Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/xsew9610

STUDY TO DETERMINE DIAGNOSTIC ACCURACY OF FIRST TRIMESTER GLYCOSYLATED HAEMOGLOBIN FOR PREDICTION OF GESTATIONAL DIABETES MELLITUS

Dr. G Thenmozhi[1], SHRUTHI S[2], Sanjana D.[3*]

[1]Professor and HOD, Department of Obstetrics and Gynaecology, Government Chengalpattu Medical College and hospital drthenmozhi135@gmail.com ORCID ID - 0009-0007-9820-9409
[2]Associate Professor, Department of Obstetrics and Gynaecology, Government Chengalpattu Medical College and Hospital .Mail id - drshruthi87@gmail.com ORCID ID- 0009-0007-5662-9106
[3*]Senior Resident, Department of Obstetrics and Gynaecology, Government Chengalpattu Medical College and Hospital. Mail ID - sanjana.devarajulu@gmail.com ORCID ID - 0009-0000-7340-8339

***Corresponding Author: Sanjana D.**
* Senior Resident Department of Obstetrics and Gynaecology, Government Chengalpattu Medical College and Hospital. Mail ID - sanjana.devarajulu@gmail.com ORCID ID - 0009-0000-7340-8339

Abstract

Background:
Gestational Diabetes Mellitus (GDM) is a rising public health concern, particularly in South Asian populations with inherent insulin resistance. Early identification of high-risk pregnancies is critical to minimize maternal and fetal complications. Glycosylated hemoglobin (HbA1c), a marker of average blood glucose over 2–3 months, may offer a convenient early screening option when measured in the first trimester.

Objective:
This study aimed to evaluate the diagnostic accuracy of first-trimester HbA1c in predicting GDM and to determine an optimal HbA1c cutoff that could serve as a risk stratification tool in routine antenatal care.

Methods:
A prospective cohort study was conducted at a tertiary care hospital over six months. A total of 100 pregnant women with gestational age 8–13 weeks were enrolled. First-trimester HbA1c was measured using high-performance liquid chromatography. All participants underwent a 75 g OGTT at 24–28 weeks, and GDM was diagnosed as per IADPSG criteria. Data were analyzed using SPSS, and the diagnostic accuracy of HbA1c was assessed through sensitivity, specificity, and ROC analysis.

Results:
GDM was diagnosed in 15% of participants. All GDM cases had a first-trimester HbA1c $\geq$ 5.7%, showing 100% specificity but reduced sensitivity. A significant association was observed between GDM and obesity ($p < 0.001$), with all cases occurring in obese women. HbA1c $\geq$ 5.7% demonstrated strong predictive value but cannot replace OGTT due to limited negative predictive capacity.

Conclusion:
First-trimester HbA1c $\geq$5.7% is a useful high-specificity screening tool for GDM but lacks sufficient sensitivity to serve as a standalone diagnostic test. When combined with mid-pregnancy OGTT, it enhances early detection and facilitates targeted interventions.

Keywords: Gestational Diabetes Mellitus, HbA1c, First Trimester Screening, OGTT

INTRODUCTION

Gestational Diabetes Mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy. It poses a significant burden on maternal and fetal health, often associated with increased risks of complications such as preeclampsia, macrosomia, neonatal hypoglycemia, and long-term metabolic disorders in both mother and child[1].

The prevalence of GDM is rising globally, with India showing some of the highest reported rates ranging from 10–20%, depending on region, urbanization, and diagnostic criteria used [2]. Factors contributing to this include obesity, sedentary lifestyle, advanced maternal age, and strong familial predisposition to type 2 diabetes mellitus. South Asian ethnicity is independently associated with an increased risk due to inherent insulin resistance [3].

Screening for GDM is typically done between 24–28 weeks of gestation using the Oral Glucose Tolerance Test (OGTT). The International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria advocate a one-step 75 g OGTT, while the American College of Obstetricians and Gynecologists (ACOG) supports a two-step method. In India, universal screening is recommended due to the high prevalence and risk in the population [2].

Early identification of women at risk for GDM is essential to prevent adverse outcomes. Glycosylated hemoglobin (HbA1c), a marker of average plasma glucose concentration over the preceding 2–3 months, has emerged as a potential early predictor. Measuring HbA1c in the first trimester could help stratify risk before the onset of peak insulin resistance typically seen in the second and third trimesters [4]. Elevated first-trimester HbA1c levels have been linked with a higher probability of GDM development later in pregnancy [5].

