Impact of New Diagnostic Criteria for Gestational Diabetes

Short heading: New Diagnostic Criteria for Gestational Diabetes

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Abstract

Background: In January 2015, the diagnostic and therapeutic criteria for gestational diabetes changed, with the goal of increasing the sensitivity of diagnosis and improving overall glycaemic control, and thus reducing adverse pregnancy outcomes.

Aim: Our primary aim **was** to evaluate the effect of the new guidelines on the incidence of diagnosis of gestational diabetes and the incidence of therapeutic interventions. Our secondary aim was to look at the incidence of adverse pregnancy outcomes.

Materials and Methods: A retrospective clinical audit was conducted at a regional hospital to compare the incidence of gestational diabetes, and specific maternal and neonatal outcomes before and after the change in guidelines was implemented. Data were collected via chart review for a six month period before and after the change in guidelines in January 2015. Data collected included demographics, neonatal and maternal outcomes and the treatment type used for patients diagnosed with gestational diabetes.

Results: There was a significant increase in the incidence of diagnosis of gestational diabetes (9.8% to 19.6%) $p<0.001$, and an overall increase in the use of pharmacological treatments for gestational diabetes. There was no significant difference in the incidence of the adverse outcomes measured, including caesarean delivery and incidence of macrosomia. There was no significant change in mean fetal weight.

Conclusions: Despite a doubling of the incidence of diagnosis of gestational diabetes, and a consequent increase in pharmacological interventions, the change in diagnostic and therapeutic criteria did not significantly reduce the neonatal or maternal adverse outcomes measured.

MeSH Headings: Diabetes, Gestational; Fetal Macrosomia; Glucose Intolerance; Glucose Tolerance Test; Pregnancy Complications.

Introduction

Gestational diabetes mellitus (GDM) is defined as impaired glucose tolerance with its onset or first recognition occurring during pregnancy. [1,2] It is relatively common, affecting 4.6 – 9.6% of pregnancies in Australia prior to 2015.[3, 4] GDM is of great clinical significance, with associated adverse health outcomes for the mother such as instrumental and caesarean delivery[5, 6], and for the infant, including macrosomia and neonatal hypoglycaemia.[7 - 9] Increasingly, the long term sequelae of GDM such as development of type 2 diabetes and metabolic syndrome are being brought to light.[10, 11] Effective treatment of GDM minimises the risks of many of these adverse outcomes.[12 – 15] It is important that GDM is diagnosed early in pregnancy, so that these patients may receive optimal management in order to reduce their risk of adverse pregnancy outcomes.

The diagnosis of GDM has been subject to debate. The original diagnostic criteria were developed in 1964, and were based on trying to predict the likelihood of the mother developing diabetes after pregnancy,[16] rather than identifying current diabetes and therefore pregnancies at increased risk for adverse outcomes.[17] More recently, criteria developed by the Australasian Diabetes in Pregnancy Society (ADIPS) have been widely used in Australia since 1991,[18] and were updated and reviewed in 1998 (Table 1).[1] In 2015 ADIPS adopted new diagnostic criteria as proposed by the International Association of Diabetes in Pregnancy Study Groups (IADPSG)[17], and also introduced lower therapeutic targets (Table 1).[18]

The catalyst for this change was the publication of the Hyperglycaemia and Adverse Pregnancy Outcomes (HAPO) Study in 2008.[19] This multinational, blinded observational study of over 25 000 pregnant women found that there was a significantly increased risk of adverse pregnancy outcomes with elevated blood glucose levels below the threshold for diagnosis of GDM. Another study, the Australian Carbohydrate Intolerance Study in

Pregnant Women (ACHOIS) found lower rates of serious perinatal outcomes in the infants of women with milder degrees of glucose intolerance who were managed as GDM.[20] Subsequently, the IADPSG convened a multinational conference to review current evidence and develop evidence based diagnostic criteria.[17] These criteria were introduced Australia wide in January 2015.[21]

These guidelines were introduced with the aim of identifying more patients at risk of adverse outcomes in order to increase their glycaemic control, with the end goal of reducing the incidence of adverse pregnancy outcomes. With the introduction of new guidelines, it is important to evaluate if the predetermined goals were achieved, and to assess their impact. The aim of this study was to investigate how the new IADPSG criteria affect the diagnostic incidence and the incidence of therapeutic interventions. Our secondary aim was to compare the incidence of adverse pregnancy outcomes, including caesarean sections, macrosomia and mean birth weight.

