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Pregnancy outcomes in women with an early diagnosis of gestational diabetes mellitus ☆

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ABSTRACT

Aim: To examine pregnancy outcomes in women with gestational diabetes mellitus (GDM) based on the timing of diagnosis.

Method: We compared demographics, blood sugars and outcomes between women diagnosed before (n = 167) or after 24 weeks' gestation (n = 1202) in a single hospital between 2009 and 2012. Because early screening is risk-based we used propensity score modelling and conditional logistic regression to account for systematic differences.

Results: Women diagnosed with GDM before 24 weeks were more likely to be obese and they were less likely to have excess gestational weight gain (35 vs. 45%, p = 0.04). Early diagnosis was associated with more frequent therapy including glyburide (65 vs. 56%, p < 0.001) and insulin (19 vs 6%, p < 0.001). After propensity score modelling and accounting for covariates, early diagnosis was associated with an increased risk for macrosomia (OR 2, 95% 1–4.15, p = 0.0498). Early diagnosis was not associated with other adverse outcomes. In a subgroup analysis comparing women treated with glyburide prior to 24 weeks compared to those diagnosed after 24 weeks, early diagnosis in women treated with glyburide was associated with an increased risk for macrosomia (OR 2.3, 95% CI 1.1–5.4, P = 0.04).

Conclusion: Women diagnosed with GDM before 24 weeks have unique features, are at risk for adverse outcomes, and require targeted approaches to therapy.

1. Introduction

Treatment of gestational diabetes mellitus (GDM) improves maternal and neonatal outcomes [1–3]. While there is an ongoing debate regarding the optimal GDM screening strategy [4], numerous professional societies now support universal GDM screening between 24 and 28 weeks of gestation [5–8]. Insulin resistance increases with advancing gestation [9], and screening at 24–28 weeks is recommended to coincide with peak insulin resistance while allowing sufficient time for treatment benefit. However, the higher prevalence of obesity and diabetes outside of pregnancy raises concern that some pregnant women may develop gestational diabetes prior to 24 weeks' gestation or present with undiagnosed

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pre-gestational diabetes. Several professional organizations recommend diabetes testing at the first prenatal visit for either all women [8] or those with risk factors such as age greater than 35, obesity, prior GDM, previous macrosomic infant, family history of diabetes and PCOS [5,7]. Higher first trimester fasting glucose levels, even below those typically diagnostic of diabetes, increase the risk for LGA birth weight, macrosomia, and cesarean delivery [10]. This knowledge has prompted many physicians to treat women diagnosed with GDM prior to 24 weeks, and these women may have more advanced pathophysiology and a higher risk for poor maternal and neonatal outcomes.

In a recent study, Sweeting et. al. described higher rates of adverse pregnancy outcomes in women diagnosed with GDM before 24 weeks, with the highest risk occurring in those women diagnosed with GDM at less than 12 weeks [11]. However, after accounting for baseline maternal characteristics including maternal obesity, gestational weight gain, and fasting glucose the timing of GDM diagnosis was no longer associated with differences in large for gestational age (LGA) birth weight or macrosomia [11]. Women in this cohort were exclusively treated with insulin, which is in contrast to the United States where glyburide has become the most common treatment for GDM in recent years [12]. Therefore, we set out to better characterize treatment patterns and maternal and neonatal outcomes between women with an earlier (<24 weeks) and later (≥24 weeks) diagnosis of gestational diabetes in a US cohort.

2. Material and methods

This was a secondary analysis of retrospective cohort study created to examine the clinical course and outcomes of a contemporary, well-characterized population of patients with GDM. Women with singleton gestations and GDM who were delivered at Magee-Womens Hospital (University of Pittsburgh, Pittsburgh, PA) from January 2009 to October 2012 were included. As previously described, women were identified using the ICD-9 codes 648.01 (diabetes-delivered) and 648.81 (abnormal glucose tolerance-delivered), and medical records were reviewed to confirm the diabetes diagnosis [13]. Women were deemed to have pre-gestational diabetes if they reported a diagnosis of diabetes at their first prenatal visit or if they had a first trimester HbA1c value ≥6.5% (48 mmol/-mol), and there were a total of 20 women excluded for this reason. Women with pre-gestational diabetes were excluded, and those with GDM were included only if their records were available for review and if they had either a 50-g one-hour glucose challenge test (GCT) that exceeded 200 mg/dL, or if they had two or more abnormal values on a 3 h, 100 g oral glucose tolerance test (OGTT) as defined by the Carpenter-Coustan Criteria [5]. Out of a total of 38,222 deliveries, we identified 1374 women with GDM, and only the first pregnancy during the study period was included. There were 5 women who were excluded because the precise timing of their GDM testing was unknown, leaving 1369 women for the final cohort. Regulatory approval was obtained from the University of Pittsburgh Institutional Review Board, and informed consent was not required given the retrospective nature of the study.

Women included in this study received prenatal care in the obstetric and maternal fetal medicine clinics at our hospital. Early GDM screening was performed at the discretion of the provider, and the majority of women underwent GDM testing using a non-fasting, 50 g glucose challenge test (GCT) followed by a fasting, 100 g oral glucose tolerance test (OGTT). GDM diagnosis was established by either a GCT that exceeded 200 mg/dL as per institutional policy, or if they had two or more abnormal values on a 3 h, 100 g OGTT as defined by the Carpenter-Coustan Criteria [14]. The majority of women with GDM (n = 1215, 88.7%) received their nutritional counseling through a centralized office where they were given instructions regarding their diet and recommended weight gain based on their pre-pregnancy BMI. The remainder received similar counseling but in separate locations. Self-monitoring of plasma glucose was recommended four times daily, and targets for plasma glucose included a fasting value less than 95 mg/dL and one-hour post-meal values less than 140 mg/dL [5].

Pre-pregnancy BMI was calculated from the pre-pregnancy weight reported in the medical record, and the reported pre-pregnancy weight had a strong correlation with the measured weight at the first prenatal visit ($r = 0.98$, $p < 0.001$). Maternal pre-pregnancy overweight and obesity was reported as an index of weight-for-height (body mass index, BMI), and overweight/obesity was defined using the WHO guidelines for classification of BMI [15]. Gestational weight gain was defined as insufficient, sufficient, or excessive for each pre-pregnancy BMI category as defined in the Institute of Medicine 2009 guidelines [16]. In order to assess the association between excess gestational weight gain and pregnancy outcomes in those women who delivered preterm we estimated the maximal recommended weight gain at the gestational age at which they were delivered. We performed these calculations by multiplying the maximal weekly weight gain in the second and third trimesters times the number of weeks preterm the patient was delivered and subtracting this value from the maximum recommended weight gain for each BMI category [17].

To assess maternal glycemic control, 7 days of consecutive blood sugars were obtained from the medical record at 4 week intervals. Blood sugar data were available for 1147/1369 women (83.8%), and the mean fasting and postprandial blood sugars were calculated across gestation. We also obtained information regarding medication use including dose and gestational age at initiation of therapy and type and dose of medication at delivery.

Our primary pregnancy outcomes included macrosomia, preterm delivery, hypertensive disorders of pregnancy, and neonatal morbidity. Macrosomia was defined as birth weight >4000 g, and we also compared large for gestational age (>90th percentile for gestational age) or small for gestational age (<10th percentile for gestational age) birth weight status based on US national birth weight data between those women with an early GDM diagnosis and those who were diagnosed after 24 weeks [18]. Preterm births (<37 weeks) were further characterized as spontaneous (following the spontaneous