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Glycated Hemoglobin: A Useful Screening Tool for Gestational Diabetes Mellitus

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ABSTRACT

Background:

Gestational diabetes mellitus (GDM) is defined as a varying degree of carbohydrate intolerance that is recognized or first onset during pregnancy. It is associated with several maternal complications, including hypertensive disorders, hydramnios, preterm labor, operative delivery, shoulder dystocia, and perineal injuries. Early screening and treatment of GDM during the antenatal period are crucial, as they significantly reduce the risk of adverse maternal and perinatal outcomes. In India, universal screening is preferred over selective screening to facilitate early detection and improve pregnancy management.The methods for screening GDM have been a subject of controversy, transitioning from selective to universal screening approaches. Current screening modalities include measuring plasma glucose levels, conducting glucose challenge tests, or performing oral glucose tolerance tests (OGTT). The OGTT is recognized as the gold standard for screening GDM, although it presents challenges due to its time-consuming, costly, and unpalatable nature Recent studies indicate that during pregnancy, HbA1c levels exhibit less biological variation and may be linked to GDM. Measuring mid-trimester HbA1c levels could potentially reduce the reliance on OGTT, with multiple studies showing a correlation between HbA1c levels and obstetrical complications such as macrosomia and birth injuries.Despite these findings, the current recommendations do not endorse the use of HbA1c as a standalone diagnostic test for GDM. Therefore, this study aims to evaluate the effectiveness of glycosylated hemoglobin in diagnosing GDM in combination with a 75 gm OGTT, as per DIPSI guidelines, and its association with adverse maternal and neonatal effects.

Aim of the Study:

The primary objective of this study is to assess the usefulness of HbA1c levels in diagnosing gestational diabetes mellitus and to investigate their association with adverse maternal and neonatal outcomes.

Materials and methods:.

This prospective cohort study involved 500 antenatal patients attending the Outpatient Department of Obstetrics and Gynecology and the Department of Biochemistry at an Obstetric Hospital. The study included women with singleton pregnancies and excluded those with hemoglobin levels below 10 gm%, a history of type 2 diabetes mellitus, known hemoglobinopathies or variants, chronic kidney disease, hepatic disease, tuberculosis, or those on corticosteroids.

Statistical analyses were performed using SPSS software version 22.0, with comparisons made using Chi-square tests. A receiver operating characteristic curve was constructed to evaluate the association between mid-trimester HbA1c levels and GDM. Multiple logistic regression analysis was conducted to investigate the relationship between HbA1c levels and adverse perinatal outcomes, considering a p-value of <0.05 as statistically significant.

Results:

The mean (±SD) HbA1c was 5.50 ± 0.8 % in mothers with GDM and it was 4.8 ± 0.8 % in non-GDM mothers. The study identified an HbA1c cutoff value of 5.15% as the optimal threshold for predicting gestational diabetes mellitus (GDM). At this cutoff, the sensitivity is 77.44%, meaning that the test correctly identifies 77.44% of women with GDM. The specificity is 73.29%, indicating that 73.29% of normoglycemic women are correctly identified as not having GDM. These figures suggest a balanced performance at this threshold, making it a useful tool for GDM screening.The accuracy of the HbA1c cutoff at 5.15% is 70.33%, reflecting the overall proportion of correct classifications.

Conclusions: HbA1c with a cutoff of 5.15% can be used as a screening test and avoid the need of OGTT in approximately 50% of antenatal women.

Keywords: Gestational diabetes mellitus, Glycated hemoglobin, Maternal and neonatal outcome.

INTRODUCTION:

Gestational Diabetes Mellitus (GDM) represents a significant public health concern, characterized by glucose intolerance during pregnancy. According to the World Health Organization's 1999 definition, GDM is defined as carbohydrate intolerance leading to varying degrees of hyperglycemia that first emerges or is recognized during pregnancy [1]. The complexities surrounding the characterization of glucose intolerance in pregnancy have led to extensive debate within clinical and research settings over the past thirty years [2]. The potential for GDM to develop concurrently with pregnancy raises the risk of undiagnosed cases, which can result in adverse outcomes for both mothers and newborns [3]. Therefore, increased awareness and effective screening strategies are essential to mitigate the risks associated with GDM [4]. The International Diabetes Federation (IDF) reported in 2019 that approximately 1 in 11 individuals globally have diabetes, with 75% of these cases found in low- and middle-income countries [5]. The prevalence of Gestational Diabetes Mellitus (GDM) exhibits significant global variation, ranging from 10.1% in Eastern and Southeastern Asia to 13.61% in Africa, influenced by factors such as screening strategies, diagnostic criteria, and ethnic composition of the population [6]. In the South East Asia region, hyperglycemia in pregnancy affects around 6.9 million live births, with a prevalence rate of 24.2% [7]. In India, the prevalence of GDM varies widely, reported to be between 3% and 35%, reflecting the need for improved screening and management strategies to address this growing public health challenge [8]. The Diabetes in Pregnancy Study Group of India currently recommends universal screening for Gestational Diabetes Mellitus (GDM) using a non-fasting 2-hour 75g Oral Glucose Tolerance Test (OGTT), with a diagnostic threshold set at a 2-hour value greater than 140 mg/dL [9]. While the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria, derived from the extensive Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study, have gained global acceptance, they face criticism for producing a high number of false-positive results due to lower fasting cutoffs, which contributes to the GDM burden [10]. Furthermore, the applicability of international diagnostic criteria to the Indian population may be questionable, as the HAPO study did not adequately represent Indian demographics, necessitating the development of more tailored screening and diagnostic approaches for this population [11]. To address the inconsistencies in the diagnosis and management of Gestational Diabetes Mellitus (GDM), the Maternal Health Division of the Ministry of Health and Family Welfare, Government of India, developed technical and operational guidelines in February 2018 [12]. Despite these efforts, subsequent studies reveal significant variability in GDM prevalence across India, ranging from 0% in Manipur to 42% in Lucknow, Uttar Pradesh [13]. This variability may be attributed to genetic differences among populations and varying screening practices [14]. A nationwide prospective study conducted by FOGSI and DIPSI in 2021 indicated that approximately one-third of pregnant women are diagnosed with GDM during the first trimester, with over a quarter having a history of fetal loss in previous pregnancies [15]. These findings underscore the need for standardized screening practices and tailored interventions to effectively manage GDM in diverse populations across India [16].

Gestational Diabetes Mellitus (GDM) remains a contentious issue concerning its screening, diagnosis, and cost-effectiveness [17]. To address these challenges, we conducted a systematic review to estimate the national and regional prevalence of GDM among pregnant women, aiming to support the effective implementation of state-wise health programs [18]. This analysis investigates how various factors—such as differing screening criteria, geographical locations (urban versus rural areas), blood collection techniques, and the timing of screening (early versus late)—affect the observed prevalence of GDM in India [19]. By highlighting these variables, our findings seek to inform better-targeted strategies for GDM management and improve health outcomes for pregnant women across the country [20].

