International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Amreen S et al. Int J Reprod Contracept Obstet Gynecol. 2018 Feb;7(2):524-528
www.ijrcog.org

pISSN 2320-1770 | eISSN 2320-1789

DOI: http://dx.doi.org/10.18203/2320-1770.ijrcog20180166

Original Research Article

Use of glycosylated HbA1c and random blood sugar as a screening tool for gestational diabetes mellitus in first trimester

Shaiesta Amreen, Anjali Suneel*, Ananya Shetty, Akhila Vasudeva, Pratap Kumar

Department of Obstetrics and Gynecology, Kasturba Medical College, Manipal University, Manipal, Karnataka, India

Received: 14 December 2017
Accepted: 08 January 2018

***Correspondence:**
Dr. Anjali Suneel,
E-mail: dranjalisuneel@yahoo.in

ABSTRACT

Background: GDM cases go unidentified with inadequate screening methods in first trimester which in turn increases the maternal and neonatal morbidity which is preventable. The purpose of the study was to find out a cut off level for HbA1c and RBS at first trimester for screening Gestational diabetes mellitus (GDM).
Methods: Observational study on pregnant women in a tertiary care teaching institution. Early screening with HbA1c and RBS at booking visit and followed up to second trimester GTT at 24-28 weeks. Pregnant women were divided into 2 groups based on GTT results. Pregnant women with overt diabetes and multiple pregnancy were not included in the study.
Results: Out of the 151 subjects, 76 cases were diagnosed with GDM while the other 75 were found to be non-GDM by following the 75g GTT approved by IADPSG. According to our study optimal cut-off for HbA1C was found to be 5.496±0.48 %, as it gives a sensitivity of 80% and specificity of 55.3%. Optimal cut-off for RBS was found to be 112±0.77 mg/dl, as it gives a sensitivity of 35.55 and specificity of 94.7%.
Conclusions: Glyco Hb A1c and RBS can be used as screening tool for the diagnosis of GDM. The likelihood of having GDM at a cutoff of Glyco HbA1c 5.5% is 1.8 times and RBS level 112mg/dl is 7 times in pregnant women.

Keywords: Glucose challenge test, Glycosylated HbA1c, GDM, First trimester screening

INTRODUCTION

Gestational Diabetes Mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy. It is well known that GDM is associated with maternal and fetal morbidity such as polyhydramnios, preeclampsia, operative delivery, macrosomia, shoulder dystocia, intrauterine growth retardation, neonatal hypoglycaemia and perinatal mortality.

The prevalence of GDM varies from 3.8% to 21% in various parts of India based on geographic location and diagnostic methods used.[1] Indians are at eleven fold increased risk of developing glucose intolerance during pregnancy than European women.[2] Recently WHO adopted the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria, which has resulted in an increase in the detected incidence of GDM.[3] The guidelines recommends that at 24-28 weeks a 75 g oral glucose tolerance test (OGTT) should be done for all pregnant women.

GTT is an inconvenient test as it consumes time, the pregnant women must fast and wait for 2 hours and should have at least 3 venipunctures. They also have nausea and vomiting due the 75 g glucose and delayed gastric emptying. Moreover, the universal screening recommendation has increased the testing burden. With these methods there was a possibility of missing patients with abnormal sugars in first trimester.

The fallacy of definition of GDM is that the gestational age for diagnosis is not clear. Despite numerous studies and researches, the authorities are yet to reach a consensus for ideal screening method. The new guidelines laid down by International Association of Diabetes in Pregnancy Study Group (IADPSG) clearly specifies to screen for diabetes in early pregnancy using Fasting Blood Sugar (FBS) or Glycosylated haemoglobin A1C or Random Blood Sugar (RBS) with their threshold being >126 mg/dl, >6.5%, >200 mg/dl respectively, to recognise early the patients with risk of complications due to GDM.[4] The IADPSG guidelines for screening GDM are an important breakthrough as it allows detection of such a state with single prick. Currently there is lack of data supporting use of Glycosylated haemoglobin A1C or Random Blood Sugar (RBS) as a screening tool for detection of GDM in Indian women.

There is an apparent need for a universally acceptable, much simpler and accessible test for GDM screening in first trimester. Glycosylated HbA1c is currently a good measure to know sugar control.[5]

GDM cases go unidentified with inadequate screening methods which in turn increases the maternal and neonatal morbidity which can be preventable. Health Care costs can be reduced by avoiding strategies which result in false positive cases. This retrospective study is hence aimed to assess the usefulness of Glycosylated hemoglobin A1C and Random Blood Glucose in screening the antenatal women for Gestational Diabetes Mellitus in first trimester.

