International Journal of Health Sciences and Research
www.ijhsr.org ISSN: 2249-9571

Original Research Article

Glycated Albumin a Better Screening Tool cum Short Term Glycemic Marker over HbA1c in Gestational Diabetes

Suresh Babu Kondaveeti[1], I. Anand Shaker[2], R.Chidambaram[3]

[1]PhD Scholar in Medical Biochemistry, Bharath University, Selayur, Chennai, Tamilnadu.
[2]PhD Guide in Medical Biochemistry, Bharath University, Selayur, Chennai, Tamilnadu.
[3]Director, R&D (Medical), Dept. of Radiology, Sri Lakshmi Narayana Institute Of Medical Sciences, Affliated to BharathUniversity,Selayur, Chennai, Tamilnadu

Corresponding Author: Suresh Babu Kondaveeti

Received: 05/06//2014 *Revised: 01/07/2014* *Accepted: 04/07/2014*

ABSTRACT

Objective- Glycated albumin has a half life of 20-25days and may be a better short term marker of glycemic control than haemoglobin A1C. Our main objective was to determine the correlation between GA and HbA1c along with a simultaneous 50-gram glucose tolerancetest (OGTT) during the first trimester of pregnancy in diagnosis as well as monitoring of gestational diabetes mellitus (GDM).
Material and Methods- This prospective cohort study enrolled 350 with no history of type 1 or type 2 diabetes pregnant woman irrespective of trimesters visit to MAPIMS hospital Melmaruvathur. All the participants gone through 75g OGTT. Woman with elevated OGTT levels (135-200 mg/dl) again underwent for 2 hr GTT. Blood was collected and analysed for FP glucose, Glycated Albumin and HbA1C.The statistical analysis was done by using SPSS, version 16.0.
Results- Of 350 eligible patients, 110 had GDM and 40 patients did not, per OGTT. The percentage of patients with GA values (Reference range 14-16%) equal to or above sequential cut points. The mean HbA1c of GDM patients were 5.5±1.02.
Conclusion-This study suggests that GA is better sensitive marker in measuring GDM when compared with HbA1c values which are within the normal range and there is only little correlation with OGTT.

Key Words- Glycated Albumin, HbA1C, GDM.

INTRODUCTION

Gestational Diabetes Mellitus defined as carbohydrate intolerance with onset or first recognition during pregnancy. [1] The prevalence of GDM in India varied from 3.8 to 21% in different parts of the country, depending on the geographical locations and diagnostic methods used. GDM has been found to be more prevalent in urban areas than in rural areas. [2] Compared to selective screening, universal screening for GDM detects more cases and improves maternal and neonatal prognosis. [3] Hence, universal screening for GDM is essential, as it is generally accepted that women of Asian origin and especially ethnic Indians are at a higher risk of developing GDM and subsequent type 2 diabetes. [4] Screening for GDM is achieved by glucose

challenge test (GCT) followed by oral glucose tolerance test(OGTT). [5,6]

The OGTT regarded as inconvenient and requires fasting, so there is need of more convenient other screening alternatives. The value of HbAlc in the assessment of glucose control is well established. Use of HbAlc as an index of glycemic control is excellent for long-term assessment but is poorly responsive in the short term. Using Glycated haemoglobin (HbA1C) in GDM screening is controversial. [7-10] But Glycosylated proteins like Albumin have been useful as a measureof recent changes in blood glucose [11] and have been proposed to be useful in following diabetic pregnant patients in whom glycemic control must be maintained all the time. [12] So in our study we tried to evaluate the Glycated albumin as a better screening as well as short term glycemic control in GDM over HbA1c.

MATERIALS & METHODS

The objective of the present study was to determine the Efficacy of Glycated albumin as a better screening tool cum short term glycemic control over HbA1c in GDM. Ethical clearance was obtained from the institutional ethical committee (Regd.No. MAPIMS/IEC/24/2011) as well as oral informed consents were obtained from the subjects. The present study was conducted from January 2011 to December 2013.

In this prospective cohort study,We screened 350 consecutive pregnant women for diabetes and pregnancy who were attending our College Hospital MAPIMS,Melmaruvathur,irrespective of trimesters, with a 50-g OGTT. Women with a history of type 2 diabetes and GDM were excluded from this study. Blood sampleswere drawn at fasting and at 1 and 2 hr forestimating plasma glucose. The plasma glucose was estimated by GOD-POD method using an Olympus autoanalyzerIn the fasting sample. In addition to plasma glucose, Glycated albumin and HbA1c were measured. Plasma GA levels were measured by an enzymatic method by using albumin specific protease, ketoamine oxidase and an albumin assay reagent on a Hitachi Auto analyser (Lucica GA-L, Asahi Kasei Pharma Corp, Tokyo, Japan).HbA1C was estimated by high-performance liquid chromatography (Bio-Rad). Diagnosis of GDM was based on the World Health Organization criteria of a 2-hr plasma glucose level criteria of a 2-hr plasma glucose level. [13] Family history, previous obstetric history, treatmentfor any concomitant diseases, and food habits were obtained. All of the patientsunderwent routine physical examination.

