



ASSOCIATION OF HbA1C IN FIRST TRIMESTER OF PREGNANCY WITH GESTATIONAL DIABETES MELLITUS-AN OBSERVATIONAL STUDY

Obstetrics & Gynaecology

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KEYWORDS

INTRODUCTION

Carbohydrate intolerance of variable severity with onset or first recognition during the present pregnancy is defined as gestational diabetes mellitus (GDM)¹ and is the most prevalent metabolic abnormality during pregnancy. This condition could pre-exist in an unrecognized form or begin simultaneously with pregnancy and, in some cases, persist after delivery.

Pregnancy is a diabetogenic state¹ as there are various hormones released during pregnancy which causes insulin resistance

1. Placental hormones- Human Placental Lactogen, Placental growth factor, Insulinase
2. Other hormones- progesterone, estrogen and cortisol.

As a result, pregnant women are more prone to diabetes.

It has been reported by the government of India that GDM prevalence ranges from 9.9%-17.8% in different parts of India, given the fact there are huge differences in lifestyle and socioeconomic status of the population of India.²

About 50% of females with GDM develop diabetes mellitus type- 2 within 20 years.

According to some studies, about 4-50% females with PCOD develop GDM during pregnancy.⁶

Screening Tests for GDM³

Single step test

DIPSI (Diabetes in Pregnancy Study Group India) criteria- glucose levels ≥ 140 mg/dL after 2 hours of consumption of 75 grams glucose irrespective of the fasting status or the last meal consumed is diagnosed as GDM. Test done are as follows-

- At first contact of ANC.
- At 24-28 weeks, if first test was negative

CRITERIA	IN PREGNANCY	NON PREGNANT
2 hr ≥ 200 mg/dl	Diabetes mellitus	Diabetes mellitus
2 hr ≥ 140 mg/dL-199 mg/dl	GDM	Impaired glucose tolerance
2 hr < 140 mg/dl	Non – GDM	Non diabetic

The Government of India (MoHFW) recommends **universal screening** by OGTT(DIPSI) test at first ANC visit as the Indian population is at the higher risk of developing Diabetes mellitus.²

This single step screening method is also recommended by FOGSI. (2020)

If GDM is not diagnosed in first visit, repeat testing is to be done at 24-28 weeks of gestation.

In early pregnancy, chances of hypoglycaemia are high due to increased insulin sensitivity and recurrent nausea & vomiting. Therefore, OGTT(DIPSI) done in first trimester is not reliable. Whereas, HbA1c shows glucose concentration of previous 2 months.

HbA1c levels in pregnant females and its relation to the risk of

congenital anomalies in the fetus⁵ –

- HbA1c $< 7\%$ – no greater risk for anomalies
- 7-8.5% – risk of 5% for anomalies
- $> 10\%$ – risk of anomalies rises to 22%

Effect of Diabetes on pregnancy¹

With overt diabetes, the embryo, fetus, and mother frequently experience serious complications directly attributable to diabetes.

Fetal complications include-

- Spontaneous abortion
- Preterm delivery
- Malformation in the baby- Cardiovascular malformations are the most common malformation in the baby of a mother with overt diabetes.
- Sudden intra uterine deaths
- Polyhydramnios

Neonatal Complications include-

- RDS
- Hypoglycemia
- Hypocalcemia
- Hyperbilirubinemia and polycythemia
- Cardiomyopathy
- Long term cognitive developmental problems
- Inheritance of diabetes- The risk of developing type 1 diabetes in either parent is expected is **3 -5 percent**. Type 2 diabetes has a much stronger genetic component. if both parents have type 2 diabetes, the risk of developing it approaches **40 percent**.

Maternal Complications include-

- Risk of developing pre-eclampsia
- Diabetic retinopathy
- Diabetic neuropathy
- Diabetic ketoacidosis
- Increased rates of infections

Effect of pregnancy on diabetes¹

With the possible exception of diabetic retinopathy, the long term course of diabetes is not affected by pregnancy.



