

Obstetric Outcomes & Its Association with First Trimester Glycosylated Haemoglobin In A Tertiary Care Centre In South Kerala

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HIGHLIGHTS

- Early HbA1c predicts outcomes
- High HbA1c increases GDM
- HbA1c linked hypertension
- Elevated HbA1c increases LSCS
- Early screening improves detection

Key Words:

First-trimester HbA1c
Gestational Diabetes Mellitus
Obstetric Outcomes
Perinatal Outcomes

ABSTRACT

Introduction: The prevalence of abnormal glucose metabolism among women in Kerala is increasing steadily, posing significant concerns for maternal and the fetal health. Early maternal hyperglycemia has been associated with adverse obstetric outcomes and long-term metabolic risks in offspring. However, routine screening for Gestational Diabetes Mellitus (GDM) is typically performed later in pregnancy, potentially missing early risk indicators. First-trimester HbA1c has emerged as a promising early marker for identifying women at higher risk. **Aims & Objective:** This study aimed to determine the association between first-trimester glycosylated haemoglobin (HbA1c) levels and obstetric outcomes in women delivering at a tertiary care centre in Southern Kerala. **Materials & Methods:** A retrospective cohort study was conducted among 664 postpartum women at Pushpagiri Medical College Hospital. Participants were equally divided into two groups based on first-trimester HbA1c levels: $<5.9\%$ and $\geq 5.9\%$. Data regarding sociodemographic characteristics, clinical history, laboratory investigations, and obstetric outcomes were collected from medical records. Statistical analysis was performed using SPSS version 25, applying chi-square tests for categorical variables, independent t-tests for continuous variables, and calculation of relative risks. A p-value of less than 0.05 was considered statistically significant. **Results:** Women with HbA1c $\geq 5.9\%$ showed significantly higher rates of GDM, gestational hypertension, earlier deliveries, increased likelihood of LSCS, adverse perinatal outcomes, and higher mean birth weight compared to those with lower HbA1c levels. No significant differences were observed in maternal age, pre-pregnancy BMI, or obstetric history. **Conclusion:** The elevated first-trimester HbA1c is strongly associated with adverse maternal and neonatal outcomes, supporting its role as an effective early screening tool for identifying high-risk pregnancies.



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INTRODUCTION

Pregnancy is a unique physiological state marked by complex hormonal and metabolic adaptations that support fetal growth and development, with maternal glucose metabolism playing a central role as the primary energy source for the fetus. Maintaining optimal glycemic control is essential for both maternal and fetal health, as early pregnancy hyperglycemia has been increasingly linked to adverse obstetric and neonatal outcomes. Glycosylated hemoglobin (HbA1c), which reflects average blood glucose levels over the preceding two to three months, serves as a reliable marker of long-term glycemic status. Measuring HbA1c during the first trimester provides an opportunity to identify women at risk of complications before the onset of physiological insulin resistance later in pregnancy, thereby enabling early interventions [1,2].

The prevalence of abnormal glucose metabolism among women of reproductive age in Kerala has risen significantly due to urbanization, sedentary lifestyles, dietary changes, and increasing obesity rates. Evidence suggests that fetal exposure to maternal hyperglycemia begins early in gestation and can lead to accelerated fetal growth even before the diagnosis of gestational diabetes mellitus (GDM). Additionally, such exposure has long-term consequences, predisposing offspring to obesity, insulin resistance, and type 2 diabetes later in life, highlighting the importance of early detection and management of dysglycemia [3,4]. GDM, defined as glucose intolerance first recognized during pregnancy, arises when maternal insulin resistance exceeds pancreatic β -cell compensation, resulting in elevated blood glucose levels. This leads to increased placental glucose transfer, stimulating fetal hyperinsulinemia & promoti-

