A comparitive study in diagnosis and management of gestational diabetes mellitus with oral glucose challenge test and HbA1C

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Abstract

Introduction: Diabetes mellitus in pregnancy is one of the major complications during pregnancy. Pregnancies with gestational diabetes mellitus are associated with distinct spectrum of adverse maternal and perinatal outcomes such as birth injury, fetal growth abnormalities, increased rates of Caesarean section, and long-term risk for both the mother and baby. Numerous screening procedures and diagnostic guidelines have been used based on the suitability of test to the individual and population characteristics, cost of test and screening accuracy. Still debate exists on the most suitable test for screening of GDM as different diagnostic criterias followed in different countries. Hence Universal screening tool for GDM is necessary, which is economical, suitable and feasible especially in Indians, who are at higher risk of developing GDM. Current evidence suggests mainly two tests; Oral glucose challenge test (OGCT) and glycosylated hemoglobin (HbA1C) for diagnostication and prognostication of GDM. Of this, OGCT, WHO recommended, is a simple and cost-effective screening tool.

Materials and Methods: It is a prospective study conducted at Adichunchanagiri Institute of Medical Sciences, B.G.Nagar, Mandya. 100 cases were selected randomly at 24–28 gestational weeks and all 100 cases underwent OGTT, OGCT and HbA1C. In OGCT > 140mg/dl and in HbA1C >5% taken as positive.

Conclusion: According to available evidence, overall diagnostic efficiency of OGCT is superior to HbA1C and fructosamine throughout a broad range of clinical settings. OGCT is a patient friendly test, as it is performed regardless of the timing of last meal, causing minimum interference in the routine activities of the mother. An early diagnosis of diabetes and strict glucose control are crucial for preventing or delaying the onset of serious, life-threatening complications. Although OGCT, HbA1C remains the standard for diagnosing diabetes and glycemic monitoring emerging evidence attests that additional biomarkers such as fructosamine.

Keywords: Gestational diabetes mellitus, Oral glucose challenge test, Glycosylated hemoglobin.

Introduction

Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance of variable severity with recognition or onset during pregnancy irrespective of the treatment with diet or insulin.[1] GDM is one of the most common medical conditions complicating pregnancy. Pregnancies associated with GDM are associated with adverse maternal and fetal outcomes like future diabetes, birth injury, fetal growth abnormalities, prematurity, shoulder dystocia, increased rates of Caesarean section.[1,2] GDM is a state of glucose intolerance with the onset or first detection during pregnancy with or without remission after the end of pregnancy.[4]

GDM has future implications beyond the index pregnancy, increasing pregnancy morbidity and higher plausibility of subsequent diabetes in the mother, identifying two generations at risk of future diabetes[5] and immediate serious obstetric complications like birth injury, prematurity, shoulder dystocia, fetal growth abnormalities, increased incidence of caesarean section, as well as long term complications to both mother and fetus. The risk of adverse perinatal and maternal outcomes is directly proportional to the degree of hyperglycemia, with a linear relationship between maternal glucose and various neonatal outcomes.[6] Hence, detection and care of women with GDM

becomes necessary in the strategy for the primary prevention of diabetes.

Screening for GDM is selective or universal screening. During first antenatal visit, FBS or RBS done, then screening glucose challenge test (GCT) at 24–28 weeks, followed by oral glucose tolerance test (OGTT).

1. As per ADA guidelines, any of the criterion met for diagnosis of GDM: fasting $\geq$ 92 mg/dl (5.1 mmol/l), 1-hour $\geq$180 mg/dl (10.0 mmol/l) or 2-hr value $\geq$153 mg/dl (8.5 mmol/l),[7-10]
2. According to DIPSI criteria, 75gm glucose given orally irrespective of time and meals, 2-hours value $\geq$ 140 mg/dl is a single step, non-fasting procedure.[11]

The current diagnostic and prognostic strategies in diabetes are strongly based on two historical tests, plasma (or capillary) glucose and HbA1c. The efficient diagnosis and accurate monitoring of diabetic patients are cornerstones for reducing the risk of diabetic complications.

Numerous screening guidelines and tests have been developed based on the population characteristics, accuracy and cost. Various screening tests in use are: Random blood glucose estimation, Fasting blood glucose estimation, 75 g glucose challenge test (GCT), 75/100 g oral glucose tolerance test (OGTT), Serum fructosamine estimation, Glycosylated haemoglobin (HbA1c) estimation.[3,12] But

controversies exist, as to which test to be used, when, why, where, and on whom should the screening be done.

