Serial fetal abdominal circumference measurements in predicting normal birth weight in gestational diabetes mellitus

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ABSTRACT

Objectives: To construct a clinical management matrix using serial fetal abdominal circumference measurements (ACMs) that will predict normal birth weight in pregnancies complicated by gestational diabetes (GDM) and reduce unnecessary ultrasound examination in women with GDM.

Study design: Retrospective cohort study of 144 women with GDM in a specialist obstetric-diabetes clinic. Women with GDM who delivered singleton infants were identified from a clinical register. Regression analysis was used to identify associations between serial ACMs, maternal parameters and normal birth weight (birth weight between the 10th and 90th percentiles). Predictive clinical models were designed with the aim of identifying normal birth weight infants with the lowest number of fetal ultrasound scans.

Results: Compared to mothers of large-for-gestational-age (LGA) infants, mothers of normal weight infants had lower fasting glucose measurements at diagnosis (5.9 mmol/l ± 1.0 vs. 6.6 mmol/l ± 0.7, p < 0.05), lower maternal weight at delivery (90 kg ± 17 vs. 96 kg ± 17, p < 0.05), and a lower rate of prior LGA infants (31% vs. 60%, p < 0.05). Maternal weight and a history of prior LGA delivery were identified as useful predictors of fetal weight in predictive models. Serial ACMs below the 50th, 75th and 90th percentiles could predict normal birth weight with 100%, 97% and 96% positive predictive value respectively when used in these risk factor based models. Two measurements sufficed in low-risk pregnancies.

Conclusion: Serial ACMs can predict normal birth weight in GDM.

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1. Introduction

Predicting birth weight in pregnancies complicated by diabetes is fraught with difficulty [1–3]. Fetal ultrasound can be of limited utility in predicting birth weight, as there is significant inter-operator variability [2]. Similarly, maternal body mass index and gestational age can affect accuracy [3]. Despite these limitations, fetal ultrasound is the tool used most often in clinical practice to estimate fetal growth.

A key goal of fetal growth monitoring is identifying large-for-gestational-age (LGA) infants, but the optimal screening stratagem for LGA in gestational diabetes mellitus (GDM) has yet to be established. This may result in women with GDM undergoing multiple ultrasound evaluations which may be unnecessary. Using the new International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria for the diagnosis of GDM increases the incidence of the condition, with resultant costs for the healthcare system [4,5]. In this current era of near-universal screening a strategy involving unnecessary ultrasound examinations may not be cost-effective, and a more rational approach is needed [5]. Therefore, we plan to develop a clinical practice matrix using serial fetal abdominal circumference measurements to predict normal birth weight in pregnancies complicated by GDM. Such a tool would reduce the exposure of women to repeated unnecessary ultrasound examinations, and would enable us to rationalize use of ultrasound within our unit. First, however, we need to analyze the maternal and fetal growth data from our clinic to identify the ultrasound limits and maternal parameters that could be predictive of normal birth weight in our cohort.

Previous studies have demonstrated the value of using fetal abdominal circumference measurements in the third trimester to quantify risk of birth weight deviations in diabetic and non-diabetic populations [6,7]. Fetal abdominal circumference measurements below the 75th percentile have been recommended as a threshold below which the risk of macrosomia is reduced [8]. We evaluated serial ACM measurements in the third trimester to predict birth weight using the 50th, 75th and 90th percentile thresholds. We also evaluated specific maternal

Abbreviations: GDM, gestational diabetes; HbA1c, glycosylated haemoglobin; NPH, Neutral Protamine Hagedorn insulin; LGA, large-for-gestational age.

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parameters to add to the positive predictive value of the serial fetal abdominal measurements.

2. Materials and methods

This retrospective cohort study evaluated 144 women with a first-time diagnosis of GDM who presented to a single multidisciplinary diabetes clinic for antenatal care from 2006 to 2010. Inclusion criteria were: (1) a diagnosis of GDM based on a 100 g glucose tolerance test using the Fourth International Workshop Conference on Gestational Diabetes Mellitus criteria [9], (2) documented serial fetal biometry with at least two fetal abdominal circumference measurements per pregnancy, (3) singleton pregnancy as confirmed on fetal ultrasound at presentation for obstetric care, (4) gestational age determined by fetal biometry on initial clinical review, and (5) delivery at term, defined as 37 completed weeks' gestation.

