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ORIGINAL ARTICLE

Comparison of Diagnostic Accuracy of Non-fasting DIPSI and HbA1c with Fasting WHO Criteria for Diagnosis of Gestational Diabetes Mellitus

Pikee Saxena[1] · Puja Verma[1] · Binita Goswami[2]

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About the Author

Dr. Saxena Pikee is M.D. Obstetrics and Gynaecology, FICOG, MNAMS, has done a Post Graduate Certificate Course in Hospital Management and Post Graduate Diploma in Clinical Research. She is a Professor at the prestigious Lady Hardinge Medical College and SSK Hospital, New Delhi, India. She has more than 100 International and National publications. She has been awarded 21 gold medals for her research work in both National and International forum. She is involved as principal investigator in several research projects including DST and ICMR. Dr Saxena is the honorary General Secretary of Board of Management of the Delhi Diabetic Forum. She is the Executive Editor of Indian Journal of Medical Specialities and Co-Editor of the Journal of Delhi Diabetic Forum.

Abstract

Background To compare diagnostic accuracy of non-fasting DIPSI and HbA1c with fasting WHO 1999 as gold standard for diagnosis of gestational diabetes mellitus (GDM).

Methods Pregnant women attending antenatal clinic underwent a 2-h 75-gm GCT in non-fasting state (DIPSI). HbA1c was also determined at the same sitting. A 2-h 75-gm GCT was repeated for all women after 72 h in a fasting state (WHO criteria). GDM was diagnosed if plasma glucose was ≥140 mg/dl by either test or if HbA1C ≥6%.

Results Of the 800 women evaluated, 51 were diagnosed as GDM by WHO criteria, 63 by DIPSI, and 40 by HbA1c. The sensitivity of DIPSI test with respect to WHO 1999 was 98.04% and specificity 98.26%. The diagnostic accuracy was 98.25%. The area under the ROC curve for DIPSI was 0.988 ($p < 0.001$) (95% confidence interval: 0.960–1.000). The sensitivity of HbA1c with respect to WHO GTT was 47.06%, specificity 97.86%, and diagnostic accuracy 94.63%. The ROC curve between WHO GTT and HbA1c covered an area of 0.805 ($p < 0.01$) (95% confidence interval: 0.731–0.879).

Dr. Saxena Pikee is an M.D. Obstetrics and Gynaecology, FICOG, MNAMS, has done a Post Graduate Certificate Course in Hospital Management and Post Graduate Diploma in Clinical Research. She is a Professor at the prestigious Lady Hardinge Medical College and SSK Hospital, New Delhi, India; Puja Verma as Postgraduate Student of Obstetrics and Gynaecology; Binita Goswami as Associate Professor of Biochemistry.

✉ Pikee Saxena
pikeesaxena@hotmail.com

[1] Department of Obstetrics and Gynaecology, Lady Hardinge Medical College and SSK Hospital, New Delhi 110001, India

[2] Department of Biochemistry, Lady Hardinge Medical College and SSK Hospital, New Delhi 110001, India

Conclusions Non-fasting DIPSI criteria had high diagnostic accuracy compared to gold-standard WHO GTT and can be an effective and practical alternative to the latter. HbA1c had a low sensitivity although the specificity was good and therefore is not a suitable test for screening GDM.

Keywords GDM · WHO GTT · DIPSI · HbA1C

Introduction

Gestational diabetes mellitus (GDM) is a major health problem in many parts of the world, and the prevalence rates vary considerably depending on the population screened and the type of diagnostic method used.

Early detection and achieving normoglycemia during pregnancy can prevent complications not only during pregnancy but also later in life for both the mother and her baby. Therefore, the need for universal screening is well recognized specially in Indian women who have 11-fold higher risk of developing GDM compared to Caucasian women [1].

Many women in developing countries avail antenatal care late in second or third trimester or may approach the health facility during labor without attending any antenatal clinic. In the last decade, as per the National data, health indicators including utilization of antenatal care services were as poor as 50–60% in rural areas [2], and there is a dropout of nearly one-third in the follow-up visits. In India, every year about 27 million pregnancies occur, and all these women need to be screened for GDM. Considering the wide gap between the target and reality, a practical, cost-effective, easy, and convenient screening test is required so that the women can be tested during their initial visit even in a non-fasting state as many may not return subsequently in a fasting state.