The traditional WHO method of OGTT with 75 gram glucose is cumbersome, time consuming and poorly tolerated by pregnant females. The patient must be in fasting state and wait for 2 hours and have minimum of 3 blood samples. The pregnant women are prone to nausea and vomiting, along with gestational edema leading to difficult venous access, impacting test result. Thus, there is rising need for a universal screening test, which is simpler and easily accessible. The current recommendation for the diagnosis is DIPSI method[13] (One step procedure): 75 gram of glucose load. Glycosylated haemoglobin (HbA1c) is presently the most approved modality for chronic glycaemia outside of pregnancy.[9]

Hemoglobin A1c (HbA1c) is the final product of an irreversible enzymatic glycation of glucose moiety to plasma proteins, i.e., haemoglobin. HbA1c level reflects the average plasma glucose level over the RBC lifespan, roughly 120 days, correlated with the degree of glycation.

HbA1c testing done as a single non-fasting blood test and reflects glucose levels over the previous 4-8weeks. In contrast to finger-prick glucose testing, it has exhibited greater accuracy, reliability, higher analytical stability and improved standardization with less inter-laboratory or inter-observer variations, less affected by meals, fasting state, diurnal variation, acute stressors or medications, thus, more comfortable for pregnant women.[3]

Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study[14] clarified the higher risk of adverse outcome significantly associated with increased levels of maternal HBA1C, and higher glycemia levels during pregnancy, thus escalating further more severe risk of overt diabetes.[15]

In this current study conducted on assessing the role of HbA1c as a parallel prospective comparison with single step GCT as a screening tool for detecting GDM in pregnant women attending antenatal care at AIMS, Mandya.

Objectives

The aim of the study was to diagnose and evaluate GDM with oral glucose challenge test, oral glucose tolerance test, and determination of the utility of HbA1c. To evaluate the association of HbA1c levels and OGTT in pregnant women with GDM.

Materials and Methods

The study was undertaken after informed consent from the patients and with the prior approval of the institutional ethical committee. The current study was a prospective study conducted at Sri Adichunchanagiri Institute of Medical Sciences, B.G.Nagar, Mandya, Karnataka during June 2017- Sep 2017. 100 cases were selected randomly between 24–28 gestational weeks attending antenatal care in the department of OBG.

Inclusion Criteria

All pregnant women ≥18 years old presented between 24–28 weeks gestation, singleton pregnancy.

Exclusion Criteria

Pregnancies <24 and >28 weeks gestational age, Overt Diabetes, multiple gestation.

Methodology

All pregnant women who visit antenatal care and satisfy inclusion criteria were included in the present study. Data is gathered regarding demographic data, anthropometric measurements, significant past history, family history, and obstetric history using a standard questionnaire. 100 pregnant women screened for the study between 24 – 28 weeks gestation.

According to DIPSI guidelines, Oral Glucose Challenge Test (OGCT) is performed as an OPD procedure without regard to last meal time. 75gm glucose is given orally irrespective of fasting status or timing of last meal. Venous blood sampling done after 2 hours and post 2 hours blood glucose value ≥140mg/dl is diagnostic of GDM.

As per ADA guidelines, Oral Glucose Tolerance Test (OGTT) is performed as both screening and diagnostic test. The patient required to be in a state of good health, on normal carbohydrate diet, 8-10 hour overnight fasting. A venous blood sample collected in fasting state, then 75 grams of glucose in 300 ml of water, given within 5 min. Next blood samples collected at 1, 2 and 3 hours of the glucose load and tested for blood glucose using the Abbott glucose hexokinase method or using commercial kits.

HbA1C level checked from random sample measured using immunoassay. HbA1c levels correlate with the mean blood glucose levels over the red blood cell life span, i.e., degree of glycation/glycosylation reflecting glucose levels over the preceding 4–8 weeks.

Statistical Analysis

Patient attributes were calculated as percentages, and as mean and standard deviation, or median using descriptive statistics. The correlation between HbA1c levels and GTT values were determined using plot analysis. The discriminative measure of HbA1c used in the detection of GDM assessed by ROC curve. Sensitivity, specificity, false-positive predictive value and false-negative predictive value were also evaluated.

In the present study, the diagnosis of GDM defined as:

1. As per ADA guidelines, any of the criterion met for diagnosis of GDM: fasting ≥ 92 mg/dl (5.1 mmol/l), 1-hour ≥180 mg/dl (10.0 mmol/l) or 2-hr value ≥153 mg/dl (8.5 mmol/l)[7,9,10]

2. As per DIPSI criteria, 75gm glucose given orally irrespective of time and meals, 2-hours value ≥ 140 mg/dl.[10,11]

3. In this study, an arbitrary cut-off value for HbA1c at >5% been taken to detect GDM.

Results

In this study, 100 pregnant women recruited screened using OGCT, HbA1c and fasting 75 gram OGTT. The mean age was 24.6±2.57 and median age of 25 years, and major age group of 26 years. The mean gestational age was 26.38 weeks (SD 1.11) with median gestational age of 26.5 weeks. According to ADA OGTT, the mean fasting glucose levels of 113.48±10.81 mg/dl, 181.14±49.37 mg/dl at 1 hour and 183.34±40.78 mg/dl at 2 hour. The mean HbA1c levels was 4.98±0.82 % and mean OGCT glucose levels was 166.87±16.96 mg/dl.