• This 6050-g macrosomic infant was born to a woman with diabetes.

Effects of GDM on mother and fetus¹

Adverse consequences of gestational diabetes mellitus differ from those of pregestational diabetes. Unlike in women with overt diabetes, women with gestational diabetes do not have fetuses with substantially higher rates of anomalies than the general obstetrical population. From the data collected from Swedish Medical Birth Registry, major malformation rates in overt diabetes mellitus was 2.3% and in GDM was 1.8%.

Effects on fetus include-

- Neonatal hypoglycaemia
- Fetal macrosomia

Effects on mother include-

- High risk of developing diabetes mellitus type 2 in further life. The incidence for the same is 50% within 20 years post pregnancy.
- Higher rates of Caesarean section.
- Higher rates of instrumental delivery.
- Increased frequency of hypertension.

Utility of HbA1c for diagnosis of Gestational Diabetes Mellitus

The normal range of HbA1c is less than 6.5% in non-pregnant state. Normal range for HbA1c during pregnancy is less than 5.7%. HbA1c may have a role in screening and management of GDM.

According to government of India, the DIPSI guidelines are followed to diagnose gestational diabetes mellitus. Early screening of pregnant women can lead to early screening of GDM patients. The treatment of early GDM can improve impaired glucose tolerance in the second trimester, and reduce the incidence of GDM complications. HbA1c in early pregnancy has a positive impact on the screening and diagnosis of GDM patients. For eg., patients with elevated HbA1c in the first trimester of pregnancy have a higher risk of GDM. Also HbA1c is associated with an increased probability of LGA (large for gestational-age infants). The ADA considers that HbA1c < 6 at mid and late pregnancy is related with a minimization of LGA risk.⁴ Elevated first- trimester HbA1c is associated with severe maternal morbidity (SMM) or risk of death.

A hemoglobin A1c (HbA1c) level 5.7-6.4% is the recommended diagnostic cutoff for gestational diabetes. When considering HbA1c as a screening test in early pregnancy to detect substantial glucose elevations in women without known diabetes, there is a little evidence as to what diagnostic threshold should be recommended for intervention. Most data are from studies of women with preexisting diabetes. Further studies needed to verify these results. Limited data was available regarding association of HbA1c and GDM. Therefore the current study was conducted to determine the association of HbA1c in first trimester of pregnancy with gestational diabetes mellitus.

AIM:

- To assess the association between glycosylated haemoglobin and gestational diabetes mellitus.
- The **objective** of this study is:
- To study the association between HbA1c with GDM
- To identify the lower cut-off of HbA1c for GDM screening.

MATERIAL AND METHOD:

An Observational study has been carried out in pregnant women, visiting the ANC OPD in obs gyn department of RMCH, Bareilly for a period of 1 year. A total of 144 study subjects were enrolled through OPD.

Inclusion Criteria:

Pregnant women at 8-14 weeks of period of gestation with singleton pregnancy who gave the consent for the study.

Exclusion Criteria:

The patients with the following conditions were not be considered for the study

1. Overt diabetes mellitus.
2. Women with severe anaemia.
3. Pregnant women with chronic renal disease.
4. Obese pregnant woman.
5. Pregnant already diagnosed with PCOD.

After the approval of the Institutional Ethics Committee, women were informed about the need for HbA1c testing. Pregnant females between

8 to 14 weeks of POG who came to the ANC OPD was chosen for the study by applying the above criteria. Informed consent was taken.

Women with OGTT(DIPSI) less than 140 mg/dl were re-evaluated at 24 to 28 weeks of period of gestation with repeat OGTT(DIPSI) test. Subsequently, we evaluate the HbA1c level of all 144 enrolled females who have met the inclusion criteria and its association with GDM risk.

The data analysis was done by using Statistical Package for the Social Sciences (SPSS) version 23.0 for Windows. Chi- square test used for non-parametric variables and Student's t-test was used for continuous variables and $p < 0.05$ was considered as statistically significant.

