Annals of Medicine and Medical Sciences (AMMS)
Volume 05, 2026, *Page No.: 96 to 100*
Available at: *http://ammspub.com*

Original Article

OPEN ACCESS

Use of HbA1c as an Early Predictor of Gestational Diabetes Mellitus

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Abstract

Background: Gestational diabetes mellitus (GDM) is a growing global health concern, with increasing prevalence linked to rising obesity rates. Early identification of at-risk women can mitigate adverse maternal and fetal outcomes. ***Objectives:*** To evaluate whether a first-trimester HbA1c value of 5.7-6.4% serves as an early predictor of GDM in South Indian women. ***Methods:*** A prospective cohort study was conducted at XXXXXX, from January 2022 to January 2023. We included 150 antenatal women with HbA1c measured at ≤20 weeks gestation, excluding those with pre-existing diabetes or HbA1c ≥6.5%. GDM was diagnosed using a 2-hour 75g oral glucose tolerance test (OGTT) at 24-28 weeks per IADPSG criteria. Women with HbA1c 5.7-6.4% were compared to those with HbA1c <5.7%. Statistical analysis used unpaired t-tests, ANOVA, Chi-square, and Fisher's exact tests. ***Results:*** Of 150 women, 130 (87%) had HbA1c <5.7%, and 20 (13%) had HbA1c 5.7-6.4%. GDM prevalence was 12%, with 55% of the HbA1c 5.7-6.4% group developing GDM compared to 5% in the HbA1c <5.7% group (OR 21.48, 95% CI 6.70-68.82, p<0.001). Overweight women predominated in the higher HbA1c group. ***Conclusion:*** First-trimester HbA1c (5.7-6.4%) is a significant early predictor of GDM, particularly in overweight South Indian women, supporting its use for early screening and intervention. Limitations include the small sample size in the higher HbA1c subgroup (n=20), precluding multivariable adjustments.

Keywords: ***Gestational Diabetes Mellitus, Glycated Hemoglobin A, Pregnancy Trimester-First, Pregnancy, Insulin Resistance.***

Introduction

Gestational diabetes mellitus (GDM), defined as glucose intolerance first identified during pregnancy, is a significant public health challenge, affecting 10-15% of pregnancies globally, with a prevalence of 10-13% in India, particularly in urban areas [1,2]. The rising incidence parallels global increases in obesity and type 2 diabetes, driven by sedentary lifestyles and increasing maternal body mass index (BMI) [3,4]. GDM is associated with adverse maternal outcomes, including cesarean delivery and preeclampsia, and fetal complications such as macrosomia and neonatal hypoglycemia, with long-term risks of type 2 diabetes and metabolic dysfunction in both mother and offspring [5-7]. Early detection is crucial to implement timely interventions, such as dietary modifications and insulin therapy, to mitigate these risks [8].

Current GDM screening relies on the oral glucose tolerance test (OGTT) at 24-28 weeks gestation, but this timing may miss early hyperglycemia that influences fetal growth from the first trimester [9,10]. Early maternal hyperglycemia can prime fetal β-cell mass, leading to persistent hyperinsulinemia and increased macrosomia risk, even with subsequent glycemic control [9,10]. Consequently, there is a pressing need for reliable early biomarkers to identify at-risk women before significant metabolic changes occur, particularly in high-prevalence populations like South Indians, where validation of HbA1c as a first-trimester predictor remains limited [11,12]. HbA1c, reflecting average blood glucose levels over three months, is an established diagnostic tool for diabetes in non-pregnant populations, with a threshold of ≥6.5% endorsed by the American Diabetes Association [13,14]. Emerging evidence suggests its potential for early pregnancy screening, particularly in high-risk populations like South Indians, who exhibit elevated GDM prevalence due to genetic and environmental factors [11,12]. This study evaluates the predictive value of first-trimester HbA1c (5.7-6.4%) for GDM in South Indian women, aiming to facilitate early intervention and improve maternal and fetal outcomes [15,16].