Keeping this in mind, Diabetes in Pregnancy Study group India (DIPSI) recommended 75-gram glucose challenge test in non-fasting state for diagnosis of GDM. This one-step procedure is simple, feasible, and economical for diagnosis of GDM [3]. Although DIPSI criteria have been recommended by the Ministry of Health [4], Government of India, it is not being followed in many centers all over the country. Current position of DIPSI remains controversial as few recent studies have reported its poor sensitivity and specificity compared to other tests [5–7].

HbA1c is another potential single test which can be done in a non-fasting state during the initial visit and gives an idea of sugar levels over a period of 3 months. It has been used for diagnosing gestational GDM and pre-diabetes in pregnant women, and high level of HbA1c has been seen to be closely associated with adverse outcomes of women with pre-diabetics and GDM [8, 9].

Based on a large retrospective study comparing the IADPSG criteria and the WHO 2009 criteria, it was concluded [10] that WHO 2hPG of $\geq$140 mg/dl appears to be sufficient to diagnose GDM, as it picks up the majority of GDM cases diagnosed by IADPSG criteria as well. Since one blood sample of WHO criteria picks the same number of cases as the three samples of IADPSG criteria, the single WHO cut-point of 2 h PG >140 mg/dl appears to be suitable for large-scale screening for GDM in India and other developing countries. Therefore, the WHO 1999 criteria was chosen as gold standard in this study as GDM based on this criteria has been shown to predict adverse pregnancy outcome [11]. The aim of the current study was to compare the diagnostic accuracy of two non-fasting tests, DIPSI and HbA1c with fasting WHO 1999 criteria for diagnosis of GDM.

Materials and Methods

This cross-sectional study was conducted in a tertiary care hospital in India after obtaining approval from the Ethics Committee of Human Research of the Institute. Enrollment and conduct of the study were done in accordance with ICH-GCP guidelines. The study population comprised of 800 pregnant women with singleton pregnancy between 24 and 32 weeks period of gestation. Women with multiple pregnancy and already diagnosed cases of diabetes mellitus were excluded.

After informed consent, women presenting to the antenatal outpatient department were recruited and underwent a detailed history and thorough clinical examination. BMI was calculated based on the pre-pregnancy weight and height. All women were given 75-gm glucose load orally in water within 10 min irrespective of their previous meal as recommended by DIPSI. Blood sugar was measured after 2 h. HbA1c was also determined. All participants were instructed to return after 72 h in a fasting state for WHO GTT. Blood sugar was measured in a fasting state and then 2 h after glucose load. Diagnosis of GDM was made if 2 h post-glucose blood sugar was $\geq$140 mg/dl by either test or if HbA1c $\geq$6% Fig. 1. All women were reminded to come for WHO GTT in fasting state by telephonic call given 1 day prior to the test to minimize the loss of cases.

The blood sugar samples were analyzed on fully automated clinical chemistry analyzer AU480 (Olympus, Beckman coulter, USA) using commercially available kit provided by Randox, UK, using GOD/POD method. The HbA1C samples were analyzed on fully automated clinical chemistry analyzer AU480 (Olympus, Beckman coulter,

USA) using commercially available kit provided by Randox, UK, using immunoturbidimetry method.

Sample Size

Sample size was computed as in a diagnostic test study with calibrated outcome. Sensitivity and specificity of the candidate test were assumed to be 70% (with absolute precision of ±10%) and 80% (with absolute precision of ±10%), respectively, with WHO GTT as gold standard. To detect the above sensitivity and specificity with 95% confidence level, we required to enroll 40 GDM cases and 64 non-GDM cases. Further assuming prevalence of GDM of 5% in the screened population [12], we needed to screen at least 800 pregnant women in order to get about 40 women with GDM.

Statistical analysis was performed using version 17 of SPSS Software for Windows. The results were expressed as mean ± standard deviation and percentage. The sensitivity, specificity, predictive value, diagnostic accuracy, correlation, and agreement between the DIPSI and HbA1c with the gold standard, WHO GTT were computed.

Results

In the present study, mean age was 25.02 ± 3.6 year, while it was 27.98 ± 4.3 years in women with GDM. The mean BMI was significantly increased in GDM as compared to non-GDM group (27.76 ± 4.53 kg/m^2 vs. 24.89 ± 2.92 kg/m^2; $p < 0.001$). Obesity (BMI ≥30 kg/m^2) was significantly more prevalent in the GDM women as compared to non-GDM (21 vs. 4%; $p < 0.01$).

