



STUDY OF EARLY-PREGNANCY HbA1c AS A PREDICTOR OF GESTATIONAL DIABETES MELLITUS AT A TERTIARY CARE CENTRE

Dr Pallavi Walmik Tidke *	Associate Professor, Department of OBGY, R K Damani Medical College SRIMS, Chhatrapati Sambhajanagar. *Corresponding Author
Dr Aniket Shivaji Chate	Associate Professor, Department of Medicine, R K Damani Medical College SRIMS, Chhatrapati Sambhajanagar.
Dr Smita Ramesh Kakad	Assistant Professor, Department of Paediatrics, Dr. Ulhas Patil Medical College, Jalgaon.

ABSTRACT **Background:** Gestational diabetes mellitus (GDM) is conventionally diagnosed at 24–28 weeks of gestation, although metabolic abnormalities may be detectable earlier. Glycated haemoglobin (HbA1c) is convenient, does not require fasting, and may help identify pregnant women at increased risk of subsequently developing GDM. **Objectives:** To evaluate early-pregnancy HbA1c as a predictor of subsequent GDM and to assess its association with established maternal risk factors and pregnancy outcomes. **Methods:** This prospective observational study included 1,256 women with singleton pregnancies enrolled during early pregnancy in the Department of Obstetrics and Gynaecology, R K Damani Medical College SRIMS, Chhatrapati Sambhajanagar, from January to December 2025. HbA1c was measured during early pregnancy, and eligible women subsequently underwent GDM assessment at 24–28 weeks using the DIPSI 75-g oral glucose test. Maternal demographic characteristics, body mass index (BMI), family history of diabetes, previous GDM and obstetric outcomes were recorded. Receiver operating characteristic (ROC) analysis and logistic regression were used to evaluate predictive performance and associated maternal risk factors. **Results:** GDM was diagnosed in 226 of 1,256 women (17.99%). Women who subsequently developed GDM were older, had higher BMI, and more frequently had a family history of diabetes. Mean first-trimester HbA1c was significantly higher among women who subsequently developed GDM than among those who remained normoglycaemic ($5.32 \pm 0.31\%$ vs $4.94 \pm 0.36\%$; $p < 0.001$). The proportion developing GDM increased progressively from 8.53% among women with HbA1c $< 5.2\%$ to 62.90% among those with HbA1c 5.9–6.4%. At an HbA1c threshold of $\geq 5.4\%$, sensitivity was 62.83%, specificity 86.99%, positive predictive value 51.45%, and negative predictive value 91.43%; the AUC was 0.80 (95% CI 0.77–0.83; $p < 0.001$). **Conclusion:** Higher early-pregnancy HbA1c was associated with a progressively greater probability of subsequent GDM. HbA1c may be useful for early risk stratification, particularly when interpreted with conventional maternal risk factors, but it should not replace definitive glucose-based testing at 24–28 weeks.

KEYWORDS : Gestational diabetes mellitus; Glycated haemoglobin; HbA1c; First trimester; Pregnancy; Risk prediction; Oral glucose tolerance test

INTRODUCTION

Gestational diabetes mellitus is an important metabolic complication of pregnancy and is associated with increased maternal and neonatal morbidity. Increasing maternal glycaemia is continuously associated with adverse outcomes, including large-for-gestational-age birth, fetal hyperinsulinaemia, neonatal adiposity, hypertensive disorders and operative delivery.^{1,2} In women without previously recognised diabetes, conventional GDM testing is generally undertaken at 24–28 weeks of gestation.³

Metabolic alterations may begin substantially earlier, creating interest in biomarkers that could identify women at increased risk before the conventional diagnostic window. Recent Indian data reinforce the clinical relevance of this problem. The ICMR-INDIAB national study reported a weighted GDM prevalence of 22.4%, with substantial regional variation and a prevalence of 16.0% in West India.⁴

HbA1c reflects average glycaemic exposure over the preceding several weeks and offers practical advantages because it does not require fasting or administration of a glucose load. Its predictive value is particularly relevant in Indian women, in whom background dysglycaemia, adiposity patterns and GDM prevalence may differ from many Western populations. The present study therefore evaluated early-pregnancy HbA1c as a predictor of subsequent GDM in women attending a tertiary-care centre in Chhatrapati Sambhajanagar.

MATERIALS AND METHODS

This prospective observational study was conducted in the Department of Obstetrics and Gynaecology, R K Damani Medical College SRIMS, Chhatrapati Sambhajanagar, Maharashtra, India, between January 2025 and December 2025. Written informed consent was obtained from participants. The Institutional Ethics Committee approval was taken before commencing present study.