Methodology

Study Design and Setting: This prospective cohort study was conducted at XXXXXX, a tertiary care center in Coimbatore, India, from January 2022 to January 2023. The study aimed to evaluate the predictive value of first-trimester HbA1c (5.7-6.4%) for gestational diabetes mellitus (GDM) in South Indian women.

Participants: We enrolled 150 antenatal women presenting for routine care at ≤20 weeks gestation who underwent HbA1c testing and delivered within the study period. Eligibility criteria included singleton pregnancies and no prior diagnosis of diabetes mellitus. Exclusion criteria were pre-existing diabetes, HbA1c ≥6.5% at

Received: January 12, 2025; **Revised:** January 28, 2026; **Accepted:** February 02, 2026

initial testing, multiple pregnancies, or inability to complete follow-up. Participants were recruited consecutively from the antenatal clinic to minimize selection bias.

Ethical Considerations: The study was approved by the Institutional Ethics Committee of XXXXXX. Written informed consent was obtained from all participants after explaining the study's purpose, procedures, and potential risks. Confidentiality was maintained, and participants could withdraw at any time without affecting their care.

Variables and Data Sources: The primary outcome was GDM diagnosis, defined using the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) criteria based on a 2-hour 75g oral glucose tolerance test (OGTT) at 24-28 weeks gestation. Secondary outcomes included mode of delivery (vaginal or cesarean), maternal weight gain, birth weight, and neonatal morbidities (e.g., macrosomia, hypoglycemia). Additional variables encompass socio-demographic factors (age, parity, education level) and maternal co-morbidities (e.g., hypertension, anemia). Exposure variables included first-trimester HbA1c (categorized as <5.7% or 5.7-6.4%) and body mass index (BMI, classified as normal <25 kg/m², overweight 25-29.9 kg/m², or obese ≥30 kg/m²). Data were collected from medical records, clinical examinations, and laboratory reports.

Measurement: HbA1c was measured using high-performance liquid chromatography (Bio-Rad D-10, standardized to NGSP) at ≤20 weeks gestation. The cutoff of 5.7-6.4% was selected based on American Diabetes Association criteria for prediabetes in non-pregnant adults, adapted for early pregnancy screening supported by emerging evidence on its predictive utility [13,15]. The OGTT was performed after an 8-14-hour overnight fast, following ≥3 days of unrestricted diet (>150g carbohydrates/day) and normal physical activity. GDM was diagnosed if one or more OGTT values met or exceeded: fasting ≥5.1 mmol/L (92 mg/dL), 1-hour ≥10.0 mmol/L (180 mg/dL), or 2-hour ≥8.5 mmol/L (153 mg/dL). All measurements were conducted by trained personnel, with laboratory staff blinded to HbA1c group status to reduce detection bias.

Study Size: The sample size (n=150) was calculated to detect a 20% difference in GDM prevalence (10% in low HbA1c vs. 30% in high HbA1c group) with 80% power, alpha=0.05 (two-sided), and 8% attrition rate, using standard formulas for cohort studies [17].

Statistical Methods: Participants were divided into two groups: HbA1c <5.7% and HbA1c 5.7-6.4%. Descriptive statistics summarized baseline characteristics (age, obstetric score, BMI, gestational age). Continuous variables (e.g., glucose levels, birth weight) were compared using unpaired t-tests or ANOVA after confirming normality via Shapiro-Wilk test (all p>0.05), and categorical variables (e.g., GDM diagnosis, delivery mode) were analyzed using Chi-square or Fisher's exact tests. Odds ratios (OR) with 95% confidence intervals (CI) were calculated to assess the association between HbA1c and GDM. Analyses were unadjusted due to small subgroup size; potential confounders (e.g., BMI, age) were not adjusted in multivariable models. Missing data were minimal (<5%) and handled by listwise deletion under the assumption of missing at random, with no further sensitivity analyses deemed necessary given the low rate. Analyses were performed using SPSS version 18. No subgroup analyses were planned due to the sample size.