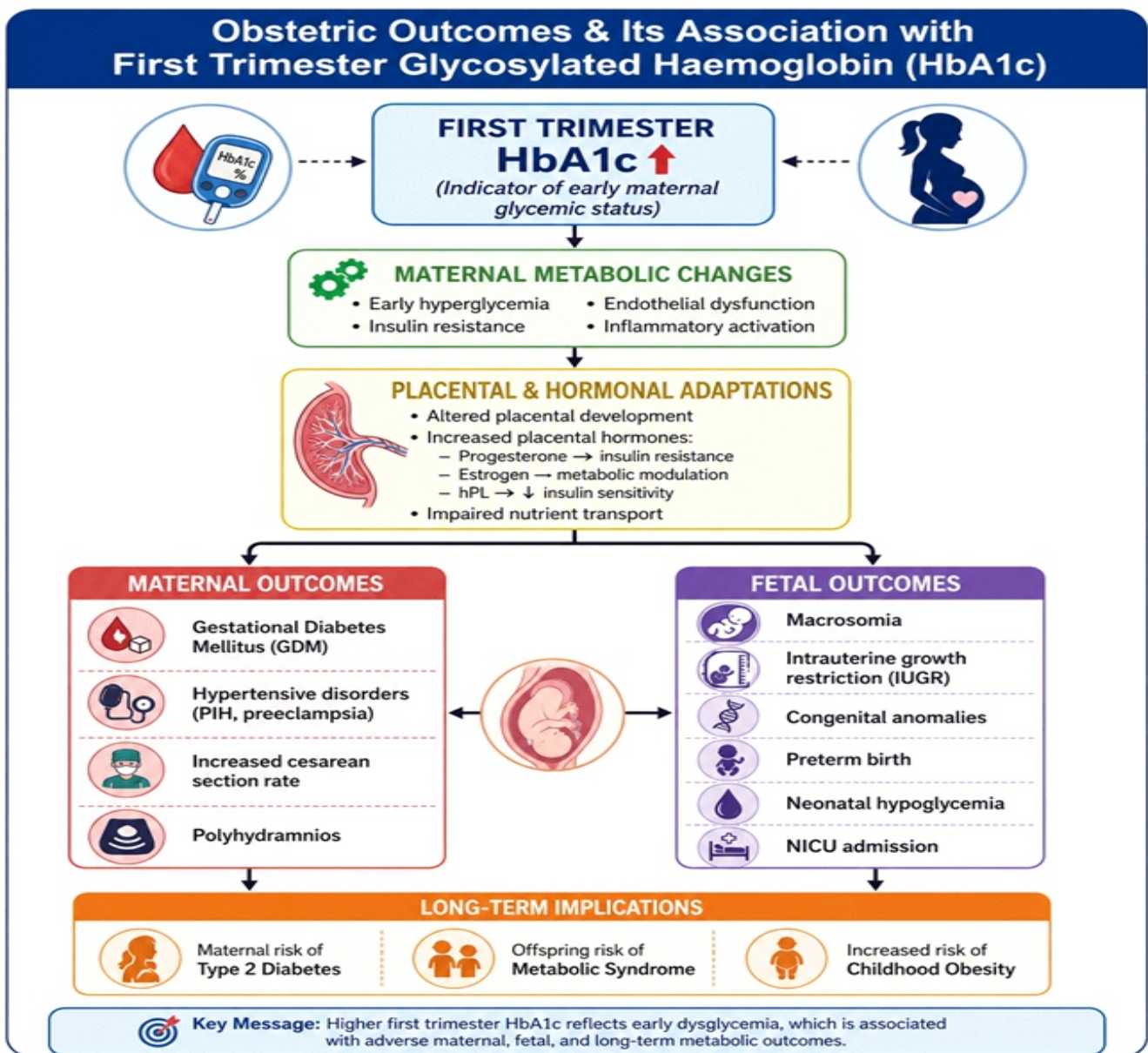


Figure 1: Association of first-trimester HbA1c with maternal metabolic alterations, placental adaptations, and adverse maternal, fetal, and long-term obstetric outcomes. Adapted from [1].

ng excessive growth, or macrosomia. Macrosomic infants are at higher risk for complications such as obstructed labor, shoulder dystocia, cesarean delivery, and neonatal hypoglycemia. Maternal hyperglycemia is also associated with placental dysfunction, oxidative stress, and increased risks of pre-eclampsia, polyhydramnios, preterm birth, and stillbirth [5,6].