RESULT

A total one hundred forty four pregnant females between 8 to 14 weeks of POG who came to the ANC OPD will be chosen for the study. OGTT(DIPSI), HbA1c and all routine ANC investigations at first trimester was done. And found that 5 (3.4%) pregnant females were showing the GDM in first trimester. The rest 139 were further evaluated with single step OGTT (DIPSI) at 24-28 weeks of gestation and further 10 pregnant females were diagnosed as GDM. A total of 129 pregnant females were found non-GDM.

Table 1: Prevalence of GDM in this study

GDM	Frequency (n=144)	Percentage
In first trimester	5	3.4%
In 24-28 wks	10	6.9%
Non-GDM	129	89.7%

The prevalence of GDM in first trimester and 24 to 28 wks was 3.4% and 6.9% respectively. Thus a total prevalence of 10.3% whereas in non GDM group was 89.7%.

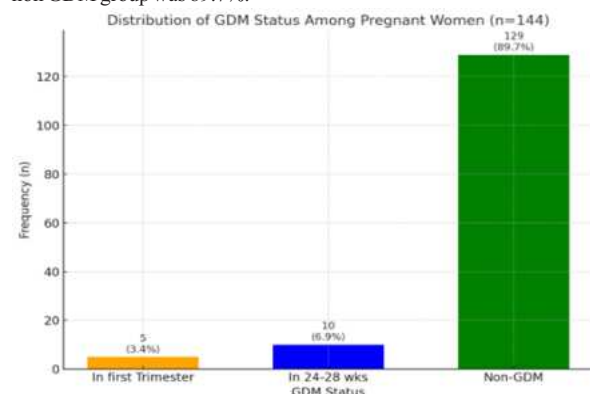
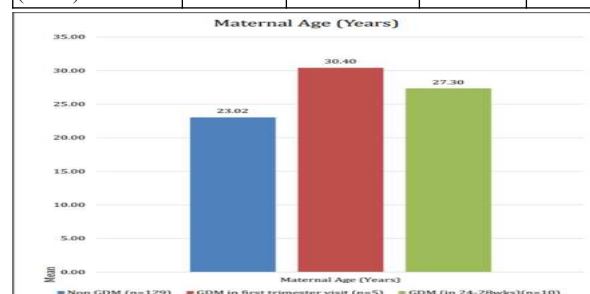
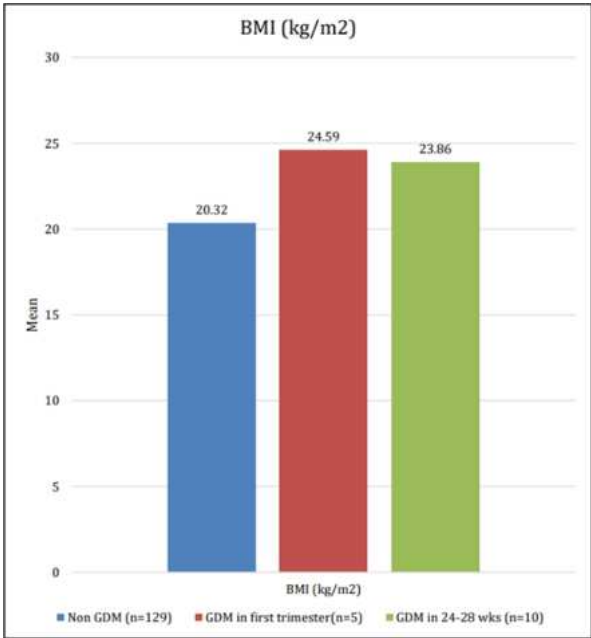


Table 2: Pregnant Women Characteristics:

	Non GDM (n=129)	GDM (in first trimester visit) (n=5)	GDM (in 24-28wks) (n=10)	p value
Maternal Age (Years) (Mean)	23.02±2.34	30.40±3.44	27.3±2.9	<0.001
BMI (kg/m ²) (Mean)	20.3±1.2	24.59±1.57	23.86±0.97	<0.001

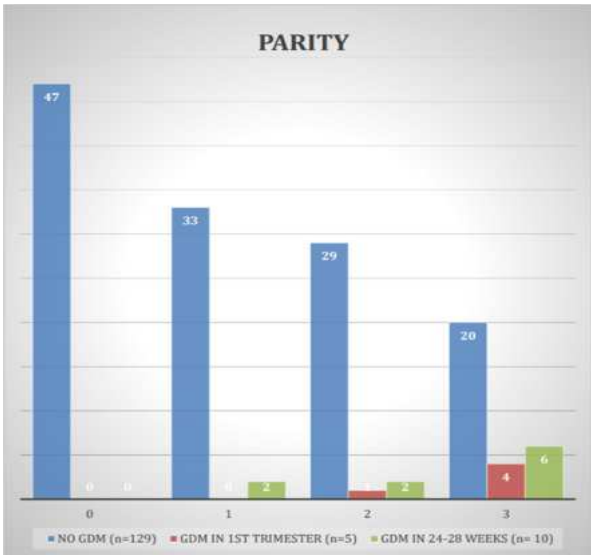




We noted that the maternal age and BMI was higher in GDM group (both groups that is, detected in first trimester and 24-28 weeks) compared to non GDM group and it was significant (p<0.001).

Table 3: Obstetric History

		Non GDM (n=129)	GDM in first trimester (n=5)	GDM in 24-28wks (n=10)	P value
Parity	0	47 (36.4%)	0	0	<0.05
	1	33 (25.5%)	0	2 (20%)	
	2	29 (22.4%)	1 (20%)	2 (20%)	
	3	20 (15.7%)	4 (80%)	6 (60%)	



Multiparous females were at higher risk of for developing GDM as compared non GDM group (p<0.05).

Table 4: Reasons For LSCS IN GDM Patients:

Reasons for LSCS	Frequency (n=5)	Percentage
PREV 2	1	20%
FETAL DISTRESS	3	60%
CPD	1	20%

Fetal distress was the main reason for LSCS in GDM patients with 60%, CPD and previous 2 LSCS were other reasons with 20%. in patients with fetal distress(n=3), 1 was induced and 2 were kept for spontaneous vaginal delivery.

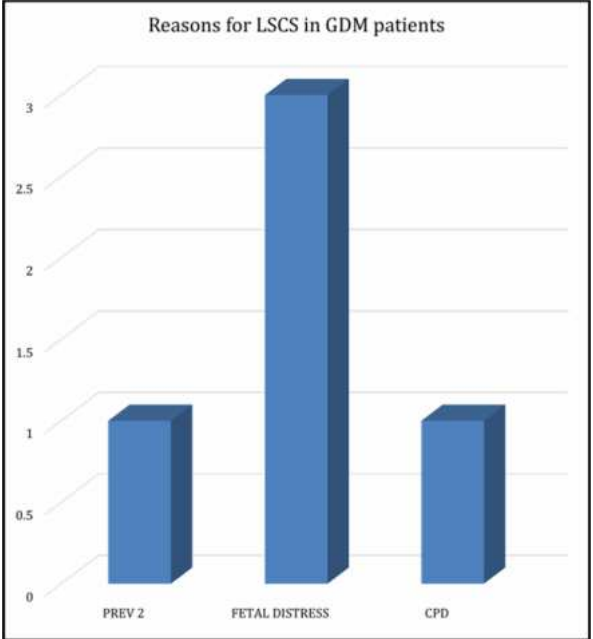


Table 5: Reasons For LSCS In Non GDM Patients

Reasons for LSCS	Frequency (n=13)	Percentage
Prev 2	3	23.08%
FETAL DISTRESS	3	23.08%
SCAR TENDERNESS	4	30.77%
CPD	2	15.38%
PLACENTA PREVIA	1	7.69%

Scar tenderness (30.77%) was the main reason for LSCS in non GDM group followed by previous 2 LSCS (23.08%) and fetal distress (23.08%), followed by CPD (15.38%). Least common reason was placenta previa 7.69%). Out of 3 LSCS for fetal distress, all were induced with misoprostol.