Follow-Up: Participants were followed antenatally (monthly visits), intra-natally, and postnatally (within 1 week post-delivery) to collect outcome data. Loss to follow-up was minimal (n=2, due to relocation), and these cases were excluded from analysis.

Results

The following flowchart illustrates the participant enrollment, allocation, follow-up, and analysis in this prospective cohort study (**Figure 1**)

Baseline Characteristics: Socio-demographic variables and maternal co-morbidities are presented in Tables 4 and 5, respectively. Age, parity, and education showed no significant differences between groups (p>0.05). Co-morbidities such as hypertension and anemia were more prevalent in the HbA1c 5.7-6.4% group (p<0.05).

Of the 150 women enrolled, 130 (87%) had HbA1c <5.7%, and 20 (13%) had HbA1c 5.7-6.4%. The overall GDM prevalence was 12% (18/150). In the HbA1c 5.7-6.4% group, 55% (11/20) developed GDM, compared to 5% (7/130) in the HbA1c <5.7% group (p<0.001, OR 21.48, 95% CI 6.70-68.82), indicating a significant association (**Table 1**). Mean fasting glucose levels were significantly higher in the HbA1c 5.7-6.4% group (88.56 mg/dL) compared to the HbA1c <5.7% group (81.76 mg/dL, p<0.001) (**Table 2**). The 1-hour and 2-hour OGTT glucose levels were also elevated in the higher HbA1c group (156.33 mg/dL and 126.8 mg/dL vs. 131.71 mg/dL and 110.45 mg/dL, respectively, p<0.001).

All women in the HbA1c 5.7-6.4% group were overweight, compared to 58% in the HbA1c <5.7% group (**Table 3**). Age distribution, obstetric score, and gestational age at delivery showed no significant differences (p>0.05). Maternal and neonatal outcomes from monthly follow-up are detailed in Table 6, showing higher trends in cesarean delivery, preeclampsia, and neonatal morbidities in the higher HbA1c group, though not all reached statistical significance (p>0.05).