First-trimester HbA1c has emerged as a practical and stable tool for early detection of pre-existing diabetes and gestational dysglycemia, offering advantages over single-point glucose measurements. Elevated HbA1c levels in early pregnancy have been associated with adverse outcomes, including preeclampsia, preterm delivery, large-for-gestational-age infants, and increased neonatal intensive care admissions. Early screening enables timely interventions such as dietary modification, pharmacologic therapy, and enhanced maternal-fetal monitoring [7,8].

Regional factors such as genetics, lifestyle, and healthcare access influence the burden of metabolic disorders, making population-specific research essential. In Kerala, increasing obesity rates, delayed childbearing, and lifestyle transitions have contributed to rising glucose intolerance, yet data on early pregnancy HbA1c and outcomes remain limited. Studying this association in a tertiary care setting can provide valuable insights for improving antenatal care and developing region-specific guidelines [9,10].

Early maternal hyperglycemia also affects fetal organogenesis and metabolic programming, leading to increased insulin production and fat deposition in the fetus. This contributes to complications such as macrosomia, neonatal hypoglycemia, respiratory distress, and long-term metabolic risks. Early identification and management through lifestyle interventions, glucose monitoring, and appropriate therapy can significantly improve outcomes. Incorporating first-trimester HbA1c screening into routine antenatal care can enhance risk stratification, reduce complications, and inform public health strategies. Overall, early glycemic control plays a critical role in improving both immediate and long-term health outcomes for mothers and their offspring [11,12]. First trimester HbA1c and its association with maternal, placental, and fetal outcomes (**Figure 1**).

This study aimed to determine the association between obstetric outcomes and first-trimester glycosylated haemoglobin levels. To achieve this, a retrospective study was conducted at a tertiary care centre in Southern Kerala, focusing on examining the relationship between first-trimester glycosylated haemoglobin values and subsequent obstetric outcomes.

MATERIAL & METHODS

This retrospective cohort study was conducted at the Department of Obstetrics and Gynaecology, Pushpagiri Institute of Medical Sciences & Research Centre, Tiruvalla, Kerala, from 2023 to 2026 for 18 months. Ethical approval has been obtained from the

Ethical Approval Committee of Pushpagiri Institute of Medical Sciences & Research Centre, Tiruvalla, Kerala.

Study Population

The study population comprised all women who delivered at PMCH during the study period with documented first-trimester HbA1c values in antenatal records. Included were women with singleton pregnancies, HbA1c measured at or before 13 weeks, delivery at PMCH, and complete antenatal, delivery, and neonatal records. Excluded were those with pre-existing diabetes, multiple gestation, chronic renal disease, prior hypertension, hemoglobinopathies, or incomplete records, enabling focus on gestational dysglycaemia for this analysis.

Data Analysis

Data were entered into Microsoft Excel and analyzed using SPSS version 25. statistics means and standard deviations for continuous variables, and frequencies and percentages for categorical variables. Inferential analysis applied the chi square test to assess associations between HbA1c categories and categorical outcomes, and the independent t test to compare means as birth weight, AFI, and gestational age. Relative risk was calculated for outcomes, with p less than 0.05 considered statistically significant.

RESULTS

The study included 664 participants with ages ranging from 20 to 37 years, with a mean age of 28.52 ± 5.33 years and a median of 28 years, indicating a predominantly reproductive-age population. The mean pre-pregnancy BMI was 24.20 ± 3.35 kg/m², with most women falling within the normal to overweight range. A positive family history of diabetes was present in 36.6% of participants. Gravidity distribution showed 40.96% primigravidae, 38.86% second gravidae, and 20.18% with three or more pregnancies. First-trimester HbA1c levels were equally distributed, with 50% below 5.9% and 50% at or above 5.9%. Nearly half (49.4%) had no prior adverse obstetric history, while previous GDM (14.61%) and preterm delivery (11.14%) were most common among those affected. Gestational diabetes mellitus was diagnosed in 34.94% of participants, highlighting a considerable burden of gestational dysglycaemia in the study population.