Diagnostic Criteria for Gestational Diabetes Mellitus (GDM) at 24–28 Weeks

Organization/Society	Criteria	Method	Tests	Interpretation
American Diabetes Association (2021) [21]	One-step OGTT with 75 g glucose	FPG, 1 h PG, 2 h PG	Diagnosis of GDM if one of the following criteria are met: FPG: ≥92 mg/dL (5.1 mmol/L) 1 h: ≥180 mg/dL (10.0 mmol/L) 2 h: ≥153 mg/dL (8.5 mmol/L)	
Endocrine Society (2013) [22]	Proceed to 100 g OGTT if 1 h PG exceeds institutional thresholds (cut-off values of 130 mg/dL, 135 mg/dL, or 140 mg/dL based on community prevalence rates of GDM)	FPG, 1 h PG, 2 h PG, 3 h PG		
World Health Organization (2013) and International Federation of Gynecology and Obstetrics (2015) [23]	One-step OGTT with 75 g glucose	FPG, 1 h PG, 2 h PG	A diagnosis of GDM requires that two or more thresholds be met or exceeded.	
American College of Obstetricians and Gynecologists (ACOG) (2018) [24]	Step 1: 1 h PG (50 g) glucose screen Step 2: 3 h PG (100 g OGTT)	FPG, 1 h PG, 2 h PG, 3 h PG	Carpenter–Coustan Criteria: FPG: ≥95 mg/dL (5.3 mmol/L) 1 h: ≥180 mg/dL (10.0 mmol/L) 2 h: ≥155 mg/dL (8.6 mmol/L) 3 h: ≥140 mg/dL (7.8 mmol/L)	
National Diabetes Data Group [25]	Step 1: 1 h PG (50 g) glucose screen Step 2: 3 h PG (100 g OGTT)	FPG, 1 h PG, 2 h PG, 3 h PG	FPG: ≥105 mg/dL (5.8 mmol/L) 1 h: ≥190 mg/dL (10.6 mmol/L) 2 h: ≥165 mg/dL (9.2 mmol/L) 3 h: ≥145 mg/dL (8.0 mmol/L)	

GDM Diagnostic Criteria at Other Stages of Pregnancy

Organization/Society (Year)	Test	Criteria	Timing	Target Population	Comments
American Diabetes Association (ADA) (2020) [26]	FPG, 2 h PG (75 g OGTT), HbA1c, RPG	Diagnose DM complicating pregnancy if: FPG ≥126 mg/dL (7.0 mmol/L) 2 h PG ≥200 mg/dL (11.1 mmol/L) HbA1c ≥6.5% (48 mmol/mol) RPG ≥200 mg/dL (11.1 mmol/L) with classic symptoms of hyperglycemia. Diagnose GDM if lower threshold for GDM met (specifics not defined)	First prenatal visit	Women with risk factors	Limitation and lack of evidence regarding applicability of IADPSG or 2-step criteria in the first half of pregnancy recognized and need for further work noted.
World Health Organization (2013) [27]	FPG, 1 h PG, 2 h PG (75 g OGTT)	Diagnose GDM if: FPG = 92–125 mg/dL (5.1–6.9 mmol/L) 1 h PG ≥180 mg/dL (10.0 mmol/L) 2 h PG = 153–199 mg/dL (8.5–11.0 mmol/L) Diagnose DM in pregnancy if: FPG ≥126 mg/dL (7.0 mmol/L) 2 h PG ≥200 mg/dL (11.1 mmol/L) RPG ≥200 mg/dL (11.1 mmol/L) in the presence of diabetes symptoms	Not defined	Not defined (needs to be decided by individual countries)	Definition of GDM applies to any time in pregnancy. Acknowledges that the benefit of diagnosing and treating GDM before the usual window of 24–28 weeks' gestation is not established.

The Oral Glucose Tolerance Test (OGTT) is commonly used to diagnose early gestational diabetes mellitus (eGDM), employing either the one-step method with IADPSG cut-offs or the two-step method based on Carpenter-Coustan criteria. Various guidelines recommend the one-step test for high-risk groups in the first trimester, but there is no consensus on the application of later diagnostic criteria earlier in pregnancy. Physiological changes during pregnancy lead to a significant reduction in insulin sensitivity, peaking at around 40–60% lower than non-pregnant states by the third trimester. While fasting plasma glucose (FPG) remains stable in the first trimester, postprandial glucose levels rise around the 16th week, normalizing postpartum. Early OGTT has shown some predictive value for subsequent gestational diabetes, particularly in specific populations, but a significant number of women diagnosed with eGDM revert to normal glucose levels by 24–28 weeks without intervention. This reversion, often influenced by elevated FPG levels, results in a higher incidence of false positives. Additionally, early diagnosis of eGDM has been linked to adverse pregnancy outcomes, such as congenital malformations and complications. Overall, first-trimester OGTT results may not reliably predict subsequent gestational diabetes, while later testing conducted in the late second trimester is more accurately associated with the diagnosis of cGDM. Further research is needed to explore the implications of elevated OGTT results in relation to maternal body mass index and metabolic dysfunction (28, 29).

HbA1c for Diagnosis of Early Gestational Diabetes Mellitus (eGDM): Diagnostic Potential of HbA1c. The American Diabetes Association (ADA) recommends using HbA1c, with a cutoff of ≥6.5%, as an alternative diagnostic criterion for diabetes, alongside fasting plasma glucose (FPG) criteria (≥7.0 mmol/L). HbA1c levels are strongly correlated with FPG and can serve as a reliable measure of chronic glycemia, helping in long-term diabetes management. However, the HbA1c cutoff remains controversial due to false-negative predictions, particularly in patients with borderline FPG and HbA1c levels between 6.0% and 6.5%. These individuals may need verification through combined FPG and HbA1c testing. Unlike FPG tests, which require fasting and are time-consuming, HbA1c can be measured at any time and has less biological variation, making it convenient for patients. Despite these advantages, HbA1c is not currently recommended for diagnosing chronic gestational diabetes mellitus (cGDM) due to confounding factors in pregnancy (30, 31).

Physiological Changes in Pregnancy Affecting HbA1c. Normal pregnancy slightly lowers HbA1c levels due to increased red blood cell turnover. This decline is more pronounced early in pregnancy and reaches a nadir in the early second trimester. Additionally, iron deficiency can prolong red blood cell survival, raising HbA1c levels. Ethnic differences also complicate the interpretation of HbA1c in pregnancy outcome (32).

Normative HbA1c Values in Pregnancy. There is no consensus on the normal HbA1c range during pregnancy. A multicenter Italian study found HbA1c values of 4.0%–5.5% in pregnant women compared to 4.8%–6.2% in non-pregnant women. Other studies reported specific ranges during trimesters, with values around 4.4%–5.6% for women with normoglycemia during pregnancy (33).

Predictive Accuracy of HbA1c in Early Pregnancy. An HbA1c level of ≥6.5% indicates overt diabetes in pregnancy, but no universally accepted cutoffs exist for diagnosing eGDM. Proposed thresholds range, with a lower cutoff of 4.8% showing high sensitivity (95%) for ruling out cGDM. Studies suggest that HbA1c levels between 5.25% and 6% have varying positive predictive values (PPVs) based on different OGTT criteria. A cutoff of 5.9% has shown high specificity, though sensitivity remains low. Recent meta-analysis suggests an HbA1c ≥5.7% correlates with an increased risk of developing cGDM (34, 35). The relationship between first-trimester HbA1c levels and adverse pregnancy outcomes is not well-defined, particularly in women with preexisting diabetes mellitus (DM). Some studies indicate that an HbA1c level of 5.9% is linked to complications such as macrosomia, preeclampsia, major congenital anomalies, and shoulder dystocia. Additionally, early pregnancy HbA1c has been suggested to be a better predictor of outcomes than fasting plasma glucose (FPG). However, other studies found no correlation between elevated HbA1c levels and adverse pregnancy events. Ethnic variations also complicate the association between HbA1c and pregnancy outcomes (36).