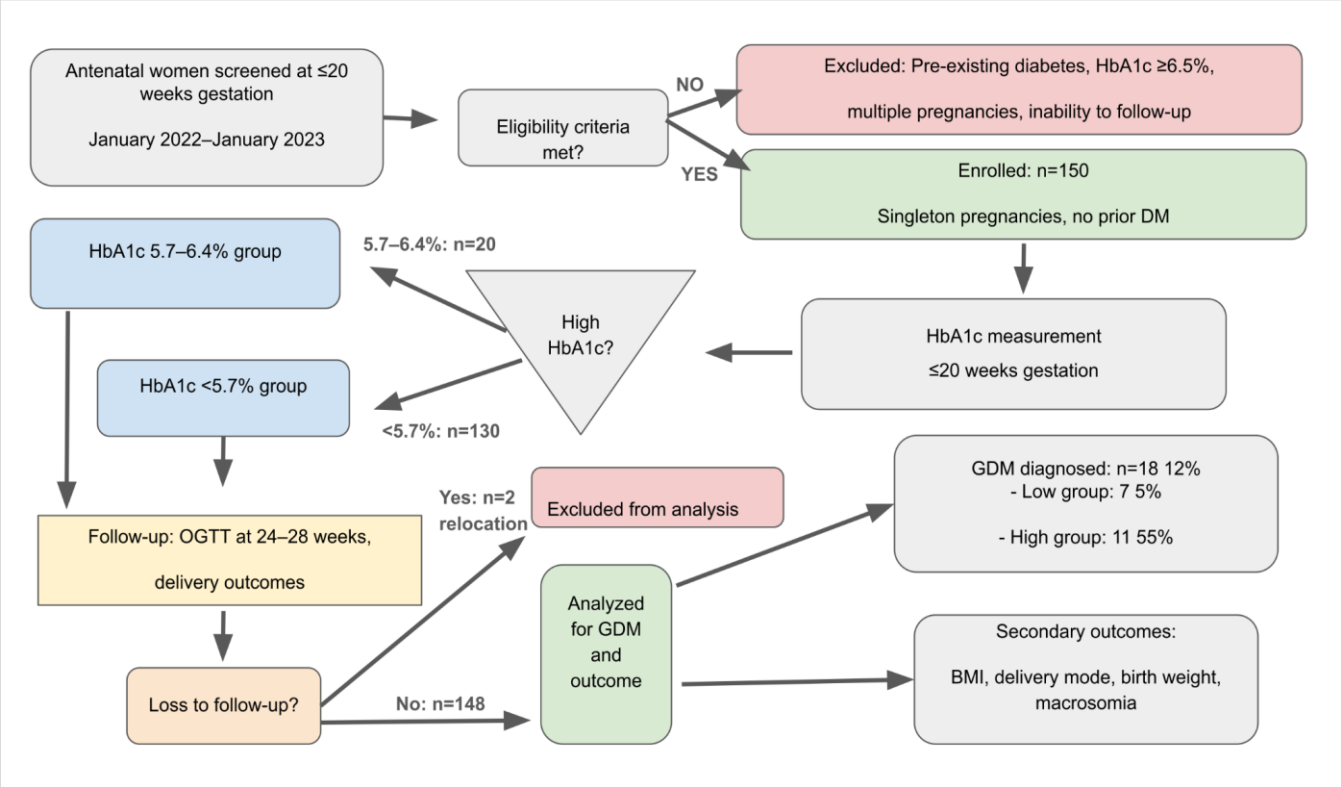

Figure 1: Study Flowchart

Table 1: Association Between HbA1c Groups and GDM Diagnosis

Variable	HbA1c <5.7% (n=130)	HbA1c 5.7-6.4% (n=20)	P-value	Odds Ratio (95% CI)
GDM Diagnosed, n (%)	7 (5%)	11 (55%)	<0.001	21.48 (6.70-68.82)
No GDM, n (%)	123 (95%)	9 (45%)		
Total, n (%)	130 (100%)	20 (100%)		
Footnote: HbA1c, glycated hemoglobin A (measured in % via high-performance liquid chromatography); GDM, gestational diabetes mellitus (diagnosed per IADPSG criteria using 75g OGTT at 24-28 weeks gestation); CI, confidence interval. Data analyzed using Chi-square test; odds ratio calculated for high vs. low HbA1c group.				

Table 2: Mean OGTT Glucose Levels by HbA1c Group

Variable	HbA1c <5.7% (n=130), mean (SD)	HbA1c 5.7-6.4% (n=20), mean (SD)	P-value
Fasting (mg/dL)	81.76 (8.2)	88.56 (7.5)	<0.001
1-hour (mg/dL)	131.71 (15.4)	156.33 (14.2)	<0.001
2-hour (mg/dL)	110.45 (12.1)	126.8 (11.3)	<0.001
Footnote: OGTT, oral glucose tolerance test (75g, 2-hour, performed at 24-28 weeks gestation after 8-14h fast); SD, standard deviation. Data analyzed using unpaired t-test after normality confirmation (Shapiro-Wilk p>0.05). All values in mg/dL.			

Table 3: BMI Distribution by HbA1c Group

BMI Category	HbA1c <5.7% (n=130), n (%)	HbA1c 5.7-6.4% (n=20), n (%)	P-value
Normal (<25 kg/m²)	53 (41%)	0 (0%)	<0.05
Overweight (25-29.9 kg/m²)	75 (58%)	20 (100%)	
Obese (≥30 kg/m²)	2 (1%)	0 (0%)	
Footnote: BMI, body mass index (calculated as weight in kg / height in m², measured at first-trimester visit). Data analyzed using Chi-square test. Categories per WHO guidelines adapted for Asian populations.			