INCLUSION CRITERIA

- Pregnant women aged ≥ 18 years.
- Singleton pregnancy.
- Enrolment during early pregnancy. (≤ 12 weeks).

- Underwent early-pregnancy HbA1c measurement.
- Completion of GDM assessment at 24–28 weeks.
- Written informed consent.

EXCLUSION CRITERIA

- Known type 1 or type 2 diabetes mellitus before pregnancy.
- Overt diabetes detected during early pregnancy.
- Multiple pregnancy.
- Known haemoglobinopathy likely to affect HbA1c interpretation.
- Recent blood transfusion.
- Severe medical disorder substantially affecting glucose or erythrocyte metabolism.
- Chronic systemic corticosteroid therapy.
- Failure to complete definitive GDM testing.
- Incomplete essential study data.

A total of 1,256 eligible women who completed early-pregnancy evaluation and subsequent GDM assessment constituted the final analytical cohort. Women were enrolled during the first trimester. Maternal age, parity, booking BMI, family history of diabetes, previous GDM and previous macrosomia were recorded.

Maternal weight and height were measured at enrolment, and BMI was calculated as weight in kilograms divided by height in metres squared. Early-pregnancy venous blood was obtained for HbA1c estimation, and HbA1c was recorded as a percentage. “At enrolment, fasting plasma glucose and random plasma glucose were also recorded as part of the baseline metabolic assessment. Eligible women underwent definitive glucose-based GDM assessment at 24–28 weeks as per DIPSI guidelines. At 24–28 weeks of gestation, participants underwent a 75-g oral glucose tolerance test irrespective of the timing of the last meal. Venous plasma glucose was measured 2 hours after administration of 75 g oral glucose. GDM was diagnosed when the 2-hour plasma glucose concentration was ≥ 140 mg/dL, according to the DIPSI criterion.

The primary outcome was GDM diagnosed during the conventional 24–28-week testing window. For descriptive analysis, early HbA1c was grouped as $< 5.2\%$, 5.2–5.4%, 5.5–5.8%, and 5.9–6.4%; HbA1c

was also analysed as a continuous variable. Maternal and neonatal outcomes assessed included gestational hypertension, preeclampsia, preterm birth, caesarean delivery, macrosomia, large-for-gestational-age birth, neonatal hypoglycaemia and NICU admission.

Continuous variables were expressed as mean±standard deviation, and categorical variables as frequency and percentage. Continuous variables were compared using the independent-samples t-test; categorical variables were compared using the Chi-square test or Fisher exact test, as appropriate. ROC analysis was used to assess discrimination of early HbA1c for subsequent GDM. Area under the ROC curve (AUC), 95% confidence interval (CI), sensitivity, specificity, positive predictive value, negative predictive value and overall accuracy were reported. Logistic regression was used to evaluate associations between maternal risk factors and subsequent GDM. Results were expressed as crude and adjusted odds ratios (ORs) with 95% CIs. A two-sided p-value <0.05 was considered statistically significant.

RESULTS

A total of 1,256 women were included in the final analytical cohort; 226 (17.99%) developed GDM and 1,030 (82.01%) remained normoglycaemic. Women who subsequently developed GDM were significantly older (29.1±4.2 vs 26.6±4.0 years; $p<0.001$) and had a higher mean BMI (26.7±3.8 vs 23.9±3.5 kg/m²; $p<0.001$). Multigravida was more frequent in the GDM group than in the non-GDM group (58.85% vs 49.13%; $p=0.008$), whereas primigravida was less frequent (41.15% vs 50.87%; $p=0.008$). A family history of diabetes was present in 35.40% of women who developed GDM compared with 18.83% of those who remained normoglycaemic ($p<0.001$). Among multigravid women, previous GDM (18.80% vs 5.73%; $p<0.001$) and previous macrosomia (15.04% vs 8.10%; $p=0.015$) were also significantly more frequent in the GDM group. Mean early-pregnancy HbA1c was significantly higher among women who subsequently developed GDM (5.32±0.31% vs 4.94±0.36%; $p<0.001$).

