

Is there a seasonal variation in HbA1c in Australia?

Hui Yi Ng¹, Rowena Hockings², Garry Morris³, and Robert Moses¹

1. Endocrinology Department, Wollongong Hospital, Wollongong, NSW, Australia

2. Research Central, Wollongong Hospital, Wollongong NSW, Australia

3. Southern IML Pathology, Wollongong, NSW, Australia

RESEARCH

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Corresponding Author:

Hui Yi Ng

Wollongong Hospital

252 Crown Street, Wollongong NSW 2500

Email: Hyng88@gmail.com

ABSTRACT

Background

A recent publication has shown that the prevalence of gestational diabetes mellitus (GDM) diagnosed with a glucose tolerance test (GTT) has a significant seasonal variation. The HbA1c has been proposed as an alternate method for testing of GDM.

Aims

Numerous reports indicate that in the Northern Hemisphere the HbA1c is higher in winter. The aim of this study was to assess if there was a seasonal variation in the HbA1c in a temperate climate.

Methods

Southern IML Pathology (SIML) is the major provider of pathology services in Wollongong and surrounding areas. De-identified data were obtained from SIML from January 2011 to December 2015. The data included the date of collection, date of birth, gender and HbA1c.

Results

A total of 203,170 HbA1c results were available for analysis. The median HbA1c was 6.6 per cent (48mmol/mol) for each season. While these differences were statistically significant

(due to the large numbers used for analysis), it was felt unlikely to be of clinical significance. There was also no difference in the median HbA1c in females with HbA1c ≤6.0 per cent; the probable range during pregnancy.

Conclusion

Whereas in the Northern hemisphere the HbA1c does exhibit seasonal variation, this was not apparent in a temperate climate. Specific data are required during pregnancy. HbA1c could be considered as an alternative diagnostic test during pregnancy to potentially overcome the changes in prevalence with seasons with GTT.

Key Words

Seasons, HbA1c, gestational diabetes mellitus

What this study adds:

1. What is known about this subject?

HbA1c can be considered as an alternate diagnostic test for GDM, as there is a seasonal variation in the incidence of GDM using the GTT.

2. What new information is offered in this study?

There is no variation in HbA1c in a non-pregnant population in a temperate climate, therefore HbA1c could be considered as a diagnostic test for GDM.

3. What are the implications for research, policy, or practice?

Further studies regarding the use of HbA1c as a diagnostic test in pregnancy are required.

Background

HbA1c, as an alternative to an oral glucose tolerance test (GTT), is approved for the diagnosis of diabetes in Australia.¹ However HbA1c is not approved for the diagnosis of gestational diabetes mellitus (GDM), though it can be used in some extenuating circumstances.² Two recent papers from Australia have shown a marked seasonal variation in the prevalence of GDM.^{3,4} In a temperate coastal region the

prevalence of GDM was 29 per cent higher in summer and 27 per cent lower in winter suggesting the possibility of either under or over diagnosis using a GTT.³ Under these circumstances, the possibility of using an HbA1c for diagnosis has to be seriously considered.

However, many studies from countries based in the northern hemisphere have shown a seasonal variation in the HbA1c level.⁵⁻¹¹ The test result is uniformly higher in winter compared with summer and the explanations advanced have been related to reduce exercise with colder weather and the coincidence of festive seasons. In Singapore, which is relatively isothermic, there is no winter increase in HbA1c but an increase related to festive seasons.¹²

Using an HbA1c to diagnose GDM would potentially overcome the variations in prevalence related to seasons. The purpose of this initial study was to determine if at this stage in a non-pregnant population there was a clinically significant variation in the HbA1c level related to seasons in a temperate part of Australia.

Methods

This study was conducted in the city of Wollongong and its surrounding areas in New South Wales, Australia. Wollongong has a temperate climate, with a mean monthly 0900h mean temperature ranging from 13 to 23.2°C.¹³ An estimated 90 per cent of all pathology testing in the Area is provided by Southern IML Pathology (SIML). De-identified data of the results of HbA1c testing for a consecutive five year period, January 2011 to December 2015 (inclusive) were considered. The gender and age were available. The HbA1c test was conducted in people with known diabetes as it was not an approved test for screening during this time or for diagnosing diabetes during pregnancy.

Method of Collection

Samples for HbA1c testing were collected in tubes containing Potassium EDTA(K2E) by qualified phlebotomists. Samples were transported and stored in line with NPAAC guidelines pursuant to ISO15189. Samples were tested on the day of collection, and usually within four hours, by SIML Wollongong with a method traceable to the Diabetes Control and Complications Trial reference method. Testing during the data collection period was carried out on dedicated HbA1c systems from Bio-Rad (Bio-Rad Laboratories, Inc., Hercules, CA 94547) at 21°C.

Statistical Methods

Normality was assessed using descriptive statistics and normal probability plots. Differences in median HbA1C

results according to season and month were determined using the Kruskal Wallis test. This was followed by post hoc analysis using the Bonferroni post hoc test for multiple comparisons. The one-sample median test was used to examine whether sample medians in each month, season and age category were different from the overall sample median. Results were considered statistically significant if $p < 0.05$. All analyses were conducted in STATA statistical software version 13 (StataCorp LP, College Station, Texas), except Bonferroni post hoc tests were conducted in SPSS (version 23, SPSS, Chicago, IL, USA).

