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Short Report

Fetal gender is not associated with either gestational diabetes mellitus or placental weight: A cohort study

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Abstract

Aim. – This study assessed whether male fetal gender increases the risk of maternal gestational diabetes mellitus (GDM) and investigated the association with placental weight.

Methods. – The study included 20,149 women without pregestational diabetes who delivered singletons at our hospital between January 2002 and December 2010. There was universal screening for GDM, and all placentas were weighed at delivery.

Results. – GDM (affecting 14.2% of women) was not associated with fetal gender (male fetuses in women without and with GDM: 51.8% vs. 51.7%, respectively; $P = 0.957$), and remained likewise after logistic-regression analysis of risk factors for GDM (OR: 1.007, 95% CI: 0.930–1.091; $P = 0.858$). Placental weights were 600 ± 126 g, 596 ± 123 g, 584 ± 118 g and 587 ± 181 g in women with GDM/female, GDM/male, no GDM/female and no GDM/male fetuses, respectively (GDM effect: $P = 0.017$; gender effect: $P = 0.41$; GDM * gender effect: $P = 0.16$).

Conclusion. – The present results suggest that fetal gender is not associated with GDM and, while placental weights were higher in cases of GDM, there were still no gender effects.

Keywords: Fetal gender; Gestational diabetes mellitus; Placenta

1. Introduction

Gestational diabetes mellitus (GDM), defined as any degree of glucose intolerance with onset or first recognition during pregnancy, is associated with adverse outcomes during pregnancy. Classical risk factors for GDM are increasing age and body mass index (BMI), family history of diabetes mellitus, personal history of GDM and a macrosomic infant [1]. A recent systematic review and meta-analysis showed an increased risk of GDM in women carrying a male fetus compared with women carrying a female fetus [2]. However, the incremental increase in relative risk (+4%) appeared to be modest in its overall magnitude and was not consistent across all studies [2]. This may be partly due to differences in study populations and GDM criteria. Another consideration is that the association between GDM and fetal gender was either not or only incompletely adjusted for risk factors of GDM in most of the studies [2].

Nevertheless, the observation is of some interest as it suggests that the fetus may affect glucose metabolism in the mother. Placentas may be structurally or functionally different depending on the sex of the fetus, with different gene, steroid and protein expressions [3]. For example, a male conceptus, considered

Abbreviations: BMI, body mass index; GDM, gestational diabetes mellitus.

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as a fetal–placental unit, might induce additional insulin resistance through higher testosterone production in the maternal circulation [4]. Heterogeneity in placental weight according to the presence of GDM and fetal gender suggests that the placenta may be partly involved, as placental weight is a measure commonly used to describe placental growth and is even a determinant of fetal growth [5]. Even more intriguing, maternal age and ethnicity were reported in one study to interact with fetal gender in determining the risk of GDM when considering most of the established risk factors of GDM [6].

In this context, the aims of our present study were:

- to assess whether the association between GDM and fetal male gender was present in our large prospective observational cohort [7,8];
- to adjust the results for confounders and investigate any interaction with other risk factors of GDM;
- to explore placental weight at delivery according to fetal gender and GDM.

2. Methods

2.1. Participants

A total of 20,653 women delivered at our university hospital between January 2002 and December 2010. Data are routinely entered at birth for all women giving birth at our hospital by the midwife assisting at the delivery, and then checked and collected during the maternity stay by a single midwife (I.P.). The data are retrospective and observational, with no need for approval by an ethics committee/institutional review board or for written informed consent. In addition, the patients' records/information are anonymous, and the database is declared to the French National Commission on Informatics and Liberty [*Commission nationale de l'informatique et des libertés* (CNIL)] [7,8].

The present study excluded women with known diabetes ($n = 204$) and/or multiple pregnancies ($n = 378$). Therefore, 20,149 pregnancies were eligible for analysis. Definitions of the parameters did not change over the 9 years of the study.

2.2. GDM screening

GDM was universally screened for and diagnosed, using a one-step screening and diagnostic test, which consisted of a 75-g oral glucose tolerance test [7,8]. GDM was defined as a fasting plasma glucose value ≥ 5.3 mmol/L and/or a 2-h plasma glucose value ≥ 7.8 mmol/L [7,8].

2.3. Placental weighing

The placenta was cleaned and weighed by the midwife together with membranes and umbilical cord, using a DYMO digital postal scale with a resolution of 2 g/O.2 oz (Newell Rubbermaid, Atlanta, GA, USA). No specific attempt was made to remove placental blood before weighing.

2.4. Statistical analyses

Descriptive data are reported as means ± standard deviations (SD), and as numbers and percentages for categorical data. The outcomes were GDM, placental weight (g), and the ratio between birth weight and placental weight. Maternal baseline characteristics were compared to determine the univariate risk factor of GDM status, using Chi^2 or Fisher's exact tests for categorical variables and *t*-tests for continuous variables (Wilcoxon tests were performed when data were not normally distributed). The association between GDM and fetal gender was analyzed by logistic-regression based on, first, a model including the factors associated with GDM with a P-value < 0.05 on univariate analysis. A second model included the parameters used in a previously published model [6]. Associations between the sex of the fetus and placental weight, and the placental/fetal ratio according to the presence or absence of GDM, were analyzed by linear-regression, and a further two adjusted linear-regression analyses were also performed. The first analysis was adjusted for gestational age at delivery, and the second one for gestational age at delivery, parity, maternal BMI and weight gain. The two-sided significance level was fixed at 5%. All tests were performed using SAS version 9.3 software (SAS Institute Inc., Cary, NC, USA).

3. Results

3.1. Women's characteristics and factors associated with GDM

Table 1 shows our study participants' characteristics. GDM prevalence was 14.2% and male gender represented 51.7% of the offspring. Fetal gender was not associated with GDM on univariate analysis ($P = 0.957$). Also, logistic-regression analyses were performed to assess the association between fetal gender and GDM after adjusting for risk factors of GDM. For these, factors associated with GDM on univariate analysis in our series were entered into our first model (Table 1); these included risk factors for GDM according to French recommendations (age ≥ 35 years, overweight status, family history of diabetes, personal history of GDM, a macrosomic infant [9]), plus multiparity, smoking before pregnancy, a personal history of miscarriage or hypertension, and ethnicity. The second model was as similar as possible to that used by Retnakaran et al. [6], and included maternal age, ethnicity, family history of diabetes, prepregnancy BMI, weight gain during pregnancy, infant birth weight and male fetus. In both our models, fetal gender was not associated with GDM [odds ratio (OR): 1.007, 95% confidence interval (CI): 0.930–1.091; $P = 0.858$ and OR: 0.986, 95% CI: 0.908–1.072; $P = 0.746$, respectively]. Although there was no association between fetal gender and GDM, an investigation into whether age ≥ 35 years, overweight status and ethnicity interacted with this association also showed this was not the case (data not shown).