Patients screened by OGCT for diagnosis of GDM, about 6 cases were diagnosed as non-GDM compared to OGTT when were subjected for further
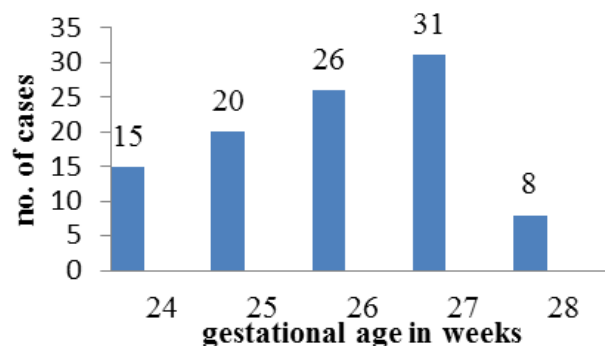

Fig. 1: Distribution of patients according to gestational age

Table 1: Distribution of patients according to ADA and DIPSI criteria

		Diagnosed as GDM	Non-GDM
ADA OGTT	Fasting	99	1
	1st hour	41	69
	2nd hour	81	19
DIPSI OGCT 2nd hour		94	6

Table 2: Distribution of patients according to screening tests

	Diagnosed as GDM	**Non-GDM**
ADA OGTT	100	0
DIPSI OGCT	94	6

Screening with OGTT (Table 1). In our study, out of 100 cases screened by OGTT, about 99% diagnosed as GDM with fasting sample itself, 41% by 1st hour sample and 81% cases by 2nd hour sample (Table 2). In comparison to 2nd hour OGTT which diagnosed 81% cases, 2nd hour OGCT has higher sensitivity, with 94% diagnosed with GDM. Thus it was ascertained that about 6% cases would be missed if DIPSI OGCT used alone. But with application of both criteria, diagnosis of GDM has very high sensitivity and specificity.

Area Under the Curve				
Test Result Variable(s): HbA1C(%)				
Area	**Standard Error[a]**	**Asymptotic Sig.[b]**	**Asymptotic 95% Confidence Interval**	
			Lower limit	**Upper limit**
.761	.048	.000	.666	.855
a. Under the nonparametric assumption				
b. Null hypothesis: true area = 0.5				
Coordinates of the Curve				
Test Result Variable(s): HbA1C (%)				
Positive if Greater Than or Equal To[a]		**Sensitivity**	**1 - Specificity**	
3.00		1.000	1.000	
4.50		.778	.351	
5.50		.381	.054	
6.50		.063	0.000	
8.00		0.000	0.000	

The smallest cutoff value is the minimum observed test value minus 1, and the highest cut-off value is the maximum observed test value plus 1. All the other cutoff values are the averages of two consecutive ordered observed test values.

Table 3: Spearman's correlation

			HbA1C (%)	Fasting	After 1 hour	After2 hours
Spearman's rho	HbA1C (%)	Correlation Coefficient	1.000	.677**	.759**	.602**
		Sig. (2-tailed)		.000	.000	.000
		N	100	100	100	100
	Fasting	Correlation Coefficient	.677**	1.000	.682**	.603**
		Sig. (2-tailed)	.000		.000	.000
		N	100	100	100	100
	After 1 hour	Correlation Coefficient	.759**	.682**	1.000	.735**
		Sig. (2-tailed)	.000	.000		.000
		N	100	100	100	100
	After 2 hours	Correlation Coefficient	.602**	.603**	.735**	1.000
		Sig. (2-tailed)	.000	.000	.000	
		N	100	100	100	100

**. Correlation is significant at the 0.01 level (2-tailed).

It was detected that, Spearman correlation between OGTT and HbA1c (Table-3) observed significant association of 1 and 2 hour OGTT with HbA1c (p≤0.0001).

The test result variable(s): HbA1C (%) has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.
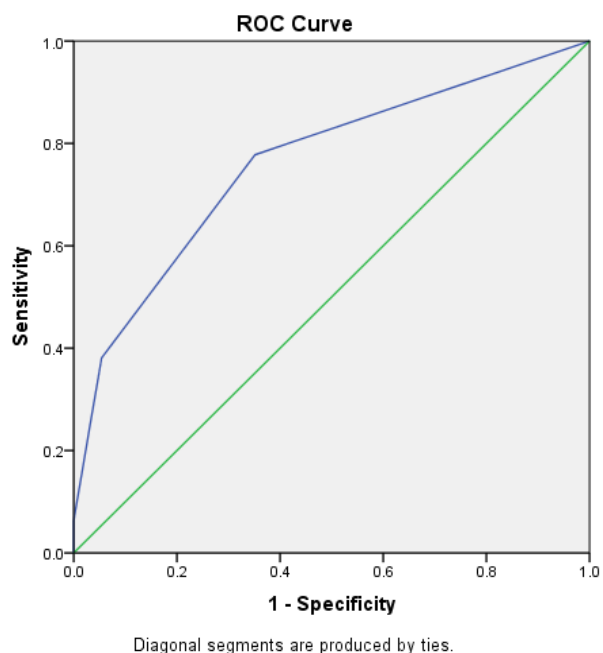

Diagonal segments are produced by ties.