Among 664 participants, 65.06% did not develop GDM, while most diagnoses occurred between 24–29 weeks, especially at 25 and 29 weeks. Glucose tolerance results were identical in the second and third trimesters, with 65.06% normal and 34.94% abnormal, indicating persistent dysglycaemia once detected (**Table 1**). Among the 664 participants, gestational hypertension was observed in 11.9%, while 88.1% remained normotensive, reflecting rates comparable to similar populations and supporting its relevance in assessing vascular complications. The mean amniotic fluid index was 14.91 ± 4.45 , with most values within the normal range, indicating adequate fluid volume. Neonatal birth weight ranged from 1.97 to 4.72 kg, with

a mean of 3.14 ± 0.40 kg, showing predominantly normal distribution. Vaginal delivery occurred in 73.34% of cases, while 26.66% underwent caesarean section. Most women (76.51%) had no medical complications, though PPRM, urinary tract infections, and PROM were noted. Normal perinatal outcomes were seen in 76.96%, while 23.04% had adverse outcomes. The mean gestational age at delivery was 37.99 ± 1.90 weeks, with most deliveries occurring at term.

In 664 participants, 92.02% had normal urine albumin in the second trimester, while 7.98% showed microalbuminuria, indicating limited renal or vascular involvement. All were normal in T1, and the same T2 distribution persisted in T3, suggesting stable rather than progressive albuminuria (Table 2). Estimated fetal weight ranged from 2.12–5.0 kg (mean 3.39 ± 0.39 , median 3.33), with most fetuses in the 3.0–3.5 kg range indicating generally appropriate near-term growth. Higher weights suggest a potential link between maternal glycaemic status and increased fetal growth (Figure 2).

Elevated first-trimester HbA1c ($\geq 5.9\%$) showed a strong association with higher rates of GDM, gestational hypertension, caesarean delivery, and adverse perinatal outcomes, all statistically significant. Overall, higher HbA1c in early pregnancy is a key predictor of maternal and fetal complications (Table 3).

Higher first-trimester HbA1c ($\geq 5.9\%$) was associated with significantly greater birth weight and markedly increased risk of GDM, while maternal age, BMI, parity, and past obstetric history were comparable between groups. Overall, elevated HbA1c is a strong predictor of adverse metabolic outcomes rather than baseline maternal characteristics (Table 4).

Elevated first-trimester HbA1c ($\geq 5.9\%$) was strongly associated with abnormal GTT results in both second and third trimesters, with over half showing glucose intolerance, while most with lower HbA1c remained normal. This significant association indicates early HbA1c as a strong predictor of persistent gestational dysglycaemia.

Comparison between first-trimester HbA1c groups showed that

women with HbA1c $\geq 5.9\%$ had a significantly higher mean amniotic fluid index (17.88 ± 4.03 cm) compared to those with HbA1c $< 5.9\%$ (11.94 ± 2.38 cm), indicating a strong association between elevated HbA1c and increased amniotic fluid volume ($p < 0.0001$). However, medical complications such as postpartum hemorrhage, PROM/PPROM, urinary tract infections, and vaginitis were similarly distributed between groups, with no significant association ($p = 0.15$). Additionally, women with higher HbA1c levels delivered at a slightly earlier gestational age (37.65 ± 1.98 weeks) compared to those with lower HbA1c (38.33 ± 1.76 weeks), a difference that was statistically significant ($p < 0.0001$) (Table 5).

The distribution of gestational age at diagnosis of gestational diabetes mellitus (GDM) was similar across both first-trimester HbA1c groups, with most cases identified between 24 and 29 weeks of gestation. Although a greater number of GDM cases occurred in the HbA1c $\geq 5.9\%$ group, reflecting its higher overall prevalence, the pattern of diagnosis timing remained comparable between groups. Statistical analysis showed no significant association between first-trimester HbA1c levels and the gestational age at GDM diagnosis ($\chi^2 = 3.03$, $p = 0.70$), indicating that early HbA1c status did not influence when GDM was detected.

All participants had normal urine albumin in the first trimester, with no association to HbA1c, but in later trimesters elevated HbA1c ($\geq 5.9\%$) was strongly linked to higher microalbuminuria rates. This significant pattern indicates early HbA1c as a predictor of subsequent renal or vascular involvement (Table 6).