A screening 100 g oral glucose tolerance test was offered to selected at-risk groups in the total pregnant population. Risk factors included: (1) a family history of diabetes mellitus, (2) previous delivery of a LGA infant, (3) maternal obesity as defined by a body mass index of 30 kg/m² or more at booking, or a body weight of 90 kg or more at booking, (4) the appearance of glycosuria during pregnancy, (5) an LGA infant on ultrasound examination, and (6) polyhydramnios on ultrasound evaluation.

Women with any of these risk factors proceeded to a 100 g glucose tolerance test between 24 and 28 weeks' gestation. In the case of glycosuria, polyhydramnios or LGA fetuses, the glucose tolerance test is performed on appearance of the risk factor.

Exclusion criteria included: (1) only one recorded fetal abdominal circumference measurement in pregnancy, (2) pre-gestational diabetes mellitus, (3) a history of GDM in a prior pregnancy, (4) pre-term delivery, and (5) small for gestational age infants (less than 10th percentile for gestational age).

Using a clinical register maintained on site, all women meeting the inclusion criteria were identified and their medical records were examined. All the maternal and fetal parameters mentioned above were recorded from the clinical records and entered anonymously into the study database. Ethical approval was obtained from the Coombe Women and Infants University Hospital ethics board in October 2011.

The maternal parameters measured were age, parity, history of delivery of an LGA infant, gestational age at diagnosis of GDM, body mass index at diagnosis, glycosylated haemoglobin (HbA1c) at diagnosis and delivery, insulin use and weight change from onset of GDM to delivery. The results of the diagnostic glucose tolerance test were also recorded in the study database.

Fetal and delivery parameters measured were fetal abdominal circumference, birth weight at delivery, gestational age at delivery, and mode of delivery. Normal birth weight was defined as a birth weight of less than the 90th percentile and above the 10th percentile for gestational age. Term was defined as 37 completed weeks' gestation.

On diagnosis of GDM, a diabetologist, diabetes midwife specialist and a dietitian reviewed the woman, and the initial treatment was a prescribed diet specific to the needs of the individual. The woman then presented for ongoing review at the multidisciplinary clinic until delivery.

Glycaemic control on dietary therapy was determined by measuring pre-prandial and one-hour post-prandial serum glucose measurements at intervals of up to 3 weeks. The limits accepted for fasting and one-hour post-prandial serum glucose measurements were 5 mmol/l and 7 mmol/l respectively. If a woman exceeded these limits on clinical review then insulin therapy was initiated.

Once insulin therapy was initiated, the woman was supplied with a glucometer and instructed to record a daily seven-point profile of capillary blood glucose measurements for the duration of the pregnancy. These measurements were to be taken immediately before meals and at one hour after meals, with a final capillary blood glucose measurement before sleep.

Insulin Aspart and Neutral Protamine Hagedorn (NPH) insulin were used in this study. Insulin Aspart was prescribed with meals and titrated to maintain a one-hour post-prandial capillary blood glucose level of 7 mmol/l or less, and was prescribed up to a maximum of three times per day with main meals. NPH insulin was prescribed with meals or before sleep up to a maximum of four times per day. The dose of NPH was titrated to the pre-prandial capillary blood glucose of the next meal, or the capillary blood glucose taken before sleep, and the glycaemic target was 5 mmol/l or less.

Fetal abdominal circumference measurements were taken on at least two separate time points from 27 weeks' gestation. The same senior obstetric staff took all measurements throughout the study. The results were recorded in millimeters and compiled into different gestational age brackets: 27–28 weeks, 29–30 weeks, 31–32 weeks, 33–34 weeks, 35–36 weeks, and 37–38 weeks.

