Seasonal Changes in the Prevalence of Gestational Diabetes Mellitus

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OBJECTIVE

To determine the effect of different seasons on the prevalence of gestational diabetes mellitus (GDM) by using World Health Organization criteria.

RESEARCH DESIGN AND METHODS

The results of all pregnancy glucose tolerance tests (GTTs) were prospectively collected over a 3-year period in a temperate climate, and the results were grouped by season.

RESULTS

The results of 7,369 pregnancy GTTs were available for consideration. In winter, the median 1-h and 2-h glucose results after GTT were significantly ($P < 0.0001$) lower than the overall 1-h and 2-h results. The prevalence of GDM at the 1-h diagnostic level was 29% higher in summer and 27% lower in winter than the overall prevalence ($P = 0.02$). The prevalence of GDM at the 2-h diagnostic level was 28% higher in summer and 31% lower in winter than the overall prevalence ($P = 0.01$).

CONCLUSIONS

The prevalence of GDM varies according to seasons, which leads to the possible overdiagnosis of GDM in summer and/or underdiagnosis in winter. Further research into standardization of the GTT or seasonal adjustment of the results may need to be considered.

Gestational diabetes mellitus (GDM) is the most common medical problem affecting pregnancy. In the past, concern has been expressed about the effects of ambient temperature variations on glucose tolerance and the prevalence of GDM (1–4). To our knowledge, the effect of ambient temperature variations on the prevalence of GDM has not been examined on the basis of the new World Health Organization (WHO) criteria.

Current criteria and terminology for the diagnosis of hyperglycemia in pregnancy (HIP) have been outlined by the WHO (5). These were guided by the recommendations of the International Association of Diabetes and Pregnancy Study Groups (6), which were based on findings of the Hyperglycemia and Pregnancy Outcomes (HAPO) study (7). The aim of the current study was to examine the effect of different seasons on the prevalence of GDM based on WHO criteria.

RESEARCH DESIGN AND METHODS

This study was conducted in the Illawarra Area around the city of Wollongong, Australia. Wollongong is a coastal city with a temperate climate, a population of ∼280,000, and ≥3,300 births each year. The population is ethnically similar to

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Australia as a whole (8), and there is excellent integration between the public and private health-care systems. About two-thirds of all pregnancy glucose tolerance tests (GTTs) are done in the private sector by one dominant private pathology company, Southern IML (SIML), with multiple collection centers in the city and local area. The remainder are done in the major public hospital, The Wollongong Hospital (TWH). About two-thirds of deliveries take place in a publicly funded hospital and the remainder in a private hospital. Since 2010, the method of testing and the diagnostic criteria set forth by the International Association of Diabetes and Pregnancy Study Groups and subsequently endorsed by WHO have been used in the area. WHO terminology has more recently been adopted and applied.

Women with acknowledged risk factors for HIP are tested at the first available antenatal opportunity, with the method of testing, usually a fasting glucose, being at the discretion of the obstetric care provider. All women not known to have HIP are tested at 24–28 weeks gestation with a GTT. The GTTs involved an oral 75-g glucose load administered in the morning after an overnight fast, with venous blood samples taken at fasting and at 1 and 2 h. Blood samples were collected by trained phlebotomists and placed into commercial tubes containing fluoride as a preservative and centrifuged at 4,000 rpm for 10 min to separate plasma for glucose analysis. Samples collected at peripheral collection centers were stored in a refrigerator until transported to the central laboratory. Laboratory estimations of glucose were done according to manufacturer's recommendations by using a hexokinase method on either the Roche Cobas 6000 analyzer (at TWH) or the Roche Cobas 8000 analyzer (at SIML). For both laboratories, within-run and between-run precision was 1.0–1.6% (TWH) and 1.5–2.6% (SIML). The bias between the two laboratories was <0.5%.

HIP was diagnosed for any abnormal plasma glucose result. In accordance with WHO recommendations, women were subdivided into either diabetes in pregnancy (DIP) or GDM. The DIP diagnosis was based on standard 2006 WHO criteria (9), with a fasting glucose ≥7.0 mmol/L and/or a 2-h glucose ≥11.1 mmol/L. GDM was diagnosed at any time during the pregnancy if one or more of the following criteria were met: fasting glucose of 5.1–6.9 mmol/L, 1-h glucose ≥10.0 mmol/L, or 2-h glucose of 8.5–11.0 mmol/L.

The deidentified results of all pregnancy GTTs done over a 3-year period (2012–2014) were prospectively collected and considered. Some of these data have recently been examined in a prevalence study (10).