Aims and objective of present study was to evaluate the usefulness of Glycosylated Hemoglobin A1C and Random Blood Glucose for screening Gestational Diabetes Mellitus in first trimester.

METHODS

This was an observational study which was conducted in the department of Obstetrics and Gynecology of our tertiary teaching hospital. The study was approved by the Institutional Ethics Committee.

Antenatal women were advised to give blood samples for RBS and Glyco HbA1c along with the other antenatal blood investigations on her booking visit. She was followed up till the second trimester 75g GTT which is routinely done as a universal screening method. The IADPSG criteria was followed to detect women with gestational diabetes mellitus.

Exclusion criteria of this study were those with overt diabetes and multiple pregnancy.

The data collected from the hospital central laboratory database was analysed using SPSS version 16.0 software. The mean age, glycosylated HbA1C and RBS of GDM and non-GDM was compared also the sensitivity of glycosylated HbA1c and RBS at various cut off point was calculated.

RESULTS

Out of 151 pregnant women, 76 cases were diagnosed with GDM while the other 75 were found to be non-GDM by following the 75g GTT approved by IADPSG. The pregnant women were then grouped into GDM if any one value of 75g GTT (IADPSG) was abnormal. The others were grouped into non GDM group.

Table 1: Characteristics of the study participants.

Characteristics	Mean±standard deviation		P value
	With GDM n=76	Without GDM n=75	
Mean Age (in years)	30.7±4.8	28.9±4.09	0.13
Mean Glyco Hb A1c	5.496±0.48	5.1±0.43	<0.05
Mean RBS (mg/dl)	112.77±2.6	91±1.48	<0.05

Mean age of the women with GDM in years was 30.4±4.8 compared to 28.9±4.09 in the non GDM group.

According to present study mean Glyco HbA1C was found to be 5.496±0.48% in the women diagnosed with GDM. The mean Glyco HbA1c in the non GDM group was 5.1±0.43.

Table 2: Value of first trimester Glyco HbA1c and RBS for screening of GDM - mid trimester GTT as gold standard for diagnosis.

	At cut off value of Glyco Hb 5.5	At cut off of RBS at 112mg/dl
Sensitivity	80%	35.5%
Specificity	55.3%	94.7%
Positive predictive value	63.8%	87%
Negative predictive value	73.7%	59.2%
Likelihood ratio of developing GDM	1.8 times	7 times

Glyco HbA1c at 5.5% had a sensitivity of 80% and specificity of 55.3%.

Taking 5.5% as cut off screen positive (Glyco Hb >5.5%) were 57 and screen negative (Glyco HbA1c <5.5%) were 94. Out of the screen positive 42 patients were truly GDM.

Mean RBS was found to be 112±0.77 mg/dl in women with GDM while mean RBS of women with non GDM was 91±1.48. Considering 112mg/dl as cutoff for screening of GDM in first trimester, it gives a sensitivity of 35.5% and specificity of 94.7%. The screen positive

patients (RBS >112mg/dl) were 31 and screen negative (RBS <112mg/dl) were 120. Out of the screen positive only 4 were wrongly diagnosed as GDM. While among the screen negative 49 women were missed to be diagnosed.

DISCUSSION

An early screening of GDM before 20 weeks is desirable. By early interventions which can be targeted at the screened positive population, we can reduce the growing burden on health care.

Complications are higher in diabetic pregnancy than non-diabetic pregnancies. Diabetes in early pregnancy at the embryonic development phase leads to miscarriages, congenital malformations and stillbirths. Majority of investigators find 2-3 fold increase in fetal malformations in women with GDM though there is no universal agreement.[6] A study has found that elevated level of glyco Hb was associated with congenital anomaly. The risk of congenital malformation is related to maternal glycemic status as poor glycemic control has teratogenic effect during embryogenesis.[7]

HbA1c is the product of an irreversible non-enzymatic binding of glucose to plasma proteins, specifically haemoglobin (Hb). It can be measured till the lifespan of red cell which is approximately 3 months. Anaemia in pregnancy combined with haemodilution and increase in red cell turnover have hampered the acceptance of Glyco Hb as a screening tool. Especially in our country India where anaemia in pregnancy is very common it becomes difficult to accept this method.

Present study has shown that, pregnant women with normal GTT were younger to women with GDM. This finding is consistent with the fact that risk of GDM increases with the advancing. Studies in the past have shown that maternal age more than 25 years is most predictive factor of GDM.[8]

50% subjects in present study were found to be GDM which shows the high prevalence in our south indian population where the study was conducted. The prevalence of GDM has increased probably because of stringent second trimester screening by IADPSG criteria.