The maternal characteristics, delivery characteristics, and fetal abdominal circumference measurements, of normal birth weight and LGA infants were compared. The differences were tested for significance using Student’s t-test, or the Mann–Whitney U test for parameters that were not normally distributed. The fetal abdominal circumference measurements were then categorized by percentile. The 75th percentile was used as a threshold below which risk of delivery of a LGA fetus decreased, in keeping with recent recommendations [8]. The percentile groups were classed as those with a fetal abdominal circumference:

- consistently above the 75th percentile
- consistently above the 50th percentile but below and including the 75th percentile
- consistently below and including the 50th percentile

Our sample size was 96 to give a confidence level of 95% based on a minimum incidence of normal birth weight in a local population with GDM of 76% [4]. An established percentile curve for the local population was used [10,11]. Univariate linear and logistic regression analyses were used to test each maternal parameter for significant associations with fetal birth weight. Those parameters found to have a significant association with normal birth weight were used in multivariate models. Statistical significance was assumed at p < 0.05. Statistical analysis was completed with the R software (version 2.9.2).

3. Results

Over the three-year study period, 144 women with GDM were identified, and 137 met the inclusion criteria and were included in the final analysis. This included 111 individuals (81%) who had progressed to supplemental insulin therapy by delivery.

Of the seven women who were excluded, three were found not to meet the inclusion criteria for diagnosis of GDM on review of their initial glucose tolerance tests, three delivered small-for-gestational age infants (birth weight less than the 10th percentile for gestational age), and one had a pregnancy which resulted in a pre-term delivery. A total of 102 women (74%) delivered an infant defined as normal birth weight and 35 infants (26% of total group) were delivered at term with a birth weight greater than the 90th percentile for gestational age. The maternal and fetal characteristics are tabulated in Table 1.

The absolute birth weights were greater in insulin users than in non-insulin users (3.73 ± 0.61 kg vs. 3.48 ± 0.54 kg, p = 0.04). Women using insulin had a higher HbA1c at diagnosis than women
not using insulin (5.9 ± 0.7% vs. 5.5 ± 0.6%, p = 0.03), but his difference had been lost by delivery (6.2 ± 0.8% vs. 5.9 ± 0.8%, p = 0.12). Insulin use, however, was not associated with normal birth weight or LGA on regression analysis (p = 0.09). The women using insulin did not have a significantly higher rate of LGA infants than women not using insulin (27% vs. 20%, p = 0.21). Birth weight was not associated with HbA1c at diagnosis or delivery on regression analysis.

A total of 326 ultrasound examinations were included for analysis. The percentile group characteristics are outlined in Table 2. A comparison of fetal abdominal circumference measurements at each gestational age was made between normal birth weight and LGA groups. The fetal abdominal circumference measurements were significantly greater in the LGA group at every gestational age category (p < 0.05).

In order to predict normal weight deliveries, we tested a number of models using fetal abdominal circumference percentile thresholds, and incorporated maternal variables into these models with the aim of improving accuracy. Birth weight was included in these models to identify the associated variables that could be used in a prospective clinical matrix. Using regression analysis the following variables were found to be associated with an increased risk of the delivery of a LGA infant:

(a) A history of previous LGA infant (p = 0.003).
(b) The fasting blood glucose on the diagnostic glucose tolerance test (p = 0.03).

Maternal weight at booking (p = 0.04) and at delivery (p = 0.002).
(d) Change in weight from GDM diagnosis to delivery (p < 0.001)

Given that our aim was to develop a practical model for use in clinical practice, instituting an ultrasound surveillance schedule at booking, we did not use birth weight at delivery and weight gain in our models.

All pregnancies in which the fetal abdominal circumference was consistently measured at or below the 50th percentile (N = 33, 24% of total cohort) went on to deliver fetuses weighing below the 90th percentile for gestational age. Therefore, two abdominal circumference measurements below the 50th percentile yielded a positive predictive value of 100% with a sensitivity and specificity of 32% and 100% respectively. This group had a significantly lower maternal weight at booking (p < 0.001) when compared to the rest of the cohort. They had a lower parity (0.009) and were less likely to have previously delivered a LGA infant (p = 0.01).