Statistical Methods

Normality was assessed by using the Shapiro-Wilk test. The χ^2 test was used to determine the proportion of women with GDM diagnosed based on fasting, 1-h, and 2-h results, categorized by season. Differences in median fasting, 1-h, and 2-h results according to season were determined by Kruskal-Wallis test. This was followed by Bonferroni post hoc test for multiple comparisons. Results were considered statistically significant if $P < 0.05$. All analyses were conducted with SPSS version 22 software (IBM Corporation, Chicago, IL).

Ethical Approval

This audit conforms to the standards established by the National Health and Medical Research Council for ethical quality (11). The University of Wollongong and Illawarra Shoalhaven Local Health District Health and Medical Human Research Ethics Committee do not require the audit reported herein to be reviewed.

RESULTS

A total of 7,633 GTTs were performed, of which 264 were excluded due to missing glucose results, and 26 were excluded because the results were diagnostic of DIP and because seasonal variations would unlikely alter this diagnostic category. Of the remaining 7,343 GTTs, 229 were likely to be from the same woman in one pregnancy or the same woman in different pregnancies. These were not excluded because the primary aim was to examine the effect of seasonal variations on glucose results and, hence, the prevalence of GDM.

The median monthly glucose results from the fasting, 1-h, and 2-h blood samples overall and per month together with mean monthly temperature at 0900 h (12) are shown in Supplementary Table 1. The prevalence of GDM for each month based on fasting glucose alone or in combination with either an elevated 1-h or 2-h level and the prevalence of GDM based on either the 1-h or the 2-h glucose level after exclusion of women with a raised fasting glucose level are also shown in Supplementary Table 1.

The mean temperature at 0900 h in Wollongong ranges from 22.3°C in January to 13.0°C in July. For further analysis, the results have been grouped into traditional seasons (December, January, February being summer). The median glucose results overall and per season are shown in Table 1. The prevalence of GDM based on fasting glucose alone or in combination with either an elevated 1-h or an elevated 2-h result and the prevalence of GDM based on either the 1-h or the 2-h result after exclusion of women with a diagnostically raised fasting glucose level (n = 516) are shown in Table 2.

CONCLUSIONS

These data do not show a clinically significant seasonal variation in fasting glucose or prevalence of GDM on the basis of an elevated fasting result. However, they do show a marked seasonal variation in both 1-h and 2-h glucose levels after a GTT. Both results are significantly lower in winter than the overall median. These variations are sufficient to alter the seasonal prevalence of GDM. The prevalence of GDM in winter based on either the 1-h or the 2-h glucose results are significantly lower than the overall prevalence. There is a >50% variance in prevalence between winter and summer.

These differences in prevalence were found in a coastal city with a temperate climate. The mean temperature at 0900 h varied by <10°C between winter and summer. In practical terms, winter temperatures never fall to <5°C at any time of the day, and summer morning temperatures are rarely >30°C. Seasonal differences in the prevalence of GDM could become more pronounced in areas where there is a greater variation in ambient temperature. In parts of the world where the seasons are accompanied by major temperature variations, there are other factors that may need to be considered in determining the variation in prevalence of GDM, including the duration of daylight hours and the possible effect of these hours on light-sensitive hormones (vitamin D, melatonin, serotonin) and seasonal variations in food

Table 1—Glucose levels according to season for pregnancy GTT (*n* = 7,343)

	Summer	Fall	Winter	Spring	Overall	*P* value
Fasting (mmol/L)	4.4 (4.2–4.7)	4.4 (4.1–4.7)	4.4 (4.2–4.7)	4.4 (4.2–4.7)	4.4 (4.2–4.7)	
1 h (mmol/L)	7.1 (6.0–8.2)	6.9 (5.9–8.1)	6.7 (5.0–7.8)*	6.9 (5.9–8.2)	6.9 (5.9–8.1)	<0.0001
2 h (mmol/L)	5.9 (5.1–6.7)	5.9 (5.0–6.8)	5.6 (4.8–6.6)*	5.9 (5.1–6.8)	5.8 (5.0–6.7)	<0.0001

Data are median (interquartile range). *Post hoc analysis indicates that winter values were significantly lower than overall values.

intake, weight, and activity. Not all these factors, however, would necessarily alter results in the same direction or contribute to a lower prevalence of GDM in winter. The diagnosis of type 2 diabetes is more likely in the winter months (13), and HbA_{1c} may also be higher in the winter (14).

The first report of a variation in the prevalence of GDM with ambient temperature was by Schmidt et al. (3) in 1994 in Brazil. The 1-h and 2-h glucose results were significantly higher with changes in the 0900 h ambient temperature from 5–14°C to 25–31°C. This was sufficient to cause a change in the prevalence of GDM. In 1995, Moses et al. (4) did not find a change in the prevalence of GDM with seasonal change in Australia with the criteria then currently in use (15), but they did find an increase in the 2-h glucose with each increase of 1°C. A report from Plymouth, England (16), where there is a relatively low prevalence of GDM, found numerically but not statistically significant lower rates in the colder months.

