



1,5 Anhydroglucitol in gestational diabetes mellitus

Thyparambil Aravindakshan Pramodkumar ^a, Ramamoorthy Jayashri ^a, Kuppan Gokulakrishnan ^a, Kaliyaperumal Velmurugan ^a, Rajendra Pradeepa ^a, Ulagamathesan Venkatesan ^a, Ponnusamy Saravanan ^b, Ram Uma ^c, Ranjit Mohan Anjana ^a, Viswanathan Mohan ^{a,*}

^a Madras Diabetes Research Foundation & Dr. Mohan's Diabetes Specialities Centre, WHO Collaborating Centre for Non-communicable Diseases Prevention and Control, ICMR Centre for Advanced Research on Diabetes, Gopalapuram, Chennai, India

^b Division of Health Sciences, Warwick Medical School, University of Warwick, Coventry, United Kingdom

^c Department of Obstetrics and Gynecology, Seethapathy Clinic and Hospital, Chennai, Tamil Nadu, India

ARTICLE INFO

Article history:

Received 25 April 2018

Received in revised form 17 October 2018

Accepted 28 November 2018

Available online 5 December 2018

Keywords:

1,5 Anhydroglucitol

Gestational diabetes mellitus

Oral glucose tolerance test

Receiver operating characteristics

Glycemic variability

Glycated hemoglobin

ABSTRACT

Objective: 1,5 Anhydroglucitol (1,5 AG) is reported to be a more sensitive marker of glucose variability and short-term glycemic control (1–2 weeks) in patients with type 1 and type 2 diabetes. However, the role of 1,5 AG in gestational diabetes mellitus (GDM) is not clear. We estimated the serum levels of 1,5 AG in pregnant women with and without GDM.

Methods: We recruited 220 pregnant women, 145 without and 75 with GDM visiting antenatal clinics in Tamil Nadu in South India. Oral glucose tolerance tests (OGTTs) were carried out using 82.5 g oral glucose (equivalent to 75 g of anhydrous glucose) and GDM was diagnosed based on the International Association of Diabetes and Pregnancy Study Group criteria. Serum 1,5 AG levels were measured using an enzymatic, colorimetric assay kit (Glycomark®, New York, NY). Receiver operating characteristic (ROC) curves were used to identify 1,5 AG cut-off points to identify GDM.

Results: The mean levels of the 1,5 AG were significantly lower in women with GDM ($11.8 \pm 5.7 \mu\text{g/mL}$, $p < 0.001$) compared to women without GDM ($16.2 \pm 6.2 \mu\text{g/mL}$). In multiple logistic regression analysis, 1,5 AG showed a significant association with GDM (odds ratio [OR]: 0.876, 95% confidence interval [CI]: 0.812–0.944, $p < 0.001$) after adjusting for potential confounders. 1,5 AG had a C statistic of 0.693 compared to Fructosamine (0.671) and HbA1c (0.581) for identifying GDM. A 1,5 AG cut-off of $13.21 \mu\text{g/mL}$ had a C statistic of 0.6936 (95% CI: 0.6107–0.7583, $p < 0.001$), sensitivity of 67.6%, and specificity of 65.3% to identify GDM.

Conclusion: 1,5AG levels are lower in pregnant women with GDM compared to individuals without GDM.

© 2018 The Authors. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

The prevalence of gestational diabetes mellitus (GDM), one of the most common metabolic disorders during pregnancy, is increasing worldwide possibly due to advancing maternal age and increasing obesity rates.¹ Women with GDM are also more prone to develop type 2 diabetes mellitus (T2DM) in the future.² Women with GDM need to maintain good glycemic control to reduce the incidence of maternal

and fetal complications.^{3,4} Some studies have demonstrated that abnormal fetal growth depends not only on chronic hyperglycemia but also on glucose variability.⁵ Markers of glycemic control such as glycated hemoglobin (HbA1c) and Fructosamine (FA) are routinely used as chronic glycemic control over 2–3 months and 2–3 weeks respectively. However, they do not provide information about glycemic variability.⁶

