, and arterial hypertension in adulthood [10], [11]. In addition, GDM has been
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51 88 linked to delayed development and stunted fetal growth [12]. This linkage may exacerbate the
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54 89 adverse health outcomes of SGA. Epidemiological studies show that SGA infants born to
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57 90 mothers with GDM have higher rates of neonatal complications or death [13], [14]. They are
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60 91 also at higher risk of developing long-term cardiovascular offspring hospitalization [15]. Given

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4 92 the seriousness of the consequences, identifying its potential influencing factors is of great
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6 93 significance for the screening and prevention of SGA births among GDM pregnant women.
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9 94 Maternal glycemia is widely recognized for its association with perinatal outcomes,
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11 95 including its impact on offspring' birthweight [16]. According to Hyperglycemia and Adverse
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13 96 Pregnancy outcomes (HAPO), women with higher glucose levels are considered to be at greater
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15 97 risk [17]. Current prenatal treatment goals emphasize tight glucose monitoring and strict
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17 98 glucose control [18], [19]. Consequently, women experiencing hypoglycemia are generally
18
19 99 deemed to be at low risk for antenatal care. Several investigations have reported an association
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21 100 between maternal hypoglycemia and FGR or SGA [20]–[23]. Presently, the pregnancy factors
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23 101 related to SGA infants born to women with GDM remain unclear. Moreover, few studies have
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25 102 examined the association between maternal glycemic level associated with SGA infants born
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27 103 to mothers with GDM. After the diagnosis of GDM, timely recognition of glycemic
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29 104 abnormalities is critical for normal fetal growth and development. Therefore, the purpose of
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31 105 this study was to explore the influencing factors during pregnancy associated with SGA infants
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33 106 born to mothers with GDM in China.
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43 107 **Methods**

44 108 **Study design and population**

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47 109 This case-control study included pregnancies affected by GDM who delivered between
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49 110 January 2019 and December 2020 from a tertiary Maternal and Child Health Hospital in Fuzhou
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51 111 City, Fujian Province. All pregnant women followed a routine prenatal care protocol,
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53 112 scheduling frequent visits to the health system to identification of risk factors and initiation of
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4 113 preventive care measures [24].
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6 114 Eligible participants were pregnant women diagnosed with GDM based on 75-gram oral
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9 115 glucose tolerance test (OGTT) conducted between 24 and 32 weeks of gestation, following the
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11 116 modified International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria
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14 117 [25]. Diagnosis criteria included one or more elevated glucose levels: fasting plasma glucose
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17 118 level ≥ 5.1 mmol/L, 1-h plasma glucose level ≥ 10.0 mmol/L, and 2-h plasma glucose level ≥ 8.5
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19 119 mmol/L [25]. Pregnant women with multiple gestations, a clinical diagnosis of pregestational
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22 120 diabetes mellitus (PGDM), or overt diabetes (fasting plasma glucose (FPG) ≥ 7.0 mmol/L or
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25 121 2-h ≥ 11.0 mmol/L) were excluded. A total of 6,839 participants were enrolled, all of whom
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27 122 had complete demographic and clinical data.
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30 123 All participants in this study were categorized into the SGA group (case group, <10th
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32 124 percentile), AGA group (controlling group, between 10 and 90th percentile), and LGA group
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35 125 (>90th percentile) according to the association between gestational age and birth weight.
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37 126 Finally, for each SGA infant, four gestation age-matched AGA infants were randomly selected
38
39
40 127 using PSM analysis with gestation age-matched (Figure 1).
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43 128 **Patient and public involvement**

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45 129 No patients involved.
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48 130 **Data collection and study outcomes**

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51 131 Maternal demographic characteristics, pregnancy characteristics and pregnancy
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53 132 complications, and outcomes were collected retrospectively by one researcher from the
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56 133 electronic medical record database of the one hospital in our study. In addition, we collected
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4 134 glycemic levels including 75g OGTT glycemia, FPG, 2-h postprandial glucose, and HbA1c in
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6 135 the 2nd trimester. Based on the number of abnormal OGTT values, women with GDM were
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9 136 stratified into 1, 2, or 3 items of abnormal OGTT values, respectively (Supplementary material
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14 138 The primary outcome of this study was SGA babies born to women with GDM.
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17 139 Gestational age was determined by subtracting the date of last menstrual period (LMP) reported
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20 140 by the mother or by the first ultrasound scan (USS) from the date of birth. SGA was defined as
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22 141 birth weight below the 10th percentile for gestational age and sex, based on birth weight curves
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25 142 in Chinese [26], [27].

26 27 143 **Statistical analysis**

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30 144 All statistical analyses were performed using IBM SPSS, version 27.0, and R, version
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33 145 4.1.3. We applied a 1:4 nearest-neighbor matching with a caliper of 0.01, a preset value for
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36 146 propensity score matching (PSM), to lessen the potential selection bias and obtain matched data.
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38 147 The outcomes were compared between the SGA group and the AGA group among GDM
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41 148 pregnant women. Continuous variables were presented as mean \pm standard deviation (SD) or as
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44 149 medians (interquartile range [IQR] 25th percentile–75th percentile), compared by using
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47 150 independent *t*-test or the Mann–Whitney test. Categorical variables were presented as the
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50 151 frequency with percentages and analyzed by the Chi-square test or Fisher's exact test.

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53 152 We examined the risk factors associated with SGA infants born to mothers with GDM
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56 153 using the Binary logistic regression model. Variables were carefully chosen to ensure
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59 154 parsimony of the final model (forward LR, entry 0.05, removal 0.10). Further, to explore the

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4 155 association between maternal glycemc levels and SGA, adjusted for parity, previous uterine
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6 156 scar, history of low birth weight, history of macrosomia, gestational hypertensive disorder,
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9 157 oligohydramnios, anemia, pre-pregnancy BMI, height, Gestational weight gain (GWG) rate,
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12 158 and ketonuria in 1st trimester. A two-sided p-value of <0.05 was considered statistically
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14 159 significant in all analyses.

160 **Ethics approval**

161 This study was approved by the Ethics Committee (No.2019-161). Given all maternal and
162 neonatal data were extracted from the hospital electronic medical record system by a unique
163 identifier with no participant involved in the design, the written informed consent was waived.

164 **3 Results**

165 **3.1 Selection of GDM pregnant women**

166 A total of 6,839 GDM pregnant women were enrolled in the study according to eligible
167 and exclusion criteria, including 382 SGA infants, 964 LGA infants, and 5,493 AGA infants.
168 After the 1:4 PSM analysis, 382 SGA infants were selected and 1,528 AGA infants were
169 randomly matched with the SGA group according to the gestational age at birth (Figure 1).
170 After propensity analysis, the mean (*SD*) gestational age at birth was 38.6 (*SD* = 1.61) weeks
171 in the AGA group and 38.59 (*SD* = 1.62) weeks in the SGA group, there was no evidence of
172 differences in the gestational age between the two groups (*P* = 0.983).

173 **3.2 Characteristics and univariate analysis of AGA and SGA**

174 The average age of the participants was 31.67 (*SD* = 4.36) years old. Among all women,
175 Han Chinese accounts for 97.91%. Approximately 50% of the participants in both groups had

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4 176 a college or university education. More than 50% of the women in the SGA group were
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6 177 nulliparous, which was slightly more than the percentage of women in the AGA group (35.3%)
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9 178 who were nulliparous ($P < 0.001$). The previous uterine scar was shown statistically significant
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11 179 ($P < 0.05$).

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14 180 In terms of pregnancy history, there were no statistically significant differences observed
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16 181 in the occurrence of abortion or miscarriage, preterm delivery, fetal distress, or GDM. However,
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18 182 a statistically significant association was found between a history of macrosomia ($P = 0.012$)
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20 183 and low birth weight ($P = 0.04$). Regarding pregnancy complications, statistically significant
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22 184 differences were identified in the occurrence of oligohydramnios ($P < 0.001$) and anemia ($P =$
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24 185 0.034). In addition, height, pre-pregnancy BMI, and GWG rate were shown statistically
25
26 186 significant (all $P < 0.05$). Regarding the glycemic level, 75g OGTT 0 h and 2 h glycemia, as
27
28 187 well as ketonuria in 1st trimester, fasting glucose, and 2-h postprandial glucose in the 2nd
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30 188 trimester, showed statistically significant ($P < 0.05$). However, 75g OGTT 1 h and HbA1c in
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32 189 the 2nd trimester did not exhibit significant differences ($P > 0.05$). The characteristics of the
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34 190 SGA group and AGA group are presented in Table 1 and Table 2.