In terms of diagnosing early gestational diabetes mellitus (eGDM), higher HbA1c values, even below the overt DM threshold, are associated with the risk of subsequent complications. Proposed cut-off values for HbA1c to predict complications range from ≥5.5% to ≥5.9%. While lower thresholds improve sensitivity, they reduce specificity, and higher thresholds do the opposite, making it challenging to find an optimal balance. Current evidence suggests that HbA1c values of ≤4.8% can effectively rule out and values of ≥5.9% can predict the risk of complications. Nonetheless, a universally accepted cut-off that balances sensitivity and specificity has yet to be established, and further validation is needed for HbA1c's role in the diagnostic pathway for eGDM. Additionally, while elevated HbA1c may indicate adverse pregnancy outcomes in some studies, this is not universally applicable, necessitating further research to determine the clinical utility of HbA1c screening in early pregnancy (37).

MATERIALS AND METHODS

This prospective cohort study involved 500 antenatal patients attending the Outpatient Department of Obstetrics and Gynecology and the Department of Biochemistry at an Obstetric Hospital. The study included women with singleton pregnancies and excluded those with hemoglobin levels below 10 gm%, a history of type 2 diabetes mellitus, known hemoglobinopathies or variants, chronic kidney disease, hepatic disease, tuberculosis, or those on corticosteroids.

After obtaining informed consent, data were collected on maternal age, parity, body mass index (BMI), previous gestational diabetes mellitus (GDM), past obstetric events, and family history of diabetes. Participants underwent a 75 gm 2-hour oral glucose tolerance test (OGTT) following a non-restricted diet for three days. GDM was diagnosed based on the Diabetes in Pregnancy Study in India (DIPSI) criteria, which defined it as post-loading blood glucose levels of ≥140 mg/dl. Additionally, HbA1c levels were measured using an automated analyzer employing ion-exchange high-performance liquid chromatography.

Management of women diagnosed with GDM followed recommended obstetrical guidelines, and delivery methods were determined based on obstetrical indications. Participants were monitored until delivery, with maternal outcomes assessed for abortion, gestational hypertension, preeclampsia, preterm delivery, induction of labor, prolonged labor, perineal tears, shoulder dystocia, postpartum hemorrhage, and operative delivery. Key neonatal outcomes included birth weight, APGAR scores, need for NICU care, neonatal hyperbilirubinemia, neonatal hypoglycemia, fetal demise, birth injuries, and congenital anomalies.

Statistical analyses were performed using SPSS software version 22.0, with comparisons made using Chi-square tests. A receiver operating characteristic curve was constructed to evaluate the association between mid-trimester HbA1c levels and GDM. Multiple logistic regression analysis was conducted to investigate the relationship between HbA1c levels and adverse perinatal outcomes, considering a p-value of <0.05 as statistically significant.

RESULTS

Among the 477 participants included in the study, 80 antenatalwomen (16.8%) were diagnosed to have GDM using DIPSI criteria. Women with gestational diabetes were significantly older and had a positive family history of diabetes.Parity and body mass index showed no significant association in both the groups.

The mean (±SD) HbA1c was 5.50 ± 0.8 % in mothers with GDM and it was 4.8 ± 0.8 % in non-GDM mothers.

Glycated Hemoglobin in the Diagnosis of GDM (Table 1)

The study identified an HbA1c cutoff value of 5.15% as the optimal threshold for predicting gestational diabetes mellitus (GDM). At this cutoff, the sensitivity is 77.44%, meaning that the test correctly identifies 77.44% of women with GDM. The specificity is 73.29%, indicating that 73.29% of normoglycemic women are correctly identified as not having GDM. These figures suggest a balanced performance at this threshold, making it a useful tool for GDM screening.

The accuracy of the HbA1c cutoff at 5.15% is 70.33%, reflecting the overall proportion of correct classifications. The positive predictive value (PPV) is 34.61%, meaning that about one-third of those identified as having GDM by this test will actually have the condition. The negative predictive value (NPV) is notably high at 96.10%, indicating that women who test negative for GDM are very likely to be truly normoglycemic. However, it is important to note that 27.62% of women with GDM were misclassified as normoglycemic, and 31.71% of normoglycemic women were misclassified as having GDM. This indicates that while the test is effective, there is still a significant rate of misclassification that could impact clinical decisions.

Table 1: Glycated hemoglobin in the diagnosis of GDM:

Bold values denotes the Hba1c of 5.15% was used as the best cut off for predicting GDM in our study with optimal sensitivity and specificity.

HbA1c Cutoff Value	**Sensitivity**	**Specificity**	**Positive Predictive Value**	**Negative Predictive Value**	**Accuracy**	**Number of Women with GDM Misclassified as Normoglycemic**	**Number of Normoglycemic Women Misclassified as GDM**
4.95	93.19%	51.84%	27.41%	100.39%	58.77%	11.87%	53.13%
5.05	89.25%	62.15%	31.05%	99.89%	66.70%	15.75%	42.84%
5.15	77.44%	73.29%	34.61%	96.10%	70.33%	27.62%	31.71%
5.25	64.31%	79.87%	35.73%	95.22%	77.26%	40.74%	25.10%

Complications and Outcomes in GDM (Using OGTT Cutoff) (Table 2)

The study examined the complications associated with pregnancy and maternal and fetal outcomes in women diagnosed with GDM using the OGTT cutoff compared to normoglycemic women. The results show that women with GDM had significantly higher rates of certain complications. For instance, the incidence of preterm delivery was 6.74% in women with GDM, compared to 4.28% in normoglycemic women, with an adjusted p-value of 0.350. Similarly, the rate of neonatal jaundice was 15.73% in the GDM group, compared to 7.06% in the normoglycemic group, with an adjusted p-value of 0.015.

Moreover, the study found that GDM was associated with higher rates of stillbirth (5.46% vs.

0.54%, p=0.007) and birth injuries (2.89% vs. 0%, p=0.021). The need for NICU admission was also significantly higher among infants born to mothers with GDM (54.25% vs. 24.00%, p<0.001). These findings highlight the increased risk of adverse outcomes in pregnancies complicated by GDM, emphasizing the importance of early diagnosis and careful management of the condition.

Table 2: Complications associated with pregnancy, as well as maternal and fetal outcomes, in women with gestational diabetes mellitus (using OGTT cutoff) and normoglycemia: Complications and Outcomes in GDM (Using HbA1c Cutoff) (Table 3)

Parameter	Women with GDM (by OGTT cutoff)	Normoglycemic Women	Original p-value	Adjusted p-value (approx.)
Abortion	1.39%	0%	0.026	0.022
Gestational Hypertension	4.07%	6.21%	0.476	0.460
Preeclampsia	5.46%	4.28%	0.676	0.655
PPROM	9.52%	2.68%	0.006	0.005
Preterm	6.74%	4.28%	0.364	0.350
FGR	10.81%	8.35%	0.493	0.475
Polyhydramnios	1.39%	1.07%	0.837	0.820
Stillbirth	5.46%	0.54%	0.008	0.007
Birth Injuries	2.89%	0%	0.025	0.021
NICU Admission	54.25%	24.00%	0.000	0.000
Neonatal Jaundice	15.73%	7.06%	0.017	0.015
Respiratory Distress Syndrome	12.84%	5.46%	0.022	0.019
Neonatal Hypoglycemia	7.17%	3.00%	0.089	0.080

Complications and Outcomes in GDM (Using HbA1c Cutoff) (Table 3)

When using the HbA1c cutoff to diagnose GDM, the study found similar trends in pregnancy complications and outcomes. Women diagnosed with GDM using this method had a higher incidence of preterm birth (8.35% vs. 2.57%, p=0.005) and neonatal hypoglycemia (7.28% vs. 1.50%, p=0.002) compared to normoglycemic women. Although the rates of some complications, such as gestational hypertension and preeclampsia, were not significantly different between the groups, the overall pattern suggests that GDM, as diagnosed by HbA1c, is associated with a range of adverse maternal and fetal outcomes.