1,5 Anhydroglucitol (1,5 AG) is one of the major polyols in human fluids and is structurally similar to glucose.⁷ It is absorbed mainly from ingested food and is distributed to all organs and tissues.⁸ Under normal glycemic conditions, levels of 1,5 AG is constantly maintained through renal filtration followed by reabsorption in the proximal tubules.⁹ As it competes with glucose for its reabsorption in the renal tubules, glycosuria will lead to reduction in the serum 1,5 AG level.¹⁰ Hence, when blood glucose levels exceed the threshold of glucosuria, reabsorption of 1,5 AG is competitively inhibited and excreted in urine.¹¹ This mechanism hence allows it to be utilized as a marker of glycemic control and

Abbreviations: 1,5 AG, 1,5 Anhydroglucitol; GDM, gestational diabetes mellitus; OGTT, Oral glucose tolerance tests; ROC, Receiver operating characteristic.

Conflicts of interest: There are no conflicts of interest.

* Corresponding author at: Madras Diabetes Research Foundation & Dr. Mohan's Diabetes Specialities Centre, 4 Conran Smith Road, Gopalapuram, Chennai - 600086, India.

E-mail addresses: drmoahans@diabetes.ind.in

URL: <https://www.drmoahansdiabetes.com>

URL: <https://www.mdrrf.in> (V. Mohan).

<https://doi.org/10.1016/j.jdiacomp.2018.11.010>

1056-8727/© 2018 The Authors. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

in contrast to HbA1c and FA whose levels are higher in uncontrolled diabetes, where as levels of 1,5 AG are lower.^{7,12} There are some reports that 1,5 AG levels predicted T2DM better than HbA1c.¹³

Clinical studies have also reported 1,5 AG as a short-term post-prandial marker for hyperglycemia.¹⁴ We recently showed that circulatory levels of 1,5 AG significantly reduced as glucose intolerance increases with NGT individuals having the highest values followed by IGT and T2DM and also reported on the usefulness of 1,5 AG as an additional tool to assess short-term glycemic control, compared to serum FA and HbA1c in Asian Indians.¹⁵

Earlier studies have demonstrated that changes in plasma levels of 1,5AG during pregnancy may reflect a mild alteration of carbohydrate metabolism and that 1,5 AG could act as an adjunct marker for HbA1c in pregnant women with diabetes.^{16,17} Boritza et al. reported that 1,5 AG could be used as a reliable marker for moderate glycemic control during early pregnancy.¹⁸ In this context, it is useful to study the association of 1,5 AG with GDM among Asian Indians who have higher prevalence of GDM, an earlier age of onset and lower body mass index.¹⁹ Asian Indian women with GDM are also known to be more susceptible to T2DM, and the conversion to T2DM occurs earlier in South Asians compared to other ethnic groups.²⁰ The aim of this study was to determine the association of 1,5 AG in Asian Indian pregnant women with and without GDM.

2. Materials and methods

The study subjects for this case-control study were recruited from antenatal clinics in rural and urban centers in Tamil Nadu, Southern India. Consecutive pregnant women with gestational age <28 weeks visiting the antenatal clinics were included in the study. Inclusion criteria were as follows: pregnant women who consented for testing, aged ≥18 years of age, gestational age <28 weeks and singleton pregnancy. The study groups comprised 75 women with GDM and 145 women without GDM. Clinical information including obstetric history, family history of diabetes as well as current and past medications was collected using a structured questionnaire. The oral glucose tolerance test (OGTT) was done using 82.5 g oral glucose (equivalent to 75 g of anhydrous glucose) which was dissolved in 300 mL of water and given to the pregnant women who consumed it within 5 min. Further venous samples were drawn at fasting, 1 h and 2 h on oral glucose tolerance test and measurement of 1,5 AG were simultaneously performed in 7% (n = 15), 82% (n = 180), and 11% (n = 25) of pregnant women in the first, second and third trimester of their pregnancy, respectively. In addition HbA1c and FA was measured in the fasting state.

We calculated a sample size of 98 which had a power of >95% to detect a difference of 4.4 µg/mL between groups for 1,5 AG, with a standard deviation of 0.5 and an alpha error of 0.05. GDM was diagnosed using the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria if 1 or more values equalled or exceeded the following thresholds: fasting plasma glucose of 5.1 mmol/L (92 mg/dL), 1-h plasma glucose level of 10.0 mmol/L (180 mg/dL) or a 2-h plasma glucose level of 8.5 mmol/L (153 mg/dL).²¹ We included women with singleton pregnancy and excluded those with pre-existing diabetes mellitus, hyper or hypothyroidism, or renal disease. A complete medical history was obtained, including any past or family history of diabetes, as well as current medications. Institutional Ethics Committee approval was obtained before the start of the study and written informed consent was obtained from the study participants.