Risk factors including age >25 years, BMI >25 kg/m^2, family history of diabetes, history of previous abortions, and stillbirths in GDM groups by WHO, DIPSI, and HbA1c are depicted in Fig. 2. The mean hemoglobin in study population was 10.27 ± 6.51 gm/dl. In cases of GDM, the mean blood sugar by DIPSI was 166.43 ± 4.64 mg/dl and by WHO criteria was 178.52 ± 31.47 mg/dl. The mean HbA1C value of 800 women was 5.06 ± 0.54% and of women diagnosed as GDM was 6.43 ± 0.78%.

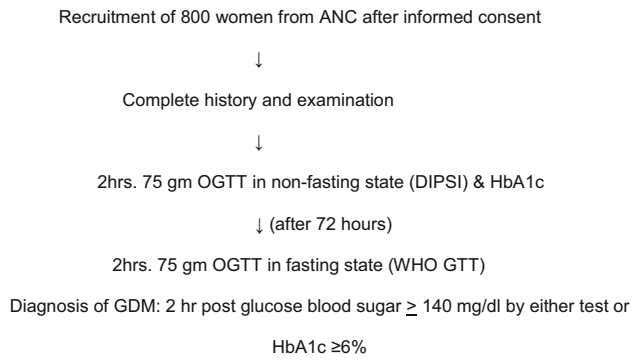

Fig. 1 Patient flowchart

Comparison of GDM by WHO GTT and DIPSI (Table 1).

Women diagnosed as GDM by WHO GTT were 51 and by DIPSI were 63. The sensitivity of DIPSI with regard to WHO GTT was 98.04%, specificity 98.25%, positive predictive value 79.37%, negative predictive value 99.86%, and diagnostic accuracy 98.25% Table 1. Agreement (kappa value) between DIPSI and WHO GTT was 0.868 ($p < 0.001$). The ROC curve between WHO and DIPSI covered an area of 0.981 ($p < 0.001$) with 95% confidence interval (0.960–1.000). Pearson's correlation between WHO and DIPSI was 0.781 ($p < 0.000$).

Comparison of GDM by WHO GTT and HbA1c (Table 1).

Total number of cases of GDM detected by HbA1c was 40. The sensitivity of HbA1c with respect to WHO GTT was 47.06%, specificity 97.86%, positive predictive value 60.0%, negative predictive value 96.45%, and diagnostic accuracy 94.63% Table 1. The agreement (kappa value) between WHO GTT and HbA1c was 0.499 ($p < 0.01$). The ROC curve between WHO GTT and HbA1c covered an area of 0.805 (p value < 0.01) with 95% confidence interval (0.731–0.879). Pearson's Correlation between WHO and HbA1c was 0.459 ($p < 0.000$).

On comparing sensitivity and specificity of different DIPSI value in comparison with WHO GTT for GDM (Table 2), values between 139.5 and 142 mg/dl demonstrated maximum sensitivity (96%) and specificity (98%).

Discussion

The prevalence of GDM in the present study was 6.25%. According to other studies done in North India, the prevalence of GDM was between 6 and 7% which is similar to the present study [13, 14].

As is evident from the results of this study, family history diabetes, previous history of abortions, and stillbirths were significantly higher in GDM as compared to non-GDM women (Fig. 2).

In the present study, we observed that 187 (24.96%) women had previous history of abortion. Sharma et al. [13] found 24.9% of their GDM patients with a positive family history of perinatal losses. The increased rates of previous stillbirth and abortions in women with GDM are due to fluctuations in blood sugar levels, reduced blood flow through placenta, placental necrosis, amniotic fluid abnormalities, congenital and metabolic abnormalities, polycythemia, etc.

This study compared the diagnostic efficacy of non-fasting tests DIPSI and HbA1c with WHO OGTT for