Statistical Analysis

The statistical analysis was done by using SPSS, version 16.0. One Way ANOVA method was applied to observe the association between GA and HbA1c. A p value of $\leq$ 0.0001 was considered as statistically significant.

RESULTS

Among the 350 women screened, 155 (50.5%) were in the first trimester of pregnancy. In this group, 55 (33.7%) had GDM (14.56% of the total women screened), and their mean age, BMI, and gestational weeks at screening during the first trimester were 29.63 ± 4.62 years, 25.96 ± 3.00 kg/m^2, and 9.20 ± 2.03 weeks, respectively. In women with normal glucose tolerance, the mean age, BMI, and gestational weeks at screening during the first trimester were 24.0 ± 3.00 years, 24.54 ± 2.41 kg/m^2, and 9.15 ± 3.24 weeks, respectively (Table-1). There was no statistically significant difference among age, BMI, and gestational weeks of the women in the normal glucose tolerant and GDM groups ($P > 0.05$). The mean GA and A1C levels of the women with normal glucose tolerance was14.25 ± 1.65%, 5.36 ± 0.36%, and that of the GDM women

detected in the first trimester was16.75 ± 1.85% (Table-2).

The mean GA and HbA1C levels of the 122 (30.5%) GDM women, irrespective of trimesters, was found to be 17%, 6%. Applying this cutoff level of 17% and 6% (Table-3), we divided the women diagnosed as having GDM or normal glucose tolerance in the first trimester into four groups (Table-4). Group 1: There were 38 (12.94%) women with a 2-h plasma glucose level ≥140 mg/dl and GA ≥17,HbA1C ≥6%. Group 2: A total of 27 (20.6%) women had a 2-h plasma glucose level ≥140 mg/dl andGA ≥16.5 HbA1C ≥5.5%. Group 3: In this group, there were 10 (3.9%) women with a 2-h plasma glucose level ≤140 mg/dl GA ≤ 15.5%HbA1C ≤ 5%. Group 4: This group included 159 (61.9%) women with a 2-h plasma glucose level <140 mg/dl and GA≤ 15% HbA1C <6% respectively.

Table -1Demographical dataof enrolledcases

Groups	Number Of Cases	Mean age in years	Mean BMI in kg/m^2	Mean gestational weeks
Group A	122	29.63±4.62	25.96±3.00	9.20 ± 2.03
Group B	228	24.0 ± 3.00	24.54±2.41	9.15 ± 3.24

Group A-pregnant women with GDM (positive OGTT)
Group B-pregnant women without GDM (Negative OGTT)
GDM-Gestational Diabetes Mellitus, GA-Glycated Albumin, HbA1c- HemoglobinA1c

Table -2Mean GA and HbA1c in First trimester GDM and Non GDM pregnant women

Groups	Number	Mean GA (%)	Mean HbA1c (%)
Group A	55	16.75 ± 1.85%,	5.96 ± 0.63%.
Group B	100	14.25 ± 1.65%	5.36 ± 0.36%

Table-3 Sensitivities(%) both GA and HbA1c at cut point value(16% & 6 %) of the following

GA cut off value (%)	Sensitivity (%)	HbA1c cutoff value (%)	Sensitivity (%)
≥ 14	100	≥ 5.0	98
≥15	98.6	≥ 5.5	95
≥16	89.4	≥ 6.0	86.1
≥16.5	68.7	≥ 6.5	64.4
≥17	42.4	≥ 7.0	36.5

Table-4. Correlation of 2 hr Plasma glucose values with GA and HbA1c valuesamong pregnant women irrespective of the trimester with GDM and without GDM

Groups	Cases in number	2 hr Plasma glucose conc (mg/dl)	GA (%)	P value	HbA1c (%)	P value
Goup 1	38	≥140	≥17	< 0.0001	≥6	< 0.0001
Group 2	27	≥140	≥16.5	<0.0001	≥5.5	< 0.0001
Group 3	34	≤140	≥15.5	<0.0001	≤5	< 0.0001
Group 4	251	≤140	≤15	<0.0001	≤4.5	< 0.0001