2.1. Biochemical test

Plasma glucose (hexokinase method) was measured using Beckman Coulter AU2700 (Fullerton, CA, USA). HbA1c was measured by high-performance liquid chromatography using the Variant II Turbo (Bio-Rad, Hercules, CA, USA). The intra and inter-assay coefficients of variation for the biochemical assays ranged between 3.1% and 7.6%. FA

(NBT/kinetic) was also measured using Beckman Coulter AU2700 (Fullerton, CA, USA). The assay has a sensitivity of 10 µmol/L, and intra- and inter-assay coefficients of variation ranged between 0.9% and 2.9%. All measurements were performed in our laboratory, which is certified by the College of American Pathologists (CAP) and the National Accreditation Board for Testing and Calibration Laboratories (NABL).

2.2. 1,5 Anhydroglucitol measurements

Serum 1,5 AG levels were assessed using an enzymatic, colorimetric assay kit (Glycomark®, New York, NY)²² using the Beckman Coulter AU2700 (Fullerton, CA, USA). The 1,5 AG assay had, a sensitivity of 1.5 µg/mL, linearity <50 µg/mL, and coefficients of variation ranged between 2.4% and 4.9%.

2.3. Statistical analysis

Student's *t*-test or one-way ANOVA (with Tukey's HSD) as appropriate were used to compare groups for continuous variables and the Chi-square test or Fisher's exact test as appropriate was used to compare proportions. Pearson's correlation analysis was carried out to determine the correlation between 1,5 AG, Fasting, 1 h plasma glucose (1HrPG) and 2 h plasma glucose (2HrPG). Multiple logistic regression analysis was performed using GDM as the dependent variable and 1,5 AG as the independent variable after adjusting for age, HbA1c, and family history of diabetes. Receiver operating characteristic (ROC) curves were plotted for 1,5 AG and sensitivity and specificity for identifying GDM were calculated for various 1,5 AG cut-off points. The C statistic was estimated, and by interpolation from the area under the curve, the point closest to the upper-left corner, which maximized sensitivity and specificity, was selected as the optimal cut-off point; this identified the highest number of subjects with or without GDM.²³ All analyses were done using the Windows-based SPSS statistical package (version 22.0, SPSS Inc., Chicago, IL) and *p* < 0.05 was considered statistically significant.

3. Results

The clinical and biochemical features of the study participants are shown in Table 1. Age (*p* < 0.001), FA (*p* < 0.001), fasting blood glucose (*p* < 0.001), 1HrPG (*p* < 0.001), and 2HrPG (*p* < 0.001) were higher in individuals with GDM. However HbA1c levels were not statistically different between the groups.

Fig. 1 shows that the mean levels of the 1,5 AG were significantly lower in GDM women (11.8 ± 5.7 µg/mL) compared to women without GDM (16.2 ± 6.2 µg/mL (*p* < 0.001).

Pearson correlation analysis showed that 1HrPG (*r* = −0.175, *p* < 0.01) and 2HrPG (*r* = −0.174, *p* < 0.01) were significantly correlated with 1,5 AG. However there was no correlation between 1,5 AG and fasting plasma glucose (*r* = −0.108, *p* = 0.110).

Multiple logistic regression analysis was performed using GDM as the dependent variable and 1,5AG as the independent variable

Table 1
Clinical and biochemical characteristics of the pregnant women.

Variable	Without GDM (n = 145)	With GDM (n = 75)	<i>p</i> value
Age (years)	24.9 ± 2.6	27.4 ± 4.8	<0.001
Mean period of gestation (weeks)	21 ± 4.7	23.3 ± 5.6	<0.001
Family history of diabetes n (%)	21(14.5%)	38(50.7)	<0.001
HbA1c (%)	5.0 ± 0.4	5.1 ± 0.7	0.179
Fructosamine (µmol/L)	154.9 ± 46	182.8 ± 51	<0.001
Fasting plasma glucose (mg/dL)	80 ± 7	87 ± 12	<0.001
1 h plasma glucose (mg/dL)	121 ± 25	164 ± 46	<0.001
2 h plasma glucose (mg/dL)	99 ± 16	146 ± 42	<0.001

Abbreviations: GDM - gestational diabetes mellitus, HbA1c - glycated hemoglobin. Bold values indicates *p* < 0.001 is statistically significant.

