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Research Paper

Single Fasting Plasma Glucose Versus 75-g Oral Glucose-Tolerance Test in Prediction of Adverse Perinatal Outcomes: A Cohort Study

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ABSTRACT

Background: There remains uncertainty regarding whether a single fasting glucose measurement is sufficient to predict risk of adverse perinatal outcomes.
Methods: We included 12,594 pregnant women who underwent a 75-g oral glucose-tolerance test (OGTT) at 22–28 weeks' gestation in the Born in Guangzhou Cohort Study, China. Outcomes were large for gestational age (LGA) baby, cesarean section, and spontaneous preterm birth. We calculated the area under the receiver operator characteristic curves (AUCs) to assess the capacity of OGTT glucose values to predict adverse outcomes, and compared the AUCs of different components of OGTT.
Results: 1325 women had a LGA baby (10.5%). Glucose measurements were linearly associated with LGA, with strongest associations for fasting glucose (odds ratio 1.37, 95% confidence interval 1.30–1.45). Weaker associations were observed for cesarean section and spontaneous preterm birth. Fasting glucose have a comparable discriminative power for prediction of LGA to the combination of fasting, 1 h, and 2 h glucose values during OGTT (AUCs, 0.611 vs. 0.614, $P = 0.166$). The LGA risk was consistently increased in women with abnormal fasting glucose (≥5.1 mmol/l), irrespective of 1 h or 2 h glucose levels.
Conclusions: A single fasting glucose measurement performs comparably to 75-g OGTT in predicting risk of having a LGA baby.

1. Introduction

Large for gestational age (LGA), defined as a birth weight ≥ 90th percentile for gestational age, is the predominant adverse outcome associated with maternal hyperglycemia (Langer et al., 2005; Metzger et al., 2008). LGA is the main factor underlying birth trauma and preterm birth, as well as obstructed labor, that leads to cesarean delivery (Kc et al., 2015; Zhang et al., 2008). Long-term effects of LGA for the offspring include obesity, the metabolic syndrome, type 2 diabetes and insulin resistance (Damm et al., 2016).

In clinical practice, the main aim of gestational diabetes mellitus (GDM) treatment is to control glucose metabolism and thus reducing fetal macrosomia and obstetric complications as well as to prevent obesity in the offspring. Treatment of GDM is supposed to decrease the risk of fetal macrosomia (Crowther et al., 2005; Landon et al., 2009). In 2010, the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) recommended new criteria for GDM diagnosis, based on odds ratios of abnormal birth weight, cord C-peptide and percent body fat observed in the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study (Metzger et al., 2008), with the primary aim of prevention of obesity risk among high-risk offspring. The test criteria include relatively lower cut-off values and single abnormal of a fasting, 1 h or 2 h glucose measured by an universal, single stage screening of 2 h 75-g oral glucose-tolerance test (OGTT) is adequate to make a diagnosis, which consequently increased the prevalence of GDM in many countries including China adopted this criteria (Cundy et al., 2014). Although

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OGTT has been well recognized as the "gold standard" for GDM diagnosis, it has many disadvantages of not reproducible, time-consuming and fairly demanding for both the pregnant women and the laboratory (Davidson, 2002; Hanna and Peters, 2002). Given the uncertainty of the utility of each glucose measurement in the prediction of fetal macrosomia and the significant resource implications of the IADPSG criteria, there remains controversy regarding this screening methodology for identification of macrosomia risk during pregnancy (Kalter-Leibovici et al., 2012).

In the setting of developing countries with limited resource, the screening and management of high-risk population may be more important and cost-effective than GDM diagnosis. Fasting plasma glucose (FPG) provides a cheap, acceptable reliable, reproducible alternative GDM screening method to the OGTT for the last three decades (Mortensen et al., 1985; Zhu et al., 2013), with renewed attention following introduction of the IADPSG criteria. Early studies suggested that FPG had significantly higher predictive value for LGA in comparison to post-load glucose, independent of maternal BMI and 2 h glucose value (Disse et al., 2013; Legardeur et al., 2014). A recent systematic review also found that fasting glucose concentration has stronger associations with LGA than post-load glucose concentration (Farrar et al., 2016). FPG performance has been largely determined by utility to GDM detection using specific criteria, with limited information regarding prediction of adverse pregnancy outcomes (Agarwal, 2016). However, the U.S. Preventive Services Task Force has suggested that the gold-standard for GDM screening tests, should include an acceptable, agreed set of relevant pregnancy outcomes (Donovan et al., 2013). There remains uncertainty regarding whether a single FPG measurement is sufficient for prediction of increased risk of adverse perinatal outcomes.

The aim of the study was to evaluate the performance of single FPG measurement versus a complete 75-g OGTT for screening women at increased risk of perinatal outcomes, primarily abnormal birth weight, in a large contemporary cohort of Chinese pregnant women.

