

## The use of HbA<sub>1c</sub> as an aid in the diagnosis of gestational diabetes mellitus

O. Sevket, A. Sevket, A. Ozel, R. Dansuk & S. Kelekci

To cite this article: O. Sevket, A. Sevket, A. Ozel, R. Dansuk & S. Kelekci (2014) The use of HbA<sub>1c</sub> as an aid in the diagnosis of gestational diabetes mellitus, Journal of Obstetrics and Gynaecology, 34:8, 690-692, DOI: [10.3109/01443615.2014.925855](https://doi.org/10.3109/01443615.2014.925855)

To link to this article: <https://doi.org/10.3109/01443615.2014.925855>



Published online: 23 Oct 2014.



Submit your article to this journal [↗](#)



Article views: 455



View related articles [↗](#)



View Crossmark data [↗](#)



Citing articles: 3 View citing articles [↗](#)

OBSTETRICS

## The use of HbA<sub>1c</sub> as an aid in the diagnosis of gestational diabetes mellitus

O. Sevket<sup>1</sup>, A. Sevket<sup>1</sup>, A. Ozel<sup>1</sup>, R. Dansuk<sup>1</sup> & S. Kelekci<sup>2</sup>

Department of Obstetrics and Gynecology,<sup>1</sup>Faculty of Medicine, Bezmialem Vakif University, Istanbul and  
<sup>2</sup>Katip Celebi University, Izmir, Turkey

The ability of HbA<sub>1c</sub> was evaluated in the diagnosis of gestational diabetes mellitus (GDM) and for the implications of its use in clinical practice. A total of 339 pregnant women with an estimated gestational age of 24–28 weeks were evaluated for GDM using an oral glucose tolerance test (OGTT) based on International Association of Diabetes and Pregnancy Study Group (IADPSG) criteria. A ROC curve was drawn to determine the sensitivity and specificity of HbA<sub>1c</sub> in detecting GDM. An HbA<sub>1c</sub> cut-off value of  $\geq 5.2\%$  had sensitivity of 64.15% and specificity of 67.48% in diagnosing GDM, and a positive predictive value of 26.77%. Using two cut-offs in the 'rule-in and rule-out' algorithm, 94.4% of the GDM cases would have been detected but 33% (43 of the 130) women would have been misclassified. HbA<sub>1c</sub> is not suitable to use alone for the diagnosis of GDM and is not useful in decreasing the need for OGT testing.

**Keywords:** Gestational diabetes mellitus, HbA<sub>1c</sub>, OGTT

### Introduction

Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance that begins or is first recognised in pregnancy (ACOG 2001). GDM is one of the most common medical complications of pregnancy, with an overall prevalence of 3–5% but reaching as high as 18%, depending on the population and diagnostic criteria. While the oral glucose tolerance test (OGTT) is accepted as the diagnostic gold standard, it has the drawbacks of being inconvenient, poorly reproducible, expensive and unsuitable for large-scale screening (WHO 1999; ADA 2004; Metzger et al. 2010).

HbA<sub>1c</sub>, a haemoglobin variant, is an accepted and standardised measure of glycated haemoglobin and was used as a marker of glycaemic control over the preceding 120 days for patients (Goldstein et al. 2004). HbA<sub>1c</sub> has less intra-individual variability (Little et al. 2007), and is easily measured with a single blood test; therefore, it requires neither multiple blood draws nor fasting followed by consumption of a concentrated glucose beverage. Few studies have assessed HbA<sub>1c</sub> as a screening test for GDM and it is controversial (Agarwal et al. 2005; Metzger et al. 2008; Rajput et al. 2012). The aim of this prospective study was to evaluate the ability of HbA<sub>1c</sub> to diagnose

GDM, and to examine implications of its use for this purpose in clinical practice.

### Materials and methods

This study was a prospective, observational study conducted between June 2011 and January 2012 at Bezmialem Vakif University, Department of Obstetrics and Gynecology, Istanbul, Turkey. The study protocol was approved by the Research and Ethics Committee of the Bezmialem Vakif University Hospital. We excluded from the study any woman who had known diabetes, who made errors in protocol or who was suffering from anaemia or other severe illness.

