Haemoglobin A1c as a screening tool to identify pre-diabetes and diabetes in postpartum women with gestational diabetes

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Abstract
The primary objective of this study was to determine the right test and time for postpartum screening of women with gestational diabetes to identify diabetes mellitus or impaired glucose tolerance.

Retrospective data were collected on women with gestational diabetes followed at the Center for Diabetes and Metabolic Care at Saint Francis Hospital and Medical Center, Hartford, Connecticut, USA.

Of the 150 women included in this study, blood work was completed in 42 (28%) of the subjects. Of the women completing laboratory tests, 23 of them (56.1%) had an abnormal test result. Using the standard tests, 15 (41.7%) of the women tested positive based on HbA1c ≥5.7% (39mmol/mol), six (16.7%) based on fasting glucose ≥100mg/dl (5.6mmol/L), and 10 (27%) based on 2-hour 75g oral glucose tolerance test (OGTT) ≥140 mg/dl (7.8mmol/L). However, due to better negative predictive value, HbA1c was more accurate than 2-hour OGTT.

Of the standard testing available, HbA1c alone identified the majority of the subjects with an abnormal test. Copyright © 2016 John Wiley & Sons.

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Key words
gestational diabetes; diabetes and pregnancy; haemoglobin A1c

Introduction
Gestational diabetes mellitus (GDM) is diagnosed in women who have carbohydrate intolerance with onset or recognition during pregnancy; 4–14% of all pregnancies are complicated by GDM. The prevalence varies based on the screening methods used and the population studied.1–3 GDM not only predisposes the mother to risk of developing GDM with subsequent pregnancies but also of type 2 diabetes (T2DM) within five years of the birth.1–3 In addition, the offspring is at a higher risk of developing diabetes mellitus later in life.1–4 It is projected that up to 50% of women with GDM will develop diabetes within two to three decades after pregnancy.1–3 Postpartum screening between six to 12 weeks is recommended for women who had GDM during pregnancy to identify those with persistent glucose intolerance or new-onset T2DM, and thereafter every one to three years depending on risk factors.1,2

Despite recommendations for screening, screening rates remain suboptimal in this population irrespective of the timing of the screening. Traditionally, the screening has been done around six weeks postpartum to time it around health care visits and also to allow for time for the increased glucose levels in pregnancy to return to normal. A study showed no difference in screening with a fasting glucose and postprandial glucose measured following 2-hour 75g oral glucose tolerance test (OGTT) before six weeks postpartum.5

Kim et al.4 showed that measuring postprandial glucose using a 2-hour 75g OGTT has a greater sensitivity than fasting plasma glucose for diagnosis of diabetes. However, if the mother is breast feeding an infant during the 75g OGTT, it may lead to lower 2-hour plasma glucose.6

The haemoglobin A1c (HbA1c) is another test that can identify individuals at risk for diabetes. Even though the HbA1c concentration is not affected by breast feeding, its concentrations six weeks postpartum could be affected by perinatal haemoglobin shifts and prenatal treatments, and may not correlate well with glucose concentrations.6 For this reason the American Diabetes Association (ADA) has recommended that the HbA1c not be
HbA1c as a screening tool to identify pre-diabetes and diabetes in postpartum GDM

Original article

These women were seen by the educators at the Metabolic Care (CDMC) at Saint Francis Hospital and Medical Center from September 2013 to June 2014. Pregnant women over the age of 18 and diagnosed with GDM were included in the study. Subjects with pre-existing diabetes were excluded. These women were seen by the diabetes educators in the prenatal period. Education included information about GDM and nutrition. In addition, they were educated regarding the increased risk of developing GDM in subsequent pregnancies and T2DM in the future, and the importance of postpartum screening. As part of routine care, all women with GDM were encouraged to be screened with a fasting glucose, a 2-hour 75g OGTT and HbA1c around 12–16 weeks postpartum.

Patients were scheduled to receive a telephone call four to six weeks postpartum reminding them about the screening, as well as a mailed laboratory requisition.

Sensitivity, specificity, predictive value and accuracy were calculated for laboratory tests alone and in combination. Data were also analysed to see if there was a correlation between reminders to the patients and incidence of screening performed.