The effects of changes in ambient temperature on 1-h and 2-h GTT results were investigated by Moses et al. (17) in healthy males in a climate chamber. The 2-h glucose result increased nonlinearly with increasing temperature, with the rise being apparent between 25°C and 30°C. A later study by Dumke et al. (18), again in healthy males in a climate chamber, found a significant rise in both insulin and glucose with higher temperatures.

The effect of ambient temperature on glucose tolerance is most likely caused by a redistribution of blood between the arterial and venous systems in relation to changes in core temperature (18,19). The increased arterialization of venous blood leads to higher glucose levels in venous samples. It could be hypothesized that the rise in the post-GTT glucose results is more pronounced in pregnant women relative to the thermal response of increased subcutaneous fat and a more hyperdynamic circulation.

The strengths of this study are that the data were collected prospectively and that the study was conducted in an ethnically representative population for the country and used results from both public and private sectors. A potential limitation of the study is the emerging realization that fluoride preservative provides an incomplete inhibition of glycolysis (20). Conversion of glucose to a glycolytic intermediate still occurs in uncentrifuged and unrefrigerated tubes, resulting in the loss of glucose at a rate of 5–7% per hour. This loss would have the greatest impact on the fasting sample. However, in this study, samples were either centrifuged for analysis of glucose concentration within 30 min of collection or kept refrigerated if centrifugation was delayed. A weakness of the study is that we did not at the time take into account the daily temperatures in the collection centers and whether the centers were climate controlled.

We examined the prevalence of GDM based on WHO criteria, which use a lower fasting glucose than all the criteria WHO has either replaced or considered as an alternative. In Australia, for example, of the women given a GDM diagnosis, the previously used criteria (13) were diagnostic of only 8% (21) to 17% (22) on the basis of the fasting glucose result, whereas with the current WHO criteria, >50% of GDM is diagnosed on the fasting result (10). Thus, although there is seasonal variation in the prevalence of GDM, it is likely that the widespread adoption of WHO criteria will potentially reduce this variation.

More women are given a diagnosis of GDM in the summer than in the winter months, which calls into question whether women are overdiagnosed in summer or underdiagnosed in winter. A post hoc consideration of HAPO data related to season of testing may provide some answers. From the HAPO data, the highest prevalence of GDM based on either the 1-h or the 2-h samples (or the lowest rate on the basis of the fasting sample) was found in Bangkok, Thailand (23). Bangkok could be considered warm to

Table 2—Prevalence of GDM according to season

Glucose (mmol/L)	Summer (*n* = 279)	Fall (*n* = 228)	Winter (*n* = 219)	Spring (*n* = 271)	Overall (*n* = 997)	*P* value
Fasting, 5.1–6.9 (*n* = 516)						0.35
% (95% CI)	6.6 (5.4–7.7)	6.6 (5.5–7.8)	6.9 (5.8–6.1)	7.9 (6.7–9.2)	7.0 (6.4–7.6)	
n	122	116	131	147	516	
1 h, ≥10.0 (*n* = 244)						0.02*
% (95% CI)	4.6 (3.6–5.6)	3.4 (2.5–4.3)	2.6 (1.9–3.3)	3.6 (2.7–4.5)	3.6 (3.2–4.1)	
n	80	56	46	62	244	
2 h, 8.5–11.0 (*n* = 237)						0.01†
% (95% CI)	4.4 (3.4–5.4)	3.4 (2.5–4.3)	2.4 (1.7–3.1)	3.6 (2.7–4.5)	3.5 (3.1–3.9)	
n	77	56	42	62	237	

The prevalence of GDM based on fasting glucose may include women who also had either a raised 1-h or a raised 2-h glucose level. The prevalence of GDM based on a raised 1-h or 2-h glucose level are after exclusion of women with a raised fasting level (*n* = 516). *Post hoc analysis indicates that prevalence is 29% higher than the overall in summer and 27% lower than the overall in winter. †Post hoc analysis indicates that prevalence is 28% higher than the overall in summer and 31% lower than the overall in winter.

hot with no marked seasonal variation. However, Singapore, with a tropical climate, had nearly one-half the women receiving a diagnosis on the fasting result, so ethnicity and the ambient temperatures of the collection centers may need to be taken into consideration. Variations in ambient temperature on core temperature may also have an influence for therapeutic decisions based on postprandial glucose monitoring. If the prevalence of GDM is being influenced by ambient temperature, then research is required to see how long a period of acclimatization may be required before the test is conducted. However, in most parts of the world where climate control is not an option and climate extremes are common, consideration of an adjustment of the diagnostic glucose levels may be required to correct the prevalence to an overall result. Alternatives to the GTT, such as glycated hemoglobin, may need to be considered in this context.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

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