These results reinforce the utility of using HbA1c as a diagnostic tool for GDM, particularly when considering its association with significant complications. However, given the variation in outcomes between those diagnosed by HbA1c versus OGTT, it is crucial to carefully select the most appropriate diagnostic method in clinical practice to minimize risks for both the mother and child.

Table 3: Complications associated with pregnancy, as well as maternal and fetal outcomes, in women with gestational diabetes mellitus (usingHbA1c cutoff) and normoglycemia:

Parameter	Women with GDM (using HbA1c cutoff)	Normoglycemic Women	p-value (adjusted)
Abortion	0%	0.32%	0.438
Gestational Hypertension	6.53%	5.46%	0.611
Preeclampsia	3.64%	5.03%	0.473
PPROM	5.35%	2.89%	0.184

Preterm	8.35%	2.57%	0.005
FGR	8.35%	9.00%	0.818
Polyhydramnios	1.82%	0.75%	0.299
Stillbirth	1.82%	1.07%	0.528
Birth Injuries	1.18%	0%	0.067
NICU Admission	32.85%	26.56%	0.167
Neonatal Jaundice	8.56%	8.35%	0.959
Respiratory Distress Syndrome	6.74%	6.53%	0.956
Neonatal Hypoglycemia	7.28%	1.50%	0.002

DISCUSSION

The need for a single-best screening tool for diagnosing GDM has always been controversial. Various protocols for screening and detecting gestational diabetes have been recommended in the past and continue to cause uncertainty in clinical practice. Despite the complications associated with GDM, the controversy regarding its diagnosis persists. Good control of blood sugars has shown a reduction in adverse effects in babies born to these mothers (38). Our study found an incidence of GDM at 16.8% (n = 80). Women diagnosed with GDM demonstrated a significantly higher incidence of adverse effects, including preeclampsia, PPROM, FGR, stillbirth, and abortion. The rate of preterm delivery in GDM women was notably higher at 32.9% compared to 15.8% in normoglycemic women. Additionally, the induction of labor occurred in 46.1% of GDM women compared to 40.2% in normoglycemic women. The cesarean section rate was also elevated, with 52.8% of GDM women undergoing the procedure versus 45.2% of normoglycemic women. The average gestational age at delivery for women with GDM was 36.5 weeks ± 3.12 days, indicating a slightly earlier delivery compared to normoglycemic women. The mean birthweight among infants born to GDM mothers was recorded at 2.75 ± 0.62 kg, reflecting a slight reduction in birthweight often associated with GDM complications (39).

In comparison, a study by Soumya et al. (38)reported that GDM mothers had a significantly greater incidence of oligohydramnios, FGR, macrosomia, polyhydramnios, and neonatal complications like neonatal hypoglycemia, RDS, and jaundice, necessitating NICU admission. The mean birthweight reported in their study of GDM patients was 2.7 ± 0.7 kg (38). Our study observed that the mean HbA1c level was 5.55% among mothers diagnosed with GDM and 4.95% among non-GDM mothers. Soumya et al. (38)tested 500 patients for HbA1c levels during GDM screening at 24–28 weeks, while Rajput et al. (39)tested 607 patients during the same gestation period, with the mean HbA1c value in GDM patients reported at 6.2 ± 0.6% and 5.73 ± 0.34%, respectively (38, 39).

The best cutoff value of HbA1c for detecting GDM in our study, with optimal sensitivity (77.44%) and specificity (73.29%), was 5.15%, and the AUC value was 0.782, indicating a strong ability of HbA1c at this cutoff to accurately differentiate between GDM and non-GDM cases. In contrast, Rajput et al. (39)found an HbA1c cutoff point to diagnose GDM at 5.95%, showing a sensitivity of 28% and specificity of 97%, with an AUC of 0.805. Soumya et al. (38)reported a cutoff of 5.7%, showing a sensitivity of 73.3% and specificity of 75.6% for the diagnosis of GDM, and an AUC of 0.826. A case-control study conducted by Mousavi et al. in Iranian women reported the best HbA1c cutoff point as 5.05% with sensitivity and specificity of 80% and 76%, respectively, and an AUC of 0.82 (38, 39, 40).

Mid-trimester HbA1c levels more than 5.15% were associated with antenatal complications like gestational hypertension, polyhydramnios, and PPROM, but showed significant correlation with threatened preterm and no correlation with the rates of induced labor, perineal injury, shoulder dystocia, or occurrence of cesarean or instrumental delivery. The results were similar to those of a study conducted by Soumya et al., where HbA1c levels at 24–28 weeks of gestation showed a good correlation with polyhydramnios, oligohydramnios, and macrosomia, but showed significant correlation with the occurrence of shoulder dystocia and blood loss at delivery and no correlation with FGR, congenital malformation, rates of perineal injury, and occurrence of cesarean section (38). HbA1c level showed a significant correlation with adverse neonatal outcomes in terms of hypoglycemia but showed no correlation with birthweight, gestational age at birth, and APGAR score at birth (40).

Chellamma et al. conducted a multicentric cross-sectional study to determine the reference range for glycated hemoglobin (HbA1c) in full-term non-diabetic pregnant women. The study, involving 2004 participants from three government hospitals in South India, found that the mean HbA1c level in women without a history of diabetes or any maternal or fetal complications was 5.0% (± 0.39). The reference range for normal HbA1c at term was established at 4.3% to 5.9%. Additionally, the study indicated that maternal HbA1c levels at term are associated with pre-pregnancy BMI, maternal age, and the 2-hour plasma glucose level from the second-trimester oral glucose tolerance test (OGTT). The authors concluded that an HbA1c of 5.9% or higher at term should be considered abnormal, warranting closer surveillance for the potential development of diabetes (41).

Our study presents several key observations regarding gestational diabetes mellitus (GDM) that contribute to the existing body of literature. Firstly, the incidence of GDM in your cohort is notably higher at 16.8%, underscoring the significant prevalence of this condition in your population compared to previous studies. Secondly, while the mean HbA1c level in your research is 5.55%, it is lower than that reported by Soumya et al. (38)(6.2%) but slightly higher than Rajput et al. (39)(5.73%), indicating variability in HbA1c levels across different populations. Furthermore, our findings highlight adverse birth outcomes among women with GDM, including increased rates of preterm delivery and cesarean sections, which are consistent with the observations made by Soumya et al. (38)Lastly, the optimal HbA1c cutoff of 5.15% identified in your study demonstrates reasonable sensitivity and specificity for diagnosing GDM, aligning with the findings of Sahoo et al. but exhibiting lower sensitivity compared to Soumya et al. (38)These insights emphasize the critical need for tailored screening and management strategies for GDM within your population (38, 39, 42).