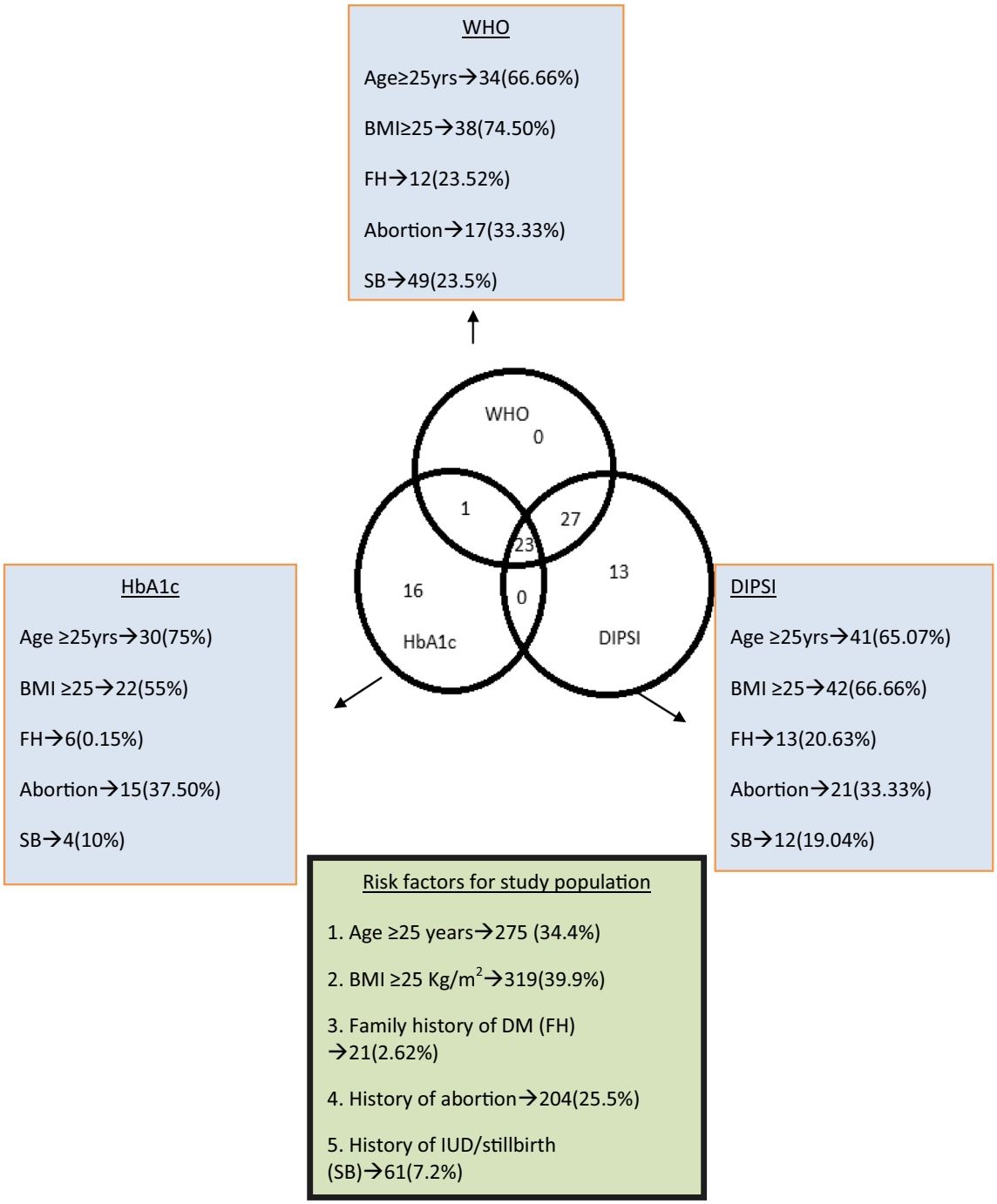

Fig. 2 Risk factors for GDM groups

practical, one-step diagnosis of gestational diabetes mellitus during the first visit itself as many women may not return for a subsequent checkup in a fasting state. In this study, four patients were diagnosed as GDM by fasting WHO 1999 criteria, all of whom were picked up by DIPSI also. According to the DIPSI group, the rationale of performing this type of OGTT is that after a meal, a normal non-diabetic pregnant woman would be able to maintain normal blood sugar level (<140 mg/dl) despite the glucose challenge due to a brisk and adequate insulin release [3]. In women with GDM, there will be a further increase in plasma glucose value after an OGTT due to impaired insulin secretion and increasing insulin resistance [3].

