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Gestational Diabetes Mellitus and Seasonal Variation

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Abstract

Aims

The aim of this study was to investigate whether there was seasonal variation in biochemical measurements and the incidence of GDM in a cohort of women screened selectively where laboratory standards were implemented stringently

Methods

The one step, 2-hr 75g oral glucose tolerance test (OGTT) was conducted in a cohort with at least one maternal risk factor for GDM at 26-28 weeks' gestation after an overnight fast and the latest laboratory standard was adhered to. Fasting serum specimens were obtained at the same visit for insulin and c-peptide measurement.

Results

A total of 202 women attended for the OGTT at a mean gestation of 27.5±1.0 weeks gestation with a GDM rate of 53.5%(n=108) in this at-risk cohort. There was no difference in the fasting, 1-hr or 2-hr glucose or insulin or c-peptide levels across the seasons. The percentage of women diagnosed with GDM also did not vary according to the seasons.

Discussion

In this well characterised population where laboratory standards were implemented strictly and glycolysis was inhibited, we found that there was no seasonal variation in the results of maternal glucose, insulin, HOMA-IR or C-peptide measured at the time of an OGTT at 26-28 weeks gestation. Previous studies showing a minor seasonal variation in GDM rates may be explained by variations in glycolysis rates depending on differences between winter and summer in room temperature where the phlebotomy was performed.

Keywords: Gestational diabetes mellitus, Oral glucose tolerance test, Laboratory methods, Pregnancy, Seasonal Change.

Introduction

One of the epidemiological challenges in contemporary obstetrics is the wide variation in the reported prevalence of Gestational Diabetes Mellitus (GDM) globally. It varies depending on whether screening is selective or universal, the test used, whether it is a one-step or two-step process, on what diagnostic criteria are used, on preanalytical and analytical laboratory standards, on the gestation at screening, the setting for screening and on the population screened.[1,2] In a post hoc analysis of the 15 centres in the Hyperglycaemia and Adverse Pregnancy Outcomes (HAPO) study the prevalence varied from 9.3% to 25.5% (overall 17.8%).[3]

In a secondary analysis of a recent study, we investigated whether there was seasonal variation in biochemical measurements and the incidence of GDM in a cohort of women screened selectively where laboratory standards were implemented stringently.[3]

Methods

This study was conducted in a large maternity hospital between October 2017 and November 2018. Women who were aged ≥18 years with sonographic confirmation of a singleton viable pregnancy and at least one maternal risk factor for GDM were included. Written consent was obtained. The one step, 2-hr 75g oral glucose tolerance test (OGTT) was conducted after an overnight fast (of ≥8 hours) and the latest laboratory standards were adhered to and have previously been reported.[2] Fasting, 1-hour and 2-hour samples reached the laboratory on ice for prompt centrifugation after a mean duration of 17±9.7, 13±9.0 and 13±8.9 minutes respectively.

An additional fasting venous blood sample was collected in a Sarstedt EDTA Monovette 7.5ml tube and plasma aliquots were stored at -80°C for the duration of the study. The samples were sent in bulk to an external company with GMP compliance and ISO 13485 and 9001 accreditations for analysis using the Bio-plex Pro Human Diabetes Assay (Bio-Rad Laboratories, Cat #171A7001M, Lot #64213365). This assay analyzed for 10 biochemical markers including insulin and c-peptide.

Statistical analysis was conducted using SPSS version 24.0 (IBM Corp). Data were assessed for normality and analysed using non-parametric tests and binary regression analysis. This study was approved by the Hospital's Research Ethics Committee.

Results

Of the 275 women recruited, 202 attended for the OGTT at a mean gestation of 27.5±1.0 weeks gestation. The mean age was 31.5±5.3 years and the mean BMI was 30.6±6.1kg/m^2. In this selectively screened cohort whose blood glucose samples had the highest international preanalytical and analytical standards applied, the GDM rate was 53.5%.

Table 1 compares the median levels of fasting plasma glucose (FPG), 1-hr glucose, 2hr glucose, insulin, the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) and c-peptide according to the season when the analysis was conducted. There was no difference in any of the glucose or biomarker levels across the seasons. The percentage of women diagnosed with GDM also did not vary according to the seasons.

Table 1: Maternal glucose, insulin, HOMA and C-peptide and the GDM rate according to the four seasons.

	Spring (n=27)	Summer (n=33)	Autumn (n=42)	Winter (n=100)	P value
Fasting plasma glucose (mmol/L, median (IQR))	5.1 (0.5)	5.0 (0.7)	5.0 (0.6)	5.0 (0.6)	0.774
1-hr plasma glucose (mmol/L, median (IQR))	8.6 (3.6)	8.8 (3.1)	8.0 (2.9)	7.6 (2.9)	0.175
2-hr plasma glucose (mmol/L, median (IQR))	6.2 (1.8)	5.8 (2.2)	5.9 (1.6)	6.0 (1.5)	0.182
GDM diagnosed (%, n)	59.3% (16)	63.6% (21)	45.2% (19)	52.0% (52)	NS~
Insulin (pg/ml, median (IQR)) *	252.7 (170.6)	289.5 (161.3)	287.7 (175.5)	267.6 (210.4)	0.522
HOMA-IR (median (IQR)) *	1.6 (1.2)	1.9 (1.1)	1.8 (1.3)	1.7 (1.4)	0.276
C-peptide (pg/ml, median (IQR)) *	1728.4 (708.3)	1705.5 (658.4)	1597.5 (952.6)	1660.5 (689.5)	0.638

Abbreviations: IQR- interquartile range, GDM - gestational diabetes mellitus, HOMA-IR - Homeostatic Model Assessment of Insulin Resistance.
~Binary regression analysis showed no association between GDM diagnosis and any of the seasons investigated (all p>0.05)
**n=27, 33, 40 and 96 for Spring, Summer, Autumn and Winter respectively.*

Discussion

In this well characterised population where laboratory standards were implemented strictly and glycolysis was inhibited, we found that there was no seasonal variation in the results of maternal glucose, insulin, HOMA-IR or C-peptide measured at the time of an OGTT at 26-28 weeks gestation. We also found no seasonal variation in the prevalence of GDM. Previous studies showing a minor seasonal variation in GDM rates may be explained by variations in glycolysis rates depending on differences between winter and summer in room temperature where the phlebotomy was performed.

A strength of this study was strict adherence to the latest international laboratory standards supervised by a single researcher (EOM). A potential weakness of the study is that it is a small single centre study conducted in a country where the climate is mild and the seasonal variations in outdoor temperature is relatively small. However, the cohort was well characterised biochemically with particular attention to preanalytical sample handling.

Recent studies have reported seasonal variations in the prevalence of GDM. In a recent secondary analysis of the two Australian HAPO centres in Brisbane and Newcastle enrolled in 2001-6 (n=2120), maternal measurements at the time of the OGTT were correlated to monthly temperature records from the Australian Bureau of Meteorology.[4] There was a small but significant increase during winter in fasting plasma glucose (FPG), HA1C and HOMA-IR. Another Australian study of 7369 OGTTs in the three years 2012-4, however, concluded that GDM was possibly over-diagnosed in summer and underdiagnosed in winter.[5]

As a result of this study and previous research we suggest that variations in OGTT measurements are more likely due to variations in maternal sample handling rather than seasonal variations. Our findings highlight the need for larger epidemiological studies of seasonal variations in different climates globally in both hemispheres.

Declaration of Conflicts of Interest:
The authors declare no conflicts of interest.

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