Fig. 2

Discussion

Pregnant mothers with GDM are at high risk of future incidence of diabetes predominantly type-2 diabetes. Thus GDM women are an optimal group for the primary prevention of diabetes.[15] Thus, a universal screening procedure, which is simple and satisfactory, for detection of women with GDM may be considered.

Pregnancy is a state of insulin resistance.[16] As the pathophysiology of GDM is distinctive from diabetes mellitus in the non-pregnant population, GDM may be an index of high risk of non-insulin dependent type 2 Diabetes mellitus in the postnatal period. Placental hormones such as growth hormone, progesterone, corticotropin-releasing hormone, placental lactogen, together act to increase insulin resistance in the pregnant females, thus ensuring sufficient nutrient supply to the growing fetus. In the event of insufficient pancreatic stores or activity to counteract the high insulin resistance, there is high incidence of development of GDM.

Due to increased burden of GDM in Indian population,[4,17] there was a strong necessity to establish a standard diagnostic criteria for diagnosis of GDM. Various diagnostic guidelines were proposed to be effective in diagnosis of GDM such as American College of Obstetricians and Gynecologists (ACOG) guidelines, American Diabetes Association (ADA) guidelines, IADPSG guidelines and National Institute of Health and Clinical Excellence (NICE) guidelines.[18]

In view of standardization of the diagnosis, WHO advocates 2-hour 75 g oral glucose tolerance test (OGTT) with a positive diagnosis in plasma glucose concentration ≥140 mg/dL at 2 hours. A modified form of WHO criteria-DIPSI is a one-step method with a single glucose measurement after administration of 75 gram oral glucose load, irrespective of fasting status. It is interpreted as diagnosis of GDM if 2- hour plasma glucose is ≥ 140 mg/dl.[15]

In our study, about 94% patients of GDM diagnosed by DIPSI, which is in consensus with study by Polur et al.,[18] with 92% cases and Nallaperumal et al.,[19] with 98% cases diagnosed by DIPSI. But detected only 81% of cases if 2nd hour sample of ADA criteria was considered.

Due to the existence of different genetic variations in the levels of glycation of hemoglobin, which is not dependent on glycaemia, thus are evident from ethnic differences in HbA1c. Thus reference ranges of HbA1c for the specific population should be provided before enacting HbA1c as a screening test in GDM to the population.[20] Khalafallah et al.,[3] conducted a similar study on comparison between HbA1c levels and the OGTT results in pregnant women have also reported no significant correlation in

GDM pregnant patients. In present study, mean HbA1c levels were 4.98% (SD 0.82). It was deduced that significant association exists with respect to 1 and 2 hour OGTT with HbA1c (p≤0.0001).

Related to the present study, Rajput et al.,[21] conducted a study on 607 women between 24 weeks and 28 weeks gestation, to evaluate for GDM using OGTT on ADA criteria and HbA1c. HbA1c with a cut-off value ≥5.4% found sensitivity of 85.7% and specificity of 61.1%. But in our study, an arbitrary cut-off value for HbA1c at >5% to detect GDM showed sensitivity of 38% and specificity of 99%. Anjalakshi C et al., done a study comparing GCT Test with OGTT, showed no significant correlation between these two tests.[22]

Conclusion

An early diagnosis of diabetes and a strict glucose control are crucial for preventing or delaying the onset of serious, even life-threatening complications.

Traditional WHO or ADA type of OGTT requires fasting status and cumbersome to the pregnant mother whereas DIPSI is a non-fasting state, patient-friendly, cost effective, single step method which has the same sensitivity and specificity in screening and diagnosing GDM.

The use of HbA1c as a screening test for GDM is yet to be investigated, as diagnosis of GDM might be missed in some pregnant patients. So it should be commented with caution when considered a new GDM diagnosis because HbA1c levels usually lasts for 4 to 8 weeks of erythrocyte life span. Thus, the utilization of HbA1c levels as a screening method for GDM within the specific population needs further evaluation. But incorporation as additional method for diagnosis of GDM helps in aiding the current testing methods with prognostic value even outside pregnancy.

Conflict of Interest: None.

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