The sensitivity of the DIPSI test was 98.04% and specificity was 98.26% when compared to WHO OGTT. The diagnostic accuracy was 98.25%. Sharma et al. [13] found DIPSI to be 100% sensitive and 100% specific in diagnosing GDM. According to a study conducted by

Table 1 Comparison between (a) WHO and DIPSI and (b) WHO and HbA1c

	WHO GTT (+)		WHO GTT (−)	
	n	%	*n*	%
DIPSI				
≥140 mg/dl	50	98.04%	13	1.74%
<140 mg/dl	1	1.96%	736	98.25%
Total	51	100%	749	100%
HbA1c				
≥6%	24	47.06%	16	2.14%
<6%	27	52.94%	733	97.86%
Total	51	100%	749	100%

Table 2 Different sensitivity and specificity at different glucose values

Glucose value (DIPSI) mg/dl	Sensitivity (%)	Specificity (%)
103.5	100	52
109.5	96	69
136.5	96	97
139.5	96	98
141.0	96	98
142.0	96	98
143.0	92	99
149.5	76	99
161.0	53	100

Badikillaya et al. [15], the sensitivity was 100% and a specificity of 89% was observed. While in a study conducted by Mohan et al. [7], it was observed that the sensitivity of DIPSI criteria was as low as 27.7% with a good specificity of 97.7% (Table 3).

DIPSI recommends that when a pregnant woman comes to antenatal clinic on first visit, she should undergo 2-h, 75-gram oral glucose challenge test irrespective of duration of last meal. If 2-h blood glucose is ≥140 mg/dl, she should be diagnosed as gestational diabetes mellitus [3]. This test is simple, feasible, and economical. In developing countries like India, pregnant women rarely come to antenatal clinic in a fasting state [3]. Thus performing a non-fasting GCT is a very useful test and most suitable for India.

Table 3 Comparison of WHO GTT and DIPSI by different authors

References	Sample size	Sensitivity (%)	Specificity (%)
Present study	800	98.04	98.26
Sharma et al. [13]	500	100	100
Badikillaya et al. [15]	200	100	89
Mohan et al. [7]	1031	27.7	97.7

Due of nausea and vomiting associated with pregnancy, it is difficult for pregnant women to drink glucose empty stomach [3]. So, glucose testing in non-fasting state improves acceptability.

The WHO has accepted the IADPSG criteria as the new WHO criteria in 2013 [16] although it recognizes a few important and pertinent observations with regard to GDM testing. GTT is resource intensive, and many health services, especially in low-resource settings, are not able to routinely perform OGTTs in pregnant women [16]. In these circumstances, many health services do not test for hyperglycemia in pregnancy. Taking multiple venous samples as recommended by ADA, IADPSG requires extra cost, manpower, and resources [16]. Doing a two-step test is also not feasible as many women may be lost to follow-up. Thus, diagnosing GDM with a single sample is practical and economical. Moreover, the pregnant women will not be pricked multiple times for taking venous samples [16].

Recently Sagili et al. [17] compared the IADPSG and WHO 1999 criteria, and their effects on neonatal birth weight as IADPSG criteria for GDM has been adopted by most associations across the world including the American Diabetes Association and WHO. They found the prevalence of GDM using IADPSG and WHO 1999 criteria to be 12.6 and 12.4%, respectively. Both GDM criteria groups did not differ in neonatal birth weight and macrosomia rate. Elevated fasting plasma glucose alone picked up only one GDM in the previous WHO criteria group.

Recently, Ministry of Health and Family welfare, Government of India, has also recommended DIPSI test for the diagnosis of GDM [4].

Out of 800 women, 40 (5%) had HbA1c ≥6%. Out of these 40 women 24 were diagnosed as GDM by WHO GTT, making the sensitivity of HbA1c to be 47.06%. The number of false positive cases was 16 (2.14%). Rajput et al. [18] in their study found that the mean HbA1c value in women with GDM was significantly higher than women without GDM (5.73 ± 0.34% compared to 5.34 ± 0.35%). HbA1c cutoff value of ≥5.95% had sensitivity of 28.6% and specificity of 97.2% in diagnosing GDM, while an HbA1c cutoff value of ≥5.45% had sensitivity of 85.7% and specificity of 61.1% in diagnosing GDM [18].

Conclusions

Non-fasting DIPSI criteria may be recommended for diagnosis of GDM due to its high diagnostic accuracy and agreement with gold standard, WHO 1999. This test has several advantages over WHO GTT as this single test, serving both as a screening and diagnostic test, does not require the patient to come in a fasting state and is

economical. Therefore, it seems to be an appropriate and practical test which could be used for universal screening of pregnant women in developing countries during the initial visit. HbA1c has a good specificity but poor sensitivity and therefore does not serve as a good screening test.

Compliance with Ethical Standards

Conflict of interest Authors have no conflict of interest in the findings of this study.

Ethical Statement This study was initiated after approval from the Ethics Committee of Human Research of the Institute. Enrollment and conduct of the study were done in accordance with ICH-GCP guidelines.

Human and Animal Rights All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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