Data are reported as mean ± SD unless indicated otherwise.

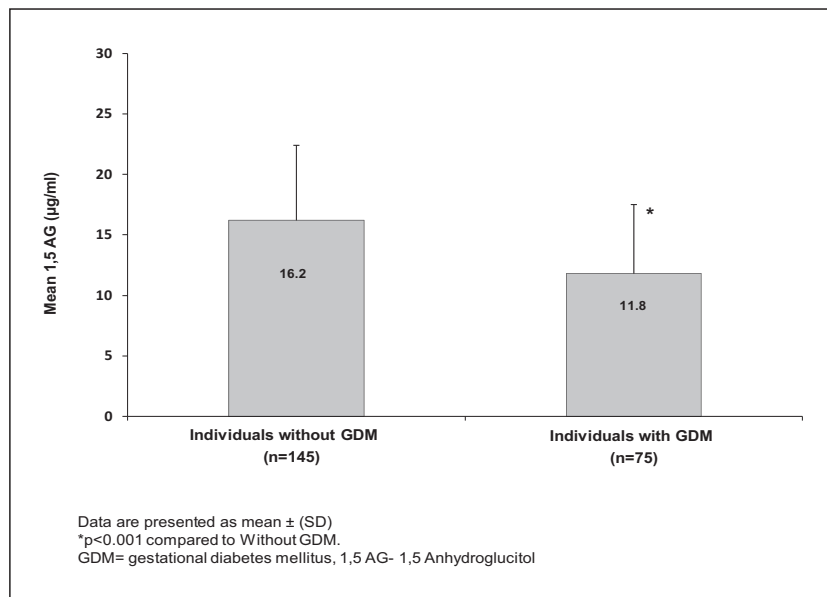


Fig. 1. Mean levels of 1,5 AG in individuals with and without GDM.

(Table 2). 1,5 AG showed a significant association with GDM (odds ratio [OR]: 0.880, 95% confidence interval [CI]: 0.834–0.929, $p < 0.001$). This association remained statistically significant even after adjusting for age, family history of diabetes, BMI and gestational age (OR: 0.876, 95% CI: 0.812–0.944, $p < 0.001$).

ROC curves were constructed to derive the cut-off point for 1,5AG levels with the best sensitivity and specificity to identify women with GDM. A 1,5 AG cut-off point of 13.21 $\mu\text{g/mL}$ had a C statistic of 0.6936 (95% CI: 0.6107–0.7583, $p < 0.001$), a sensitivity of 67.6% and specificity of 65.3% for identifying GDM. The C statistic improved to 0.7801 after adjusting for age and family history of diabetes (Fig. 2). The ROC curves with various glycemic parameters 1,5 AG, FA and HbA1c to detect GDM is shown in Supplementary Fig. 1 a. Of the three, 1,5 AG had the highest AUC for GDM (AUC = 0.693) followed by FA (AUC = 0.671) and HbA1c (AUC = 0.581). On analyzing combinations, it was found that the combination of fasting plasma glucose and 1,5 AG predicted GDM better (AUC = 0.752) compared to traditional glycemic markers as shown in Supplementary Fig. 1 b.

If we use 1,5AG cut-off less than 13.21 $\mu\text{g/mL}$, we found that 65.3% of GDM compared to 32.4% of individuals without GDM had values below the cut point (Fig. 3).

We also stratified GDM individuals according to their HbA1c levels <6% and found that 65% of those with HbA1c <6% had 1,5 AG of <13.2 $\mu\text{g/mL}$ (Supplementary Fig. 2).

4. Discussion

This study shows the following findings. First, the mean 1,5 AG levels were significantly lower in subjects with GDM. Second, 1,5 AG showed a significant correlation with 1HrPG and 2HrPG. Third, 1,5 AG was significantly associated with GDM after adjusting for age, family history of diabetes, BMI and gestational age. Fourth, among the three individual glycemic parameters, we observed that the 1,5 AG had the best C statistic compared to FA and HbA1c. Additionally, a 1,5 AG cut off-point of 13.21 $\mu\text{g/mL}$ could be used to identify 65% of GDM.