P value <0.0001 is significant

DISCUSSION

Gestational diabetes is associated with significant perinatal morbidity and mortality. [14,15] It is usually assymptomatic and thus a screening test that is simple and reliable is required The screening for glucose intolerance is usually performed at ~24–28 weeks of gestation. But the early detection of glucose intolerance in pregnant women helps in limiting the influence of maternal hyperglycemia on fetal growth. [16,17]

This study has shown that one third of the pregnant women (99 out of 350) with confirmed diagnosis of GDM had elevated GA(>16.5%) levels and HbA1c(>6%) . this suggests a reasonable sensitivities of GA over HbA1c when compared with 2 hr plasma glucose concentration. The study has also shown the average GA levels of 251 patients (without GDM) with normal OGTT

results was < 15%. We were able to establish from our study the mean GA and HbA1c level in women with GDM at diagnosis during different trimesters as 16.5%(17± 0.65), 6% (6.04 ± 0.81). We analyzed our finding, taking into consideration the OGTT, GA andHbA1C values, to categorize the women in whom glucose intolerance was diagnosed in early pregnancy as pre-GDM, GDM, or normal glucose tolerant.

In group 1, women diagnosed with GDM had GA levels ≥17% HbA1c ≥6%. In them, glucose intolerance was detected in the early weeks of pregnancy, and they were likely to be pre-GDM or have type 2 diabetes before conception but were detected during pregnancy. The women in group 2 were diagnosed to have GDM by OGTT, but their GA levels ≥16.5 HbA1C level was <6%. In them, the abnormal glucose tolerance would have manifested in the early weeks of pregnancy, but the duration of exposure to hyperglycemia was not long enough to effect the changes in the A1C level but proteins such as Glycated albumin shows rapid response to change in blood glucose concentration. Thus, these women were considered to have pregnancy-induced glucose intolerance (GDM). Women in group 3 had normal OGTTs but GA ≥15.5%, HbA1C ≥6%. Historically, they had pregnancy-induced disturbances in alimentation, which occurs in some women in the early weeks of pregnancy. This would probably have resulted in a normal OGTT. They are an ominous group and are more likely to be pre-GDM and need repeat OGTTs in subsequent trimesters. On follow-up, we found that all women in group 3, who had normal glucose tolerance, developed GDM in the subsequent trimester. In group 4, there were 251 women who had a 2-h plasma glucose level <140 mg/dl and GA ≤15%, HbA1C also <6%.

Our findings suggests that GA can be a alternative potential screening role over HbA1c along with abnormal OGTT. By using HbA1c as screening measure in these cases with the cut off value (6%) 34.4% of cases missed but in case of GA the percentage is only 12.9%.Previous studies addresses the diagnostic potential of HbA1c in GDM were discrepant and they lacked consensus. [7] The most recently published studies addressing the screening potential of HbA1c in GDM were both reported by same investigators within the last eight years. [9-10]

A study conducted in Glasgow compared the respective value of serial measurements of GA, GPP (Glycated Plasma Proteins), and HbA1c (Glycated Hemoglobin), determined by affinity chromatography, in early pregnancy in 14 insulin-dependent diabetic womenAs the patients showed rapid improvement in glycemic control with intensive diabetic education and monitoring, the observed rate of decline in the concentration of GA or Glycated plasma proteins was approximately twice that of the declinein concentration in HbA1c concentration. The results demonstrate that measurement of GA or GPP gave an earlier indication to the clinician of improved diabetic control. The study also proposed that GA and GPP were less likely than HbA1c assays to be affected by non-diabetic conditions, such as patients who are anemic, received blood transfusions or are treated by hematinics. Hematinics are commonly prescribed in pregnancy and can cause misinterpretation of HbA1c values. [18]

Similar study conducted by other group of researchers concluded that “GA could be a better marker for glycol metabolic control with respect to HbA1c in cases of pre-gestational diabetes” (i.e. in pregnancy of type 1 or type 2 diabetic women) because of larger excursion of glycemic levels in these subjects, with respect to GDM pregnancies. [19] A

symposiumheld in 1999 on point-of-care testing recommended the immediate adoption of glycated albumin testing for gestational diabetes. This recommendation has not yet been acted upon due to the lack of a convenient and inexpensive test for glycated albumin. [20]

Our study has obvious limitations, first of all our study designed as prospective cohort study because of small number of subjects when compared with normal OGTT. Secondly our study did not evaluate the clinical status or outcome of the subjects (baby weight & neonatal complications) with GA as well as HbA1c levels which are desirable in studies involving diagnostic tests.