HbA1c testing is advantageous due to its convenience—non-fasting, single blood draw, and stable sample handling. However, its utility as a standalone diagnostic tool for GDM remains controversial due to inter-individual variability, influence of hemoglobinopathies, and differing cutoff thresholds [2],[4].

Several studies have explored the predictive value of early pregnancy HbA1c levels. Valadan et al [4] demonstrated that a first-trimester HbA1c level ≥5.7% could predict GDM with reasonable accuracy. Similarly, Wu et al. [5] constructed a predictive model incorporating HbA1c and other risk factors to stratify GDM risk during early pregnancy. Nonetheless, there remains a lack of consensus on ideal thresholds and diagnostic sensitivity compared to OGTT.

This study was designed to evaluate the diagnostic accuracy of first-trimester HbA1c in predicting GDM, and to identify an optimal cutoff level that could serve as an early warning marker in the Indian population. Given the limitations of OGTT—including patient compliance, fasting requirements, and timing—HbA1c could offer a simpler alternative or an adjunct in high-risk cases.

By bridging the gap between early detection and timely intervention, the study aims to contribute toward refining screening protocols in resource-constrained and high-burden settings like India.

MATERIALS AND METHODOLOGY

This prospective cohort study was conducted in the Department of Obstetrics and Gynaecology at Government Chengalpattu Medical College and Hospital, Chengalpattu, over a period of six months. The aim was to evaluate the diagnostic accuracy of first-trimester glycosylated haemoglobin (HbA1c) in predicting the development of gestational diabetes mellitus (GDM). The primary objectives were to assess the sensitivity, specificity, and predictive value of first-trimester HbA1c in the early identification of GDM. The secondary objectives included identifying an optimal HbA1c cutoff for GDM prediction and studying its association with maternal risk factors such as pre-pregnancy BMI and socioeconomic status.

Pregnant women receiving regular antenatal care at the hospital were screened for eligibility. The inclusion criteria were women aged 18–35 years, with a confirmed gestational age of 8–13 weeks via ultrasound, who provided informed written consent and were compliant with antenatal follow-up.

The exclusion criteria included known pregestational diabetes mellitus, chronic anaemia, hemoglobinopathies (e.g., sickle cell disease), coagulopathies, thrombocytopenia, history of GDM in a previous pregnancy, and pregnancies with fetal anomalies or chromosomal abnormalities.

After enrollment, detailed demographic and clinical histories were collected using a structured proforma. Maternal age, parity, educational level, socioeconomic status (based on modified Kuppuswamy scale), dietary preferences, family history of diabetes, and pre-pregnancy weight were recorded. Body mass index (BMI) was calculated based on measured height and pre-pregnancy weight.

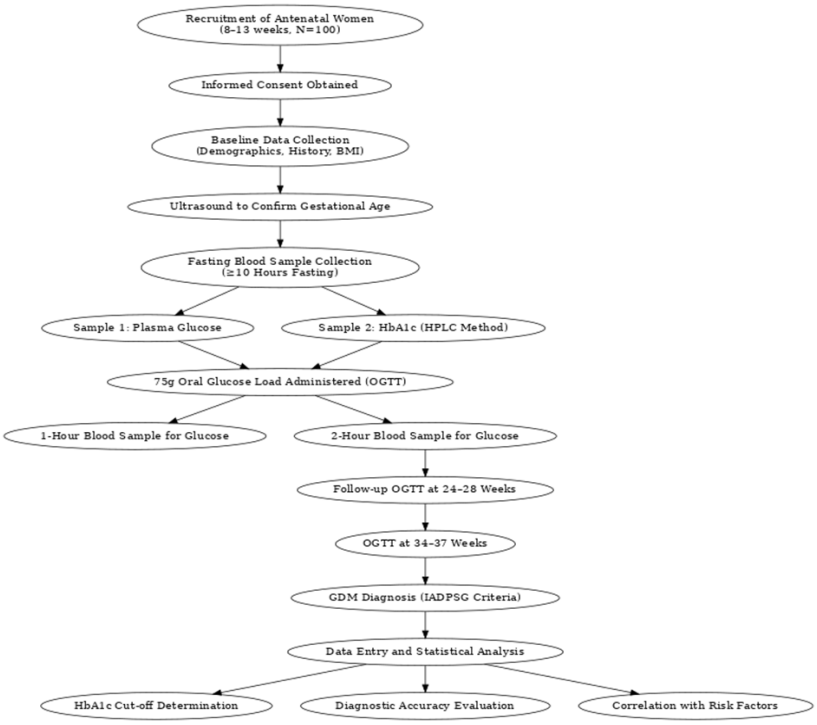
All participants underwent a 75 g oral glucose tolerance test (OGTT) between 8 and 13 weeks of gestation. Blood glucose levels were measured at fasting, 1-hour, and 2-hour intervals using the enzymatic hexokinase method. In parallel, venous blood was collected in an EDTA vial and stored at −70°C until processed for HbA1c by high-performance liquid chromatography (HPLC), as endorsed by the American Diabetes Association for diabetes screening in non-pregnant adults (American Diabetes Association, 2024).