191 **3.3 Multivariable logistic regression analysis for the factors of SGA**

192 The multivariable analysis indicated that history of low birth weight (OR=5.01, 95%CI
193 1.21-20.72, $P=0.026$) was an independent risk factor for SGA. Mothers with gestational
194 hypertensive disorder were more likely to have SGA (Gestational hypertension: OR=2.78,
195 95%CI 1.68-4.59, $P < 0.001$; preeclampsia and eclampsia: OR=6.31, 95%CI 3.35-11.91, $P <$
196 0.001). The risk of SGA was fourfold greater in pregnant women with oligohydramnios than in

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4 197 women with normal amniotic fluid (OR=4.22, 95%CI 2.5-7.12, $P < 0.001$). Mothers with lower
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7 198 height had a higher risk of SGA (150–154.9 cm: OR=2.02, 95% CI 1.46-2.79, $P < 0.001$; 145–
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9 199 149.9 cm: OR=1.95, 95%CI 1.21-3.14, $P=0.006$; < 145 cm: OR =7.42, 95%CI 1.76-31.25,
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12 200 $P=0.006$) compared with >155 cm height. Underweight pre-pregnancy had a 64% more chance
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15 201 of SGA (OR = 1.64, 95%CI 1.17-2.3, $P = 0.004$) than normal. Also, mothers who had
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17 202 inadequate weight gain during pregnancy had a 37% more chance of SGA than appropriate gain
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20 203 (OR=1.37, 95%CI 1.05-1.8, $P = 0.023$).

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22 204 However, the multivariate analysis also revealed that multiparous was a protective factor
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25 205 (OR=0.55, 95%CI 0.43-0.71, $P < 0.001$) compared to nulliparity. The SGA risk was reduced
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28 206 by previous uterine scar experience (OR=0.57, 95%CI 0.39-0.83, $P=0.004$). Anemia was
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31 207 associated with a decreased incidence of SGA (OR=0.71, 95%CI 0.53-0.96, $P=0.027$). Two or
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34 208 three items with elevated blood glucose values on OGTT showed a lower probability of SGA
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37 209 (OR=0.67, 95%CI 0.52-0.86, $P=0.002$; OR=0.32, 95%CI 0.18-0.55, $P < 0.001$) than one
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40 210 elevated item. Ketonuria levels ranging from 0.5 to 3.9 mmol/l in the 1st trimester had a lower
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43 211 risk of SGA than < 0.5 mmol/l. (OR=0.59, 95%CI 0.42-0.81, $P=0.001$). The forest map of
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46 212 multivariate logistic regression analysis is shown in Figure 2.

213 3.4 Association between Blood glucose level and the risk of SGA

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48 214 We further explored the relationship between OGTT, glycemic control level in the 2nd
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51 215 trimester and SGA. Specifically, multivariate analysis revealed that when adjusted for parity,
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54 216 previous uterine scar, history of macrosomia, history of low birth weight, gestational
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57 217 hypertensive disorder, oligohydramnios, anemia, pre-pregnancy BMI, height, GWG rate, and
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4 218 ketonuria in 1st trimester. 75g OGTT 0 h, 75g OGTT 2 h, and 2-h postprandial glucose in 2nd
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6 219 trimester were associated with a decreased risk for SGA (OR=0.4, 95% CI 0.29-0.55, $P < 0.001$;
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9 220 OR=0.88, 95% CI 0.81-0.95, $P=0.002$; OR = 0.81, 95% CI 0.73-0.9, $P < 0.001$). However, 75g
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11 221 OGTT 0 h glycemia exhibited a stronger association with SGA outcomes than 2-h OGTT and
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14 222 2-h postprandial glucose in the 2nd trimester. In contrast, HbA1c in the 2nd trimester was
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17 223 associated with an increased risk of SGA (OR=2.4, 95% CI 1.64-3.52, $P < 0.001$) (Table 3).

224 **4 Discussion**

225 In this Case-Control study, several key maternal demographic characteristics (height, BMI,
226 and GWG rate), pregnancy characteristics (parity, previous uterine scar, and history of LBW),
227 pregnancy complications (hypertensive disorders, oligohydramnios, and anemia), OGTT (0h,
228 2h) and glycemic control level (2-h postprandial glucose and HbA1c in the 2nd trimester) were
229 identified as risk factors for SGA in women with GDM.

230 Maternal height exerts the most significant influence. Our results confirmed maternal
231 stature below 145cm is a strong indicator for SGA, aligning with previous studies [28]. This
232 may contribute to inadequate self-nutrition in GDM pregnant women who are of short stature.
233 The transition to a sugar-controlled diet may have a significant impact on the adequate supply
234 of nutrients for fetal growth. Further, both GWG and BMI serve as reflections of maternal
235 nutritional status. Our study reveals that inadequate weight gain and underweight BMI were
236 associated with an increased risk of SGA in women with GDM, consistent with prior research
237 [29]. This heightened risk may be attributed to pregnant women experiencing inadequate
238 weight gain or being underweight, potentially indicating chronic malnutrition, which can be

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4 239 detrimental to fetal growth and development. Therefore, it is imperative that hospitals offer
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6 240 comprehensive health education, monitor pregnancy nutrition, and implement personalized
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9 241 nutrition therapy for women diagnosed with GDM.
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11 242 Nulliparous pregnant women with gestational diabetes mellitus (GDM) exhibited an
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14 243 increased susceptibility to small for gestational age (SGA) births in our study, corroborating
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17 244 findings from a prior retrospective Chinese study [30]. This heightened risk can be attributed
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20 245 to physiological disparities between nulliparous and multiparous women. Multiparous women
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22 246 showcased superior uteroplacental circulation, optimizing oxygen and nutrient delivery to the
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25 247 fetus and creating a conducive environment for fetal growth [30]. Conversely, nulliparous
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27 248 women displayed potential hemodynamic differences, including a higher pulsatility index of
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30 249 the uterine artery (UtA-PI) and elevated blood impedance, contributing to an elevated risk of
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33 250 SGA [31], [32]. Moreover, multiparous women were likely to possess a higher degree of
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36 251 maternal adaptation to gestational changes, encompassing improved blood volume expansion
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38 252 and hormonal regulation, thus fostering a favorable environment for fetal growth and
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41 253 diminishing the likelihood of SGA. Notably, differences in risk perception and prenatal care
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44 254 practices were apparent. Multiparous women, drawing on their experience, demonstrated
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47 255 proactive management skills for dietary changes and glycemic control, resulting in more
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50 256 effective prenatal care and potentially reducing the risk of SGA. Conversely, nulliparous
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53 257 women's relative inexperience might contribute to delayed or suboptimal prenatal care,
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56 258 impacting fetal growth outcomes.