CONCLUSION

Our study suggests that GA may be a reasonably sensitive screening measure for prediction of GDM as well as a good short term glycemic control in GDM. So GA can be used as screening adjunct with GTT in alternative to HbA1c. Further studies required to evaluate specificity and other diagnostic parameters of GA before endorsing it as an alternative screening tool in populations.

AKNOWLEDGEMENT

The authors are thank full to the Management, MAPIMS, Melmmaruvathur, Tamilnadu, India, for providing the necessary facilities and for permitting us to carry out this research work. Also, the authors are very much thankful to all the Physicians, OB&G DepartmentMAPIMS Hospitals who had referred the cases .

Funding: No funding sources
Conflict of interest: None declared

REFERENCES

1. Seshiah V, Balaji V, Balaji MS. Scope for prevention of diabetes‘focus intrauterine milieu interieur.J Assoc Physicians India 2008;56:109-13.
2. Seshiah V, Balaji V, Balaji MS, et al. Pregnancy and diabetes scenario around the world: India.Int J Gynaecol Obstet. 2009;104(Suppl 1):S-35.
3. Cosson E. Screening and insulin sensitivity in gestational diabetes. Abstract volume of the 40th Annual Meeting of the EASD, September 2004;A 350.
4. DornhorstA Paterson CM, Nicholls JS, et al. High Prevalence of gestational diabetes in women from ethnic minority groups. Diabet Med. 1992;9(9):820-5.
5. The American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes care 2007;30:S42-7.
6. Alberti KG, Zimmetpz. Definition, Diagnosis and Classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of diabetes mellitus.Provisional report of a WHO consultation. Diabetes Med 1998;15:539-53.
7. Pollack A, Brehm R, Lisclotte H et al. Total glycosylated hemoglobin in mothers of large for gestational age infants.*Biol Neonate* 1981; 40: 129–135.
8. Griffith RJ, Vinali PS, Stickland MH, etal.Heamoglobin A1c in normal and diabetic pregnancies. Eur J ObstetGynecolreprodBiol 1987;24:195-200.
9. Agarwal MM, Hughes PF, Punnose J, et al. Gestational diabetes screening of a multi ethnic, high risk population using Glycated proteins. Diabetes Res ClinPract 2001;51:67-73.
10. Agarwal M, Dhatt G, Punnose J, et al. Gestational diabetes: A reappraisal of HBA1c as a screening test. ActaObstetGynecolScand 2005;84:1159-63.
11. Editorial: Glycosylation and disease. Lancet 2:19-20, 1984
12. Kennedy L, Mehl TD, Riley WJ, Merimee TJ: Non enzymatically glycosylated serum protein in diabetes

mellitus: an index of short term glycemiaDiabetologia 21:94-98,198 .
13. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. Diabet Med. 1998;15(7):539-53.
14. Philipson EH, Kalhan SC, Rosen MG, Edelberg SC, WilliamsTG, Riha MM: Gestational diabetes mellitus: is further improvement necessary? Diabetes 34 (Suppl. 2):55—60, 1985.
15. Sepe SJ, Connell FA, Geiss LS, Teutsch SM: Gestational diabetes incidence, maternal characteristics, and perinatal out. Diabetes 34 (Suppl. 2): 13-16, 1985.
16. Buchanan TA, Kitzmiller JL: Metabolic interactions of diabetes and pregnancy. Annu Rev Med 45:245–260, 1994.
17. Reiher H, Fuhrmann K, Noack S, Woltanski KP, Jutzi E, Hahn von Dorsche H, Hahn HJ: Age-dependent insulin secretion of the endocrine pancreas in vitro from fetuses of diabetic and nondiabeticpatients.Diabetes Care 6:446–451, 1983
18. Leiper J, Talwar D, Robb D, Lunan C, MacCuish A. Glycosylated Albumin and Glycosylated Proteins: Rapidly Changing Indices of Glycaemia in Diabetic Pregnancy. Quarterly Journal of Medicine. 1985;55(218):225-231.
19. Paroni R, et al, Performance characteristics and clinical utility of an enzymatic method for the measurement of glycated albumin in plasma, ClinBiochem. 2007; 40(18):1398-1405.
20. Hicks, J.M., et al. Recommendations and opinions for the use of point-of-care testing for hospitals and primary care: summary of a 1999 symposium. ClinicaChimicaActa.2001; 303(1-2): 1-17.

How to cite this article: Kondaveeti SB, Shaker IA, Chidambaram R. Glycated albumin a better screening tool cum short term glycemic marker over HbA1c in gestational diabetes. Int J Health Sci Res. 2014;4(8):160-165.

****