Serial fetal abdominal circumference measurements below the 75th percentile were significantly associated with a normal birth weight in our cohort (p < 0.05). Serial AC measurements consistently at or below the 75th percentile predicted normal birth weight with a positive predictive value of 93%, sensitivity of 61% and specificity of 86%. A total of 43 women (31% of cohort) had serial measurements less than the 75th percentile.

In women with a weight at booking of 90 kg or less, and without a history of LGA, serial fetal abdominal circumference

### Table 1
Maternal and fetal characteristics of the large for gestational age group (LGA) and normal birth weight group (NBW).

<table>
<thead>
<tr>
<th></th>
<th>LGA</th>
<th>NBW</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>35</td>
<td>102</td>
<td></td>
</tr>
<tr>
<td>Age at booking to clinic (years)</td>
<td>33 ± 5</td>
<td>33 ± 5</td>
<td>0.38</td>
</tr>
<tr>
<td>Gestational age at diagnosis of GDM (weeks)</td>
<td>24 ± 9</td>
<td>24 ± 9</td>
<td>0.27</td>
</tr>
<tr>
<td>Parity</td>
<td>2 ± 2</td>
<td>2 ± 2</td>
<td>0.13</td>
</tr>
<tr>
<td>BMI at booking to clinic (kg/m²)</td>
<td>34 ± 5</td>
<td>32 ± 6</td>
<td>0.07</td>
</tr>
<tr>
<td>Weight at booking to clinic (kg)</td>
<td>91 ± 15</td>
<td>85 ± 18</td>
<td>0.05</td>
</tr>
<tr>
<td>Weight at delivery (kg)</td>
<td>96 ± 17</td>
<td>90 ± 17</td>
<td>0.039</td>
</tr>
<tr>
<td>Weight change from GDM diagnosis to delivery (kg)</td>
<td>5.3 ± 7.2</td>
<td>3.9 ± 4.7</td>
<td>0.1</td>
</tr>
<tr>
<td>History of previous LGA delivery (% of parous women per group)</td>
<td>60%</td>
<td>31%</td>
<td>0.001</td>
</tr>
<tr>
<td>HbA1c at booking to clinic (%DCCT)</td>
<td>5.9 ± 0.8</td>
<td>5.8 ± 0.7</td>
<td>0.4</td>
</tr>
<tr>
<td>HbA1c at delivery (%DCCT)</td>
<td>6.2 ± 0.9</td>
<td>6.1 ± 0.8</td>
<td>0.35</td>
</tr>
<tr>
<td>Insulin use (% of group)</td>
<td>86%</td>
<td>79%</td>
<td>0.2</td>
</tr>
<tr>
<td>Gestational age at delivery (weeks)</td>
<td>39 ± 1</td>
<td>39 ± 1</td>
<td>0.45</td>
</tr>
<tr>
<td>Birth weight (kg)</td>
<td>4.45 ± 0.48</td>
<td>3.42 ± 0.39</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fasting blood glucose on GTT (mmol/l)</td>
<td>6.6 ± 0.7</td>
<td>5.9 ± 1.0</td>
<td>0.019</td>
</tr>
<tr>
<td>One-hour blood glucose on GTT (mmol/l)</td>
<td>13.0 ± 1.9</td>
<td>13.3 ± 1.8</td>
<td>0.4</td>
</tr>
<tr>
<td>Two-hour blood glucose on GTT (mmol/l)</td>
<td>10.4 ± 2.0</td>
<td>12.0 ± 3.1</td>
<td>0.2</td>
</tr>
<tr>
<td>Three-hour blood glucose on GTT (mmol/l)</td>
<td>9.1 ± 2.1</td>
<td>8.2 ± 2.7</td>
<td>0.18</td>
</tr>
</tbody>
</table>

BMI = body mass index; GDM = gestational diabetes mellitus; GTT = glucose tolerance test. Data are presented as mean ± standard deviation or as percentage of total group unless otherwise stated.