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59 259 Our research findings revealed an intriguing association wherein a history of a previous
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4 260 uterine scar appeared to reduce the risk of SGA births among pregnant women with GDM.
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6 261 Remarkably, cesarean sections are widely preferred by Chinese women, with a national rate
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9 262 reaching 36.7% in 2018, the highest in Asia [33]. In the context of Chinese obstetric practices,
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11 263 where multiparity is linked with a higher likelihood of opting for cesarean sections, it raises the
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13 264 possibility that the protective influence on SGA outcomes could be influenced by the
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15 265 prevalence of cesarean deliveries. It is important to emphasize that while a history of cesarean
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17 266 section may be associated with a lower risk of SGA, it does not imply that cesarean section
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19 267 itself is a recommended method for preventing SGA. The choice of delivery method should
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21 268 still be based on medical evaluations, taking into account the specific circumstances of the
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23 269 current pregnancy and medical indications.
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30 270 Women with GDM face an increased risk for Hypertensive disorders (HD) due to insulin
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32 271 resistance and the underlying pathology of the metabolic syndrome [34]. HD is closely
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34 272 associated with birth weight [35], and when combined with GDM, it elevates the risk of adverse
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36 273 outcomes. This corresponds with our findings that gestational hypertension as well as
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38 274 preeclampsia and eclampsia are risk factors for delivering SGA in pregnant women with GDM.
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40 275 HD can induce spasms in maternal umbilical blood vessels and systemic small arteries,
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42 276 impacting maternal-fetal circulation and insufficient oxygen supply. Consequently, this affects
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44 277 the intrauterine growth and development of the fetus [36]. The presence of hypertensive
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46 278 disorders with a decrease in serum vascular endothelial growth factor (VEGF) and placental
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48 279 growth factor (PlGF) levels, alongside an increase in soluble fms-like tyrosine kinase-1 (sFLT-
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50 280 1) levels. These changes may reflect underlying placental dysfunction and are related to
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4 281 inhibition in fetal growth and development [37], [38]. Oligohydramnios, often seen in
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6 282 conjunction with hypertensive disorders [39], may indicate complicated pregnancies, signifying
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9 283 chronic suboptimal placental function [40]. Such conditions could reduce fetal resources and
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11 284 are associated with SGA. Thus, maternal blood pressure should be closely monitored and
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14 285 regular ultrasound examinations should be performed to assess changes in pregnancy status.

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17 286 Contrary to earlier research, this study discovered that maternal anemia during pregnancy
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19 287 reduces the incidence of SGA [41]. One possible explanation is that women with GDM are
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22 288 particularly attentive to their diet, incorporating supplementation recommended by their
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25 289 obstetricians to address anemia. Consequently, they may effectively mitigate the risk of SGA
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27 290 through appropriate nutritional support. Besides, the effect of anemia on pregnancy outcomes
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30 291 varies between gestational periods. Therefore, further research is needed to investigate the
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33 292 effect of hemoglobin concentration on SGA at different gestational ages.

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35 293 Maternal glycemic parameters significantly influence fetal growth, as highlighted by
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37 294 findings from the HAPO study. Pregnant women with elevated glucose levels face a higher risk
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40 295 of adverse pregnancy outcomes. This association is driven by various mechanisms. Firstly,
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43 296 heightened glucose levels can stimulate increased fetal insulin production, promoting excessive
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46 297 fetal growth and contributing to macrosomia [17]. Conversely, elevated glucose levels may, in
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48 298 some instances, impair placental function, leading to reduced nutrient and oxygen supply to the
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51 299 fetus, ultimately resulting in growth restriction and the birth of SGA infants [42]. Our study
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54 300 found that GDM women with 2 or 3 elevated glucose values, as opposed to just one, may
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56 301 experience a decreased risk of SGA. Besides, higher OGTT-0h and OGTT-2h were found to be

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4 302 significant predictors of SGA when the glucose values were analyzed as continuous variables.
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6 303 This may contribute to within the mild elevation range of blood glucose levels, blood glucose
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9 304 passes through the placental circulation to the fetus, and extra glucose in the fetus is stored as
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11 305 body fat [43]. There may be a protective mechanism ensuring that the fetus receives adequate
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14 306 nutrients within the normal range. However, this does not imply that higher blood glucose levels
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17 307 are better. When blood glucose rises to a certain extent, adaptive responses may be triggered,
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20 308 leading to the occurrence of SGA. Therefore, GDM women with elevated OGTT-0h and
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22 309 OGTT-2h levels are less likely to deliver SGA infants. However, they should be aware of more
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25 310 severe disturbance in glucose metabolism and insulin sensitivity and the potential for delivering
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27 311 high birth weight newborns. In addition, GDM women with low OGTT-0h and OGTT-2h do
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30 312 not need for excessively strict glucose control throughout pregnancy, but should be concerned
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32 313 about the occurrence of FGR. Therefore, personalized monitoring is crucial for assessing
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35 314 maternal blood glucose levels, allowing for the adjustment of dietary, exercise, and insulin
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38 315 management strategies based on their glycemic status.

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40 316 Our study identified an association between delivering SGA in pregnant women with
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42 317 GDM and 2-h postprandial glucose in the 2nd trimester. Measuring 2-h postprandial glucose
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45 318 helps evaluate the effectiveness of dietary modifications and glycemic control strategies [44].
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48 319 In clinical practice, pregnant women are advised to control their glycemic levels through dietary
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51 320 adjustments when diagnosed with GDM. However, due to fear of insulin and lack of knowledge
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53 321 about GDM treatment options, some women may follow an overly strict diet. Consequently,
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56 322 maternal glucose regulation is inadequate, which can lead to fetal undergrowth [21].Hence,

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4 323 pregnant women diagnosed with GDM should be warned of the potential risk of SGA if they
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6 324 are found to have low glucose values. Besides, compared to the late pregnancy period, timely
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9 325 blood glucose testing in the second trimester provides a longer time window. More attention
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11 326 should be paid to glucose status during this period. Understanding the glycemic status is a
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14 327 crucial step in adjusting the diet and exercise plan to achieve stable blood glucose levels,
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17 328 ensuring normal fetal development, and avoiding SGA.

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19 329 The multifactorial analysis revealed the association between elevated HbA1c levels in the
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22 330 second trimester and an increased risk of SGA, suggesting a potential impact of long-term
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25 331 glucose control on fetal outcomes. However, this finding different with a previous study [45],
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28 332 and contradicts the results of instantaneous glycemic measures (OGTT and 2-h postprandial
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31 333 glucose) in our study. This discrepancy may be attributed to the curvilinear relationship
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34 334 between HbA1c and fetal weight. Specifically, normal fetal weight may occur at low HbA1c
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37 335 levels, while moderately raised levels may result in macrosomia, and very high HbA1c levels
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40 336 may be associated with severe intrauterine growth restriction [46]. Future research could
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43 337 explore the relationship between glycemic control and birth weight using unrestricted cubic
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46 338 splines or subgroup analyses to evaluate their correlation. This approach would contribute to a
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49 339 more comprehensive understanding of the intricate relationship between maternal glycemic and
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52 340 fetal outcomes.

51 341 **Limitation**

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53 342 There are a few limitations to our analysis. Firstly, data regarding women's history of
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56 343 smoking and drinking was not recorded. Although the incidence of smoking and drinking

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4 344 among pregnant women is low due to Chinese customs, smoking and drinking experience may
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6 345 be potential contributors to SGA. Secondly, data was collected from a single hospital and may
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9 346 not be representative of other areas. Thirdly, this study is a case-control study even though a
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11 347 PSM analysis was conducted to minimize the bias. Lastly, this study lies in the inability to
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14 348 accurately differentiate FGR from overall SGA during the grouping process, aligning with the
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17 349 specific objectives of the study. Future research endeavors could consider employing more
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20 350 specific diagnostic criteria and focusing explicitly on FGR, offering a more comprehensive
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22 351 understanding of these distinct fetal growth conditions.

352 **Conclusion**

353 SGA infants born to women with GDM are the result of a multifactorial interaction,
354 including maternal demographic characteristics, pregnancy characteristics, pregnancy
355 complications and clinical and laboratory parameters. Notably, SGA was correlated with OGTT
356 and glycemic control levels. It is difficult to reverse once SGA has occurred, perinatal
357 monitoring and antenatal care are crucial for identifying risk factors that can help predict and
358 prevent SGA.

360 **DECLARATION**

361 **Ethics approval and consent to participate**

362 This study was performed in accordance with the Declaration of Helsinki. The study was
363 approved by the Ethical Committee of Fujian Maternal and Child Health Hospital, affiliated
364 hospital of Fujian Medical University, China (No: 2019-161). As this was a retrospective case-

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4 365 control study involving review of medical records, informed consent from individual
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6 366 participants was not obtained. However, all data collected were treated confidentially and used
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9 367 solely for the purpose of this study. Measures were taken to ensure the privacy and anonymity
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12 368 of the patients' information.