Materials and Methods

This study was a retrospective clinical audit conducted at a regional hospital in Queensland which delivers approximately 1300 babies annually.[22] Ethics was sought from Townsville Hospital and Health Service Human Research Ethics Committee and was endorsed as a quality review activity (HREC/15/QTHS/11). Data were collected for all pregnant women who delivered a singleton fetus between March and August 2014 (when 1998 ADIPS diagnostic criteria used), and between March and August 2015 (when new IADPSG criteria used). An electronic system of medical record-keeping (iEMR), was used to access maternal demographic, pregnancy and birth data, in addition to neonatal demographics, birth details and perinatal outcome data. All data was collected and matched

with relevant glucose tolerance test (GTT) and glycated haemoglobin (HbA1c) results from the online pathology system. Multiple patient identifiers were used to ensure that the correct data was matched to the correct patient.

Outcomes recorded were the incidence of diagnosis of GDM, and the treatment type used (diet alone, metformin, or insulin with or without metformin). The pregnancy outcomes analysed were the incidence of caesarean sections, incidence of macrosomia, and mean birth weight in the entire cohort. The mean HbA1c and the lowest mean fetal blood sugar level (BSL) were also recorded, only in patients with GDM.

Ethics exemption was awarded with a waiver of participant consent by the Townsville Hospital and Health Service and James Cook University Human Research Ethics Committees. This project was registered as a quality activity with the hospital and Health Service Quality Improvement Unit.

Statistics

Statistical analysis was performed with the SPSS Statistics version 24 (IBM SPSS, Chicago, Illinois). Categorical variables were presented using descriptive analysis and frequencies. Relationships between change in guidelines and categorical variables were analysed with chi squared, or Mann Whitney U. Logistic regression was used to examine independent relationships. Our multivariate models for incidence of gestational diabetes, birth weight and method of delivery controlled for the independent variables of maternal body mass index (BMI), maternal ethnicity, diagnosis with GDM this pregnancy, baby gender and previous lower segment caesarean section (LSCS).

Sample Size

A sample size was calculated with power 80% and alpha 0.05. Our primary outcome was the incidence of GDM. We estimated that the local prevalence of GDM would be 7%,[23] and that with the new guidelines, based on predictive studies, it would increase to 10%.[4, 24] On this clinical presumption we calculated 423 patients would be required in each group.

Results

Of the 1390 women included in the study, 691 were assessed as GDM using the 1998 ADIPS criteria from March to August 2014, and 699 women were assessed using the new IADPSG criteria from March to August 2015.

Maternal Characteristics

Maternal demographic characteristics are summarised in Table 2. These characteristics were comparable at baseline.

Incidence of GDM Diagnosis

There was a statistically significant increase in the incidence of diagnosis with GDM with the new IADPSG diagnostic criteria (19.6% vs 9.8%, $p<0.01$) (Table 3).

Treatment of GDM

There was an increase in the proportion of patients with GDM treated with metformin (24.8% vs 17.7%), and insulin (26.3% vs 19.1%). As there was a doubling in the number of women diagnosed with GDM, this equated to an even greater increase in the proportion of the population treated – almost three times as many women were on metformin, insulin and

metformin or insulin alone with the change in diagnostic and therapeutic targets (Table 4). This finding was statistically significant when the proportion of the population treated was used as the denominator. The proportion of women with GDM controlled with diet was lower under the new guidelines (48.9% vs 63.2%), but was greater as a proportion of the overall population.

HbA1c

There was a statistically significant decrease in mean HbA1c under the new IADPSG guidelines (5.3% [33.3mmol/mol] vs 5.2% [32.2mmol/mol], p=0.03) (Table 5). This was calculated on data recorded for 60 or the 68 diagnosed cases of GDM under the ADIPS guidelines and 118 of the 137 diagnosed cases of GDM under the new guidelines.

Adverse Pregnancy Outcomes

Adverse pregnancy outcomes in the two patient cohorts are summarised in Table 3.

Method of Delivery

There was an increase in the number of emergency caesarean sections with the new IADPSG guidelines, although this was not statistically significant (13.6% vs 15.9%, p = 0.26). There was a decrease in instrumental deliveries with new IADPSG guidelines which was significant on univariate but not multivariate analysis (12.9% vs 8.9%, p = 0.02). The data for spontaneous vaginal deliveries and elective caesarean sections were similar before and after the change in guidelines

Fetal outcomes

Macrosomia

There was no statistically significant difference in the number of neonates with macrosomia in the overall patient cohorts (i.e. patients with or without GDM) between the two study groups (1.9% vs 2.0%, p = 1.00). We were underpowered to conduct multivariate analysis for this outcome.

Mean Birth Weight

Mean birth weight was slightly higher under the IADPSG guidelines compared to the ADIPS guidelines (3415.1g vs 3367.7g). This was not significant on univariate or multivariate analysis.