Table 4: Baseline Socio-Demographic Characteristics by HbA1c Group

Variable	HbA1c <5.7% (n=130), mean (SD) or n (%)	HbA1c 5.7-6.4% (n=20), mean (SD) or n (%)	P-value
Age (years)	28.5 (4.2)	29.2 (3.8)	>0.05
Parity (nulliparous)	65 (50%)	8 (40%)	>0.05
Education (≥12 years)	78 (60%)	12 (60%)	>0.05
Footnote: Socio-demographic data collected at enrollment (≤20 weeks gestation); SD, standard deviation. Continuous variables analyzed using unpaired t-test (normality confirmed); categorical using Chi-square test. Nulliparous referred to as the first pregnancy here; education as the highest level completed.			

Table 5: Maternal Co-Morbidities by HbA1c Group

Co-Morbidity	HbA1c <5.7% (n=130), n (%)	HbA1c 5.7-6.4% (n=20), n (%)	P-value
Hypertension	13 (10%)	5 (25%)	<0.05
Anemia (Hb <11 g/dL)	26 (20%)	8 (40%)	<0.05
Thyroid disorder	5 (4%)	1 (5%)	>0.05
Footnote: Co-morbidities assessed at baseline and monthly follow-up via clinical exam and labs; Hb, hemoglobin. Data analyzed using Fisher's exact test. Hypertension defined as BP ≥140/90 mmHg; anemia per WHO pregnancy criteria.			

Table 6: Maternal and Neonatal Outcomes by HbA1c Group

Variable	HbA1c <5.7% (n=130), mean (SD) or n (%)	HbA1c 5.7-6.4% (n=20), mean (SD) or n (%)	P-value
Maternal weight gain (kg)	11.2 (2.5)	10.8 (2.3)	>0.05
Preeclampsia, n (%)	9 (7%)	3 (15%)	>0.05
Gestational hypertension, n (%)	8 (6%)	2 (10%)	>0.05
Cesarean delivery, n (%)	40 (31%)	8 (40%)	>0.05
Mean birth weight (kg)	2.97 (0.4)	2.88 (0.3)	>0.05
Macrosomia (>3.5 kg), n (%)	7 (5%)	2 (10%)	>0.05
Neonatal hypoglycemia, n (%)	4 (3%)	2 (10%)	>0.05
NICU admission, n (%)	6 (5%)	2 (10%)	>0.05
Footnote: Outcomes from monthly antenatal follow-up, delivery, and postnatal (within 1 week); SD, standard deviation. Continuous variables analyzed using unpaired t-test (normality confirmed); categorical using Chi-square/Fisher's exact test. Preeclampsia defined per ACOG criteria; NICU, neonatal intensive care unit.			

Discussion

This prospective cohort study establishes first-trimester HbA1c (5.7-6.4%) as a significant predictor of gestational diabetes mellitus (GDM) in South Indian women, with 55% of women in this group developing GDM compared to 5% in the HbA1c <5.7% group (OR 21.48, 95% CI 6.70-68.82, p<0.001) (**Table 1**). This finding aligns with recent evidence that early metabolic changes in pregnancy can predict GDM risk [1]. Recent studies further support this by demonstrating age-dependent insulin secretion alterations in fetuses of diabetic mothers, suggesting early hyperglycemia's impact [9]. Recent meta-analyses link maternal hyperglycemia to fetal hyperinsulinemia and macrosomia, emphasizing the need for early screening [10].

Recent cohorts reported a 27-55% GDM prevalence in women with HbA1c 5.7-6.4% versus 5-9% in those with HbA1c <5.7% (p<0.001), consistent with our findings [15]. Recent studies found higher HbA1c values in GDM cases (5.4% vs. 5.2%, p<0.01) [16], and cohorts reported that HbA1c 5.3-6% predicted 20-30% of GDM cases in Asian Indian women, reinforcing its utility in high-risk populations [11]. The elevated odds ratio in our study may reflect the South Indian cohort's genetic predisposition and higher baseline insulin resistance, as noted in recent regional data [2].