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14 369 **Consent for publication**

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17 370 Not applicable.

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19 371 **Availability of data and materials**

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22 372 The dataset supporting the conclusions is available from the corresponding author on
23
24 373 reasonable request.

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27 374 **Conflict of interest**

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29 375 No conflict of interest has been declared by the authors.

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34
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36
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39
40 379 **Author contributions**

41
42
43 380 Jianing Li and Yuqing Pan: Writing- Original draft preparation, Writing- Reviewing and
44
45 381 Editing, Visualization. Xiumin Jiang: Supervision, Conceptualization. Qingxiang Zheng and
46
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48 382 Xiaoqian Chen: Methodology, Validation. Yu Zhu, Rulin Liu and Ling Huang: Investigation,
49
50 383 Data curation.

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387 **Reference**

- 388 [1] L. Reitzle *et al.*, ‘Gestational diabetes in Germany: Development of screening
389 participation and prevalence’, Robert Koch-Institut, report, Jun. 2021. doi:
390 10.25646/8325.
- 391 [2] A. A. Choudhury and V. Devi Rajeswari, ‘Gestational diabetes mellitus - A metabolic
392 and reproductive disorder’, *Biomedicine & Pharmacotherapy*, vol. 143, p. 112183, Nov.
393 2021, doi: 10.1016/j.biopha.2021.112183.
- 394 [3] C. Gao, X. Sun, L. Lu, F. Liu, and J. Yuan, ‘Prevalence of gestational diabetes mellitus
395 in mainland China: A systematic review and meta-analysis’, *J Diabetes Investig*, vol. 10,
396 no. 1, pp. 154–162, Jan. 2019, doi: 10.1111/jdi.12854.
- 397 [4] J. Pedersen, ‘Weight and Length at Birth of Infants of Diabetic Mothers’, *Acta*
398 *Endocrinologica (Norway)*, vol. 16, no. 4, pp. 330–342, Aug. 1954, doi:
399 10.1530/acta.0.0160330.
- 400 [5] I. M. Langmia *et al.*, ‘Cardiovascular Programming During and After Diabetic Pregnancy:
401 Role of Placental Dysfunction and IUGR’, *Front Endocrinol (Lausanne)*, vol. 10, p. 215,
402 Apr. 2019, doi: 10.3389/fendo.2019.00215.
- 403 [6] A. U. Nayak, A. M. A. Vijay, R. Indusekhar, S. Kalidindi, V. M. Katreddy, and L.
404 Varadhan, ‘Association of hypoglycaemia in screening oral glucose tolerance test in
405 pregnancy with low birth weight fetus’, *World J Diabetes*, vol. 10, no. 5, pp. 304–310,
406 May 2019, doi: 10.4239/wjd.v10.i5.304.
- 407 [7] J. Chen *et al.*, ‘Demographic and Clinical Features of Small-for-Gestational-Age Infants
408 Born to Mothers With Gestational Diabetes Mellitus’, *Frontiers in Pediatrics*, vol. 9,
409 2021, Accessed: Nov. 19, 2022. [Online]. Available:
410 <https://www.frontiersin.org/articles/10.3389/fped.2021.741793>
- 411 [8] R. A. Pilliod, Y. W. Cheng, J. M. Snowden, A. E. Doss, and A. B. Caughey, ‘The risk of
412 intrauterine fetal death in the small-for-gestational-age fetus’, *Am J Obstet Gynecol*, vol.
413 207, no. 4, p. 318.e1–6, Oct. 2012, doi: 10.1016/j.ajog.2012.06.039.
- 414 [9] A. C. C. Lee *et al.*, ‘National and regional estimates of term and preterm babies born small
415 for gestational age in 138 low-income and middle-income countries in 2010’, *Lancet Glob*
416 *Health*, vol. 1, no. 1, pp. e26-36, Jul. 2013, doi: 10.1016/S2214-109X(13)70006-8.
- 417 [10] R. P. Anne *et al.*, ‘Propensity-Matched Comparison of Very Preterm Small- and
418 Appropriate-for-Gestational-Age Neonates’, *Indian J Pediatr*, vol. 89, no. 1, pp. 59–66,
419 Jan. 2022, doi: 10.1007/s12098-021-03878-3.
- 420 [11] Q. Chen *et al.*, ‘Association between maternal blood lipids levels during pregnancy and
421 risk of small-for-gestational-age infants’, *Sci Rep*, vol. 10, p. 19865, Nov. 2020, doi:
422 10.1038/s41598-020-76845-1.
- 423 [12] A. Yuste Gómez, M. del P. Ramos Álvarez, and J. L. Bartha, ‘Influence of Diet and
424 Lifestyle on the Development of Gestational Diabetes Mellitus and on Perinatal Results’,
425 *Nutrients*, vol. 14, no. 14, p. 2954, Jul. 2022, doi: 10.3390/nu14142954.

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2
3 426 [13] B. Barquiel, L. Herranz, N. Martínez-Sánchez, C. Montes, N. Hillman, and J. L. Bartha,
4 427 'Increased risk of neonatal complications or death among neonates born small for
5 428 gestational age to mothers with gestational diabetes', *Diabetes Research and Clinical
6 429 Practice*, vol. 159, p. 107971, Jan. 2020, doi: 10.1016/j.diabres.2019.107971.
- 8 430 [14] T. F. Esakoff, A. Guillet, and A. B. Caughey, 'Does small for gestational age worsen
9 431 outcomes in gestational diabetics?', *The Journal of Maternal-Fetal & Neonatal Medicine*,
10 432 vol. 30, no. 8, pp. 890–893, Apr. 2017, doi: 10.1080/14767058.2016.1193142.
- 12 433 [15] E. Neimark, T. Wainstock, E. Sheiner, L. Fischer, and G. Pariente, 'Long-term
13 434 cardiovascular hospitalizations of small for gestational age (SGA) offspring born to
14 435 women with and without gestational diabetes mellitus (GDM) ‡', *Gynecol Endocrinol*,
15 436 vol. 35, no. 6, pp. 518–524, Jun. 2019, doi: 10.1080/09513590.2018.1541233.
- 17 437 [16] L. N. R. Alves *et al.*, 'Investigation of maternal polymorphisms in genes related to glucose
18 438 homeostasis and the influence on birth weight: a cohort study', *J Pediatr (Rio J)*, vol. 98,
19 439 no. 3, pp. 296–302, Sep. 2021, doi: 10.1016/j.jpmed.2021.06.007.
- 21 440 [17] HAPO Study Cooperative Research Group *et al.*, 'Hyperglycemia and adverse pregnancy
22 441 outcomes', *N Engl J Med*, vol. 358, no. 19, pp. 1991–2002, May 2008, doi:
23 442 10.1056/NEJMoa0707943.
- 25 443 [18] X. Cao *et al.*, 'Comprehensive intensive therapy for Chinese gestational diabetes benefits
26 444 both newborns and mothers', *Diabetes Technol Ther*, vol. 14, no. 11, pp. 1002–1007, Nov.
27 445 2012, doi: 10.1089/dia.2012.0142.
- 29 446 [19] S. Morampudi, G. Balasubramanian, A. Gowda, B. Zomorodi, and A. S. Patil, 'The
30 447 Challenges and Recommendations for Gestational Diabetes Mellitus Care in India: A
31 448 Review', *Front Endocrinol (Lausanne)*, vol. 8, p. 56, Mar. 2017, doi:
32 449 10.3389/fendo.2017.00056.
- 34 450 [20] T. Dassios, A. Greenough, S. Leontiadi, A. Hickey, and N. A. Kametas, 'Admissions for
35 451 hypoglycaemia after 35 weeks of gestation: perinatal predictors of cost of stay', *J Matern
36 452 Fetal Neonatal Med*, vol. 32, no. 3, pp. 448–454, Feb. 2019, doi:
37 453 10.1080/14767058.2017.1381905.
- 39 454 [21] J. Leng *et al.*, 'Small-for-gestational age and its association with maternal blood glucose,
40 455 body mass index and stature: a perinatal cohort study among Chinese women', *BMJ Open*,
41 456 vol. 6, no. 9, p. e010984, Sep. 2016, doi: 10.1136/bmjopen-2015-010984.
- 43 457 [22] I. B. Delibas, S. Tanriverdi, and B. Cakmak, 'Does reactive hypoglycemia during the 100
44 458 g oral glucose tolerance test adversely affect perinatal outcomes?', *Ginekol Pol*, vol. 89,
45 459 no. 1, pp. 25–29, 2018, doi: 10.5603/GP.a2018.0005.
- 47 460 [23] S. Shinohara, Y. Uchida, M. Hirai, S. Hirata, and K. Suzuki, 'Relationship between
48 461 maternal hypoglycaemia and small-for-gestational-age infants according to maternal
49 462 weight status: a retrospective cohort study in two hospitals', *BMJ Open*, vol. 6, no. 12, p.
50 463 e013749, Dec. 2016, doi: 10.1136/bmjopen-2016-013749.
- 52 464 [24] W. Hu, H. Hu, W. Zhao, A. Huang, Q. Yang, and J. Di, 'Current status of antenatal care
53 465 of pregnant women-8 provinces in China, 2018', *BMC Public Health*, vol. 21, no. 1, p.
54 466 1135, Jun. 2021, doi: 10.1186/s12889-021-11154-4.
- 56 467 [25] International Association of Diabetes and Pregnancy Study Groups Consensus Panel *et*