Patients were followed up at regular antenatal visits, and a repeat OGTT was performed at 24–28 weeks of gestation, as recommended by the International Association of Diabetes and Pregnancy Study Groups (IADPSG, 2010), which diagnoses GDM if any one of the following thresholds is met: fasting glucose ≥92 mg/dL, 1-hour ≥180 mg/dL, or 2-hour ≥153 mg/dL. A third OGTT was performed between 34 and 37 weeks for select cases to assess for late-onset GDM.

An HbA1c level of ≥5.7% in the first trimester was considered a potential predictor of GDM, in accordance with prior findings by Valadan et al [4], who demonstrated that early HbA1c elevation could identify at-risk pregnancies. Wu et al. [5] also supported the use of early glycemic biomarkers in predictive models for GDM. However, the use of HbA1c in pregnancy is still debated due to physiological hemodilution and iron metabolism changes that may alter values.

All data were entered in Microsoft Excel and analyzed using SPSS version 23. Comparisons between GDM and non-GDM groups were made using Chi-square, Fisher's exact, and independent t-tests. ROC (receiver operating characteristic) curves were plotted to determine optimal cutoff values, and diagnostic performance was expressed as sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).

STUDY FLOW CHART



RESULTS

Table 1: Demographic Characteristics

Variable	Category
Age (years)	≤20: 9%, 21–25: 40%, 26–30: 37%, 31–35: 12%, >35: 2%
Education Level	Illiterate: 2%, Primary: 16%, Middle: 9%, High School: 40%, Diploma+: 33%
Occupation	Unemployed: 85%, Professionals: 4%, Others: 11%
Income/month (INR)	<6174: 24%, 6175–18496: 60%, 18497–30380: 13%, >30381: 3%
Pre-pregnancy BMI	Normal: 35%, Overweight: 42%, Obese: 23%

Table 1 **-** The majority of the study population fell within the 21–30 year age group, consistent with the typical reproductive age distribution. Most participants were from lower socioeconomic strata and had a high school education. A substantial proportion (42%) were overweight and 23% were obese, indicating a high baseline risk for GDM. These demographic factors are known contributors to glucose intolerance in pregnancy and underscore the need for early screening in such populations.

Table 2: GDM Status Distribution

GDM Status	Frequency	Percentage
Present	15	15.0%
Absent	85	85.0%

Table 2 - GDM was diagnosed in 15% of the study population, aligning with previously reported Indian prevalence rates of 10–20% (DIPSI Guidelines). This highlights the significant burden of GDM in urban tertiary care centers. Early identification and intervention are critical in this population to prevent adverse maternal and neonatal outcomes and reduce the long-term risk of Type 2 diabetes.

Table 3: Pre-pregnancy BMI vs GDM

Pre-pregnancy BMI	GDM Present	GDM Absent	Total
Normal	0	35	35
Overweight	0	42	42
Obese	15	8	23
Statistical Significance: $\chi^2 = 59.079$, $p < 0.001$			

Table 3 - This table shows a highly significant association between obesity and GDM ($p < 0.001$). All GDM cases in the study were observed exclusively in obese women, while none were identified in those with normal or overweight BMI. These findings reinforce global evidence that obesity is a strong independent predictor of GDM. Preconception weight optimization could be an effective strategy for GDM prevention, especially in high-risk groups.

Table 4: HbA1c vs GDM Diagnosis

HbA1c Level	GDM Present	GDM Absent	Total
< 5.7%	0	45	45
≥ 5.7%	15	40	55
Statistical Significance: Fisher's exact test, $p < 0.001$			

Table 4 - All women diagnosed with GDM had a first-trimester HbA1c ≥5.7%, indicating a strong correlation between early glycosylated hemoglobin levels and later development of GDM ($p < 0.001$). However, 45 non-GDM patients also had HbA1c <5.7%, reducing its negative predictive value. These

findings support the potential utility of HbA1c as a high-specificity screening tool, although it lacks sensitivity to be used alone for GDM diagnosis. It may be best applied in conjunction with OGTT.