Also, present study has shown that women with GDM have raised HbA1C value in first trimester. This suggests reasonable sensitivity of HbA1C as a predictor of GDM. There are studies which have shown that HbA1c >6.0 is an important risk factor for GDM though the cut-off given by ADA for GDM is >6.5.[9]

The accuracy of HbA1c as a screening test in pregnancy has been extensively studied over the past three decades and results have been inconsistent. O'Connor and colleagues found trimester specific reference interval of Glyco HbA1c in 246 non diabetic pregnant women with normal haemoglobin: the first trimester range was 4.8-5.5% (29-37 mmol/mol), second trimester 4.4-5.4% (25-36 mmol/mol) and third trimester 4.4-5.4% (25-36 mmol/mol).[10]

A meta-analysis of 43 studies from 2001 to 2012 with varying diagnostic criteria for GDM and cut off values for Glyco HbA1c was done. It involved 2812 GDM patients in China who were compared with 5918 controls. They concluded that HbA1c is a useful diagnostic tool for confirming GDM, but it should be used in parallel with conventional tests.[11]

The results of present study were consistent with a study by Rajesh Rajput et al which showed the mean HbA1c value in pregnant women with GDM to be higher than pregnant women without GDM that is 5.73±0.34% among GDM compared to 5.34±0.35% among non-GDM. Also, the study showed that by using HbA1c as a screening tool it was possible to detect 85.7% of the GDM cases correctly and only 2.8% of non-GDM would have been wrongly labelled as having GDM.[12] Khalafallah A and colleagues evaluated 480 pregnant women with Glyco Hb for detecting GDM. They suggested women with Glyco Hb >5.4% should undergo a GTT and this will reduce the burden of universal second trimester screening.[13]

A retrospective cohort study conducted by Alex Fong et al involving all women who delivered at a single hospital and who had HbA1c test performed at ≤20 weeks of gestation showed that 33% of patients whose HbA1c was 5.7-6.4% developed GDM against only 8.7% of those with HbA1c <5.7%. This study shows that GDM can develop even when the HbA1c is <6.5%, which is the recommended value by ADA.[14]

A study by Saleh et al showed the sensitivity of HbA1C at following cut-off point 5.0%, 5.5%, 6.0%, 6.5% and 7.0% (i.e., sensitivity values) to be 100%, 98.4%, 87.1%, 62.9% and 39.5%, respectively and mean HbA1c of the patients with GDM to be 6.9+0.8% against 6.4+0.6% of those without GDM (P< 0.006).[9]

Verhaeghe et al showed that there is strong correlation between HbA1C and insulin resistance.[15] Study by Ellen K et al showed that the cut-off level for HbA1c and FPG for the diagnosis of GDM was 5.3% and 4.3 mmol/L, respectively and that these two tests can be used concomitantly for screening GDM.[16] SS Kwon and colleagues concluded that HbA1c could diagnose GDM with high sensitivity and relatively low specificity. Glyco HbA1c can be used as a simple and less invasive alternative screening test when compared to OGTT in GDM patients.[17]

In our institution we routinely order for a random blood sugar level along with other antenatal investigations. As women who are at high risk of developing GDM may have abnormal glucose tolerance or insulin resistance in

pre pregnancy and in first trimester, we aimed at studying the usefulness of a RBS taken at antenatal booking visit, alongside Glyco Hb in same patients as screening test for GDM in first trimester.

There are very few studies on Random blood glucose as a screening tool for testing GDM. Results of the studies were inconsistent. A study by CL Meek et al showed that RBS was a better predictor of GDM than maternal age.[18] This also suggests reasonable sensitivity of RBS as predictor of GDM. Studies have shown that RBS more than 8 mmol/L or 144 mg/dl is associated with increased risk though the cut-off given by ADA for GDM is > 200 mg/dl.[19]

If RBS is >112mg/dl we should be alerted to the possibility that these women are highly likely to be GDM. In fact, this gives a window of opportunity of life style changes from early in pregnancy which might improve perinatal outcome. However, if RBS <112mg/dl. Negative predictive value is not good. These women need screening like any other pregnancy and significant number of women will be GDM.

CONCLUSION

Present study has shown that women with Glyco HbA1c >5.5% and RBS value >112mg/dl in first trimester are 1.8 times and 7 times respectively more likely to develop GDM. Therefore, such pregnant women may be advised measures for dietary modifications and mild exercises.

Hence, by detecting GDM in first trimester we can sensitise the women who were screened as high risk (screen positive) on the need and importance of 24-28 weeks GTT which might be a diagnostic test. Lifestyle modifications can be instilled early in first trimester in turn reducing the progression of metabolic changes and to GDM. Early anomaly scan and fetal ECHO can be done. Macrosomia rates and operative vaginal delivery can be prevented by early intervention.