### Table 2
Maternal and fetal characteristics of the cohort as percentile group.

<table>
<thead>
<tr>
<th></th>
<th>&gt;75th percentile</th>
<th>50th–75th percentile</th>
<th>&lt;50th percentile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>40</td>
<td>35</td>
<td>33</td>
</tr>
<tr>
<td>Maternal age (years)</td>
<td>33 ± 5</td>
<td>34 ± 5</td>
<td>31 ± 5</td>
</tr>
<tr>
<td>Parity</td>
<td>2 ± 1</td>
<td>2 ± 2</td>
<td>1 ± 1</td>
</tr>
<tr>
<td>Birth weight (kg)</td>
<td>4.2 ± 0.6</td>
<td>3.6 ± 0.4</td>
<td>3.2 ± 0.4</td>
</tr>
<tr>
<td>Maternal history of LGA in a previous pregnancy (% of group)</td>
<td>58%</td>
<td>35%</td>
<td>21%</td>
</tr>
<tr>
<td>Fasting blood glucose on glucose tolerance test (mmol/l)</td>
<td>6.2 ± 0.9</td>
<td>5.9 ± 1.2</td>
<td>5.9 ± 0.5</td>
</tr>
<tr>
<td>HbA1c at diagnosis (%DCCT)</td>
<td>5.9 ± 0.7</td>
<td>5.9 ± 0.9</td>
<td>6.0 ± 0.7</td>
</tr>
<tr>
<td>HbA1c at delivery (%DCCT)</td>
<td>6.2 ± 0.8</td>
<td>6.2 ± 0.8</td>
<td>6.2 ± 1.1</td>
</tr>
<tr>
<td>Weight at booking to clinic (kg)</td>
<td>92 ± 15</td>
<td>87 ± 18</td>
<td>78 ± 17</td>
</tr>
<tr>
<td>Weight at delivery (kg)</td>
<td>97 ± 17</td>
<td>91 ± 18</td>
<td>84 ± 16</td>
</tr>
<tr>
<td>Weight change from GDM diagnosis to delivery (kg)</td>
<td>5.6 ± 0.6</td>
<td>3.5 ± 3.4</td>
<td>4.2 ± 4.9</td>
</tr>
<tr>
<td>Cesarean section rate (% of group)</td>
<td>53%</td>
<td>21%</td>
<td>27%</td>
</tr>
</tbody>
</table>
measurements below the 75th percentile predicted normal birth weight with a positive predictive value of 97% and a sensitivity and specificity of 64% and 94% respectively. A total of 30 women (22%) of our cohort fell into this category.

In women with a weight at booking of less than 90 kg, and without a history of previous LGA delivery, serial fetal abdominal circumference measurements below the 90th percentile predicted normal birth weight with a positive predictive value of 96%. The sensitivity was 64% with a specificity of 91% in this model. In our cohort, 41 (30%) of the women fell into this category.

Within our cohort, 29 (21%) did not fit into these models, and had serial fetal abdominal circumference measurements that either ascended or descended through the 50th and 75th percentiles. There was a sub-group who had fetal abdominal circumference measurements less than the 75th percentile at 27–30 weeks who subsequently ascended through the percentiles. In this group, all of those who delivered LGA infants had at least one pre-defined risk factor and crossed the 75th percentile at 32–34 weeks’ gestation.

A clinical management decision matrix based on these data is outlined in Fig. 1.

4. Comments

In our clinic, women undergo several routine fetal abdominal measurements in the course of their pregnancy to identify LGA fetuses. With the current clinical move toward universal screening for GDM, and increasing rates of diagnoses as a result, this approach may not be efficient [4,5]. Therefore a rationalization of fetal growth monitoring with ultrasound in GDM is needed. The focus should be on identifying the low-risk cohort, who are currently undergoing unnecessary fetal surveillance simply based on their diagnosis of GDM.

In this study, fetal abdominal circumference measurements could predict normal birth weight with a positive predictive value of 100% if the fetal abdominal circumference remained at or below the 50th percentile on two or more measurements in the third trimester. In women with a weight of 90 kg or less at booking, and without a history of a previous LGA delivery, serial measurements below the 75th percentile predicted normal birth weight with positive predictive values of 97%. Using these criteria in our clinical decision matrix (Fig. 1) would allow us to rationalize the use of ultrasound surveillance for almost 50% of our cohort.