During the study period, all pregnant women between 24 and 28 weeks' gestation, who had been referred for GDM screening, were informed about the study by their obstetricians. Women who agreed to participate in the study signed an informed consent and were asked to come to the hospital in the fasting state. A total of three blood samples were taken from each woman. The first was after 8–12 h of overnight fasting, when venous blood samples were taken for fasting glucose and for HbA<sub>1c</sub>. Patients then ingested 75 g of glucose, and 1 h and 2 h later, venous blood samples were taken to measure plasma glucose. The patients received the diagnosis of GDM if their 2 h OGTT results met any one of the following thresholds of the International Association of Diabetes and Pregnancy Study Group (IADPSG) criteria: a fasting glucose  $\geq 5.1$  mmol/l; a 1 h plasma glucose  $\geq 10$  mmol/l; or a 2 h plasma glucose  $\geq 8.5$  mmol/l.

A rule-in and rule-out algorithm was used to evaluate the utility of HbA<sub>1c</sub> to limit the number of OGTTs needed for the diagnosis of GDM (Henderson 1993). Namely, this approach involves considering two HbA<sub>1c</sub> threshold values. The higher threshold, with an inherently increased specificity, rules-in GDM; the lower threshold, with its innate increased sensitivity, rules-out GDM. Women who have HbA<sub>1c</sub> values in between these two thresholds are indeterminate and require diagnostic OGTT.

The glucose measurements were performed on centrifuged venous blood utilising the standard commercial glucose oxidase method. The HbA<sub>1c</sub> assays were performed on EDTA whole blood utilising a Roche/Hitachi<sup>®</sup> analyser (Tokyo, Japan).

### Statistical analysis

T-tests were performed to test the difference between the two means. A ROC curve was drawn to determine sensitivity and

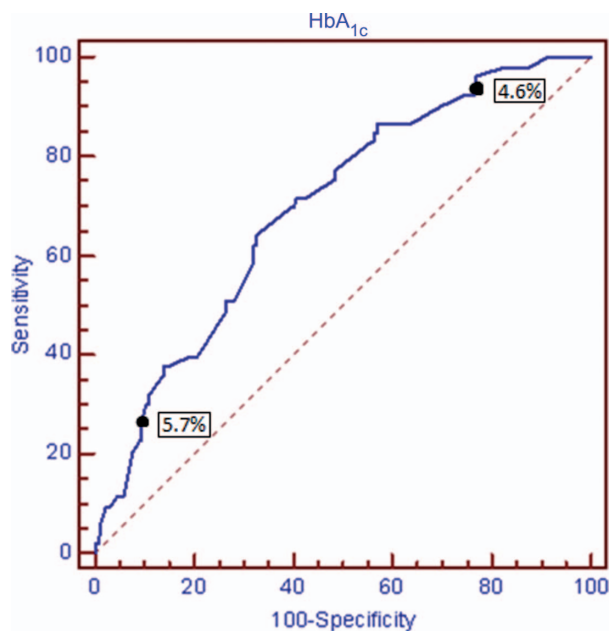


Figure 1. The ROC curve showing the sensitivity and specificity of HbA<sub>1c</sub> in detecting GDM by using IADPSG criteria.

specificity. All statistical analyses were performed using SPSS Statistics version 17.0 software.