Glyco HbA1c and Random blood sugar can be used as good screening tools for gestational diabetes in first trimester.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Mithal A, Bansal B, Kalra S. Gestational diabetes in India: Science and society. Indian J Endocrinol Metab. 2015 Nov-Dec;19(6):701-4.
2. Neelakandan R, Sethu PS. Early universal screening for gestational diabetes mellitus. J Clin Diagn Res. 2014 Apr;8(4):OC12-OC14.
3. Mohan V, Mahalakshmi MM, Bhavadharini B, Maheswari K, Kalaiyarasi G, Anjana RM et al. Comparison of screening for gestational diabetes mellitus by oral glucose tolerance tests done in the non-fasting (random) and fasting states. Acta Diabetol. 2014;51(6):1007-13.
4. Screening and Diagnosing Gestational Diabetes Mellitus. Agency for healthcare research and quality; U.S. Department of Health and Human Services. Available at https://www.ahrq.gov/research/findings/evidence-based-reports/gdmexuptp.html
5. d'Emden M. Glycated haemoglobin for the diagnosis of diabetes. Aust Prescriber. 2014;37:98-100.
6. Mills JL. Malformations in infants of diabetic mothers. Birth defects research. Part A, Clin Molecular Teratol. 2010 Oct;88(10):769.
7. Bhowmik B. First trimester complications in pregnancy with diabetes. Diabetes in pregnancy. J Pak Med Assoc. 2016 Sep;66(9 Suppl 1):S78-80.
8. Lao TT, Ho LF, Chan BC, Leung WC. Maternal age and prevalence of gestational diabetes mellitus. Diabetes Care. 2006 Apr 1;29(4):948-9.
9. Aldasouqi SA, Solomon DJ, Bokhari SA, Khan PM, Muneera S, Gossain VV. A promising screening tool in gestational diabetes mellitus. Int J Diabetes Dave Ctries. 2008;28(4):121-4
10. O'Connor C, O'Shea PM, Owens LA, Carmody L, Avalos G, Nestor L, et al. Trimester-specific reference intervals for haemoglobin A1c (HbA1c) in pregnancy. Clin Chem Lab Med. 2012;50:905-9.
11. Tian QW, Xuan C, Wang HW, Zhao JX, Yu WL, Gao G, et al. Diagnostic accuracy of glycosylated hemoglobin in Chinese patients with gestational diabetes mellitus: a meta-analysis based on 2,812 patients and 5,918 controls. Genet Test Mol Biomarkers. 2013;17:687-95.
12. Rajput R, Yadav Y, Rajput M, Nanda S. Utility of HbA1c for diagnosis of gestational diabetes mellitus. Diab Res Clin Pract. 2012;98(1):104-7.
13. Khalafallah A, Phuah E, Al-Barazan AM, Nikakis I, Radford A, Clarkson W et al. Glycosylated haemoglobin for screening and diagnosis of gestational diabetes mellitus. BMJ open. 2016 Apr;6(4):e011059.
14. Fong A, Serra AE, Gabby L, Wing DA, Berkowitz KM. Use of hemoglobin A1c as an early predictor of gestational diabetes mellitus. Am J Obstet Gynecol. 2014 Dec;211(6):641-e1.
15. Verhaeghe J, Van Herck E, Benhalima K, Mathieu C. Glycated hemoglobin in pregnancies at increased risk for gestational diabetes mellitus. Eur J Obstet Gynecol Reprod Biol. 2012 Apr;161(2):157-62.
16. Li KE, Cheung YS, Lau BY. Use of fasting plasma glucose and haemoglobin A1c in screening for gestational diabetes mellitus in high-risk antenatal patients in Hong Kong. Hong Kong J Gynaecol Obstet Midwifery. 2014;14:31-7.
17. Kwon SS, Kwon JY, Park YW, Kim YH, Lim JB. HbA1c for diagnosis and prognosis of gestational

diabetes mellitus. Diab Res Clinical Pract. 2015 Oct 31;110(1):38-43.
18. Meek CL, Murphy HR, Simmons D. Random plasma glucose in early pregnancy is a better predictor of gestational diabetes diagnosis than maternal obesity. Diabetologia. 2016 Mar 1;59(3):445-52.
19. Ostlund I, Hanson U. Repeated random blood glucose measurements as universal screening test for gestational diabetes mellitus. Acta Obstet Gynecol Scand. 2004 Jan;83(1):46-51.

Cite this article as: Amreen S, Suneel A, Shetty A, Vasudeva A, Kumar P. Use of glycosylated HbA1c and random blood sugar as a screening tool for gestational diabetes mellitus in first trimester. Int J Reprod Contracept Obstet Gynecol 2018;7:524-8.