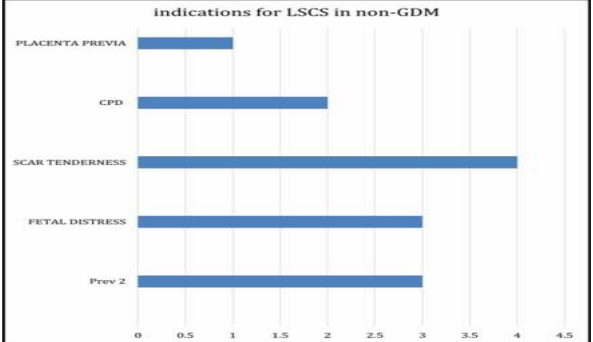


Table 6: HbA1c Levels In First Trimester GDM Patients And 24-28 Weeks GDM Patient

	HbA1c levels (mean)
In first trimester GDM patients (n=5)	5.63
In 24-28 weeks GDM patients (n=10)	5.5

Mean value of HbA1c of patients diagnosed as GDM in first trimester was 5.63% and that in patients of GDM who were diagnosed at 24-28 weeks was 5.5%.

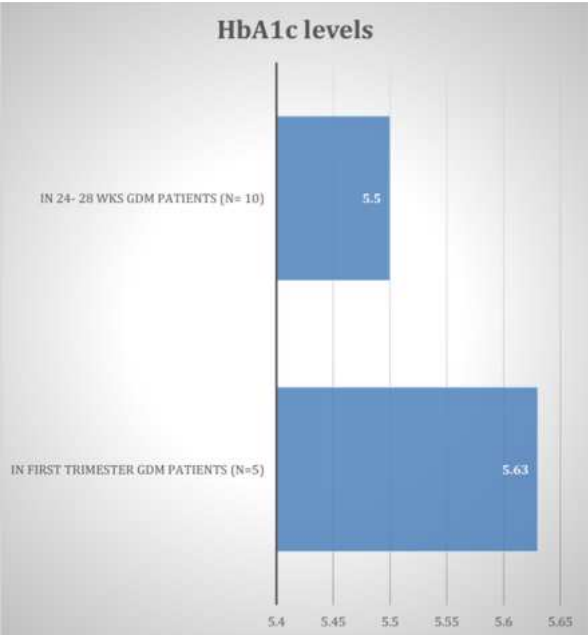
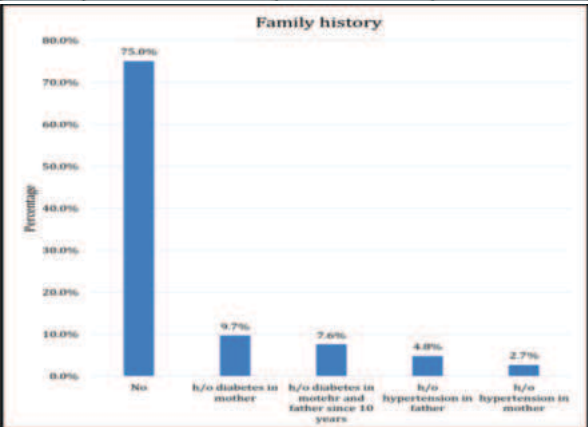


Table 7: Family History

Family history		Frequency (n=144)	Percentage
No		108	75%
Yes		36	25%
Yes	h/o diabetes in mother	14	9.7%
	h/o diabetes in mother and father since 10 years	11	7.6%
	h/o hypertension in father	7	4.8%
	h/o hypertension in mother	4	2.7%
	h/o hypertension in father and mother	0	0%



In this study we noted that 25% pregnant women were having family history like h/o diabetes in mother and father in the last 10 years (7.6%), h/o diabetes in mother (9.7%) and h/o hypertension (in father (4.8%) and in mother (2.7%).