## Results

Of the 339 subjects, the IADPSG criteria diagnosed 53 (15.6%) as having GDM. The mean maternal age, parity, BMI and gestational week of the total group was  $27.9 \pm 5.2$  years,  $0.9 \pm 0.8$ ,  $25.5 \pm 4.1$  kg/m<sup>2</sup> and  $25.7 \pm 1.0$ , respectively. The mean  $\pm$  SD HbA<sub>1c</sub> value for all patients was  $5.1 \pm 0.6\%$ . The mean HbA<sub>1c</sub> value was  $5.5 \pm 0.7\%$  in women with GDM and  $5.0 \pm 0.5\%$  in women without GDM, which was statistically significant ( $p = 0.000$ ). A ROC curve (Figure 1) was drawn to determine the sensitivity and specificity of HbA<sub>1c</sub> in detecting GDM. The area under the ROC curve of HbA<sub>1c</sub> to detect GDM was 0.697 (95% CI 0.645–0.745). An HbA<sub>1c</sub> cut-off value of  $\geq 5.2\%$  had sensitivity of 64.15% and specificity of 67.48% in diagnosing GDM. Although an HbA<sub>1c</sub> cut-off value of  $\geq 5.2\%$  had a negative predictive value of 91.04%, it had a positive predictive value of 26.77%.

The higher (5.7 mmol/l) and lower thresholds (4.6 mmol/l) were chosen based on data from the ROC curve. An HbA<sub>1c</sub> cut-off value of  $\geq 5.7\%$  had sensitivity of 26.4% and specificity of 90.5% in diagnosing GDM. An HbA<sub>1c</sub> cut-off value of  $\leq 4.6$

mmol/l had sensitivity of 96.2% and specificity of 23.0% in diagnosing GDM.

## Discussion

In March 2010, the IADPSG issued consensus guidelines to potentially attain a single approach for GDM diagnosis worldwide (Metzger et al. 2010). These guidelines recommend that every pregnant woman should undergo the OGTT, a costly and cumbersome test both for the patient and for the health provider. We wanted to evaluate the use of HbA<sub>1c</sub> as an alternative diagnostic test in order to decrease the need of the extremely demanding OGTT. A two-threshold rule-in and rule-out algorithm was used for this purpose.

In the HAPO study, HbA<sub>1c</sub> samples were taken at the same time as the OGTT but the authors concluded that the HbA<sub>1c</sub> was not a useful alternative to the OGTT (Metzger et al. 2008). Similarly, the study of Rajput et al. (2012) shows that the HbA<sub>1c</sub> cannot replace the OGTT for diagnosis of GDM. In the present study, the HbA<sub>1c</sub> value of  $\geq 5.2\%$  had a specificity of 64.1% and sensitivity of 67.4%, and thus HbA<sub>1c</sub> identified the majority of GDM in our patients. However, since HbA<sub>1c</sub> had a positive predictive value of only 26.7% for diagnosing GDM, HbA<sub>1c</sub> would not be considered an appropriate alternative for the diagnosis of GDM in our population.

This study used the new IADPSG criteria in order to limit the number of OGTTs needed for the diagnosis of GDM. The higher threshold value (with its inherently increased specificity of 90.5%) was HbA<sub>1c</sub>  $\geq 5.7$  mmol/l, and HbA<sub>1c</sub>  $\leq 4.6$  mmol/l was the lower threshold (with its innate increased sensitivity of 96.2%). Using HbA<sub>1c</sub> as the initial test, if the level of HbA<sub>1c</sub> is  $\geq 5.7$ , then the women can be labelled as having GDM. If the level of HbA<sub>1c</sub> is  $\leq 4.6$ , then the women can be labelled as normal. For women with an HbA<sub>1c</sub> level lying between 5.7 mmol/l and HbA<sub>1c</sub>  $\leq 4.6$  mmol/l, an OGTT should be performed to correctly identify those with GDM (Figure 2). Using a threshold of  $\geq 5.7\%$  to rule-in disease, 60 patients would have been considered to have GDM, of whom 40 (66.6%) would be false-positives. Using a lower cut-off of  $\leq 4.6\%$ , GDM would be ruled-out in 70 women, three (4.2%) of whom would have been misclassified as false-negatives. Using this algorithm, 94.4% of the GDM cases would have been detected, but 33% (43 of the 130) would have been misclassified. Since this algorithm would have only obviated an OGTT in one-quarter of the women in our study (25.6%), it thus demonstrates that using the combination of OGTT with HbA<sub>1c</sub> would not be useful to decrease the need of OGTT.