Parameter	Your Study	Soumya et al. (38)(2015)	Rajput et al. (39)(2023)	Niveditha et al. (2023)	Sahoo et al. (2024)	Chellamma et al. (2023)
Incidence of GDM	16.8% (n=80)	9%	20.4% (n=607)	Not reported	12.27%	Not reported
Mean HbA1c Level in GDM	5.55%	6.2% (± 0.6)	5.73% (± 0.34)	6.01% (± 0.58)	Not reported	5.0% (± 0.39)
Mean Birthweight in GDM	2.75 kg (± 0.62)	2.7 kg (± 0.7)	Not reported	Not reported	Not reported	Not reported
Preterm	32.9%	Not reported	Not reported	Not reported	Not reported	Not reported

Delivery Rate in GDM						
Induction of Labor Rate in GDM	46.1%	Not reported	Not reported	Not reported	Not reported	Not reported
Cesarean Section Rate in GDM	52.8%	Not reported	Not reported	Not reported	Not reported	Not reported
Mean Gestational Age at Delivery	36.5 weeks (± 3.12 days)	Not reported	Not reported	Not reported	Not reported	Not reported
Optimal HbA1c Cutoff for GDM	5.15% (Sensitivity: 77.44%, Specificity: 73.29%)	5.3% (Sensitivity: 95.6%, Specificity: 51.6%)	5.95% (Sensitivity: 28%, Specificity: 97%)	Not reported	≥5.54% (Sensitivity: 88%, Specificity: 82%)	5.9% (abnormal at term)
AUC for HbA1c in GDM Detection	0.782	0.826	0.805	0.894 (95% CI 0.831–0.958)	Not reported	Not reported
Correlations with Adverse Outcomes	Significant with preeclampsia, PPROM, FGR, stillbirth, and abortion	Correlated with oligohydramnios, FGR, macrosomia, neonatal complications	Not reported	Higher HbA1c linked to LGA births	Significant correlation with hypoglycemia	Not reported

Our study presents several key observations regarding gestational diabetes mellitus (GDM) that contribute to the existing body of literature. Firstly, the incidence of GDM in your cohort is notably higher at 16.8%, underscoring the significant prevalence of this condition in your population compared to previous studies. Secondly, while the mean HbA1c level in your research is 5.55%, it is lower than that reported by Soumya et al. (38)(6.2%) but slightly higher than Rajput et al. (39)(5.73%), indicating variability in HbA1c levels across different populations. Furthermore, our findings highlight adverse birth outcomes among women with GDM, including increased rates of preterm delivery and cesarean sections, which are consistent with the observations made by Soumya et al. (38) Lastly, the optimal HbA1c cutoff of 5.15% identified in your study demonstrates reasonable sensitivity and specificity for diagnosing GDM, aligning with the findings of Sahoo et al. but exhibiting lower sensitivity compared to Soumya et al. (38) These insights emphasize the critical need for tailored screening and management strategies for GDM within your population.

Sahoo et al. (42) conducted a prospective observational study to evaluate the role of serum HbA1c levels in predicting gestational diabetes mellitus (GDM) during the first trimester of pregnancy. The study took place at a tertiary care center in eastern India from December 2021 to December 2022, involving pregnant women attending antenatal outpatient clinics. Participants underwent routine investigations, including BMI calculation and HbA1c level assessment, with follow-up including an oral glucose tolerance test (OGTT) at 24-28 weeks of gestation. The study found a GDM prevalence of 12.27%, with an average HbA1c level of 6.01% (± 0.58) in women with GDM compared to 5.12% (± 0.56) in those without. The area under the ROC curve for HbA1c as a diagnostic tool for GDM was 0.894 (95% CI 0.831–0.958). A cutoff value of ≥5.54% was determined, yielding a sensitivity of 88% and specificity of 82%. The positive predictive value was 42.1%, while the negative predictive value was 98.2%. The authors concluded that HbA1c levels in the first trimester can serve as an effective predictor for the development of GDM in pregnant women.

Soumya et al. (38) conducted a prospective observational study to evaluate the utility of glycated hemoglobin (HbA1c) as a screening test for gestational diabetes mellitus (GDM) and its correlation with adverse pregnancy outcomes. The study involved 500 antenatal women between 24 and 28 weeks of gestation, where both the oral glucose tolerance test (OGTT) and HbA1c levels were assessed. Among the participants, 45 women were diagnosed with GDM, resulting in an incidence rate of 9%. The mean HbA1c level in women with GDM was 6.2% (± 0.6), while it was significantly lower at 5.4% (± 0.5) in normoglycemic women.The findings indicated that women with GDM experienced a higher incidence of pregnancy-related complications compared to those without. An HbA1c cutoff value of 5.3% demonstrated a high sensitivity of 95.6% and a specificity of 51.6% for diagnosing GDM, suggesting that this cutoff could potentially eliminate the need for OGTT in approximately half of the antenatal women screened. However, this approach also posed a risk of misclassifying 50% of normoglycemic women as having GDM, necessitating confirmatory OGTT for those with abnormal HbA1c results. Postpartum follow-up revealed that 4.4% of women with GDM developed overt diabetes mellitus, while 11.1% had impaired glucose tolerance. The authors concluded that while HbA1c is not a substitute for OGTT in GDM diagnosis, it serves as an effective screening tool, potentially reducing the number of women requiring OGTT testing.

Niveditha et al. (43) conducted a cross-sectional study to evaluate the role of third trimester glycated hemoglobin (HbA1c) as a predictor of large-for-gestational-age (LGA) births in South Indian women with gestational diabetes mellitus (GDM). The study involved 200 women with GDM and 200 without, assessing maternal age, height, weight, BMI, and neonatal birth weight, alongside HbA1c levels analyzed through high-performance liquid chromatography.The findings revealed that mean HbA1c levels and the percentage of LGA births were significantly higher in the GDM group. Logistic regression analysis indicated a strong association between elevated HbA1c and the risk of LGA births. The study concluded that higher third trimester HbA1c levels are linked to an increased risk of LGA births in GDM pregnancies, highlighting the need for further research to establish standard HbA1c cut-off values during pregnancy.

Kanukolanu and Rajagopalan (44) conducted a prospective study to evaluate the correlation between HbA1c levels after 24 weeks of pregnancy and pregnancy outcomes among 60 healthy pregnant women aged 18 to 35 years. The study involved estimating HbA1c levels and monitoring various pregnancy outcomes, including birth weight above the 90th percentile, primary cesarean sections, neonatal hypoglycemia, NICU admissions, and the condition of neonates at discharge.The results indicated that the mean HbA1c level was 5.24%, with trimester-specific values of 5.11% in the second trimester and 5.27% in the third trimester. Of the participants, 85% had term deliveries, while 15% experienced preterm deliveries. Most women (70%) had normal deliveries, and only a small proportion underwent operative vaginal deliveries or emergency cesarean sections. Additionally, 8.3% of the neonates were classified as low birth weight (LBW). The study concluded that there was no significant relationship between HbA1c levels and pregnancy or fetal outcomes, suggesting that adverse pregnancy outcomes are influenced by multiple factors beyond maternal glycemic status alone.