There is considerable controversy regarding the ideal screening and diagnosis test for GDM.²⁴ Furthermore, the current management of diabetes typically consists of daily pre- and post-prandial blood glucose monitoring. Glycated hemoglobin levels are currently not recommended for diagnosis or monitoring of GDM due to its lack of sensitivity. Moreover since HbA1c is a measurement of 2 to 3 months glycemic control and GDM typically set in the second trimester i.e. 24–28 weeks of pregnancy utility of HbA1c is rather limited. Due to the technical nature of assay, there is a mixed evidence on the utility of fructosamine for screening or diagnosing GDM.^{25,26,27} 1,5 AG reflects hyperglycemia and glucose variability, even in patients with well or moderately controlled diabetes.^{28,29} Earlier studies have shown that 1,5 AG is more sensitive than HbA1c and FA in response to short-term glycemic therapy^{30,31} and its levels were reduced in patients with T2DM.¹⁵ A

Table 2

Multiple logistic regression analysis using GDM as the dependent variable and 1,5 AG as independent variable.

Variable	OR	95% CI	p value
Unadjusted			
1,5 AG	0.880	0.834–0.929	<0.001
Model 1:			
Adjusted for age	0.887	0.838–0.938	<0.001
Model 2:			
Model 1 plus family history of diabetes	0.898	0.847–0.952	<0.001
Model 3:			
Model 2 plus BMI	0.875	0.812–0.944	<0.001
Model 4:			
Model 3 plus gestational age	0.876	0.812–0.944	<0.001

Abbreviations: 1,5 AG - 1,5 Anhydroglucitol, BMI - Body Mass Index, OR - odds ratio, CI - confidence interval

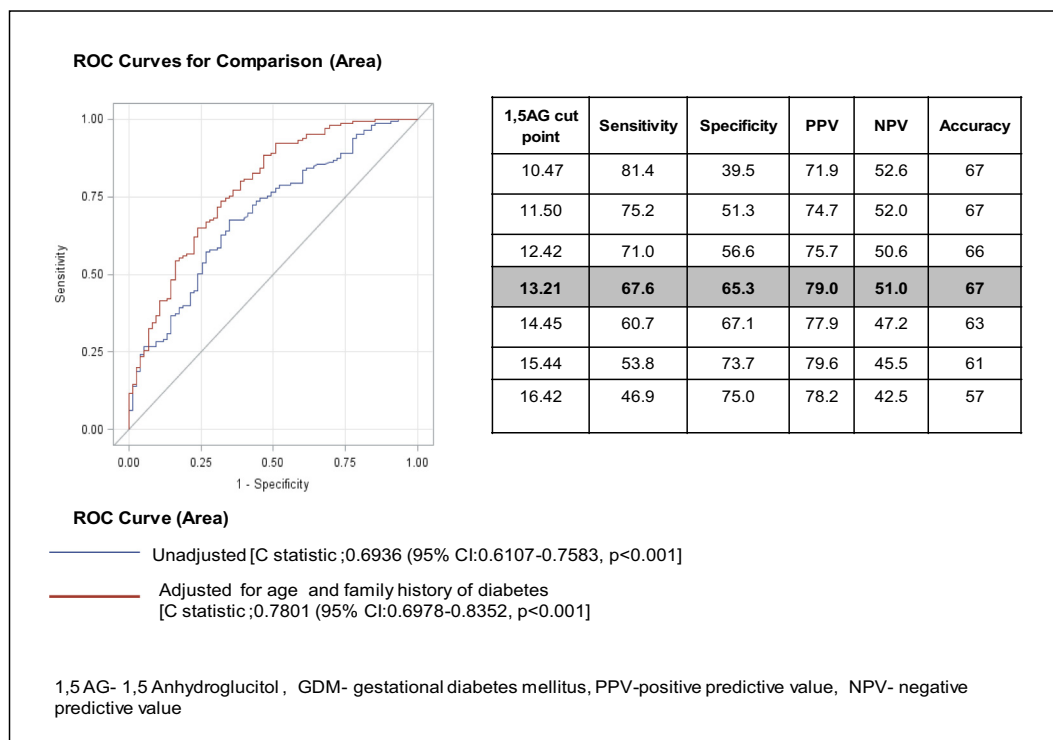


Fig. 2. ROC curves of 1,5 AG among individuals with GDM and without GDM for the unadjusted and adjusted models.