Table 8: Prevalence of GDM with positive family history

	Patients who developed GDM with positive family history (n=15)	Patients who did not developed GDM with positive family history (n=129)
n=36	11 (73.34%)	25 (19.37%)

Out of 36 patients with positive family history, 11 developed GDM. So, 11 out of 15 GDM patients (73.34%) had a positive family history and only 25 out of 129 patients of non-GDM patients (19.37%) had a positive family history showing a positive co-relation between family history and development of GDM.

Table 9: Maternal Outcome

Mode of Delivery	Non GDM (n=129)	GDM (n=15)	P value
TVD	116(89.9%)	10 (66.66%)	<0.01
LSCS	13(10.1%)	5 (33.34%)	<0.01

This study also noted that 33.34% of GDM patients needed LSCS while only 10.1% of non GDM cases needed LSCS (P<0.001).

Table 10: Incidence Of Fetal Distress In Induced Vs Spontaneous Delivery Group

	FETAL DISTRESS (n=6)	
	GDM	Non-GDM
Induced (n=52)	1	3
Spontaneous (n=80)	2	0

Out of 6 patients who had fetal distress, 33.33% from GDM group had fetal distress after induction and 66.67% had fetal distress even when they were not induced. 100% patients from non GDM group had fetal distress after induction from misoprostol. So, fetal distress was in GDM patients even when they were not induced with misoprostol.

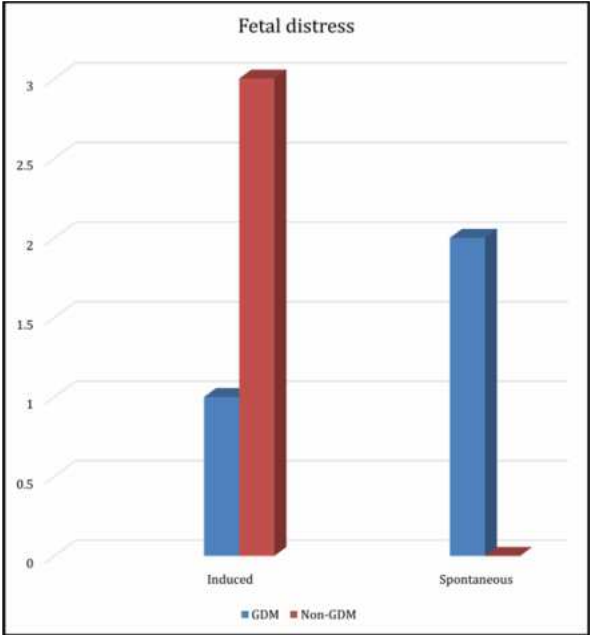


Table 11: GDM Patients Who Also Developed Pre-eclampsia

	Patients who also developed pre-eclampsia	p value
GDM group (n=15)	1	p<0.001
Non- GDM group (n=129)	0	

Out of 15 patients of GDM, 1 patients developed pre-eclampsia. None of the Non- GDM developed pre eclampsia. (p<0.001).