2. Methods

2.1. Study Design and Participants

The Born in Guangzhou Cohort Study (BIGCS) is a prospective birth cohort study conducted in the Guangzhou Women and Children's Medical Center (GWCMC), China. This hospital serves women and children in Guangzhou city, including approximately 16,000 deliveries per year. We recruited pregnant women who (1) resided in Guangzhou, (2) intended to remain in Guangzhou with their child for at least 3 years, and (3) intended to receive routine antenatal care and deliver at the GWCMC. 15,198 women participated in BIGCS and delivered between February 2012 and June 2016 were eligible for the present analysis. We excluded those women with pre-pregnancy diabetes or chronic hypertension, multiple pregnancies, termination of pregnancy or missing OGTT or delivery data. Fig. 1 shows the participants' flowchart for this study. The women who met the criteria of diabetes mellitus in pregnancy ($n = 70$, 0.5%, i.e. fasting plasma glucose ≥ 7.0 mmol/l or 2 h 75 g post-load plasma glucose ≥ 11.1 mmol/l (WHO, 2013)) were included for analysis.

At recruitment, all eligible participants provided written informed consent, and completed a self-administered comprehensive questionnaire to obtain demographic, socio-economic, environmental, lifestyle, occupational and medical information. The study protocol was approved by GWCMC Ethics Approval Board.

2.2. Oral Glucose-Tolerance Test

Eligible participants underwent a standard 2 h 75 g OGTT between 22 and 28 weeks' gestation. Women were given instructions by doctors to follow the WHO procedures to fast overnight (8–14 h) before testing. Before drawing blood, the nurses confirmed with the pregnant women

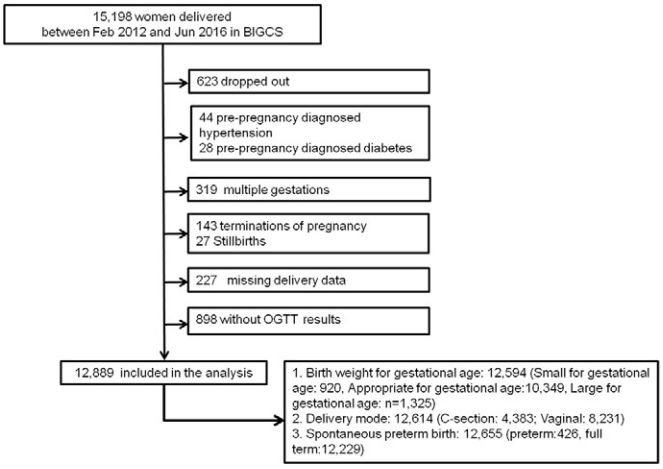

Fig. 1. The recruitment and participation flowchart.

that they have an overnight fasting. 2 ml blood samples were collected at fasting, 1 h, and 2 h after the women receipt of 300 ml water in which 75 g of anhydrous glucose dissolved, respectively, using NaF/EDTA tubes. Blood samples were stored at room temperature before 3 time-points of glucose were all drew. Once the samples were sent to the laboratory, they were centrifuged and plasma glucose was measured immediately by a hexokinase method using Beckman Coulter AU5800 automatic analyzer (Beckman Coulter®, California, United States). The laboratory has achieved ISO15189 certification by China National Accreditation Service for Conformity Assessment. At each batch, quality control plasma was set to calculate the coefficients of variation. The coefficients of variation for low and high value were 1.63% and 1.43%, respectively. If values are outside 3SD, recalibration and retest were performed to confirm the result. The glucose concentration of OGTT and testing date were extracted from the GWCMC Laboratory Information System. Women whose prenatal 75-g OGTT results met or exceeded at least one threshold of the IADPSG criteria (FPG ≥ 5.1 mmol/l, 1 h glucose ≥ 10.0 mmol/l, and 2 h glucose ≥ 8.5 mmol/l) including those have overt diabetes in pregnancy received routine clinical intervention by diet and exercise therapy. After diet control for 3 to 5 days, the women with GDM were asked to self-monitored and recorded preprandrial blood glucose (30 min before breakfast/lunch/dinner), postprandial blood glucose (30 min after breakfast/lunch/dinner), and nocturnal blood glucose at home every day. Of these women, those with FPG ≥ 5.3 mmol/l or 2 h postprandial glucose was ≥6.7 mmol/l after diet therapy were prescribed insulin or glyburide in addition to diet and exercise (Obstetrics Subgroup and Group of Pregnancy with Diabetes Mellitus, 2014). Obstetrical complications such as pregnancy hypertension disease, hydramnios, and infection were monitored by the obstetricians.

2.3. Perinatal Outcomes

The main outcomes included birthweight (continuous), birthweight Z score (continuous), LGA, cesarean section (C-section), and spontaneous preterm birth (SPTB). Birthweight and other information, including gestational age at delivery, mode of delivery, newborn gender, and pregnancy complications were obtained from medical records using the hospital-based information system. Birth weight was measured by GWCMC midwives immediately after delivery. Birthweight Z scores were calculated using a local population-based birth weight reference (He et al., 2014). LGA was defined as a birthweight larger than the 90th percentile for gestational age by gender, based on the same birth weight reference (He et al., 2014). Gestational age was estimated from ultrasound examination during the first- or second-trimester. SPTB was defined as birth following spontaneous preterm labor and/or