- 1
2
3 468 *al.*, ‘International association of diabetes and pregnancy study groups recommendations
4 469 on the diagnosis and classification of hyperglycemia in pregnancy’, *Diabetes Care*, vol.
5 470 33, no. 3, pp. 676–682, Mar. 2010, doi: 10.2337/dc09-1848.
- 7 471 [26] L. Dai *et al.*, ‘Population-based birth weight reference percentiles for Chinese twins’, *Ann*
8 472 *Med*, vol. 49, no. 6, pp. 470–478, Sep. 2017, doi: 10.1080/07853890.2017.1294258.
- 10 473 [27] B. Zhang *et al.*, ‘Birthweight percentiles for twin birth neonates by gestational age in
11 474 China’, *Sci Rep*, vol. 6, p. 31290, Aug. 2016, doi: 10.1038/srep31290.
- 13 475 [28] R. Khanam *et al.*, ‘Maternal short stature and under-weight status are independent risk
14 476 factors for preterm birth and small for gestational age in rural Bangladesh’, *Eur J Clin*
15 477 *Nutr*, vol. 73, no. 5, pp. 733–742, May 2019, doi: 10.1038/s41430-018-0237-4.
- 17 478 [29] Q.-X. Zheng *et al.*, ‘Prepregnancy body mass index and gestational weight gain are
18 479 associated with maternal and infant adverse outcomes in Chinese women with gestational
19 480 diabetes’, *Sci Rep*, vol. 12, no. 1, p. 2749, Feb. 2022, doi: 10.1038/s41598-022-06733-3.
- 21 481 [30] L. Lin, C. Lu, W. Chen, C. Li, and V. Y. Guo, ‘Parity and the risks of adverse birth
22 482 outcomes: a retrospective study among Chinese’, *BMC Pregnancy Childbirth*, vol. 21, p.
23 483 257, Mar. 2021, doi: 10.1186/s12884-021-03718-4.
- 25 484 [31] F. Prefumo, A. Bhide, S. Sairam, L. Penna, B. Hollis, and B. Thilaganathan, ‘Effect of
26 485 parity on second-trimester uterine artery Doppler flow velocity and waveforms’,
27 486 *Ultrasound Obstet Gynecol*, vol. 23, no. 1, pp. 46–49, Jan. 2004, doi: 10.1002/uog.908.
- 29 487 [32] I. Derwig *et al.*, ‘Association of placental perfusion, as assessed by magnetic resonance
30 488 imaging and uterine artery Doppler ultrasound, and its relationship to pregnancy
31 489 outcome’, *Placenta*, vol. 34, no. 10, pp. 885–891, Oct. 2013, doi:
32 490 10.1016/j.placenta.2013.07.006.
- 34 491 [33] J. Qiao *et al.*, ‘A Lancet Commission on 70 years of women’s reproductive, maternal,
35 492 newborn, child, and adolescent health in China’, *Lancet*, vol. 397, no. 10293, pp. 2497–
36 493 2536, Jun. 2021, doi: 10.1016/S0140-6736(20)32708-2.
- 38 494 [34] Y. Baumfeld *et al.*, ‘Pre-Conception Dyslipidemia Is Associated with Development of
39 495 Preeclampsia and Gestational Diabetes Mellitus’, *PLoS One*, vol. 10, no. 10, p. e0139164,
40 496 Oct. 2015, doi: 10.1371/journal.pone.0139164.
- 42 497 [35] N. Li *et al.*, ‘Preconception Blood Pressure and Risk of Low Birth Weight and Small for
43 498 Gestational Age: A Large Cohort Study in China’, *Hypertension*, vol. 68, no. 4, pp. 873–
44 499 879, Oct. 2016, doi: 10.1161/HYPERTENSIONAHA.116.07838.
- 46 500 [36] V. A. Luyckx *et al.*, ‘Effect of fetal and child health on kidney development and long-
47 501 term risk of hypertension and kidney disease’, *Lancet*, vol. 382, no. 9888, pp. 273–283,
48 502 Jul. 2013, doi: 10.1016/S0140-6736(13)60311-6.
- 50 503 [37] Y. Tang, W. Ye, X. Liu, Y. Lv, C. Yao, and J. Wei, ‘VEGF and sFLT-1 in serum of PIH
51 504 patients and effects on the foetus’, *Exp Ther Med*, vol. 17, no. 3, pp. 2123–2128, Mar.
52 505 2019, doi: 10.3892/etm.2019.7184.
- 54 506 [38] M. Badagionis, T. N. Sergentanis, P. Pervanidou, E. Kalampokas, N. Vlahos, and M.
55 507 Eleftheriades, ‘Preeclampsia and Cerebral Palsy in Offspring’, *Children (Basel)*, vol. 9,
56 508 no. 3, p. 385, Mar. 2022, doi: 10.3390/children9030385.
- 58 509 [39] N. Rabie, E. Magann, S. Steelman, and S. Ounpraseuth, ‘Oligohydramnios in complicated

- 1
2
3 510 and uncomplicated pregnancy: a systematic review and meta-analysis', *Ultrasound*
4 511 *Obstet Gynecol*, vol. 49, no. 4, pp. 442–449, Apr. 2017, doi: 10.1002/uog.15929.
- 5 512 [40] M. Vahid Dastjerdi, A. Ghahghaei-Nezamabadi, A. Tehranian, and M. Mesgaran, 'The
6 513 Effect of Sildenafil on Pregnancy Outcomes in Pregnant Women With Idiopathic
7 514 Borderline Oligohydramnios: A Randomized Controlled Trial', *J Family Reprod Health*,
8 515 vol. 16, no. 2, pp. 124–131, Jun. 2022, doi: 10.18502/jfrh.v16i2.9482.
- 9 516 [41] D. Liu *et al.*, 'Maternal Hemoglobin Concentrations and Birth Weight, Low Birth Weight
10 517 (LBW), and Small for Gestational Age (SGA): Findings from a Prospective Study in
11 518 Northwest China', *Nutrients*, vol. 14, no. 4, p. 858, Feb. 2022, doi: 10.3390/nu14040858.
- 12 519 [42] Z. Fasoulakis *et al.*, 'Intrauterine Growth Restriction Due to Gestational Diabetes: From
13 520 Pathophysiology to Diagnosis and Management', *Medicina (Kaunas)*, vol. 59, no. 6, p.
14 521 1139, Jun. 2023, doi: 10.3390/medicina59061139.
- 15 522 [43] H. D. McIntyre, J. Fuglsang, U. Kampmann, S. Knorr, and P. Ovesen, 'Hyperglycemia
16 523 in Pregnancy and Women's Health in the 21st Century', *International Journal of*
17 524 *Environmental Research and Public Health*, vol. 19, no. 24, Dec. 2022, doi:
18 525 10.3390/ijerph192416827.
- 19 526 [44] L. Monnier and C. Colette, 'Target for Glycemic Control', *Diabetes Care*, vol. 32, no.
20 527 Suppl 2, pp. S199–S204, Nov. 2009, doi: 10.2337/dc09-S310.
- 21 528 [45] Y. Xiao and X. Zhang, 'Association Between Maternal Glucose/Lipid Metabolism
22 529 Parameters and Abnormal Newborn Birth Weight in Gestational Diabetes Complicated
23 530 by Preeclampsia: A Retrospective Analysis of 248 Cases', *Diabetes Ther*, vol. 11, no. 4,
24 531 pp. 905–914, Apr. 2020, doi: 10.1007/s13300-020-00792-3.
- 25 532 [46] O. Rackham, F. Paize, and A. M. Weindling, 'Cause of death in infants of women with
26 533 pregestational diabetes mellitus and the relationship with glycemic control', *Postgrad*
27 534 *Med*, vol. 121, no. 4, pp. 26–32, Jul. 2009, doi: 10.3810/pgm.2009.07.2026.
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4 537 **Figure 1 Flow diagram of selection of GDM pregnant women in this study**