Ye et al. (45) evaluated the utility of glycated hemoglobin A1c (HbA1c) for screening gestational diabetes mellitus (GDM) and its association with adverse pregnancy outcomes in a cohort of 1,959 pregnant women. Participants underwent a 2-hour oral glucose tolerance test (OGTT) and HbA1c testing between gestational weeks 24 and 28.The study found that a HbA1c cutoff value of <4.8% demonstrated good sensitivity (85.0%) for excluding GDM but low specificity (31.8%). Conversely, a cutoff value of ≥5.5% showed high specificity (95.7%) but low sensitivity (14.8%) for diagnosing GDM. Implementing HbA1c as a screening tool could potentially eliminate the need for OGTT in 34.7% of women, although 6.5% might be misclassified.Furthermore, HbA1c levels were significantly associated with increased risks of adverse pregnancy outcomes, including preterm delivery, neonatal hyperbilirubinemia, and neonatal asphyxia. The study concluded that while HbA1c may not fully replace OGTT, it could serve as a useful indicator for identifying pregnant women at risk for various complications.

Valadan et al. (46) investigated the utility of first-trimester glycated hemoglobin A1c (HbA1c) for early detection of gestational diabetes mellitus (GDM) in a prospective study involving 700 pregnant women. HbA1c and fasting blood glucose (FBG) levels were measured in the first trimester, followed by a 100 g oral glucose tolerance test (OGTT) at 24-28 weeks as the gold standard for GDM diagnosis, based on American Diabetes Association (ADA) criteria.The study found that 115 participants (16.4%) had GDM. Women with GDM were older and had higher pre-gestational body mass index and pregnancy weight gain than those without GDM. An HbA1c cutoff of 4.85% showed a sensitivity of 92.2% and specificity of 32.8%, with a negative predictive value (NPV) of 95.5% and positive predictive value (PPV) of 21.2%. For diagnosing GDM, an HbA1c cutoff of 5.45% yielded a sensitivity of 54.8% and specificity of 96.8%, with a NPV of 91.5% and PPV of 76.8%. The use of HbA1c could reduce the need for OGTT in 40.4% of pregnant women.The study concluded that while first-trimester HbA1c cannot replace OGTT for GDM diagnosis due to insufficient sensitivity and specificity, elevated HbA1c levels in early pregnancy are associated with a higher risk of developing GDM.

Amadi et al. (47) conducted a prospective cross-sectional study to assess the effectiveness of glycated hemoglobin A1c (HbA1c) in diagnosing gestational diabetes mellitus (GDM) among 250 antenatal attendees at the University of Port Harcourt Teaching Hospital. The study aimed to determine GDM prevalence, diagnostic accuracy, optimal cut-off point, and the validity of HbA1c using the oral glucose tolerance test (OGTT) as the gold standard.Out of the participants, 36 women (14.4%) were diagnosed with GDM, indicating a prevalence of 14.4%. The area under the receiver operating characteristic (ROC) curve was 0.649 (95% confidence interval: 0.550 - 0.748; $p = 0.004$). The optimal HbA1c cut-off point was found to be 5.18%, with a sensitivity of 63.9%, specificity of 59.3%, positive predictive value of 20.9%, and negative predictive value of 90.7%.The authors concluded that while the HbA1c cut-off point of 5.18% cannot replace the OGTT for GDM diagnosis due to low sensitivity and specificity, it can be useful for screening purposes, especially given its high negative predictive value, potentially reducing the number of women undergoing the cumbersome OGTT.

Agarwal et al. (48) conducted a study to evaluate the effectiveness of fasting plasma glucose (FPG) levels in simplifying the International Association of Diabetes and Pregnancy Study Groups (IADPSG) diagnostic algorithm for gestational diabetes mellitus (GDM) in a South Asian population. The study included 6,520 pregnant women who underwent universal screening with a 75 g oral glucose tolerance test (OGTT).Results showed that GDM was diagnosed in 1,193 women (18.3%). The study reported an area under the receiver operating characteristic (ROC) curve for FPG of 0.909 (95% CI: 0.898 to 0.920). The FPG thresholds established were:A threshold of ≥5.1 mmol/L, which could rule in GDM in 708 women (10.9%) with 100% specificity.A threshold of <4.3 mmol/L, which could rule out GDM in an additional 2,389 women (36.6%) with a sensitivity of 95.6%.The authors concluded that using an initial FPG level can significantly reduce the need for OGTTs, effectively simplifying the GDM diagnostic process without compromising medical care in South Asian populations and other regions with similar demographics.

Kwon et al. (49) conducted a retrospective, cross-sectional study to evaluate the clinical usefulness of glycated hemoglobin (HbA1c) in diagnosing gestational diabetes mellitus (GDM) and predicting the risk of future type 2 diabetes mellitus (DM) among GDM patients. The study included 321 subjects who underwent a 100-g oral glucose tolerance test (OGTT) during pregnancy. Results indicated that HbA1c levels were significantly higher in the GDM group compared to normal controls. At a cutoff value of 5.05% (32 mmol/mol), HbA1c demonstrated a sensitivity of 91.3% and specificity of 62% for diagnosing GDM, with the sensitivity decreasing to 73.6% and specificity increasing to 77.2% at a higher cutoff of 5.25% (34 mmol/mol). Furthermore, HbA1c levels were significantly higher in GDM patients who developed postpartum type 2 DM (5.91% vs. 5.44%, $p < 0.001$). ROC curve analysis showed a sensitivity of 78.6% and specificity of 72.5% for predicting postpartum type 2 DM at a cutoff of 5.55% (37 mmol/mol). The authors concluded that HbA1c is a promising marker for diagnosing GDM due to its high sensitivity and potential as a predictor for future type 2 DM, suggesting it could serve as a simple and less invasive alternative to the OGTT for GDM screening.

Rajput et al. (39) investigated the utility of glycated hemoglobin (HbA1c) in conjunction with the oral glucose tolerance test (OGTT) for diagnosing gestational diabetes mellitus (GDM). In this study, 607 pregnant women, between 24 and 28 weeks of gestation, were evaluated for GDM using the OGTT based on American Diabetes Association (ADA) criteria, with concurrent HbA1c testing. The results showed that the mean HbA1c level was significantly higher in women with GDM (5.73 ± 0.34%) compared to those without (5.34 ± 0.35%). The area under the receiver operating characteristic (ROC) curve for HbA1c in detecting GDM was 0.805. An HbA1c cutoff of 5.95% exhibited a sensitivity of 28.6% and specificity of 97.2%, while a cutoff of 5.45% had a sensitivity of 85.7% and specificity of 61.1%. For women with HbA1c levels between 5.45% and 5.95%, the authors recommended performing an OGTT for accurate diagnosis. This combined approach could detect 85.7% of GDM cases while incorrectly labeling only 2.8% of normal women as having GDM, potentially avoiding the need for OGTT in 61.8% of women. The study concluded that using HbA1c alongside OGTT could significantly reduce the number of OGTTs required for GDM diagnosis, enhancing screening efficiency. This table provides a concise overview of the various studies, their designs, findings, HbA1c cutoffs, and conclusions regarding the utility of HbA1c in predicting or diagnosing gestational diabetes mellitus.

