The use of early pregnancy HbA1c in predicting excessive foetal growth in women at risk of glucose intolerance

SHORT REPORT

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EVIDENCE BRIEF

Why did we start?

Gestational diabetes mellitus (GDM) is associated with excessive fetal growth in later gestation. Traditionally, GDM is diagnosed following 75g oral glucose tolerance testing (OGTT) performed between 26-28 weeks' gestation. Subsequent intervention aims to reduce the risk of excessive fetal growth and its associated sequelae. Recent data suggest accelerated fetal growth may begin as early as 28 weeks' gestation. The identification of pregnancies at risk of early fetal growth would enable early intervention. We assessed the use of early pregnancy HbA1c in predicting excessive fetal growth.

What did we do?

HbA1c was measured at <14 weeks gestation in 948 women at risk of GDM. Comprehensive ultrasound fetal biometry was performed at 28 weeks alongside a 75g OGTT. GDM was defined using IADPSG/WHO criteria.

What answer did we get?

186 women (19.6%) screened positive for GDM. At the time of OGTT, pregnancies complicated by GDM already demonstrated higher adjusted fetal weight percentile than non-GDM pregnancies: (50.9 ±26.6 (mean ± SD) vs 46.2 ±25.7 p=0.02). This was driven by relative increases in the fetal abdominal circumference percentile in GDM compared with non-GDM pregnancies (54.7 ±24.8 vs 46.2 ±23.0 p=<0.01). Early pregnancy HbA1c was higher in the GDM vs non-GDM group: 35.8 ±4.7 vs 32.9 ±3.8 p=<0.01. A threshold for predicting excessive fetal growth was not identified in this cohort.

What should be done now?

These results demonstrate that accelerated fetal growth is evident prior to the diagnosis of GDM and highlight the need for suitable methods of early identification of pregnancies at high risk for early accelerated fetal growth due to GDM.

Background

The association of hyperglycaemia in pregnancy (gestational diabetes mellitus; GDM) with adverse maternal and fetal outcomes is clearly recognised. Traditionally the diagnosis is made at 28 weeks' gestation at which stage children of affected women already have a two-fold rate of excessive weight gain (abdominal circumference > 90th percentile). This is attributed to fetal exposure to undiagnosed high blood glucose earlier in pregnancy. Indeed almost 25% of women with GDM develop the condition before 20 weeks' gestation. Interventional studies in women diagnosed in the late second trimester have shown benefits in reducing fetal macrosomia. It is unknown whether screening in the first trimester would predict fetal macrosomia and allow more timely and effective intervention.

Secondly, The UK National Institute of Clinical Excellence (NICE) recommends selecting women for GDM testing on the basis of risk factors: BMI ≥30kg/m2, previous macrosomia (baby weighing ≥ 4.5kg), family history of diabetes, high risk ethnicity or previous gestational diabetes mellitus (GDM) (NG3, 2015). These guidelines have been widely adopted within the UK yet the identified risk factors perform poorly as predictors of GDM (positive predictive value (PPV) 20.8%). The use of ultrasound measured visceral fat has recently been propose din a proof-of-concept model as a potential marker for the risk of subsequent GDM.

Aims & Objectives

To examine this question, we undertook a prospective cohort study of 1314 women at increased risk of GDM to determine if an elevated HbA1c (39-48mmool/l) in early pregnancy (<14 weeks) can identify babies at risk of excessive weight gain in later pregnancy, as determined by ultrasound measurement of abdominal circumference at 28 weeks' gestation.
Secondly, we sought to assess the performance of ultrasound- measured maternal visceral adipose tissue depth (VAD) as a tool for GDM prediction. This is a straightforward assessment which takes around 5 minutes to perform.

Methods

HbA1c was measured at <14 weeks gestation in 948 women at risk of GDM. Comprehensive ultrasound fetal biometry was performed at 28 weeks alongside a 75g OGTT. GDM was defined using IADPSG/WHO criteria.
In a nested observational study, VAD using ultrasonography was measured at <14 weeks gestation in 123 pregnant women.

Personal and Public Involvement

The key findings summary for these studies are being drawn and will be disseminated to research participants once available.

The headline results from both the parent study and the nested observational study have been presented nationally both at the Irish Endocrine Society and Diabetes UK Professional Conferences. Further presentations are scheduled in the coming months.

News articles highlighting these findings have been disseminated to the public by Diabetes UK[1], Medscape[2] and Nursing Times[3].

A further PPI event with dissemination of results to relevant staff for maternity staff is planned once covid restrictions facilitate in the coming months.

Findings

For the parent study, 186 women (19.6%) screened positive for GDM. At the time of OGTT, pregnancies complicated by GDM already demonstrated higher adjusted fetal weight percentile than non-GDM pregnancies: (50.9 ±26.6 (mean ± SD) vs 46.2 ±25.7 p=0.02). This was driven by relative increases in the fetal abdominal circumference percentile in GDM compared with non-GDM pregnancies (54.7 ±24.8 vs 46.2 ±23.0 p=<0.01). Early pregnancy HbA1c was higher in the GDM vs non-GDM group: 35.8 ±4.7 vs 32.9 ±3.8 p=<0.01. A threshold for predicting excessive fetal growth was not identified in this cohort.

For the nested study, Of the 123 women, 26 (21.1%) developed GDM. Women with GDM had a significantly higher VAD compared with those without GDM (4.22 ±0.97cm vs 3.12 ±1.33cm p<0.01). Using receiver operator characteristic (ROC) curve analysis, a VAD of 3.98cm achieved a sensitivity of 73.1% and specificity of 72.2% for the later diagnosis of GDM in this cohort. Women exceeding this threshold were at seven-fold greater odds of later GDM diagnosis (Odds Ratio 7.0). The use of this VAD threshold in this cohort increased PPV to 41.3% with a NPV of 90.9% .

Conclusions

These results demonstrate that accelerated fetal growth is evident prior to the diagnosis of GDM and highlight the need for suitable methods of early identification of pregnancies at high risk for early accelerated fetal growth due to GDM. Secondly, ultrasound-measured VAD is an easily performed and effective tool for the prediction of GDM in at-risk pregnancies

Practice and Policy Implications/Recommendations

The key potential for practice changes in this study is with the implementation of VAD measurement as a tool for the prediction of GDM. Further work will be required to refine this technique prior to implementation.
The use of HbA1c as a predictor of excessive fetal growth or of GDM, cannot be advocated.

Pathway to Impact

Further study on the use of VAD measurement will be required prior to more widespread use. Studies should involve broad risk-profile cohorts and use multiple operators to clarify feasibility and predictive thresholds.
Pursuit of alternative biomarkers may provide useful predictors of excessive fetal growth and the dataset generated across this study will prove highly valuable in assessing any such biomarkers.

References

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