Table 1. Baseline maternal characteristics according to subsequent GDM status

Characteristic	GDM (n=226)	Non-GDM (n=1,030)	p-value
Maternal age, years	29.1±4.2	26.6±4.0	<0.001
Gestational age at HbA1c, weeks	10.8±1.5	10.7±1.6	0.371
Primigravida	93 (41.15%)	524 (50.87%)	0.008
Multigravida	133 (58.85%)	506 (49.13%)	0.008
BMI, kg/m ²	26.7±3.8	23.9±3.5	<0.001
Family history of diabetes	80 (35.40%)	194 (18.83%)	<0.001
Previous GDM*	25/133 (18.80%)	29/506 (5.73%)	<0.001
Previous macrosomia*	20/133 (15.04%)	41/506 (8.10%)	0.015
Early HbA1c, %	5.32±0.31	4.94±0.36	<0.001

BMI, body mass index; GDM, gestational diabetes mellitus; HbA1c, glycated haemoglobin.

*Calculated among multigravid women only.

Early-pregnancy glycaemic indices were consistently higher among women who later developed GDM. Mean HbA1c was 5.32±0.31% in the GDM group compared with 4.94±0.36% in the non-GDM group, corresponding to a mean difference of 0.38 percentage points ($p<0.001$). Mean fasting plasma glucose was also higher in the GDM group (84.6±7.4 vs 80.9±6.6 mg/dL; mean difference 3.7 mg/dL; $p<0.001$), as was random plasma glucose (104.8±14.2 vs 98.1±13.6 mg/dL; mean difference 6.7 mg/dL; $p<0.001$).

Table 2. Early-pregnancy glycaemic parameters according to subsequent GDM status

Parameter	GDM (n=226)	Non-GDM (n=1,030)	Mean difference	p-value
HbA1c, %	5.32±0.31	4.94±0.36	+0.38	<0.001
Fasting plasma glucose, mg/dL	84.6±7.4	80.9±6.6	+3.7	<0.001
Random plasma glucose, mg/dL	104.8±14.2	98.1±13.6	+6.7	<0.001

AUC, area under the receiver operating characteristic curve; CI, confidence interval; GDM, gestational diabetes mellitus; HbA1c, glycated haemoglobin.

HbA1c categories were selected a priori based on previously reported early-pregnancy HbA1c thresholds and to evaluate the graded relationship between HbA1c and subsequent GDM. A clear graded increase in subsequent GDM was observed across increasing early-pregnancy HbA1c categories. GDM developed in 8.53% of women with HbA1c <5.2%, 18.73% with HbA1c 5.2–5.4%, 33.95% with HbA1c 5.5–5.8%, and 62.90% with HbA1c 5.9–6.4%. The proportion developing GDM increased progressively across the HbA1c categories, reaching 62.90% in the highest category compared with 8.53% in the lowest category.

Table 3. Subsequent GDM according to early-pregnancy HbA1c category

Early HbA1c	Total women	Developed GDM	Non-GDM	GDM proportion
<5.2%	680	58	622	8.53%
5.2–5.4%	299	56	243	18.73%
5.5–5.8%	215	73	142	33.95%
5.9–6.4%	62	39	23	62.90%
Total	1,256	226	1,030	17.99%

ROC analysis demonstrated statistically significant discrimination of early-pregnancy HbA1c for subsequent GDM (AUC 0.80; 95% CI 0.77–0.83; $p<0.001$). The optimal HbA1c cutoff was identified using the maximum Youden index. At the study-specific threshold of HbA1c ≥5.4%, sensitivity was 62.83% and specificity was 86.99%. The positive predictive value was 51.45%, whereas the negative predictive value was 91.43%, with an overall classification accuracy of 82.64%. The threshold showed higher specificity than sensitivity and a high negative predictive value in this study population.

Table 4. Predictive performance of early-pregnancy HbA1c for subsequent GDM

Predictive parameter	Result
Study-specific HbA1c threshold	≥5.4%
True positive	142
False negative	84
True negative	896
False positive	134
Sensitivity	62.83%
Specificity	86.99%
Positive predictive value	51.45%
Negative predictive value	91.43%
Overall accuracy	82.64%
AUC	0.80
95% CI	0.77–0.83
p-value	<0.001

In present study, several variables remained independently associated with subsequent GDM after adjustment. Each 0.1% increase in early HbA1c was associated with 35% higher adjusted odds of GDM (adjusted OR 1.35, 95% CI 1.27–1.44; $p<0.001$). Maternal age (adjusted OR 1.08 per year, 95% CI 1.04–1.12; $p<0.001$), BMI (adjusted OR 1.13 per kg/m², 95% CI 1.08–1.18; $p<0.001$), family history of diabetes (adjusted OR 1.72, 95% CI 1.21–2.45; $p=0.003$), and previous GDM (adjusted OR 2.41, 95% CI 1.29–4.51; $p=0.006$) were also independently associated with GDM. Previous macrosomia and multigravida were significant in univariate analysis but were no longer statistically significant after multivariable adjustment.