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6 538 **Abv:** GDM: gestational diabetes mellitus; PSM: propensity score matching; AGA: appropriate
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9 539 for gestational age; LGA: Large for gestational age; SGA: small for gestational age.

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14 541 **Figure 2** Forest plot of the risk factors of SGA (Binary logistic regression analysis).

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Table1 Maternal demographic characteristic of AGA group and SGA group matched according to 1:4 PSM analysis.

Variables	Items	AGA group (n=1528)	SGA group (n=382)	χ^2/t	<i>P</i>
Maternal Age	18~35	1220(79.8)	305(79.8)	0.395	1.000 ^a
	36~45	305(20)	76(19.9)		
	≥46	3(0.2)	1(0.3)		
Nationality	The Han	1498(98)	372(97.4)	0.638	0.424
	Minority nationality	30(2)	10(2.6)		
Residence	Urban	825(54)	196(51.3)	0.884	0.347
	Rural	703(46)	186(48.7)		
Education	Elementary and below	528(34.6)	126(33)	3.476	0.324
	Secondary /	223(14.6)	45(11.8)		
	Highschool	770(50.4)	210(55)		
	College / University	7(0.5)	1(0.3)		
Occupation	Manual worker	284(18.6)	69(18.1)	2.074	0.557
	Mental worker	708(46.3)	192(50.3)		
	Unemployed	381(24.9)	86(22.5)		
	Freelance	155(10.1)	35(9.2)		
Marital status	Unmarried	27(1.8)	8(2.1)	0.685	0.730 ^a
	Married	1497(98)	374(97.9)		
	Divorced or widowed	4(0.3)	0(0)		
Height (cm)	≥155	1248(81.7)	275(72)	22.232	<0.001
	150–154.9	197(12.9)	73(19.1)		
	145–149.9	79(5.2)	29(7.6)		
	< 145	4(0.3)	5(1.3)		
Pre-pregnancy BMI (kg/m²)	Normal	1130(74)	271(70.9)	9.175	0.01
	Underweight	172(11.3)	64(16.8)		
	Overweight / Obese	226(14.8)	47(12.3)		
GWG rate	Inadequate gain	690(45.2)	199(52.1)	6.107	0.047
	Appropriate gain	539(35.3)	121(31.7)		
	Excessive gain	299(19.6)	62(16.2)		

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Table 2 Pregnancy characteristics of AGA group and SGA group matched according to 1:4 PSM analysis.

Variables	Items	AGA group (n=1528)	SGA group (n=382)	χ^2	P
Parity	Nulliparous	539(35.3)	195(51)	32.13	< 0.001
	Multiparous	989(64.7)	187(49)		
Assisted reproductive technology (ART)	No	1446(94.6)	362(94.8)	0.01	0.919
	Yes	82(5.4)	20(5.2)		
Previous uterine scar	No	1196(78.3)	337(88.2)	19.089	< 0.001
	Yes	332(21.7)	45(11.8)		
Family history	No	1367(89.5)	336(88)	2.809	0.422
	Hypertension	76(5)	26(6.8)		
	Diabetes	46(3)	13(3.4)		
	Both	39(2.6)	7(1.8)		
History of abortion or miscarriage	No	896(58.6)	251(65.7)	6.393	0.041
	Spontaneous miscarriage	348(22.8)	71(18.6)		
	Induced abortions	284(18.6)	60(15.7)		
History of preterm delivery	No	1467(96)	368(96.3)	0.087	0.768
	Yes	61(4)	14(3.7)		
History of macrosomia	No	1481(96.9)	379(99.2)	6.29	0.012
	Yes	47(3.1)	3(0.8)		
History of GDM	No	1523(99.7)	382(100)	/	0.590 ^b
	Yes	5(0.3)	0(0)		
History of fetal distress	No	1512(99)	380(99.5)	0.897	0.343
	Yes	16(1)	2(0.5)		
History of low birth weight	No	1523(99.7)	376(98.4)	/	0.011^b
	Yes	5(0.3)	6(1.6)		
Intrahepatic cholestasis of pregnancy (ICP)	No	1508(98.7)	377(98.7)	0	1
	Yes	20(1.3)	5(1.3)		

Gestational hypertensive disorder	No	1431(93.7)	324(84.8)	31.269	< 0.001^a
	Gestational hypertension	62(4.1)	31(8.1)		
	Preeclampsia and eclampsia	27(1.8)	22(5.8)		
	Chronic hypertension with superimposed preeclampsia	4(0.3)	3(0.8)		
	Chronic hypertension (of any cause)	4(0.3)	2(0.5)		
Hyperthyroid	No	1487(97.3)	376(98.4)	1.576	0.209
	Yes	41(2.7)	6(1.6)		
Hypothyroid	No	1434(93.8)	349(91.4)	3.045	0.081
	Yes	94(6.2)	33(8.6)		
Anemia	No	1149(75.2)	307(80.4)	4.508	0.034
	Yes	379(24.8)	75(19.6)		
Polyhydramnios	No	1517(99.3)	381(99.7)	/	0.479 ^b
	Yes	11(0.7)	1(0.3)		
Oligohydramnios	No	1490(97.5)	349(91.4)	32.314	< 0.001
	Yes	38(2.5)	33(8.6)		
Ketonuria in 1st trimester(mmol/l)	< 0.5	1049(68.7)	275(72)	9.963	0.007
	0.5-3.9	336(22)	59(15.4)		
	≥4	143(9.4)	48(12.6)		
Ketonuria in 2nd trimester (mmol/l)	< 0.5	1090(71.3)	293(76.7)	4.903	0.086
	0.5-3.9	308(20.2)	59(15.4)		
	≥4	130(8.5)	30(7.9)		
Elevated blood glucose in OGTT	One item	482(31.5)	161(42.1)	24.605	< 0.001
	Two items	878(57.5)	204(53.4)		
	Three items	168(11.0)	17(4.5)		
	75g OGTT 0 h glycemia (mmol/l)	4.83±0.48	4.64±0.44	7.187	< 0.001
	75g OGTT 1 h glycemia (mmol/l)	9.84±1.41	9.89±1.36	-0.585	0.559
	75g OGTT 2 h glycemia (mmol/l)	8.06±1.59	7.83±1.58	2.586	0.01

FPG in the 2nd trimester (mmol/l)	4.87±0.559	4.73±0.488	4.372	< 0.001
2-h postprandial glucose in 2nd trimester (mmol/l)	6.09±1.30	5.7±1.14	5.825	< 0.001
HbA1c in the 2nd trimester (mmol/l)	5.26±0.356	5.28±0.349	-1.008	0.314

Abv: SGA: small-for-gestational-age; AGA: appropriate-weight-for-gestational-age; OGTT: *Oral Glucose Tolerance Test*; FPG: fasting plasma glucose; HbA1c: hemoglobin A1c; the first trimester of pregnancy: 7–10 gestational weeks; the second trimester of pregnancy: 21–24 gestational weeks; the third trimester of pregnancy: 33–37 gestational weeks.