Results

A total of 150 women were included in this study. The average age at delivery was 32.2 years with mean infant gestational age of 38.6 weeks. A total of 115 patients had documentation of a follow-up phone call (77.2%), and 133 (88.7%) had documentation that a laboratory requisition was sent. Laboratory testing was completed in 42 (28%) of the subjects, with 57.1% of those having completed the blood tests within the 12–16 week postpartum period (mean = 15.3 weeks from delivery). Blood tests were completed by 31.1% of women receiving a follow-up phone call, and in 27.1% of women who were sent laboratory requisitions. Six of the 35 women with no record of a follow-up call and six of 17 with no record of a mailed laboratory requisition also completed the blood tests. Of the women completing the blood tests, 56.1% had an abnormal test, with 51.2% testing positive for pre-diabetes.

Using the three standard tests, 41.7% of women tested positive based on HbA1c ≥5.7% (39mmol/mol), 16.7% tested positive based on fasting glucose ≥100mg/dl (5.6mmol/L); and 27% tested positive based on 2-hour OGTT ≥140mg/dl (7.8mmol/L); (Table 1). Sensitivity was 71.4%, 31.6% and 85.7% for abnormal HbA1c, fasting glucose and 2-hour OGTT, respectively. However, due to better negative predictive value (NPV) of 71.4% vs 65.4%, HbA1c was more accurate (83.3% vs 75%) than 2-hour OGTT. No significant differences were found in maternal age, gestational age, or time from delivery to laboratory testing by test status (normal vs any abnormal test). Using HbA1c ≥5.7% (39mmol/mol), or fasting glucose ≥100mg/dl (5.6mmol/L), to define an abnormal test, sensitivity increased to 85.7%, NPV to 83.3%, and accuracy to 91.7%. Using either HbA1c or 2-hour OGTT >140mg/dl (7.8mmol/L) resulted in sensitivity of 91.3%, NPV of 85.7%, with accuracy of 94.6%; (Table 2).

Discussion

The carbohydrate intolerance associated with GDM frequently resolves after delivery, though it is estimated that a third of the women will have diabetes or impaired glucose tolerance at postpartum screening. The risk of developing GDM with subsequent pregnancies and developing T2DM over the next decade is high, which makes it important that women diagnosed with GDM during a pregnancy have appropriate postpartum screening and discussion to

<table>
<thead>
<tr>
<th>Process measure</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up call made (n=149)</td>
<td>115 (77.2)</td>
</tr>
<tr>
<td>Lab slip sent (n=150)</td>
<td>133 (88.7)</td>
</tr>
<tr>
<td>Completed blood work (n=150)</td>
<td>42 (28.0)</td>
</tr>
<tr>
<td>Pre-diabetes by any test (n=41)</td>
<td>21 (51.2)</td>
</tr>
<tr>
<td>Any abnormal test (n=41)</td>
<td>23 (56.1)</td>
</tr>
<tr>
<td>HbA1c ≥5.7% (39mmol/mol), (n=36)</td>
<td>15 (41.7)</td>
</tr>
<tr>
<td>Fasting OGTT ≥100mg/dl (5.6mmol/L), (n=36)</td>
<td>6 (16.7)</td>
</tr>
<tr>
<td>2-hour OGTT ≥140mg/dl (7.8mmol/L), (n=37)</td>
<td>10 (27)</td>
</tr>
</tbody>
</table>

Table 1. Process and laboratory values

<table>
<thead>
<tr>
<th>Parameter*</th>
<th>HbA1c</th>
<th>Fasting OGTT</th>
<th>2-hour OGTT</th>
<th>HbA1c or fasting OGTT</th>
<th>HbA1c or 2-hour OGTT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>71.4%</td>
<td>31.6%</td>
<td>85.7%</td>
<td>85.7%</td>
<td>91.3%</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>71.4%</td>
<td>56.7%</td>
<td>65.4%</td>
<td>83.3%</td>
<td>87.5%</td>
</tr>
<tr>
<td>Accuracy</td>
<td>83.3%</td>
<td>63.8%</td>
<td>75.0%</td>
<td>91.7%</td>
<td>94.6%</td>
</tr>
</tbody>
</table>

Table 2. Sensitivity, predictive value and accuracy
improve future pregnancy planning. Postpartum screening is recommended at six to 12 weeks for all women with GDM. Several other groups have recommended postpartum testing with fasting plasma glucose alone; others have recommended 2-hour 75g OGTTs and others have recommended HbA1c.5–10

The ADA recommends a 75g OGTT at the six to 12 week postpartum visit. National Collaborating Centre for Women’s and Children’s Health (UK) guidelines recommend using a fasting plasma glucose test six to 13 weeks after birth, or a fasting glucose test or an HbA1c≥5.6mmol/L), or a 75g OGTT 2-hour plasma glucose of 140–199mg/dL (7.8–11.0mmol/L). Diabetes is defined as repeated fasting plasma glucose ≥126mg/dL (≥7mmol/L) or 2-hour glucose ≥200mg/dL (≥11.1mmol/L).