Table 5. Univariate and multivariable predictors of subsequent GDM

Variable	Crude OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
HbA1c, per 0.1% increase	1.42 (1.35–1.50)	<0.001	1.35 (1.27–1.44)	<0.001
Maternal age, per year	1.15 (1.11–1.19)	<0.001	1.08 (1.04–1.12)	<0.001
BMI, per kg/m ²	1.23 (1.18–1.28)	<0.001	1.13 (1.08–1.18)	<0.001
Family history of diabetes	2.34 (1.71–3.20)	<0.001	1.72 (1.21–2.45)	0.003
Previous GDM	3.79 (2.15–6.68)	<0.001	2.41 (1.29–4.51)	0.006
Previous macrosomia	2.00 (1.13–3.53)	0.017	1.36 (0.73–2.53)	0.332
Multigravida	1.48 (1.11–1.98)	0.009	1.18 (0.85–1.65)	0.330

BMI, body mass index; CI, confidence interval; GDM, gestational diabetes mellitus; OR, odds ratio.

Maternal and neonatal adverse outcomes were more frequent among women with GDM. Gestational hypertension occurred in 13.27% of the GDM group versus 7.18% of the non-GDM group ($p=0.003$), and preeclampsia in 8.41% versus 4.37%, respectively ($p=0.012$). Caesarean delivery was significantly more frequent among women with GDM (42.04% vs 32.62%; $p=0.007$), and mean birth weight was higher (3085 ± 448 vs 2960 ± 421 g; $p<0.001$). Macrosomia occurred in 8.41% versus 3.59% ($p=0.001$), while large-for-gestational-age birth occurred in 12.39% versus 5.63% ($p<0.001$). Neonatal hypoglycaemia (7.52% vs 2.52%; $p<0.001$) and NICU admission (14.16% vs 8.74%; $p=0.013$) were also significantly more frequent in the GDM group. Among women with GDM, 28.32% required insulin therapy. The difference in preterm birth (12.39% vs 8.35%) did not reach statistical significance ($p=0.056$). Among women diagnosed with GDM, the requirement for insulin therapy during pregnancy was also recorded.

Table 6. Maternal and neonatal outcomes according to GDM status

Outcome	GDM (n=226)	Non-GDM (n=1,030)	p-value
Gestational hypertension	30 (13.27%)	74 (7.18%)	0.003
Preeclampsia	19 (8.41%)	45 (4.37%)	0.012
Insulin requirement among GDM	64 (28.32%)	NA	—
Preterm birth	28 (12.39%)	86 (8.35%)	0.056
Caesarean delivery	95 (42.04%)	336 (32.62%)	0.007
Birth weight, g	3085 ± 448	2960 ± 421	<0.001
Macrosomia	19 (8.41%)	37 (3.59%)	0.001
Large for gestational age	28 (12.39%)	58 (5.63%)	<0.001
Neonatal hypoglycaemia	17 (7.52%)	26 (2.52%)	<0.001
NICU admission	32 (14.16%)	90 (8.74%)	0.013

GDM, gestational diabetes mellitus; LGA, large for gestational age; NICU, neonatal intensive care unit; NA, not applicable.

DISCUSSION

In the present prospective observational study of 1,256 pregnant women, GDM was diagnosed in 17.99%. Women who subsequently developed GDM had higher early HbA1c than women who remained normoglycaemic, and the proportion developing GDM increased progressively across HbA1c categories. At the study-specific HbA1c threshold of $\geq 5.4\%$, discrimination was moderate (AUC 0.80), with higher specificity than sensitivity. These findings support the concept that early HbA1c may contribute to risk stratification but is insufficient as a stand-alone replacement for definitive glucose-based testing later in pregnancy.

The approximately 18% GDM frequency is within the range reported in contemporary Indian studies. In the STRiDE prospective cohort, Saravanan et al. reported GDM at 24–28 weeks in 19.2% of Indian participants.⁹ Khandelwal et al. reported GDM in 43 of 270 women (15.9%) in a prospective Indian cohort.¹⁰ The nationally representative ICMR-INDIAB study reported a weighted national GDM prevalence of 22.4%, with substantial regional variation and a prevalence of 16.0% in West India.⁴ Differences between studies may reflect diagnostic criteria, gestational age at testing, referral patterns and baseline metabolic risk.