All participants had normal urine albumin in the first trimester, but in later trimesters microalbuminuria (7.98%) was significantly more common in those with higher HbA1c, with persistence from T2 to T3. This suggests elevated early HbA1c is linked to subsequent endothelial or renal involvement (Table 7).

Higher first-trimester HbA1c ($\geq 5.9\%$) was associated with significantly greater estimated fetal weight (3.57 vs 3.21 kg), indicating increased fetal growth. This strong association highlights early HbA1c as a predictor of fetal overgrowth (Table 8).

Table 1: Combined Distribution of Period of Gestation at GDM Diagnosis and GTT Results (n = 664)

Category	Subcategory	Number of Participants	Percentage (%)
Period of Gestation at GDM Diagnosis (weeks)	24 weeks	37	5.57
	25 weeks	45	6.78
	26 weeks	34	5.12
	27 weeks	33	4.97
	28 weeks	40	6.02
	29 weeks	43	6.48
	NA (No GDM)	432	65.06
GTT T2 Results	Normal	432	65.06
	Abnormal	232	34.94
GTT T3 Results	Normal	432	65.06
	Abnormal	232	34.94
Total	-	664	100

Table 2: Combined Distribution of Urine Albumin Status Across Trimesters (n = 664)

Trimester	Status	Number of Participants	Percentage (%)
T1	Normal	664	100.00
	Microalbuminuria	0	0.00
T2	Normal	611	92.02
	Microalbuminuria	53	7.98
T3	Normal	611	92.02
	Microalbuminuria	53	7.98
Total	—	664	100

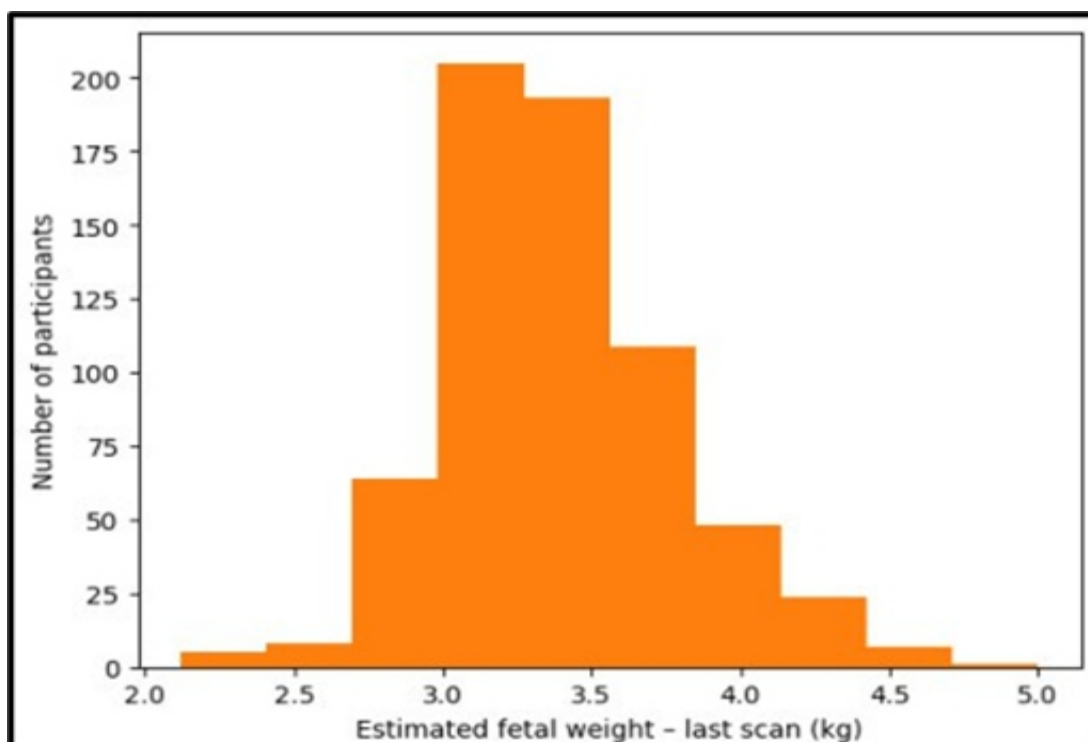


Figure 2: Estimated Fetal Weight (EFW) at Last Ultrasound Scan (n = 664)