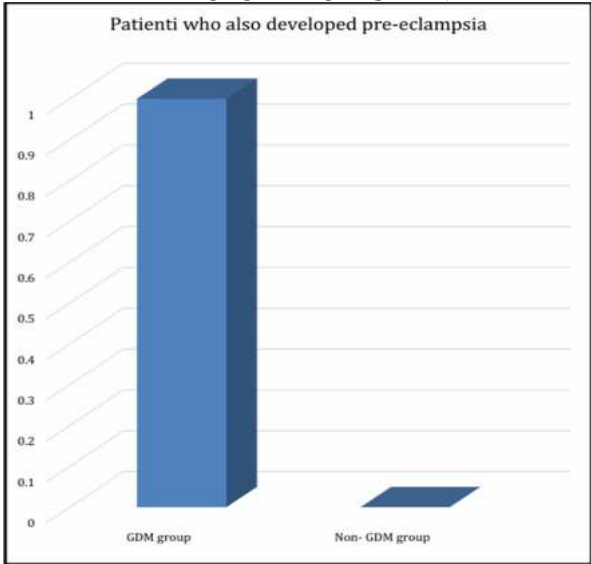


Table 12: Birth Weight Of Baby

	Non GDM (n=129)	GDM in first trimester (n=5)	GDM in 24-28 wks (n=10)	P value
Birth weight (Mean)	2.95	3.454	3.09	<0.001

There was significantly higher birth weight 3.4kg and 3.09kg in first trimester and 24-28 weeks GDM group, in comparison to 2.95 kg in non-GDM group (p<0.001)

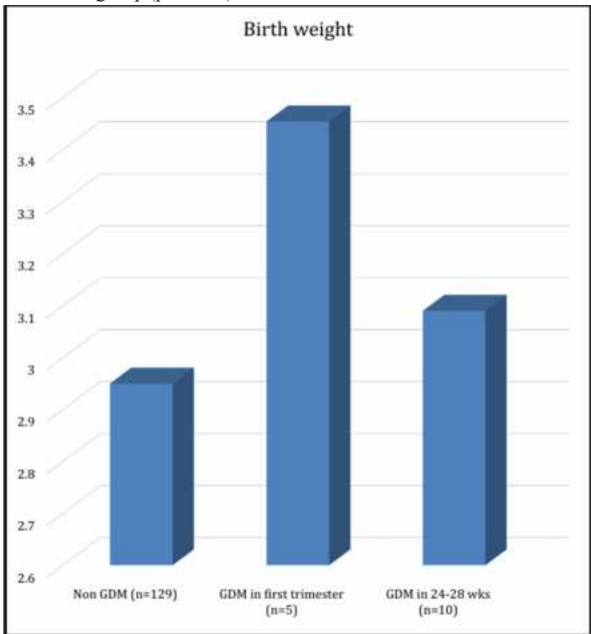


Table 13: ROC Curve Analysis(1st and 2nd Trimester GDM (n=15) And Non GDM (n=129))

Test Result Variable(s)	Area Under the Curve	Std. Error ^a	Asymptotic Sig. ^b	Asymptotic 95% Confidence interval	
				Lower Bound	Upper Bound
HbA1c	0.996	0.003	0.000	0.990	1.000

The test result variable(s): HbA1c, 1st has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

This is under the nonparametric assumptions.

By using the ROC curve analysis, we found that cutoff >5.5 HbA1c level with 100.0% sensitivity, 82.0% specificity and 96.0% accuracy to diagnose the GDM in first trimester in pregnant women. And OGTT (DiPSi) in first trimester level >140.0 mg/dl was with 80.0% sensitivity, 100.0% specificity and 99.8% accuracy.