similar trend was also observed even among subjects with GDM in this study, as women in GDM had significantly lower levels of 1,5 AG compared to pregnant women without GDM. We also observe a significant association between 1,5 AG and GDM even after adjusting for age and family history of diabetes. This observation is supported by Dworacka et al.¹⁶ who demonstrated a significant correlation between 1,5 AG and GDM. Prospective studies are needed to understand the association of 1,5 AG with GDM and its prognostic significance.

Earlier studies have reported that 1,5 AG was significantly associated with maximum glucose concentration among pregnant women.³² We found that 1,5 AG showed inverse correlation with 1HrPG glucose on OGTT and this is an important observation as elevated 1HrPG glucose

during OGTT provides a better tool to identify subjects with beta-cell dysfunction compared with HbA1c and these individuals are more prone to developing T2DM.^{33,34} Additionally, it has been demonstrated that the combination of fasting and 1HrPG glucose gives higher predictability for large-for-gestational-age newborns of mothers with GDM.³⁵

Earlier studies have reported that 1,5 AG was more sensitive and specific than HbA1c in predicting postprandial hyperglycemia.²⁸ We observed that there is no significant difference in HbA1c levels among pregnant women with and without GDM. However, 65% of GDM with lower levels of 1,5 AG ($<13.21 \mu\text{g/mL}$) had clinically acceptable HbA1c and this suggests that over half of them may have glycemic variability. This suggests the clinical importance of measuring 1,5 AG in studying glycemic variability. The strength of this study is that it is the first study which derive a cut-point for 1,5 AG in Asian Indians with GDM. Second, 1,5 AG correlates with 1HrPG and 2HrPG values and could be used as surrogate marker for expensive glucose profiling to assess glycemic variability. Longitudinal studies with serial measurements of 1,5-AG need to be done at different stages of pregnancy to further clarify the role of 1,5-AG as a marker of GDM. One of the limitations of this study is that of being a cross-sectional study and we could not assess the cause and effect relationship. Second, the sample size was relatively small.

Finally we did not perform continuous glucose monitoring or self monitoring of glucose to correlate them with 1,5 AG levels.

In summary, our data suggest that 1,5 AG levels are lower in Asian Indian pregnant women with GDM compared to individuals without GDM. More studies are needed to see if 1,5 AG could be used to predict GDM.

Acknowledgements

We thank the participants and the staff of Dr. Mohan's Diabetes Specialities Centre, Madras Diabetes Research Foundation, Chennai for their help with this study. We thank Glycomark for supply of the 1,5 Anhydroglucitol kits.

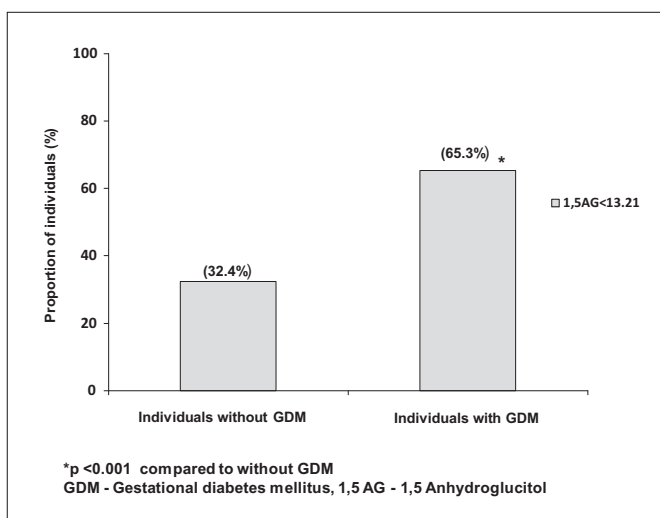


Fig. 3. Proportion of individuals with and without GDM based on the 1,5 AG cut-off value of $13.21 \mu\text{g/mL}$.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jdiacomp.2018.11.010>.