Table 3: Association of First-Trimester HbA1c with Maternal and Perinatal Outcomes (n = 664)

Outcome	Category	HbA1c < 5.9% (n = 332)	HbA1c ≥ 5.9% (n = 332)	Total	χ ² value	p-value
Gestational Diabetes Mellitus (GDM)	No	280	152	432	106.86	<0.0001
	Yes	52	180	232		
Gestational Hypertension (HTN)	No	312	273	585	20.75	<0.0001
	Yes	20	59	79		
Mode of Delivery	Vaginal	260 (78.31%)	227 (68.37%)	487 (73.34%)	10.01	0.002
	LSCS	72 (21.69%)	105 (31.63%)	177 (26.66%)		
Perinatal Outcome	Normal	291	220	511	41.62	<0.0001
	Adverse	41	112	153		
Total	-	332	332	664	-	-

Table 4: Comparison of Maternal Characteristics, Obstetric Profile, and Outcomes by First-Trimester HbA1c Group (n = 664)

Variable	Category	HbA1c < 5.9% (n = 332)	HbA1c ≥ 5.9% (n = 332)	Total	Statistical Test
Birth Weight (kg)	Mean ± SD	2.97	3.32	—	t = -12.89, p < 0.0001
Maternal Age (years)	Mean ± SD	28.34 ± 5.45	28.70 ± 5.21	—	t = -0.86, p = 0.39
Pre-pregnancy BMI (kg/m²)	Mean ± SD	24.28 ± 3.38	24.13 ± 3.32	—	t = 0.59, p = 0.56
Obstetric Score	Primi	133 (40.06%)	139 (41.87%)	272	$\chi^2 = 0.27$, p = 0.87
	G2	130 (39.16%)	128 (38.55%)	258	
	G3+	69 (20.78%)	65 (19.58%)	134	
Past Obstetric History	No adverse history	152 (45.78%)	149 (44.88%)	—	$\chi^2 = 1.95$, p = 0.86
	Previous GDM	52 (15.66%)	45 (13.55%)	—	
	Previous IUD	34 (10.24%)	35 (10.54%)	—	
	Previous macrosomia/LGA	36 (10.84%)	33 (9.94%)	—	
	Previous preeclampsia	31 (9.34%)	35 (10.54%)	—	
	Previous preterm delivery	27 (8.13%)	35 (10.54%)	—	
Gestational Diabetes Mellitus (GDM)	No	280 (84.34%)	152 (45.78%)	432	$\chi^2 = 106.86$, p < 0.0001
	Yes	52 (15.66%)	180 (54.22%)	232	
Total	-	332	332	664	-

Table 5: Association of First-trimester HbA1c with GTT T2 and GTT T3

GTT T2 (Second-trimester GTT)			
GTT T2 result	HbA1c < 5.9% (n = 332)	HbA1c ≥ 5.9% (n = 332)	Total
Normal	280 (84.34%)	152 (45.78%)	432
Abnormal	52 (15.66%)	180 (54.22%)	232
Total	332 (100%)	332 (100%)	664
Chi-square: $\chi^2 = 106.86$, p < 0.0001			
GTT T3 (Third-trimester GTT)			
GTT T3 result	HbA1c < 5.9% (n = 332)	HbA1c ≥ 5.9% (n = 332)	Total
Normal	280 (84.34%)	152 (45.78%)	432
Abnormal	52 (15.66%)	180 (54.22%)	232
Total	332 (100%)	332 (100%)	664
Chi-square: $\chi^2 = 106.86$, p < 0.0001			