Table 5: OGTT (24–28 weeks) vs GDM

OGTT Value	GDM Present (Mean ± SD)	GDM Absent (Mean ± SD)	p-value
Fasting	91.7 ± 6.3	71.6 ± 4.6	<0.001
1-hour	137.8 ± 12.2	116.1 ± 9.5	<0.001
2-hour	130.0 ± 9.8	90.1 ± 8.2	<0.001

Table 5 - This table represents the gold-standard comparison for GDM diagnosis. Statistically significant differences were observed in fasting, 1-hour, and 2-hour OGTT values between GDM and non-GDM groups (all $p < 0.001$). These results confirm the robustness of the IADPSG criteria in identifying GDM in the second trimester. Moreover, the elevated mean values in GDM cases validate the role of OGTT as a definitive diagnostic tool and highlight the limitation of relying solely on early HbA1c for diagnosis.

DISCUSSION

Prevalence of GDM (15%) observed in this study mirrors national trends in India, where prevalence ranges between 10–20%, reinforcing the growing epidemic of GDM and its public health importance in urban antenatal populations [1].

All GDM cases occurred in obese women, with none in normal or overweight categories, showing a highly significant association. This supports the findings of Song et al., who highlighted obesity as a primary driver of insulin resistance and GDM [3].

First-trimester HbA1c ≥ 5.7% demonstrated a strong association with later GDM diagnosis, suggesting it as a valuable early screening tool with high specificity, consistent with the findings of Valadan et al[4]., though not sufficient as a standalone test[4].

OGTT at 24–28 weeks proved diagnostically superior, with fasting, 1-hour, and 2-hour glucose values showing statistically significant differences in GDM patients, validating the effectiveness of IADPSG criteria in the Indian clinical context [7].

Early OGTT (8–13 weeks) showed limited utility for GDM prediction except for the 1-hour reading, which was statistically significant. This reflects the pathophysiology where insulin resistance becomes more pronounced later in gestation [5].

HbA1c is useful due to its convenience, requiring no fasting and offering stable readings over 2–3 months. However, in pregnancy, its levels may be influenced by altered iron metabolism and dilutional anaemia, reducing diagnostic reliability (American Diabetes Association).

GDM incidence was higher in women from Class 4 socioeconomic status, indicating the interplay of nutritional habits, physical inactivity, and healthcare access disparities, in line with patterns described in the DIPSI Guidelines tailored to the Indian population [2].

Increasing maternal age showed a positive correlation with GDM diagnosis, though not statistically significant. Age remains a known non-modifiable risk factor, with several studies reporting an increased risk after 25 years [8].

BMI category analysis revealed a threshold effect, where only obese women developed GDM, while overweight or normal BMI participants did not, supporting the HAPO study's findings on the strong linear relationship between obesity and GDM [9].

Elevated first-trimester HbA1c is associated with fetal anomalies, especially congenital heart and neural tube defects, which are more likely when glycemic control is poor during organogenesis. This is corroborated by observations made by MacNeill et al [10].

45% of non-GDM patients had HbA1c ≥ 5.7%, suggesting potential over-diagnosis if HbA1c is used in isolation. Major et al. noted similar trends and emphasized the importance of pairing HbA1c with OGTT for improved sensitivity [11].

Fasting glucose in OGTT was the most discriminatory variable, showing the largest mean difference between GDM and non-GDM groups, indicating its central role in early glucose dysregulation in GDM pathophysiology [12].

Pre-pregnancy weight was significantly higher in GDM patients, as shown in other studies where each unit increase in maternal weight predicted a higher risk of GDM and impaired glucose tolerance postpartum [4].

Elevated HbA1c levels have been associated with macrosomia, neonatal hypoglycemia, and perinatal complications, as described by O'Sullivan and Mahan, further supporting the need for early metabolic screening during pregnancy [13].

This study benefited from strong follow-up compliance, facilitated by the availability of HbA1c analyzers and VHN-supported antenatal linkage, as emphasized in the FIGO guidelines for integrated antenatal diabetes management in resource-limited settings [14].

CONCLUSION

First-trimester HbA1c ≥5.7% is a specific but not sensitive predictor of GDM. When combined with OGTT, it enhances early risk stratification and improves antenatal glycemic management outcomes.

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