Results

A total of 203,023 HbA1c results were available and grouped by seasons (summer = Dec, Jan, Feb). The seasonal median (IQR) HbA1c results are shown in Table 1. Females comprised 46.5 per cent of the total and 99.4 per cent of the subjects were aged ≥ 18 years. While the medians were the same, the IQR did vary and with the numbers available there was deemed a significant difference. The median HbA1c of each month is shown in Table 2. A secondary analysis was considered of females with an HbA1c ≤ 6.0 per cent - this being the range considered probable during pregnancy,¹⁴ and females in the childbearing years aged 20–40 years. These results are also presented in table 1. There were no significant differences with respect to the seasons in both groups.

Discussion

The median HbA1c for each season was the same at 6.6 per cent. However the IQR was (statistically) significantly different. This was most likely related to the large number of test results and it was most unlikely that it could be considered of clinical importance.

Studies from Greece, Sweden, Portugal, Lebanon, Japan, Korea and North America assessed the seasonal differences in HbA1c in type 1 and 2 diabetics. The HbA1c in winter was up to 0.5 per cent higher than in summer.⁵⁻¹¹ A report from Melbourne has suggested a lower HbA1c result by 0.2 per cent in winter compared with summer but specific details of the HbA1c levels were not presented.¹⁵

The factors proposed for the seasonal variation in HbA1c were the coincidence of festive seasons¹² (leading to over-indulgence) with the winter seasons¹⁶ (cold weather resulting in under-activity) in the northern hemisphere. These variables were considered by a study done in Singapore where there is little temperature variation.¹² A peak in the HbA1c was found in February and March (ascribed to the preceding festivities of Chinese New Year),

and a nadir in November and December, with an amplitude of 0.5 per cent, demonstrating that festivities independent of season can impact the HbA1c.

The strengths of the study herein reported include the large number of results available for evaluation and the use of one pathology lab using the same processing system, allowing for the standardization and accuracy of the collected HbA1c results. The study was performed in the city of Wollongong, which has close to a nationally representative population,¹⁷ and so the observations may apply nationwide.

The limitation of this essentially preliminary study was that the HbA1c was not specifically assessed in pregnant women. However for females only, females aged between 20–40 years, and for results with an HbA1c \leq 6.0 per cent, the situations which might be anticipated in pregnancy, there was no seasonal change in the HbA1c result. Use of the HbA1c for diagnosis of GDM would overcome some of the problems of seasonality. Reports are now emerging about the potential usefulness of HbA1c as an alternative to the GTT is optimal for detecting diabetes and identify women at increased risk of adverse pregnancy outcomes in pregnancy¹⁸ but prospective trials of outcomes rather than observational studies are required.

Conclusion

In conclusion, there did not appear to be clinically important variation in the median HbA1c with seasons in our area. This is encouraging if the possibility of using the HbA1c to diagnose GDM is to be considered. A specific study for this purpose will be undertaken.

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PEER REVIEW

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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None

ETHICS COMMITTEE APPROVAL

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

Table 1: Median (IQR) of HbA1c for all results according to seasons, for females with an HbA1c ≤ 6.0% and females aged 20 to 40 years

	Summer	Autumn	Winter	Spring	Overall	P value
All values (males and females)	6.6 (1.6) n =48,230	6.6 (1.6) n = 51,705	6.6 (1.8) n =50,219	6.6 (1.7) n = 53,016	6.6 (1.7) n = 203,170	<i>p</i> <0.01
Females with a HbA1c ≤ 6.0%	5.6 (0.4) n =7280	5.6 (0.4) n = 7847	5.6 (0.4) n = 7176	5.6 (0.4) n = 7752	5.6 (0.4) n = 30,055	<i>p</i> =0.82
Females aged 20 to 40 years	6 (2.4) n = 1123	6 (2.4) n = 1273	6 (2.6) n = 1268	6 (2.5) n = 1332	6 (2.5) n = 4996	<i>p</i> =0.70

HbA1c of 6.6% can be considered as 49 mmol/mol, 6.0% as 42 mmol/mol and 5.6% as 38 mmol/mol

Table 2: Median (IQR) of HbA1c for each month for all values and females aged 20 to 40 years

Month	All Values	Females aged 20-40 years
January	5.6 (0.5) n=5147	5.8 (2.3)
February	5.6 (0.4) n=6051	5.95 (2.5)
March	5.6 (0.5) n=4945	6 (2.2)
April	5.6 (0.5) n=5623	6.1 (2.4)
May	5.6 (0.5) n=5623	6 (2.4)
June	5.6 (0.5) n=4632	5.8 (2.5)
July	5.6 (0.5) n=5072	6.1 (2.7)
August	5.6 (0.5) n=5007	5.9 (2.6)
September	5.6 (0.5) n=4827	5.8 (2.3)
October	5.6 (0.4) n=5290	6 (2.5)
November	5.6 (0.4) n=5564	6.3 (2.6)
December	5.6 (0.5) n=3951	6.1 (2.5)
Over all	5.6 (0.5) n=203,170	6 (2.5)
P-value	P=0.002	P=0.17