Table 6: Association of First-trimester HbA1c with Urine Albumin Status

Urine Albumin – T1		
Status	HbA1c < 5.9% (n=332)	HbA1c ≥ 5.9% (n=332)
Normal	332 (100%)	332 (100%)
Chi-square: $\chi^2 = 0.00, p = 1.00$		
Urine Albumin – T2		
Status	HbA1c < 5.9% (n=332)	HbA1c ≥ 5.9% (n=332)
Normal	280 (84.34%)	152 (45.78%)
Microalbuminuria	52 (15.66%)	180 (54.22%)
Chi-square: $\chi^2 = 106.86, p < 0.0001$		
Urine Albumin – T3		
Status	HbA1c < 5.9% (n=332)	HbA1c ≥ 5.9% (n=332)
Normal	280 (84.34%)	152 (45.78%)
Microalbuminuria	52 (15.66%)	180 (54.22%)
Chi-square: $\chi^2 = 106.86, p < 0.0001$		

Table 7: Association of First-trimester HbA1c with Urine Albumin Status (n = 664)

Urine Albumin – T1	
Status	HbA1c < 5.9% (n = 332)
Normal	332 (100.00%)
Chi-square: $\chi^2 = 0.00, p = 1.00$	
Urine Albumin – T2	
Status	HbA1c < 5.9% (n = 332)
Normal	317 (95.48%)
Microalbuminuria	15 (4.52%)
Total microalbuminuria (T2)	53 (7.98%)
Chi-square: $\chi^2 = 8.12, p = 0.004$	
Urine Albumin – T3	
Status	HbA1c < 5.9% (n = 332)
Normal	317 (95.48%)
Microalbuminuria	15 (4.52%)
Total microalbuminuria (T3)	53 (7.98%)
Chi-square: $\chi^2 = 8.12, p = 0.004$	

Table 8: Estimated Fetal Weight (Last Scan) by First-trimester HbA1c Group

HbA1c group	n	Mean EFW (kg) ± SD
HbA1c < 5.9%	332	3.21 ± 0.22
HbA1c ≥ 5.9%	332	3.57 ± 0.44
Independent t-test: $t = -13.16, p < 0.0001$		

DISCUSSION

Maternal glucose metabolism plays a crucial role in determining pregnancy outcomes, particularly during early gestation when placentation and fetal organogenesis occur. Increasing evidence suggests that dysglycaemia in the first trimester, even before the diagnosis of gestational diabetes mellitus (GDM), is associated with adverse maternal and perinatal outcomes. Glycosylated haemoglobin (HbA1c), reflecting average blood glucose over the previous two to three months, serves as a stable and practical marker for identifying early gestational hyperglycaemia, offering advantages over single-point glucose measurements. Early assessment enables timely preventive interventions. The rising prevalence of glucose intolerance among women in Kerala, driven by lifestyle changes and increasing obesity, has further emphasized the need for early screening strategies [1,4].

The present study population had a mean maternal age of 28.52 ± 5.33 years, comparable to previous studies, indicating representation of the optimal reproductive age group. Maternal age did not significantly influence HbA1c levels, supported its independent role as a metabolic marker. The mean pre-pregnancy BMI was 24.20 ± 3.35 kg/m², consistent with earlier findings, although no significant association was observed between BMI and HbA1c levels, suggested that early dysglycaemia may occur independent of adiposity. A positive family history of diabetes was noted in 36.6% of participants, reinforcing the role of genetic predisposition in influencing glycaemic status and risk of GDM [13,14].

The distribution of gravidity and adverse obstetric history was comparable across HbA1c groups, indicating that first-trimester HbA1c reflects current metabolic status rather than past obstetric events. In this study, 50% of women had HbA1c $\geq 5.9\%$, providing a balanced comparison. A strong association was observed between elevated HbA1c and the development of GDM, with significantly higher incidence among women with HbA1c $\geq 5.9\%$, consistent with previous research highlighting its predictive value. Although most GDM cases were diagnosed between 24 and 29 weeks, elevated first-trimester HbA1c preceded diagnosis, supporting its role in early risk stratification [15].

Elevated HbA1c was also significantly associated with gestational hypertension, likely due to endothelial dysfunction and abnormal placentation. Women with higher HbA1c levels had increased rates of cesarean delivery, possibly due to complications such as fetal macrosomia and GDM. Perinatal outcomes were significantly poorer in the high HbA1c group, with increased rates of preterm birth, macrosomia, and neonatal complications, consistent with previous findings [13,15].