References

- Hunt KJ, Schuller KL. The increasing prevalence of diabetes in pregnancy. *Obstet Gynecol Clin North Am* 2007;34:173–99.
- Kim C, Newton KM, Knopp RH. Gestational diabetes and the incidence of type 2 diabetes: a systematic review. *Diabetes Care* 2002;25:1862–8.
- HAPO Study Cooperative Research Group, Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, et al. Hyperglycemia and adverse pregnancy outcomes. *N Engl J Med* 2008;358:1991–2002.
- Evers IM, de Valk HW, Mol BW, ter Braak EW, Visser GH. Macrosomia despite good glycaemic control in type 1 diabetic pregnancy; results of a nationwide study in the Netherlands. *Diabetologia* 2002;45:1484–9.
- Dalfrà MG, Chillelli NC, Di Cianni G, Mello G, Lencioni C, Biagioni S, et al. Glucose fluctuations during gestation: an additional tool for monitoring pregnancy complicated by diabetes. *Int J Endocrinol* 2013;2013:279021.
- Bonora E, Calceterra F, Lombardi S, Bonfante N, Formenti G, Bonadonna RC, et al. Plasma glucose levels throughout the day and HbA1c interrelationships in type 2 diabetes. *Diabetes Care* 2001;24:2023–9.
- Yamanouchi T, Akanuma Y. Serum 1,5-anhydroglucitol (1,5 AG): new clinical marker for glycemic control. *Diabetes Res Clin Pract* 1994;24 Suppl:S261–8.
- Yamanouchi T, Tachibana Y, Akanuma H, Minoda S, Shinohara T, Moromizato H, et al. Origin and disposal of 1,5-anhydroglucitol, a major polyol in the human body. *Am J Physiol* 1992;236:E268–73.
- Akanuma Y, Morita M, Fukuzawa N, Yamanouchi T, Akanuma H. Urinary excretion of 1,5-anhydro-D-glucitol accompanying glucose excretion in diabetic patients. *Diabetologia* 1988;31:831–5.
- Yamanouchi T, Akaoka I, Akanuma Y, Akanuma H, Miyashita E. Mechanism for acute reduction of 1,5-anhydroglucitol in rats treated with diabetogenic agents. *Am J Physiol* 1990;258:423–7.
- Ma C, Sheng J, Liu Z, Guo M. Excretion rates of 1,5-anhydro-D-glucitol, uric acid and microalbuminuria as glycemic control indexes in patients with type 2 diabetes. *Sci Rep* 2017;7:44291.
- Yamanouchi T, Shinohara T, Ogata N, Tachibana Y, Akaoka I, Miyashita H. Common reabsorption system of 1,5-anhydro-D-glucitol, fructose, and mannose in rat renal tubule. *Biochim Biophys Acta* 1996;1291:89–95.
- Kim MJ, Jung HS, Hwang-Bo Y, Cho SW, Jang HC, Kim SY, et al. Evaluation of 1,5-anhydroglucitol as a marker for glycemic variability in patients with type 2 diabetes mellitus. *Acta Diabetol* 2013;50:505–10.
- Dungan KM. 1,5-Anhydroglucitol (GlycoMark) as a marker of short-term glycemic control and glycemic excursions. *Expert Rev Mol Diagn* 2008;8:9–19.
- Pramodkumar TA, Jayashri R, Gokulakrishnan K, Velmurugan K, Pradeepa R, Anjana RM, et al. Relationship of glycemic control markers - 1,5 anhydroglucitol, fructosamine, and glycated hemoglobin among Asian Indians with different degrees of glucose intolerance. *Indian J Endocrinol Metab* 2016;20:690–5.
- Dworacka M, Wender-Ozegowska E, Winiarska H, Borowska M, Zawiejska A, Pietryga M, et al. Plasma anhydro-D-glucitol (1,5-AG) as an indicator of hyperglycaemic excursions in pregnant women with diabetes. *Diabet Med* 2006;23:171–5.
- Hashimoto K, Koga M. Indicators of glycemic control in patients with gestational diabetes mellitus and pregnant women with diabetes mellitus. *World J Diabetes* 2015;6:1045–56.
- Boritzka KC, dos Santos-Weiss IC, da Silva Couto Alves A, Réa RR, Pedrosa FO, de Souza EM, et al. 1,5 Anhydroglucitol serum concentration as a biomarker for screening gestational diabetes in early pregnancy. *Clin Chem Lab Med* 2014;52:e179–81.
