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The discordance between HbA1c and glucose tolerance testing for the postpartum exclusion of diabetes following gestational diabetes

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ABSTRACT

Aims: To assess the concordance between the HbA1c and the oral glucose tolerance test (OGTT) for the diagnosis of diabetes and prediabetes following gestational diabetes (GDM) in an ethnically diverse population.
Methods: Women with GDM underwent a concurrent OGTT and HbA1c test 6–12 weeks postpartum.
Results: There were 114 women with GDM who had a 75 g 2-h OGTT and HbA1c at 9.0 ± 3.2 weeks postpartum. Five subjects had diabetes using OGTT criteria, and 4 by HbA1c criteria. No subjects had diabetes on both criteria. The overall concordance between the OGTT and HbA1c for the diagnosis of diabetes, prediabetes, or normal glucose tolerance was only 54% (κ coefficient 0.058, $p = 0.41$). Gravidity, the 2-h glucose level on the OGTT during pregnancy, and the 3rd trimester HbA1c predicted discordance between the postpartum OGTT and HbA1c.
Conclusions: There is poor concordance between the OGTT and HbA1c for the diagnosis of diabetes and prediabetes following GDM. This reflects that the two tests measure different aspects of dysglycemia. In the post-GDM population, the HbA1c misses cases of diabetes as identified by the OGTT. We recommend that the OGTT be retained for postpartum diabetes testing following GDM.

1. Introduction

Women with gestational diabetes (GDM) have an approximate 50% future risk of developing diabetes, 6–7 times that of women who have not had GDM [1,2]. A high proportion of the progression to either prediabetes or type 2 diabetes occurs within the first five years after the pregnancy [3]. It is recommended that women with GDM be reassessed early postpartum with an oral glucose tolerance test (OGTT) to

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exclude the presence of persistent diabetes, and if negative, to undergo screening for diabetes annually to every 3 years [4,5]. The importance of regular screening for diabetes after a pregnancy complicated by GDM is not only for early detection of diabetes to prevent future diabetes complications, but also to ensure adequate pre-pregnancy planning and lifestyle modifications for glucose-intolerant women [6].

The glycated hemoglobin (HbA1c) test is now recognized internationally for the general diagnosis of diabetes as it carries obvious benefits in terms of convenience [4,7]. Not surprisingly, the question of whether a HbA1c is a reasonable alternative test for postpartum assessment of diabetes following GDM has arisen. However it is not currently endorsed by the ADA [4]. Given that the HbA1c and OGTT measure different aspects of dysglycemia the two tests may identify two different cohorts of people with glucose intolerance, and this may well be more marked when testing for diabetes after a GDM pregnancy. Indeed, early data from cohorts of women up to 36 months postpartum [8], one year postpartum [9,10], and even up to 5 years postpartum [11], suggest discordance between glycemic measures whereby the HbA1c has a poor sensitivity and specificity for the detection of glucose intolerance as based on a fasting glucose or 2-h glucose level.

As yet however, there are limited data regarding the concordance of the HbA1c and OGTT specifically at the time of initial postpartum testing at 6–12 weeks. The current study aimed to examine this prospectively in a cohort of women with GDM.

2. Materials and methods

Women with GDM attending the Westmead Hospital Diabetes in Pregnancy Clinic were invited to undertake a follow-up OGTT and concurrent HbA1c 6–12 weeks postpartum, over the period of November 2010 to March 2012. Approval was received from the local health district's human research ethics committee. The standard hospital protocol is to screen for GDM with a 50 gram non-fasting glucose challenge test at 24–26 weeks gestation, and proceed to a diagnostic 75 g OGTT if the result is $\geq$7.8 mmol/L. GDM is defined by the Australasian Diabetes in Pregnancy Society (ADIPS) criteria (fasting glucose $\geq$5.5 mmol/L and/or 2-h glucose $\geq$8.0 mmol/L) [12]. GDM is managed as per ADIPS guidelines [12], and women are referred to the multidisciplinary Diabetes in Pregnancy Clinic only if they are thought likely to require insulin or more intensive management.