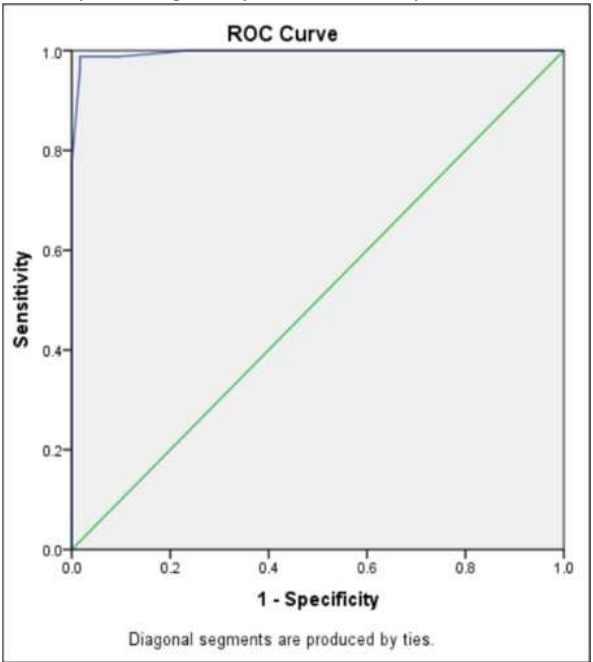


Table 14: Cutoff, Sensitivity, Specificity and Accuracy of HbA1c and OGTT in 1st trimester

Variables	Cutoff	Sensitivity	Specificity	Accuracy
HbA1c	5.5	100%	82%	96%
OGTT (DiPSi)	140	80%	100%	99.2%

DISCUSSION

This study was conducted in Rohilkhand medical college, Bareilly on a total of 144 patients meeting the exclusion and inclusion criteria. The prevalence of Tripathy et al (2022) was 11.5 %, Valadan M et al (2022) was 16.4%, Amylidi S et al (2015) was 14.7 %. In our study, the prevalence of GDM was 10.3% which was comparable to studies of Valadan et al and Amylidi S et al. The result of Singh V et al (2023) was 28 kg/m², Amylidi S et al (2015) was 26.4 kg/m², Sujithra et al (2018) was 26 kg/m². In our study, the mean of BMI in GDM cases was 24.5kg/m². it was comparable to studies of Singh V et al. It was 26 kg/m² in the study conducted by Sujithra et al. The average age of GDM patients in our study was 29 years and it was comparable to study conducted by Amylidi et al, Valadan M et al and Hinkle S et al where the average age was 31 years, 32 years and 30 years respectively. Percentage of LSCS in GDM patients was 33.34% in our study. It was comparable to the study conducted by Benainges et al with 29.4% of LSCS done in GDM patients. In Hughes et al study, HBA1C and OGTT are done in antenatal mothers 41mmol/mol) developed diabetes and they are at increased risk of adverse pregnancy outcomes. In Amylidi et al study, women at high risk with first trimester HBA1C ≥6% are predisposed to GDM. These women are at risk of developing diabetes mellitus and so they must be given appropriate advice on diet and lifestyle modifications early in pregnancy. In Jay D et al study, HBA1C cut off point for diagnosing GDM before 20 weeks of pregnancy is 5.4%. The association between HBA1C changes in diagnosing GDM before 20 weeks and BMI are highly significant. it was comparable to our study with HBA1C levels cut-off at ≥5.56%. In our study GDM cases had complications in neonates such as respiratory distress syndrome (13.4%) while the incidence of RDS in non-GDM was low (2.3%). 6.6% of GDM patients developed pre-eclampsia later in pregnancy. The APGAR score were lower in GDM group.

SUMMARY

Our study was done in the Obstetrics department of Rohilkhand Medical College, Bareilly. The prevalence of gest diabetes mellitus in our study was 19.4%. The mean age of mother diagnosed with GDM in

first trimester was 30 years and that of mothers diagnosed in 24 to 28 weeks of gestation was 27 years. BMI was higher in GDM patients as compared to non – GDM patients. GDM was more common in multiparous women. Around 33.34% percent of pregnant females with GDM delivered by LSCS, most common indication being fetal distress. 6.6% females developed pre-eclampsia later in the pregnancy. The cutoff of HbA1c at which females developed GDM was 5.56%.

CONCLUSION

First trimester HBA1C $\geq 5.56\%$ is useful in predicting pregnant women who develops GDM, so they must be given appropriate advice of diet and lifestyle modification early in pregnancy. Respiratory distress syndrome, APGAR 1 minute, preeclampsia, are highly significant with HBA1C $\geq 5.56\%$ Thus, first trimester HBA1C helps in screening of GDM and to prevent bad maternal and fetal outcomes.

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