Even though the recommendations of high-income countries are similar, the lack of uniformity makes it challenging.11,12 As a result there is also poor compliance with screening. There are many reasons why women may not be screened in the postpartum period. These include: mothers have not been educated about the risk of diabetes to them and their offspring; mothers’ time management with a newborn; inertia to repeat the OGTT; or poor communication between the providers.13–15

In our study of 150 women, blood work was completed in only 28% of the subjects. Research has shown that mailed patient reminders can increase adherence with the screening recommendations. In a randomised control trial, the response rate was 60.5% in the group in which both patient and doctor received reminders for screening, and was only 14.3% if no postal reminders were given.14–17 In our study, we found that the percentage of individuals who had the laboratory testing done following a phone call or mailing the laboratory requisition (31.1%) was very low, and the time and resources spent in trying to reach these individuals did not correlate with the response rate.

Key points

- Even though the carbohydrate intolerance associated with gestational diabetes resolves after delivery, the risk of developing type 2 diabetes over the next decade is high
- It is very important to screen women postpartum
- HbA1c does not require fasting or ingestion of a glucose load and this makes it a very convenient test to use in the postpartum period

Given the fact that the HbA1c is not an accurate measure in the immediate postpartum,16,18 and there is no reported agreement between HbA1c and blood glucose in this population,19 we decided to change the window of screening to 12–16 weeks, and screened women with all the three tests: HbA1c, fasting glucose and the 2-hour OGTT.

We found that 57.1% of those having completed the laboratory testing did so within the 12–16 week postpartum period. Using the three standard tests, our results showed that 56.1% (23) had an abnormal test, with 51.2% (21) testing positive for pre-diabetes. No significant differences were found in maternal age, gestational age, or time from delivery to laboratory test status. In our study, of the screening tests when performed after 12 weeks postpartum, HbA1c identified the majority of the patients with an abnormal test when compared to the fasting plasma glucose alone or the OGTT. HbA1c does not require fasting or ingestion of a glucose load and so this makes it a very convenient test to use in the postpartum period.

The fasting plasma glucose test when used alone as a screening test postpartum will miss approximately a third of the development of diabetes mellitus and will not allow for the detection of impaired glucose tolerance. In our study, we found that combining an HbA1c and a fasting glucose would identify more individuals with an abnormal glucose tolerance. This, along with the ease of testing, may improve postpartum testing rates in women with GDM. We have clinical evidence that in women with an abnormal glucose tolerance, T2DM can be delayed or prevented by lifestyle modifications or drug therapy. Given the high risk of development of diabetes in this population, identification, treatment and planning pregnancy in women developing diabetes after GDM should reduce subsequent early fetal loss and major congenital malformations.

Limitations to this study include small sample size, the lack of assessment of demographics to see if it played a role in non-compliance, and we did not evaluate if women were breast feeding during the period of screening. We also did not give other time windows to see if there would be a better compliance.

It is important to improve awareness and education of women with GDM and the development of T2DM in addition to educating clinicians regarding postpartum care recommendations. More research is required to improve compliance with screening.

Conclusion

The carbohydrate intolerance associated with GDM frequently resolves after delivery, though it is estimated that a third of the women will have diabetes or impaired glucose tolerance at postpartum screening. In spite of repeated efforts to contact the patient and mail laboratory requisitions, adherence to standard followed up was low. Nevertheless, of the women screened, we found 56% had an abnormal test. Of the standard testing available, HbA1c alone identified the majority of the subjects with an abnormal test. However, when used in combination with a fasting or 2-hour postprandial test, sensitivity, NPV and accuracy increased.

This study underscores the limitations of standard care in the target population, and warrants more research on effective interventions and laboratory parameters.

Acknowledgements

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Declarations of interest
There are no conflicts of interest declared.

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