On the postpartum OGTT, diabetes was diagnosed on the basis of World Health Organization (WHO) and American Diabetes Association (ADA) criteria (diabetes: fasting glucose $\geq$7.0 mmol/L or 2-h glucose $\geq$11.1 mmol/L) [4,7]. Prediabetes (impaired glucose tolerance (IGT) and impaired fasting glycemia (IFG)) was diagnosed on the basis of the ADA criteria (IGT: 2-h glucose 7.8–11.0 mmol/L; IFG: fasting glucose 5.6–6.9 mmol/L) [4]. With the HbA1c, diabetes was determined on the basis of the ADA and WHO criterion of $\geq$6.5% (48 mmol/mol) [4,7]. Prediabetes was diagnosed in accordance with the ADA criteria of 5.7–6.4% (39–46 mmol/mol) [4]. Women with GDM who obtained their postpartum OGTT at an outside laboratory, who were treated with glucocorticoids or metformin during pregnancy, or who were treated with hypoglycemic therapy postpartum were excluded from analysis.

Blood glucose was measured using the coupled hexokinase/glucose-6-phosphate dehydrogenase method with the Roche/Hitachi Modular P system (Roche Diagnostics, Basel, Switzerland). HbA1c was measured using ion exchange high pressure liquid chromatography (VARIANT II Hemoglobin HBA1C Program; BIORAD, Hercules, CA, USA), which is standardized to the IFCC and aligned to the DCCT.

Descriptive statistics are presented as mean $\pm$ SD. Concordance between the OGTT and HbA1c results was estimated by calculation of the Cohen kappa coefficient (κ). Spearman's rank correlation coefficient (ρ) was used to examine the correlation between continuous variables that were not normally distributed. The Pearson chi-square test or nonparametric tests (Kruskal–Wallis and Jonckheere–Terpstra tests) were used to examine the discordance between the OGTT and HbA1c results among dichotomous or continuous variables. P values <0.05 were considered significant. In our categorical analyses, we regarded diabetes as the most severe category of glucose intolerance, and prediabetes as a lesser category of glucose intolerance. Statistical analysis was carried out using SPSS Version 21 (Armonk, New York: IBM Corp).

3. Results

Data for 114 eligible women were available for analysis. The mean age of the women was 32.3 years. A quarter of the patients had a history of GDM in a prior pregnancy. The mean BMI was 25.8 $\pm$ 5.4 and average weight gain during pregnancy was 8.4 $\pm$ 4.8 kg. On the diagnostic OGTT, the mean fasting glucose was 4.6 $\pm$ 1.3 mmol/L and the 2-h glucose level was 8.7 $\pm$ 2.2 mmol/L. The mean HbA1c at 34–38 weeks gestation was 5.6% (38 mmol/mol). Notably, there was a diverse ethnic mix amongst the women, with a particularly high proportion of 34.2% of South Asian background. The other prominent ethnicities included East Asian (27%), Middle Eastern (18.4%), Caucasian (14%), and African (3.4%).The vast majority of women (95.6%), were treated with insulin, due to the referral criteria of the clinic.

OGTT and HbA1c measurements were performed at 9.0 $\pm$ 3.2 weeks postpartum. On the basis of the postpartum OGTT, 5 (4%) subjects had diabetes and 19 (17%) had prediabetes (17 IGT, 2 IFG). For these 24 women with abnormal postpartum OGTTs, the mean fasting glucose level was 4.9 $\pm$ 0.8 mmol/L and 2-h glucose level was 9.3 $\pm$ 1.8 mmol/L, with 75% (18/24) fulfilling criteria for prediabetes or diabetes based on the 2-h glucose level alone. On the basis of the postpartum HbA1c, 4 (4%) subjects had diabetes and 47 (41%) had prediabetes. No women had diabetes by both OGTT and HbA1c criteria.

Table 1 shows the lack of agreement between postpartum OGTT and HbA1c categories of glucose intolerance. The overall concordance was only 54%, with a κ coefficient of 0.058 ($p = 0.41$). When the subjects were examined individually, 36% had a higher category of glucose intolerance on the HbA1c including 37 women with IGT and 1 women with diabetes with corresponding normal glucose tolerance on OGTT. Eleven

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