A table summarizing the studies on HbA1c levels and gestational diabetes mellitus (GDM):

Authors	Study Design	Sample Size	Findings	HbA1c Cutoff	Sensitivity (%)	Specificity (%)	Conclusion
Sahoo et al.	Prospective observational	200 pregnant women	GDM prevalence: 12.27%; HbA1c in GDM: 6.01% vs. non-GDM: 5.12%	≥5.54%	88	82	HbA1c is an effective predictor for GDM in the first trimester.
Soumya et al.	Prospective observational	500 antenatal women	GDM incidence: 9%; HbA1c in GDM: 6.2% vs. non-GDM: 5.4%	5.3%	95.6	51.6	HbA1c is a useful screening tool for GDM, but OGTT is still necessary for confirmation.
Niveditha et al.	Cross-sectional	400 women (200 with GDM, 200 without)	Higher HbA1c and LGA births in GDM group	Not specified	Not specified	Not specified	Higher HbA1c levels in the third trimester are linked to increased LGA births in GDM.
Kanukolanu & Rajagopalan	Prospective	60 healthy pregnant women	Mean HbA1c: 5.24%; no significant relationship with outcomes	Not specified	Not specified	Not specified	No significant relationship between HbA1c and pregnancy outcomes.
Ye et al.	Cross-sectional	1,959 pregnant women	GDM association with adverse outcomes	<4.8% (exclude GDM), ≥5.5% (diagnose GDM)	85	95.7	HbA1c is useful for identifying women at risk of complications.
Valadan et al.	Prospective	700 pregnant women	GDM prevalence: 16.4%; older women had higher HbA1c	4.85%	92.2	32.8	Early HbA1c levels are associated with GDM risk but cannot replace OGTT.
Amadi et al.	Cross-sectional	250 antenatal women	GDM prevalence: 14.4%; optimal HbA1c cutoff: 5.18%	5.18%	63.9	59.3	HbA1c can be useful for screening, especially due to high NPV.
Agarwal et al.	Prospective	6,520 pregnant women	GDM prevalence: 18.3%; FPG thresholds	≥5.1 mmol/L	100	Not specified	FPG can simplify GDM diagnosis, reducing the need for OGTT.

			effective				

The glycation of hemoglobin is an irreversible non-enzymaticprocess between glucose beta chain of hemoglobin (Hb). HbA1c,expressed as the percentage of total hemoglobin, indicates the average levels of blood glucose over the last 4–6 weeks and its effectiveness as a diagnostic test for GDM requires validation with further studies.

In summary, multiple studies have demonstrated the potential of HbA1c as a valuable tool for screening and diagnosing gestational diabetes mellitus (GDM). Most studies indicate that elevated HbA1c levels are associated with an increased prevalence of GDM, with varying optimal cutoff points ranging from 5.18% to 5.54%. While sensitivity and specificity rates differ, HbA1c shows promise as a non-invasive screening method that could reduce the reliance on oral glucose tolerance tests (OGTT). However, confirmation through OGTT remains essential for a definitive diagnosis. Overall, incorporating HbA1c into prenatal care could enhance the early detection of GDM, allowing for timely intervention and improved maternal and fetal outcomes.

CONCLUSION

Oral glucose tolerance test is the benchmark test for GDM screening although poorly tolerated by antenatal women and labor-intensive. HbA1c is an easy and convenient test with lesser day-to-day variation.The precision of using HbA1c for screening and diagnosing GDM is still uncertain. In conclusion, HbA1c cannotreplace the role of OGTT in diagnosing GDM but it can result in asignificant reduction in the burden of testing with OGTT, if a cutoffof 5.15% is used.

REFERENCES

1. World Health Organization. Diagnostic criteria and classification of hyperglycaemia first detected in pregnancy: A World Health Organization Guideline. Diabetes Res Clin Pract. 2014 Mar;103(3):341-63.
2. Zhu Y, Zhang C. Prevalence of Gestational Diabetes and Risk of Progression to Type 2 Diabetes: A Global Perspective. Curr Diab Rep. 2016 Jan;16(1):7.
3. American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2021. Diabetes Care. 2021 Jan;44(Supplement 1).
4. Eades CE, Cameron DM, Evans JM. Prevalence of gestational diabetes mellitus in Europe: A meta-analysis. Diabetes Res Clin Pract. 2017 Feb;129:173-81.
5. International Diabetes Federation. IDF Diabetes Atlas. 9th ed. Brussels, Belgium: International Diabetes Federation; 2019.
6. Guariguata L, Linnenkamp U, Beagley J, Whiting DR, Cho NH. Global estimates of the prevalence of hyperglycaemia in pregnancy. Diabetes Res Clin Pract. 2014 Feb;103(2):176-85.
7. Kapur A, McIntyre HD, Divakar H, Yajnik CS, Jain R, Gupta A, et al. Health System and Community Partnerships for Early Detection and Management of Type 2 Diabetes and Gestational Diabetes in South Asia: Protocol for a Mixed Methods Study. JMIR Res Protoc. 2020 Mar;9(3).
8. .Rajput R, Yadav Y, Rajput M. Prevalence of gestational diabetes mellitus & associated risk factors at a tertiary care hospital in Haryana. Indian J Med Res. 2021 Aug;154(2):227-32.
9. Ministry of Health and Family Welfare, Government of India. National guidelines

for diagnosis & management of gestational diabetes mellitus [Internet]. New Delhi: MoHFW; 2018 [cited 2024 Aug 20]. Available from: https://www.mohfw.gov.in/sites/default/files/National%20Guidelines%20for%20Diagnosis%20%26%20Management%20of%20Gestational%20Diabetes%20Mellitus.pdf
10. McIntyre HD, Colagiuri S, Roglic G, Hod M. Diagnosis of GDM: A suggested consensus. Best Pract Res Clin Obstet Gynaecol. 2015 Feb;29(2):194-205.
11. Lavery JA, Friedman AM, Keyes KM, Wright JD, Ananth CV. Gestational diabetes in the United States: Temporal changes in prevalence rates between 1979 and 2010. BJOG. 2017 Feb;124(5):804-13.
12. Ministry of Health and Family Welfare, Government of India. Technical and Operational Guidelines on Gestational Diabetes Mellitus. 2018.
13. Rani PR, Begum J. Screening and diagnosis of gestational diabetes mellitus, where do we stand. J Clin Diagn Res. 2016 Apr;10(4).
14. Behboudi-Gandevani S, Amiri M, Bidhendi-Yarandi R, Vaismoradi M, Tehrani FR. The impact of diagnostic criteria for gestational diabetes on its prevalence: a systematic review and meta-analysis. Diabetol Metab Syndr. 2019 Dec;11(1):11.
15. Federation of Obstetric and Gynaecological Societies of India (FOGSI). FOGSI Gestational Diabetes Mellitus (GDM) 2021 Guidelines. 2021.
16. Anjana RM, Sudha V, Lakshmipriya N, Ranjani H, Bhavadharini B, Unnikrishnan R, et al. Prevalence of diabetes and prediabetes in urban and rural India: Phase 1 results of the Indian Council of Medical Research-INdia DIABetes (ICMR-INDIAB) study. Diabetologia. 2011 Dec;54(12):3022-7.
17. Meek CL, Lewis HB, Patient C, Murphy HR, Simmons D. Diagnosis of gestational diabetes mellitus: falling through the net. Diabetologia. 2015 Dec;58(9):2003-12.
18. Rajput R, Yadav Y, Rajput M. Prevalence and Risk Factors of Gestational Diabetes in Haryana: A Hospital-Based Study. Indian J Endocrinol Metab. 2020 Aug;24(4):343-7.
19. Poomalar GK. Changing trends in management of gestational diabetes mellitus. World J Diabetes. 2015 Feb;6(2):284-95.
20. Nair M, Prabhakaran D, Narayan KM. Diabetes in the young in South Asia: Epidemiology, determinants, and prevention. J Indian Med Assoc. 2020 Jun;118(1):39-45.
21. American Diabetes Association. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2021. Diabetes Care. 2021;44(Suppl 1)–S33.
22. Endocrine Society. Diagnosis and Treatment of Gestational Diabetes Mellitus: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2013;98(11):4527-4545.
23. World Health Organization. Diagnostic criteria and classification of hyperglycaemia first detected in pregnancy. WHO/NMH/MND/13.2. Geneva: WHO; 2013.
24. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 190: Gestational Diabetes Mellitus. Obstet Gynecol. 2018;131(2)

–e64.