It has been shown that more than two fetal abdominal measurements do not enhance the predictive value of fetal abdominal circumference for birth weight [12,13]. Using the 90th percentile, two fetal abdominal circumference measurements have been shown to identify 92% of infants, using a risk factor model [12]. Without risk factors, 88% of infants were identified [12]. We find that the 75th percentile yielded a greater positive predictive value than the 90th percentile with regard to predicting normal birth weight, especially if the mother did not have the pre-defined risk factors of maternal body weight greater than 90 kg or a
history of a LGA delivery. This would allow us to rationalize screening for almost 50% of our cohort.

We propose using two fetal abdominal circumference measurements in our cohort; the first at 27–30 weeks and the second at 37–38 weeks in non-obese nulliparous women or in non-obese multiparous women without a history of previous LGA delivery, as outlined in Fig. 1.

There is a role for a third fetal abdominal circumference measurement at 32–34 weeks to evaluate the high-risk group (Fig. 1). This gestational age has been previously identified as an accelerated growth period in LGA fetuses in diabetic pregnancies [14–16]. In our cohort, women with at least one risk factor who measured less than the 75th percentile at 27–30 weeks could ascend through the percentiles. Those who delivered LGA infants in this group crossed the 75th percentile at a gestational age of 32–34 weeks. This gestational age has also been shown previously to be useful in risk stratification for LGA using the 90th percentile [6].

Using maternal weight at booking adds to the positive predictive value of the fetal abdominal circumference measurements in our models. We consider women with greater body weights and weight gain in pregnancy to be at higher risk of LGA delivery, in agreement with previously published work [17–20]. Maternal weight may be more predictive of fetal birth weight than glycaemic markers [21]. Our findings support these established data.

Insulin users were more likely to deliver heavier infants, and to have higher Hba1c levels at diagnosis on comparison of means between the two groups. On regression analysis, however, this association was not seen. Evidence of LGA fetuses and hyperglycaemia are both indications for consideration of insulin therapy. Therefore, these data are consistent with our clinical practice that hyperglycaemic women or women with evidence of a LGA fetus are likely to be prescribed insulin. We believe that the difference in birth weight between insulin users and non-users is a factor of the effect of hyperglycaemia on fetal growth, rather than an effect of insulin on fetal growth.

Our study is a single-center cohort study with a specialist multidisciplinary clinic and consistent glycaemic therapy and targets, utilizing the same staff with the same ultrasound department. There were, however, limitations in our study. Firstly, the fetal abdominal circumference measurement schedule was not identical in each case, and there was scope for the clinician to scan women more or less frequently depending on perceived risk for birth weight deviation. The application of our proposed schedule as outlined above will need to be tested prospectively, and we are undertaking this study presently. Secondly, as there was a risk factor-based screening system in place for GDM, women with the established risk factors may be over-represented when compared to a cohort subject to universal or near-universal screening. Finally, we did not control for inter-operator variability, which has been shown to be highly significant [2].

Predicting normal birth weight using fetal ultrasound in pregnancies complicated by GDM remains difficult. Our study supports the use of fetal abdominal circumference in the third trimester to predict normal birth weight. Serial measurements consistently below the 50th percentile predict normal birth weight with 100% specificity. In low risk women, serial AC measurements below the 75th percentile predict normal birth weight with a 97% positive predictive value. We propose the use of maternal weight at booking and a history of a previous LGA delivery as risk factors for LGA delivery in women with GDM. Furthermore, we suggest they are used in conjunction with serial fetal abdominal circumference measurements to predict fetal birth weight.

Successfully predicting normal birth weight would allow rationalization of resources in increasingly busy GDM clinics, and reduce the exposure of low-risk women to unnecessary ultrasound measurements and hospital visits.

Conflicts of interests

We have no relevant interests to disclose.

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References