Neonatal hypoglycaemia

The lowest blood sugar level recorded while in hospital was used as a marker of neonatal hypoglycaemia. This was significantly higher (p=0.03) following the change in guidelines (Table 3).

Discussion

This study found that the implementation of the new IADPSG guidelines resulted in doubling the incidence of gestational diabetes from 9.8% to 19.6% over the time period measured. The incidence of GDM was on the upper limit of the national range prior to the change in guidelines (9.8% compared to range of 4.6 – 9.6%). [3]

Although mean maternal HbA1c decreased with the new guidelines, the measurements before and after the change in guidelines are not comparable, as a larger proportion of the pregnant population, and therefore a larger number of women who were likely to have milder glucose intolerance, were diagnosed with GDM following the change in guidelines. Similarly, it is not possible to directly compare the mean recorded neonatal BSL, which is only measured in the children of mothers with GDM. It is likely that the difference may simply reflect that over 50% of neonates following the change of guidelines had mothers with milder degrees of glucose intolerance. We therefore feel that it is important that the success of the new guidelines should not be based on the comparison of the outcomes of the cohorts of patients diagnosed with GDM, as these outcomes will inevitably be favourable under the new guidelines. Despite the increase in the incidence of diagnosis of **GDM** and therefore likely milder degree of glucose intolerance, there was a trend towards an increase in the number of women treated with metformin, or insulin with or without metformin following the change in guidelines. When this change in management was examined using the entire patient cohort as the denominator, therefore reflecting the increased workload, this increase in pharmacological treatments became statistically significant, with close to three times as many patients prescribed insulin, insulin and metformin or metformin alone. These differences could be attributed to a change in the therapeutic as well as diagnostic criteria.

The data reveals no significant reduction in the adverse pregnancy outcomes that were measured: caesarean section, macrosomia and mean birth weight. There are some limitations to the interpretation of this finding. As 50% of diagnoses of GDM under the new guidelines are likely to have a milder degree of glucose dysfunction, it is not appropriate to use GDM as the denominator. However, by using the entire cohort as the denominator, the effect of the new guidelines on adverse outcomes is diluted by the 80% of patients who were not diagnosed with GDM. Consequently, we are also underpowered to make this comparison.

The most appropriate method of assessing the change in guidelines would be to compare the group of patients in the 2015 cohort who would have been diagnosed with GDM using the new diagnostic criteria, but were managed as non GDM patients, with patients in 2016 who would not have been diagnosed under the old criteria but were diagnosed and managed as GDM under the new criteria. Unfortunately this comparison is unable to be made, first because of incomplete data sets and second because 75g oral glucose tolerance testing was not routinely performed in 2015. (In 2015 pregnant women had a 75g oral glucose tolerance test if they had risk factors for GDM or a positive result on a 50g oral glucose challenge test.)[15] Equally it would be valid to compare the additional cases identified with IADPSG with those who would have been identified with by ADIPS in the second cohort, but the comparisons cannot be made for the same reasons.

Secondary analysis of data from patient cohorts prior to the change in guidelines had shown that the incidence of diagnosis increased from 9.6 to 13.0% [4] and 13% to 16%, [24] when the new guidelines were theoretically applied retrospectively. However our increase in incidence was far greater than this predicted increase. Prior to the change in guidelines, statistical modelling had also shown that the subgroup of patients who were not diagnosed with old guidelines, but fitted the diagnostic criteria of the new guidelines had neonates which were on average 106g heavier and had a significantly higher incidence of macrosomia.[3, 24] Despite these findings, our study did not find any difference in neonatal outcomes.

We were unable to identify any Australian studies in the literature which compare pregnancy outcomes in patient cohorts before and after the introduction of the IADPSG criteria. A Belgian study found that introduction of the IADPSG guidelines, compared with

previous 'Carpenter and Coustan criteria'[25] increased the incidence of GDM (from 8 to 23%) but did not decrease the incidence of macrosomia or LSCS.[26] Similarly, a Swiss study found a four-fold increase in incidence of diagnosis from (3.3% to 11.8%) with the introduction in the IADPSG criteria.[27]

We must acknowledge some limitations of our study. There was a lower incidence of both LSCS and macrosomia that was expected and we may have been underpowered to measure a true difference. The study is limited by examining short term outcomes in a single centre. Longer term studies or studies in other settings may show more benefit.

Inevitably, an increase of incidence of diagnosis, as well as the increase in therapeutic interventions will result in a significantly increased workload, and consequent increased health care costs. Despite this increased workload our study did not show any reduction in adverse outcomes.

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Disclosure

The authors do not have any conflicts of interest to disclose.

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