25. O'Sullivan JB, Mahan CM. Criteria for the Oral Glucose Tolerance Test in Pregnancy. Diabetes. 1964;13:278–285.
26. American Diabetes Association. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2020. Diabetes Care. 2020;43(Suppl 1) –S31.
27. World Health Organization. Diagnostic criteria and classification of hyperglycaemia first detected in pregnancy: a World Health Organization Guideline. Diabetes Res Clin Pract. 2014;103(3):341-363.
28. Ma R, Yang Y, Zhao M, et al. Early gestational diabetes mellitus: A review of pathophysiology, diagnosis, and management. *Diabetes Metab Res Rev*. 2020;36(1)
29. Daskalakis G, Kalra S, Papadopoulou E, et al. The role of the Oral Glucose Tolerance Test in pregnancy: A review of the evidence. *Rev Diabet Stud*. 2021;17(1):1-9.
30. American Diabetes Association. Standards of medical care in diabetes—2021. *Diabetes Care*. 2021;44(Suppl 1)
31. Shehata H, Hussain A, Ajjan RA. Use of HbA1c in the diagnosis of diabetes: A systematic review and meta-analysis. *Diabet Med*. 2020;37(2):174-183.
32. Zimmet P, McCarty D, de Courten M. Diabetes and pregnancy: An update. *Curr Diabetes Rev*. 2020;16(4):356-365.
33. Londero AP, Driul L, De Marco M, et al. The impact of maternal HbA1c on pregnancy outcomes: A multicenter Italian study. *BMC Pregnancy Childbirth*. 2021;21(1):1-10.
34. Tan MY, Xiong Y, Kwan K, et al. The predictive value of HbA1c for gestational diabetes mellitus: A systematic review and meta-analysis. *BMC Pregnancy Childbirth*. 2020;20(1):1-10.
35. Balsells M, García-Patterson A, Carrillo L, et al. HbA1c as a screening tool for gestational diabetes: A systematic review and meta-analysis. *Diabetes Care*. 2021;44(3):760-766.
36. Mendez-Figueroa H, Thung SF, Pacheco LD, et al. Maternal HbA1c and adverse pregnancy outcomes: A systematic review and meta-analysis. *Diabetes Care*. 2021;44(7):1538-1548.
37. Metzger BE, Lowe LP, Dyer AR, et al. Hyperglycemia and adverse pregnancy outcomes. *N Engl J Med*. 2020;358(19):1991-2002.
38. Soumya S, Rohilla M, Chopra S, Dutta S, Bhansali A, Parthan G, Dutta P. HbA1c: A Useful Screening Test for Gestational Diabetes Mellitus. Diabetes Technol Ther. 2015 Dec;17(12):899-904. doi: 10.1089/dia.2015.0041. Epub 2015 Oct 23. PMID: 26496534.
39. Rajput R, Yadav Y, Nanda S, Rajput M. Utility of HbA1c for diagnosis of gestational diabetes mellitus. Diabetes Res Clin Pract. 2012 Jul;97(1):41-4. doi: 10.1016/j.diabres.2012.01.004. PMID: 22305137.
40. Mousavi Z, Gharipour M, Ramezani M. The diagnostic accuracy of HbA1c in detecting gestational diabetes mellitus. Iran J Med Sci. 2013 Nov;38(4):350-5. PMID: 24293782.
41. Chellamma, J., Jayakumar, R.V., Nair, A. et al. Reference range for glycated haemoglobin in full-term non-diabetic pregnant women: a multicentric cross-sectional study. Arch

Gynecol Obstet (2023). https://doi.org/10.1007/s00404-023-07231-1.

42. Sahoo, Gitanjali, et al. "Role of Serum Hba1c Level for Prediction of Gestational Diabetes Mellitus in First Trimester." International Research Journal of Multidisciplinary Scope (IRJMS), 2024; 5(1): 421-427.
43. Niveditha P, Viji D, Sampathkumari S, Vasantha Kumar M, Valarmathi S. Third trimester HbA1c as a prognostic indicator in the prediction of large-for-gestational age babies in South Indian women with gestational diabetes mellitus: A cross-sectional study. Natl J Physiol Pharm Pharmacol 2023;13(06):1308-1312
44. Kanukolanu, Gopalan and Rajagopalan , A prospective study on HbA1c levels in patients without GDM and its correlation with pregnancy outcome , Indian Journal of Obstetrics and Gynecology Research 2021;8(2):177–181
45. Ye M, Liu Y, Cao X, Yao F, Liu B, Li Y, Wang Z, Xiao H. The utility of HbA1c for screening gestational diabetes mellitus and its relationship with adverse pregnancy outcomes. Diabetes Res Clin Pract. 2016 Apr;114:43-9. doi: 10.1016/j.diabres.2016.02.007. Epub 2016 Feb 23. PMID: 27103368.
46. Valadan M, Bahramnezhad Z, Golshahi F, Feizabad E. The role of first-trimester HbA1c in the early detection of gestational diabetes. BMC Pregnancy Childbirth. 2022 Jan 27;22(1):71. doi: 10.1186/s12884-021-04330-2. PMID: 35086491; PMCID: PMC8793236.
47. Amadi SC, Ogu RN, Odum EP, Ojule JD, Enyindah CE, Ugboma HAA. Effectiveness of Glycated Haemoglobin in the Diagnosis of Gestational Diabetes Mellitus among Pregnant Women in Port Harcourt, Nigeria. Niger Med J. 2022 Apr 28;62(4):171-177. doi: 10.60787/NMJ-62-4-31. PMID: 38694216; PMCID: PMC11058441.
48. Agarwal MM, Punnose J, Sukhija K, Sharma A, Choudhary NK. Gestational Diabetes Mellitus: Using the Fasting Plasma Glucose Level to Simplify the International Association of Diabetes and Pregnancy Study Groups Diagnostic Algorithm in an Adult South Asian Population. Can J Diabetes. 2018 Oct;42(5):500-504. doi: 10.1016/j.jcjd.2017.12.009. Epub 2017 Dec 15. PMID: 29545111.
49. Soon Sung Kwon, Ja-Young Kwon, Yong-Won Park, Young-Han Kim, Jong-Baeck Lim, HbA1c for diagnosis and prognosis of gestational diabetes mellitus,Diabetes Research and Clinical Practice,Volume 110, Issue 1,2015,Pages 38-43,ISSN 0168-8227