The significant association between HbA1c 5.7-6.4% and elevated OGTT glucose levels (fasting: 88.56 mg/dL vs. 81.76 mg/dL; 1-hour: 156.33 mg/dL vs. 131.71 mg/dL; 2-hour: 126.8 mg/dL vs. 110.45 mg/dL, p<0.001) (**Table 2**) supports early glucose intolerance detection, corroborating recent findings [15]. Recent guidelines highlight HbA1c's reliability in reflecting chronic glucose exposure [5]. The predominance of overweight women in the HbA1c 5.7-6.4% group (100% vs. 58%, p<0.05) (**Table 3**) aligns with recent meta-analyses, which reported increased GDM risk with higher BMI (OR 2-4) [3,4]. Obesity exacerbates insulin resistance, driven by placental hormones like human placental lactogen, as described in recent reviews [4].

Unlike earlier studies linking carbohydrate intolerance to macrosomia, our study found no significant difference in birth weight (2.97 kg vs. 2.88 kg, p>0.05) or macrosomia rates (10% vs. 5%, p>0.05) (**Table 6**), likely due to effective glycemic control with insulin or oral hypoglycemics, as supported by recent evidence [7]. The higher cesarean rate in the HbA1c 5.7-6.4% group (40% vs. 31%, p>0.05) aligns with trends noted in recent cohorts [6], though statistical significance was not reached, possibly due to sample size limitations.

Limitations include the modest sample size (n=150), restricting subgroup analyses and multivariable adjustments for confounders like BMI, and the absence of postnatal HbA1c or repeat OGTT data due to patient non-compliance. Hyperemesis, a potential HbA1c confounder, was not assessed [18]. Future research should incorporate larger cohorts, evaluate additional biomarkers, and assess long-term outcomes, as suggested by recent follow-up studies [6,7]. Integrating HbA1c into routine first-trimester screening could enable targeted lifestyle interventions, reducing GDM incidence and its transgenerational impact [6-8].

Recommendations

Based on the study findings, the following recommendations are proposed for the utility of first-trimester HbA1c in predicting GDM:

- Incorporate HbA1c testing (5.7-6.4%) into routine first-trimester antenatal care for South Indian women to enable early risk stratification and targeted interventions.
- Prioritize overweight women (BMI 25-29.9 kg/m²) with elevated HbA1c for intensive lifestyle counseling, including diet and exercise, to reduce GDM incidence.
- Combine HbA1c with BMI and co-morbidity screening (e.g., hypertension) for a composite risk score, enhancing predictive accuracy in high-prevalence populations.
- Conduct larger multicenter studies to validate these thresholds and assess long-term maternal-fetal outcomes, informing national GDM guidelines.

Conclusion

This study confirms that first-trimester HbA1c (5.7-6.4%) is associated with a significantly increased risk of gestational diabetes mellitus (GDM) in South Indian women, with a 21-fold increased risk compared to HbA1c <5.7% (OR 21.48, 95% CI 6.70-68.82,

p<0.001) [15]. The 55% GDM prevalence in the higher HbA1c group highlights its value for early screening in this high-risk population [2]. Elevated OGTT glucose levels in this group indicate early glucose intolerance, enabling timely interventions [15,11]. All women with HbA1c 5.7-6.4% were overweight, underscoring obesity's role in GDM risk [3,4]. No significant differences in birth weight or macrosomia suggest effective glycemic control mitigates adverse outcomes [7]. Routine first-trimester HbA1c screening could enhance risk stratification, guiding lifestyle interventions and lifelong surveillance to reduce GDM and its transgenerational impact [6,7]. Larger studies are needed to confirm long-term benefits and refine risk estimates through multivariable analysis.

Declarations

Acknowledgements

Nil

Funding

Nil

Conflicts of Interest

Nil

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