Using these two cut-offs in the rule-in and rule-out algorithm plus different ranges of HbA<sub>1c</sub> for the ADA and the IADPSG criteria, Rajput et al. (2012) found that the OGTT could be

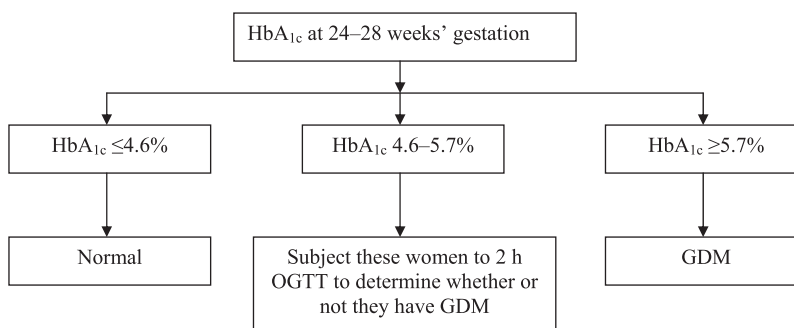


Figure 2. Flow diagram showing utility of HbA<sub>1c</sub> in combination with OGTT for diagnosing GDM per IADPSG criteria.

avoided in approximately 40% (IADPSG) and 60% (ADA) of women. Similar to our study, Agarwal et al. (2005) with the same methodology found that OGTT would not be needed in 25.1% of women and another 27% would be misclassified. They concluded that HbA<sub>1c</sub> is not a good test to screen for GDM.

Our own conclusion is that HbA<sub>1c</sub> is not an appropriate alternative for the diagnosis of GDM and is not useful in decreasing the need for OGT testing.

## Acknowledgement

The authors appreciate the contributions and editorial assistance made by S. Delacroix.

**Declaration of interest:** The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

## References

- ACOG. 2001. Practice Bulletin. Clinical management guidelines for obstetrician-gynecologists. Number 30, September 2001 (replaces Technical Bulletin Number 200, December 1994). Gestational diabetes. *Obstetrics and Gynecology* 98:525–538.
- ADA. 2004. Gestational diabetes mellitus. Position statement from the American Diabetes Association. *Diabetes Care* 27:88–90.
- Agarwal M, Dhath G, Punnose J, Koster G. 2005. Gestational diabetes: a reappraisal of HbA<sub>1c</sub> as a screening test. *Acta Obstetrica et Gynecologica Scandinavica* 84:1159–1163.
- Goldstein DE, Nathan D, Little RR, Peterson CM, Lorenz RA, Sacks DB et al. 2004. Tests of glycemia in diabetes. *Diabetes Care* 27:1761–1773.
- Henderson AR. 1993. Assessing test accuracy and its clinical consequences: a primer for receiver operating characteristic curve analysis. *Annals of Clinical Biochemistry* 30:521–539.
- Little RR, Rohlfing CL, Tennill AL, Connolly S, Hanson S. 2007. Effects of sample storage conditions on glycosylated hemoglobin measurement: evaluation of five different high performance liquid chromatography methods. *Diabetes Technology and Therapeutics* 9:36–42.
- Metzger BE, Gabbe SG, Persson B, Buchanan TA, Catalano PA, Damm P et al. 2010. International Association of Diabetes and Pregnancy Study Groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. *Diabetes Care* 33:676–682.
- Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, Coustan DR et al. 2008. Hyperglycemia and adverse pregnancy outcomes. *New England Journal of Medicine* 358:1991–2002.
- Rajput R, Yadav Y, Rajput M, Nanda S. 2012. Utility of HbA<sub>1c</sub> for diagnosis of gestational diabetes mellitus. *Diabetes Research and Clinical Practice* 98:104–107.
- WHO. 1999. Definition, diagnosis and classification diabetes and its complications. Part 1: diagnosis and classification of diabetes mellitus. Report of WHO consultation. Geneva: World Health Organization.