Table 3 Logistic regression analysis for SGA based on maternal glycemic parameters

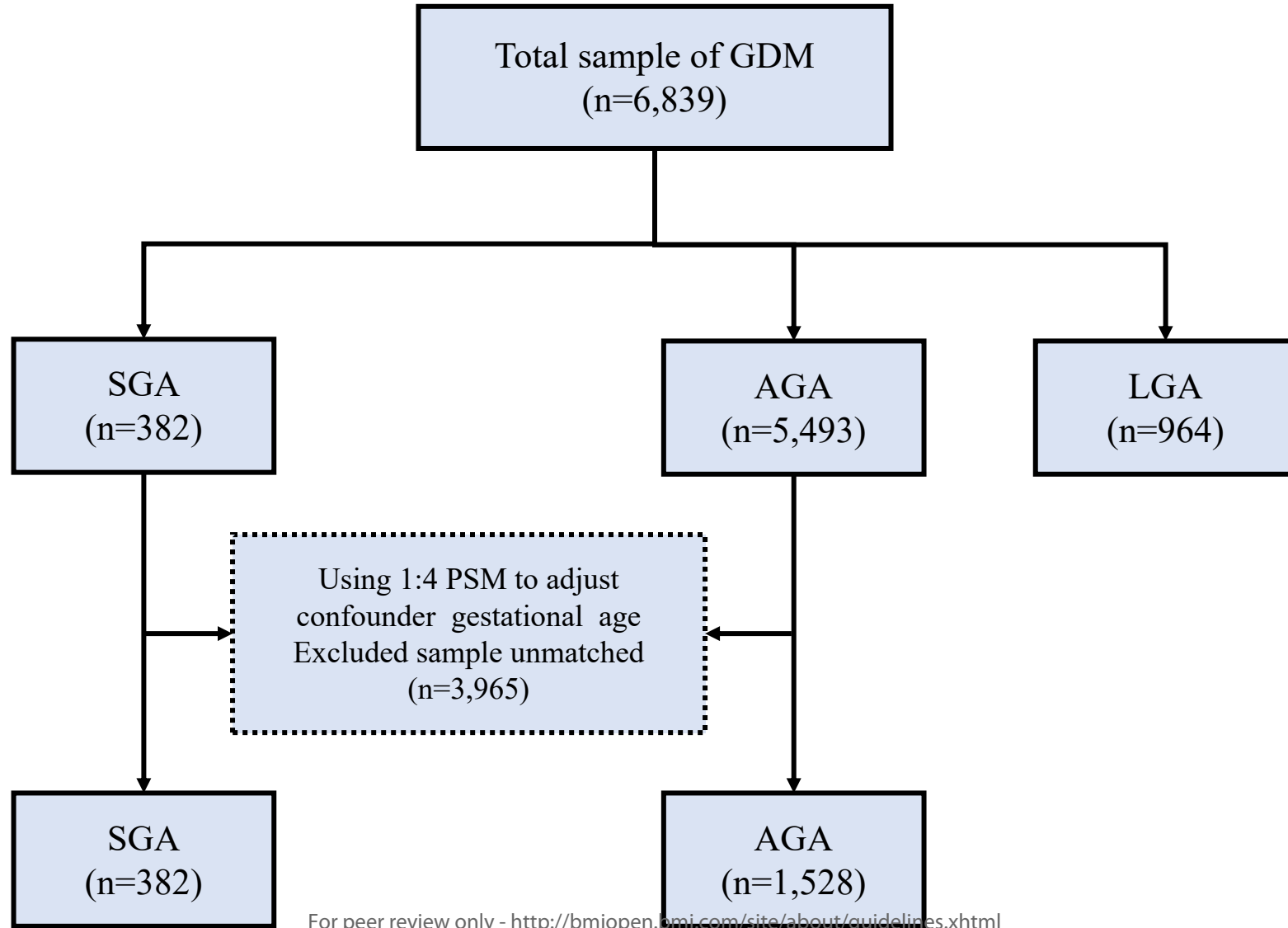
Variables	Crude OR (95% CI)	<i>P</i>	Adjusted† OR (95% CI)	<i>P</i>
75g OGTT 0 h glycemia	0.39(0.29-0.53)	< 0.001	0.4(0.29-0.55)	< 0.001
75g OGTT 1 h glycemia	1.06(0.97-1.15)	0.217	1.04(0.95-1.14)	0.365
75g OGTT 2 h glycemia	0.88(0.82-0.95)	0.001	0.88(0.81-0.95)	0.002
FPG in 2nd trimester	0.74(0.57-0.97)	0.026	0.77(0.59-1.01)	0.063
2-h postprandial glucose in 2nd trimester	0.79(0.71-0.88)	< 0.001	0.81(0.73-0.9)	< 0.001
HbA1c in the 2nd trimester	2.28(1.6-3.25)	< 0.001	2.4(1.64-3.52)	< 0.001

545 † Adjusted for parity, previous uterine scar, history of low birth weight, macrosomia,
546 gestational hypertensive disorder, oligohydramnios, anemia, pre-pregnancy BMI, height, GWG
547 rate, and ketonuria in 1st trimester.

548 **Abv:** OGTT: Oral Glucose Tolerance Test; FPG: fasting plasma glucose; HbA1c: hemoglobin
549 A1c; the third trimester of pregnancy: 33–37 gestational weeks.

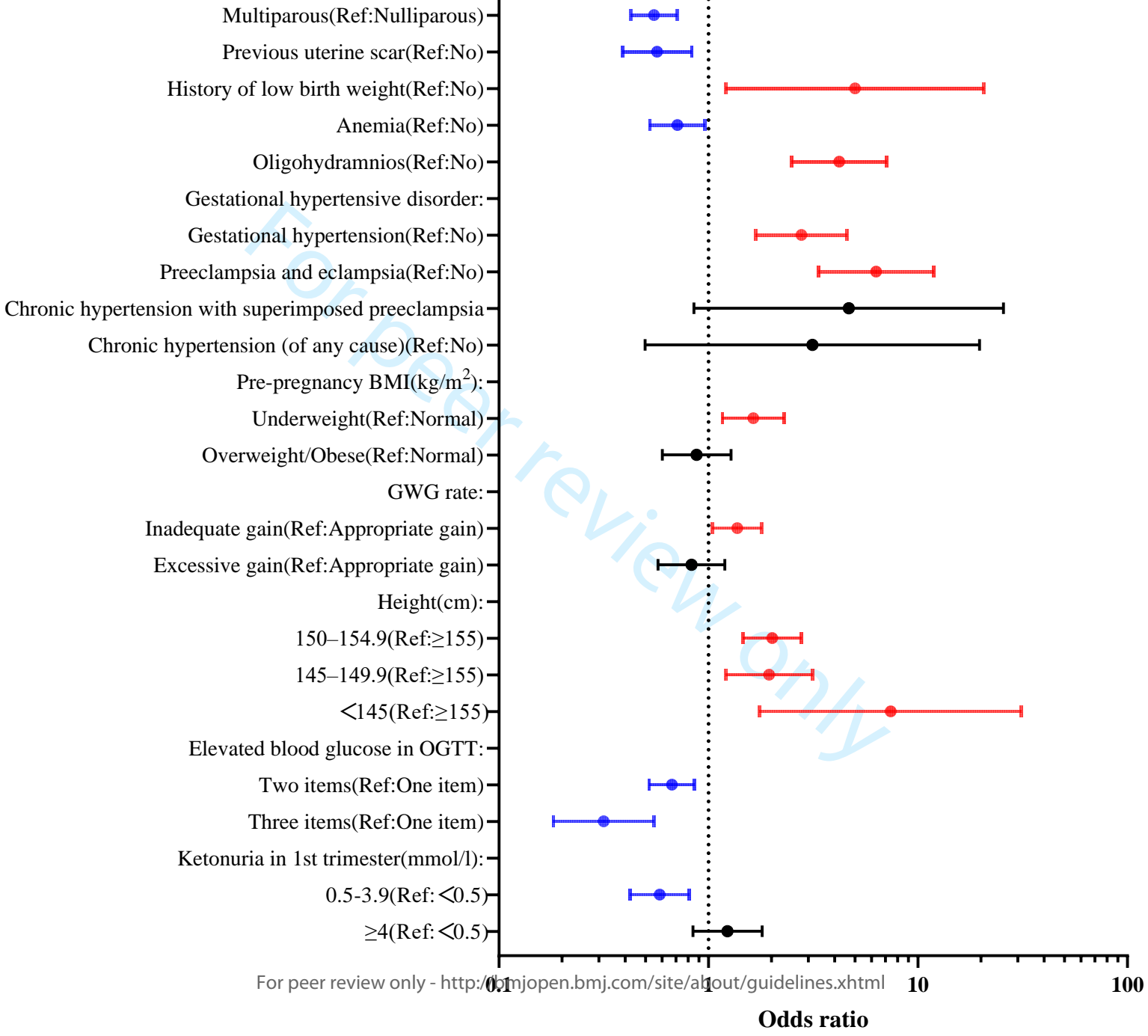
550 OR: odd ratios, CI: confidence interval.