- Mahalakshmi MM, Bhavadharini B, Kumar M, Anjana RM, Shah SS, Bridgette A, et al. Clinical profile, outcomes, and progression to type 2 diabetes among Indian women with gestational diabetes mellitus seen at a diabetes center in south India. *Indian J Endocrinol Metab* 2014;18:400–6.
- Bhavadharini B, Anjana RM, Mahalakshmi MM, et al. Glucose tolerance status of Asian Indian women with gestational diabetes at 6 weeks to 1 year postpartum (WINGS-7). *Diabetes Res Clin Pract* 2016;117:22–7.
- International Association of Diabetes and Pregnancy Study Groups Consensus Panel, Metzger BE, Gabbe SG, et al. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. *Diabetes Care* 2010;33:676–82.
- Buse JB, Freeman JL, Edelman SV, Jovanovic L, McGill JB. Serum 1,5-anhydroglucitol (GlycoMark): a short-term glycemic marker. *Diabetes Technol Ther* 2003;5:355–63.
- Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. *Radiology* 1982;143:29–36.
- Rani PR, Begum J. Screening and diagnosis of gestational diabetes mellitus, where do we stand. *J Clin Diagn Res* 2016;10:QE01–4.
- Roberts AB, Baker JR. Serum fructosamine: a screening test for diabetes in pregnancy. *Am J Obstet Gynecol* 1986;154:1027–30.
- Frandsen EK, Sabagh T, Bacchus RA. Serum fructosamine in diabetic pregnancy. *Clin Chem* 1988;34:316–9.
- Danese E, Montagnana M, Nouvenne A, Lippi G. Advantages and pitfalls of fructosamine and glycated albumin in the diagnosis and treatment of diabetes. *J Diabetes Sci Technol* 2015;9:169–76.
- Dungan KM, Buse JB, Largay J, Kelly MM, Button EA, Kato S, et al. 1,5-Anhydroglucitol and postprandial hyperglycemia as measured by continuous glucose monitoring system in moderately controlled patients with diabetes. *Diabetes Care* 2006;29:1214–9.
- Stettler C, Stahl M, Allemann S, Diem P, Schmidlin K, Zwahlen M, et al. Association of 1,5-anhydroglucitol and 2-h postprandial blood glucose in type 2 diabetic patients. *Diabetes Care* 2008;31:1534–5.
- Yamanouchi T, Ogata N, Tagaya T, Kawasaki T, Sekino N, Funato H, et al. Clinical usefulness of serum 1,5-anhydroglucitol in monitoring glycemic control. *Lancet* 1996;347:1514–8.
- McGill JB, Cole TG, Nowatzke W, Houghton S, Ammirati EB, Gautille T, et al. Circulating 1,5-anhydroglucitol levels in adult patients with diabetes reflect longitudinal changes of glycemia: a U.S. trial of the GlycoMark assay. *Diabetes Care* 2004;27:1859–65.
- Nowak N, Skupien J, Cyganek K, Matejko B, Malecki MT. 1,5-Anhydroglucitol as a marker of maternal glycaemic control and predictor of neonatal birthweight in pregnancies complicated by type 1 diabetes mellitus. *Diabetologia* 2013;56:709–13.
- Priya MM, Amutha A, Pramodkumar TA, Ranjani H, Jebarani S, Gokulakrishnan K, et al. β -Cell function and insulin sensitivity in normal glucose-tolerant subjects stratified by 1-hour plasma glucose values. *Diabetes Technol Ther* 2016;18:29–33.
- Jagannathan R, Sevik MA, Li H, Fink D, Dankner R, Chetrit A, et al. Elevated 1-hour plasma glucose levels are associated with dysglycemia, impaired beta-cell function, and insulin sensitivity: a pilot study from a real world health care setting. *Endocrine* 2016;52:172–5.
- Brankica K, Valentina VN, Slagjana SK, Sasha JM, et al. Maternal 75-g OGTT glucose levels as predictive factors for large-for-gestational age newborns in women with gestational diabetes mellitus. *Arch Endocrinol Metab* 2016;60:36–41.