Mean birth weight and estimated fetal weight were significantly higher in women with elevated HbA1c, reflecting the impact of early hyperglycaemia on fetal growth through mechanisms such as fetal hyperinsulinaemia. Additionally, elevated HbA1c was associated with abnormal glucose tolerance tests later in pregnancy

and higher amniotic fluid index, indicating increased risk of polyhydramnios. Women with higher HbA1c also delivered at earlier gestational ages, supporting evidence linking maternal hyperglycaemia with preterm birth [16,17].

No significant association was observed between HbA1c and infectious or haemorrhagic complications, suggesting that its effects are primarily metabolic. While urine albumin levels were normal in the first trimester, elevated HbA1c was strongly associated with microalbuminuria in later trimesters, indicating progressive endothelial dysfunction [18,19].

Retnakaran R & Shah BR. 2009 and **Powe CE, et. al; 2011**, highlighted that first-trimester HbA1c is a strong and independent predictor of adverse obstetric and perinatal outcomes. Early identification of dysglycaemia allows for timely interventions, improved antenatal care, and better maternal and neonatal outcomes, supporting its inclusion as a routine screening tool in pregnancy [19,20].

CONCLUSION

This retrospective cohort study at Pushpagiri Medical College Hospital in South Kerala evaluated the relationship between first-trimester HbA1c and pregnancy outcomes in 664 postpartum women divided equally into two groups ($<5.9\%$ and $\geq 5.9\%$). Elevated HbA1c was strongly associated with increased risks of gestational diabetes, hypertensive disorders, cesarean delivery, earlier births, higher neonatal birth weight, and adverse perinatal outcomes, independent of maternal age, BMI, or obstetric history. The findings highlight early pregnancy glycaemic status as a key predictor and support first-trimester HbA1c as a practical tool for early risk identification and timely intervention strategies

LIMITATIONS & FUTURE PERSPECTIVES

The study was limited by its single-centre design, relatively small sample size, and short duration, which may restrict generalizability. Future research could focus on multicenter studies with larger cohorts to validate findings, evaluate long-term outcomes, and explore innovative diagnostic and management strategies for appendicular perforation, improving patient prognosis and reducing complications.

CLINICAL SIGNIFICANCE

Timely detection and management of acute appendicitis are crucial to prevent perforation, reducing morbidity and mortality. The study identifies high-risk groups, such as males and individuals at age extremes, highlighting the need for targeted preventive strategies and clinical vigilance. Delayed presentation significantly increases perforation risk, underscoring the importance of early healthcare access and awareness campaigns. Postoperative complications, including surgical site infections and prolonged ileus, emphasize the need for thorough pre-operative risk assessment and tailored postoperative care.

Recognizing the distal third of the appendix as the most common perforation site aids surgeons in effective intraoperative planning and management.

ABBREVIATIONS

HbA1c: Glycosylated haemoglobin

GDM: Gestational diabetes mellitus

GH: Gestational hypertension

LSCS: Lower segment caesarean section

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AUTHOR CONTRIBUTIONS

All authors significantly contributed to the study conception and design, data acquisition, or data analysis and interpretation. They participated in drafting the manuscript or critically revising it for important intellectual content, consented to its submission to the current journal, provided final approval for the version to be published, and accepted responsibility for all aspects of the work. Additionally, all authors meet the authorship criteria outlined by the International Committee of Medical Journal Editors (ICMJE) guidelines.

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CONFLICT OF INTEREST

Authors declared that there is no conflict of interest.

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All necessary consent & approval was obtained by authors.

CONSENT FOR PUBLICATION

All necessary consent for publication was obtained by authors.

DATA AVAILABILITY

All data generated and analyzed are included within this research article. The datasets utilized and/or analyzed in this study can be obtained from the corresponding author upon a reasonable request.

USE OF ARTIFICIAL INTELLIGENCE (AI) & LARGE LANGUAGE MODEL (LLM)

The authors confirm that no AI & LLM tools were used in the writing or editing of the manuscript, and no images were altered or manipulated using AI & LLM.

AUTHOR'S NOTE

This article serves as an important educational tool for the scientific community, offering insights that may inspire future research directions. However, they should not be relied upon independently when making treatment decisions or developing public health policies.

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