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Supplementary material 1

1 Maternal demographic characteristic

Maternal characteristics collected included maternal age, ethnicity, educational level, occupation, marital status, place of residence, stature, pre-pregnancy Body mass index, and GWG rate.

Height: women were classified into four categories based on height < 145 cm, 145-149.9 cm, 150-154.9 cm, and ≥ 155 cm. Body mass index (BMI): BMI was calculated as weight (kg)/ [height (m)]². Using BMI, women were classified as underweight (BMI<18.5 kg/m²), normal weight (18.5–24.9 kg/m²), overweight (25–29.9 kg/m²), or obese (≥ 30 kg/m²).

Gestational weight gain rate (GWG rate): To assess the adequacy of GWG among the study population, the GWG rate of each participant, which was calculated by dividing the total GWG by gestational age in weeks, was compared with the minimum recommended GWG rate. According to the IOM 2009 guidelines, The GWG of all included participants was categorized as inadequate weight gain, normal weight gain, and excessive weight gain.

2 Pregnancy characteristics

Pregnancy characteristics collected included parity, assisted reproductive technology-conceived pregnancy (ART), previous uterine scar (previous cesarean section or myomectomy), family history of hypertension or diabetes, pregnancy history (history of miscarriage, history of GDM, history of macrosomia, history of preterm labor, history of fetal distress, history of LBW).

3 Pregnancy complications

Pregnancy complications collected included intrahepatic cholestasis of pregnancy (ICP),

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4 pregnancy-associated hypertensive disorders, hyperthyroid, hypothyroid, anemia (defined by
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6 hemoglobin < 11 g/dL before delivery) (Goonewardene, Shehata, and Hamad 2012), and
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9 pathology of amniotic fluid (oligohydramnios and polyhydramnios)
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11 The gestational hypertensive disorder was classified into four categories: gestational
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13 hypertension, preeclampsia, and eclampsia, chronic hypertension with superimposed
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15 preeclampsia, preeclampsia and eclampsia chronic hypertension (of any cause), which was
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17 diagnosed using standard criteria (Anon 2013).
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21 22 **Reference**

23
24 Anon. 2013. 'Hypertension in Pregnancy: Executive Summary'. *Obstetrics & Gynecology*
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26 122(5):1122–31. doi: 10.1097/01.AOG.0000437382.03963.88.
27
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29
30 Goonewardene, Malik, Mishkat Shehata, and Asma Hamad. 2012. 'Anaemia in Pregnancy'.
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32 *Best Practice & Research. Clinical Obstetrics & Gynaecology* 26(1):3–24. doi:
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34 10.1016/j.bpobgyn.2011.10.010.
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Reporting checklist for case-control study.

Based on the STROBE case-control guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the STROBE case-control reporting guidelines, and cite them as:

von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies.

			Page Number
Title and abstract			
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	2
Abstract	#1b	Provide in the abstract an informative and balanced summary	2-3

of what was done and what was found

Introduction

Background / [#2](#) Explain the scientific background and rationale for the 3-5
 rationale investigation being reported

Objectives [#3](#) State specific objectives, including any prespecified 5
 hypotheses

Methods

Study design [#4](#) Present key elements of study design early in the paper 5-6

Setting [#5](#) Describe the setting, locations, and relevant dates, including 5-7
 periods of recruitment, exposure, follow-up, and data collection

Eligibility criteria [#6a](#) Give the eligibility criteria, and the sources and methods of 5-6
 case ascertainment and control selection. Give the rationale
 for the choice of cases and controls. For matched studies, give
 matching criteria and the number of controls per case

Eligibility criteria [#6b](#) For matched studies, give matching criteria and the number of 7
 controls per case

[#7](#) Clearly define all outcomes, exposures, predictors, potential 5-6
 confounders, and effect modifiers. Give diagnostic criteria, if
 applicable

Data sources / [#8](#) For each variable of interest give sources of data and details of 8
 measurement methods of assessment (measurement). Describe
 comparability of assessment methods if there is more than one

group. Give information separately for cases and controls.

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4	Bias	#9	Describe any efforts to address potential sources of bias 7
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7	Study size	#10	Explain how the study size was arrived at n/a
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10	Quantitative	#11	Explain how quantitative variables were handled in the 5-6
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12	variables		analyses. If applicable, describe which groupings were
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17	Statistical	#12a	Describe all statistical methods, including those used to control 5-7
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23	Statistical	#12b	Describe any methods used to examine subgroups and n/a
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25	methods		interactions
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28	Statistical	#12c	Explain how missing data were addressed
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30	methods		
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33	Statistical	#12d	If applicable, explain how matching of cases and controls was 7
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39	Statistical	#12e	Describe any sensitivity analyses n/a
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44 Results

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47	Participants	#13a	Report numbers of individuals at each stage of study—eg 8
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57	Participants	#13b	Give reasons for non-participation at each stage 8
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1	Participants	#13c	Consider use of a flow diagram	Figure 1
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4	Descriptive data	#14a	Give characteristics of study participants (eg demographic,	8
5			clinical, social) and information on exposures and potential	
6			confounders. Give information separately for cases and	
7			controls	
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14	Descriptive data	#14b	Indicate number of participants with missing data for each	8
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19	Outcome data	#15	Report numbers in each exposure category, or summary	8
20			measures of exposure. Give information separately for cases	
21			and controls	
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27	Main results	#16a	Give unadjusted estimates and, if applicable, confounder-	8-9
28			adjusted estimates and their precision (eg, 95% confidence	
29			interval). Make clear which confounders were adjusted for and	
30			why they were included	
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37	Main results	#16b	Report category boundaries when continuous variables were	8-9
38			categorized	
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42	Main results	#16c	If relevant, consider translating estimates of relative risk into	n/a
43			absolute risk for a meaningful time period	
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48	Other analyses	#17	Report other analyses done—e.g., analyses of subgroups and	n/a
49			interactions, and sensitivity analyses	
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53	Discussion			
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56	Key results	#18	Summarise key results with reference to study objectives	10-11
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1	Limitations	#19	Discuss limitations of the study, taking into account sources of	14
2			potential bias or imprecision. Discuss both direction and	
3			magnitude of any potential bias.	
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9	Interpretation	#20	Give a cautious overall interpretation considering objectives,	14
10			limitations, multiplicity of analyses, results from similar studies,	
11			and other relevant evidence.	
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16	Generalisability	#21	Discuss the generalisability (external validity) of the study	11-14
17			results	
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22	Other Information			
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24				
25	Funding	#22	Give the source of funding and the role of the funders for the	15
26			present study and, if applicable, for the original study on which	
27			the present article is based	
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