The higher early HbA1c among women subsequently developing GDM is consistent with prior evidence. Hinkle et al. found that first-trimester HbA1c was associated with later GDM and that increasing HbA1c conferred progressively greater risk.⁵ Punnose et al. evaluated 2,275 Asian-Indian women and found first-trimester HbA1c to be independently associated with subsequent GDM, although discrimination was insufficient for HbA1c to function as a stand-alone diagnostic test.⁸ These observations support the biological concept that subtle dysglycaemia may precede the conventional diagnostic window.

The STRiDE analysis is particularly relevant to early risk stratification in India. Saravanan et al. showed that early HbA1c independently predicted later GDM and that models combining HbA1c with age, BMI and family history improved predictive performance. Their India-specific HbA1c-alone thresholds included approximately 5.4% for rule-in and 4.9% for rule-out strategies.⁹

Khandelwal et al. also evaluated first-trimester glycaemic markers in an Indian prospective cohort and reported useful discrimination for early HbA1c, while emphasizing the benefit of combining glycaemic and clinical risk variables.¹⁰ This reinforces the interpretation that HbA1c is more appropriately used as one component of a multivariable risk-stratification approach rather than as an isolated diagnostic test.

Shrivastava et al., from Dr D. Y. Patil Medical College, Pune, studied 500 pregnant women and reported increasing GDM frequency with higher HbA1c values.¹¹ Their diagnostic approach and timing differed from the present study, limiting direct numerical comparison, but the study provides relevant regional evidence linking higher HbA1c with GDM risk.

The graded rise in GDM across HbA1c categories is clinically important. Hughes et al. reported that early-pregnancy HbA1c $\geq 5.9\%$ identifies women at increased risk of dysglycaemia and adverse pregnancy outcomes.⁶ Current ADA guidance also recognises abnormal early-pregnancy glycaemic states as markers of increased metabolic risk.³ Nonetheless, interpretation requires caution because pregnancy-related changes in erythrocyte turnover and iron status can influence HbA1c values.

A sensitivity of approximately 63% indicates that HbA1c $\geq 5.4\%$ would miss a substantial proportion of women who later develop GDM if used as the sole screening criterion. The higher specificity suggests that women above the threshold constitute a higher-risk subgroup, while the high negative predictive value partly reflects the underlying GDM frequency. Systematic reviews have similarly concluded that elevated early HbA1c is associated with subsequent GDM but lacks adequate sensitivity to replace standard glucose-based assessment.^{7,12}

The physiological limitations of HbA1c deserve emphasis. Pregnancy shortens erythrocyte lifespan, which may lower HbA1c, whereas iron deficiency can increase measured HbA1c. Haemoglobinopathies, renal disease, transfusion and other disorders affecting erythrocyte turnover may also alter interpretation. These factors are particularly relevant in antenatal populations and may contribute to variation in proposed HbA1c thresholds between studies.

Taken together, the findings support early HbA1c as a convenient marker for risk stratification rather than definitive diagnosis. Women with higher early HbA1c may warrant earlier nutritional counselling, appropriate gestational-weight monitoring and closer metabolic surveillance. However, identification of increased risk is not equivalent to a diagnosis of GDM, and definitive 24–28-week glucose-based testing should continue unless future validated pathways demonstrate an alternative approach.

The strengths of this study include its prospective observational design, first-trimester assessment of HbA1c before conventional GDM testing, follow-up through the 24–28-week diagnostic window, and evaluation of HbA1c both as a continuous variable and using ROC analysis. Important limitations include the single-centre design, possible influence of iron deficiency and other conditions affecting erythrocyte turnover on HbA1c measurements, and lack of external validation of the derived HbA1c threshold. In addition, the study did not evaluate whether incorporating HbA1c into a multivariable prediction model improves clinical outcomes compared with conventional GDM screening alone.

CONCLUSION

Early-pregnancy HbA1c was associated with subsequent GDM, with a progressive increase in GDM proportion across increasing HbA1c categories. A study-specific HbA1c threshold of $\geq 5.4\%$ showed moderate sensitivity and relatively high specificity, supporting its potential role in early risk stratification rather than definitive diagnosis. Early HbA1c may help identify women who warrant closer metabolic surveillance and reinforcement of standard antenatal lifestyle counselling before conventional GDM testing. However, because HbA1c alone would miss a clinically important proportion of women who later develop GDM, standard glucose-based assessment at 24–28 weeks should continue. Larger multicentre Indian studies and external validation of combined HbA1c-based prediction models are required before routine adoption.

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