

## HbA1c IN ABNORMAL GCT IN FIRST AND SECOND TRIMESTER OF PREGNANCY AND ITS CORRELATION WITH ULTRASOUND FINDINGS AND FETAL OUTCOME

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Received : 17/10/2022  
Received in revised form : 16/11/2022  
Accepted : 30/11/2022

**Keywords:**

GDM, T2DM, Macrosomia, Hyperglycaemia, Dystocia, Polyhydramnios.

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DOI: 10.47009/jamp.2022.4.5.145

Source of Support: Nil,  
Conflict of Interest: None declared

Int J Acad Med Pharm  
2022; 4 (5); 696-701



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### Abstract

**Background:** Gestational hyperglycaemia is associated with multiple adverse outcomes for both the mother and the child. The non-desirable outcomes for the child include intra-uterine death (IUD), macrosomia, hypoglycaemia and hypocalcaemia, while maternal complications of GDM include increased hypertensive episodes, operative deliveries and incidence of TDM in future. Moreover, the offspring of GDM mothers are prone to develop metabolic diseases in the later phase of life, like Diabetes Mellitus (DM) and obesity. Timeliness and accuracy in diagnosis, therefore, remain pivotal and major drivers in the effective intervention and management of GDM. **Materials and Methods:** This is a prospective observational study to investigate whether the HbA1c level  $\geq 6.5\%$  is associated with adverse pregnancy outcomes. **Result:** Majority of the participants (n=48), had cephalic presentation. Two of the women had placenta praevia with placenta accreta spectrum. Sixty six percent (n=33) had normal amniotic fluid index. Twenty percent (n =10), had polyhydramnios. Forty percent (n= 20), had low birth weight. Forty four percent (n=22) had normal vaginal delivery and 46 (n =23) percent had operative or instrumental delivery and 10 percent (n=5) had preterm vaginal delivery. **Conclusion:** There is significant risk of association of antenatal and intrapartum complications group with Hb1Ac >6.5% in compared with those <6.5%.

## INTRODUCTION

Due to the epidemiologic transition of the population towards aging and more sedentary lifestyle related to urbanization during the past few decades, the prevalence of Type 2 Diabetes mellitus (T2DM) has been rapidly increasing and the age of onset becomes younger globally. The prevalence of Gestational Diabetes Mellitus (GDM), has increased by more than 30 % within one or two decades in a number of countries including developing countries, forming an emerging worldwide epidemic. India is labelled as the diabetes capital of the world with more than 69.2 million cases including four million women with GDM alone. The prevalence of GDM is reported to vary widely (3.8-21%) depending on the geographical location and the diagnostic criteria used in different parts of India.

The diagnostic criteria for GDM suffers from lack of consensus in terms of several cut-offs with varying regional recommendations. These tests primarily rely upon plasma glucose readings at fasting or at various intervals after glucose loading. The Diabetes in Pregnancy Study Group India (DIPSI) recommends testing 2-hour Venous plasma glucose (VPG) after a 75 g oral glucose load, known as the Oral Glucose Tolerance Test (OGTT). According to the DIPSI criteria, a 2-h VPG  $\geq 140$  mg/dL (7.8 mmol/L) under non-fasting conditions is to be used to diagnose GDM. The DIPSI criteria are convenient and an OGTT can be performed both in fasting/non-fasting situations irrespective of the last meal timing. The use of HbA1c, has become the standard of assessing glycemic control in patients with diabetes since the American Diabetes Association (ADA) recommended its use in 1988.

## Aims and Objectives

1. To determine the association between HbA1c level and deranged GCT of first and second trimesters of pregnancy.
2. To investigate whether the HbA1c level  $\geq 6.5\%$  is associated with adverse pregnancy outcomes.
3. To correlate HbA1c level with ultrasound findings and establish relationship between HbA1c and fetomaternal outcome.

## MATERIALS AND METHODS

This prospective observational study design was taken up from June 2020 till September 2022 among the Pregnant women attending the antenatal outpatient department of Obstetrics and Gynaecology, Jawaharlal Nehru Institute of Medical Sciences, Imphal and having abnormal GCT ( $\geq 140$  mg/dL) were included in the study and followed up till delivery. HbA1c was recorded after they have been enrolled in the study.

Sample size (n) will be 50 at the 95% confidence level factor and Prevalence of gestational diabetes women in Manipur 1.6% (Singh T.P et al). The absolute allowable error taken here as 3.5%. All eligible cases were consecutively enrolled as per Obstetrics and Gynaecology Department Out-Patient

Department (OPD) registered list, until the required sample size was obtained.

## Inclusion Criteria

1. Pregnant women with abnormal GCT, belonging to the age group of 18 years to 45 years.
2. Singleton pregnancies coming in their first trimester and second trimester of pregnancy (till 28th week of pregnancy).

## Exclusion Criteria

1. Women with normal GCT
2. Women with multiple pregnancies.
3. Women with pre-existing DM.

## Statistical Analysis

The collected data was entered into MS Excel Office and then transferred into IBM SPSS VERSION 22. Descriptive statistics such as frequency, percentage were used to summarize the findings. Statistical analysis like Chi square test was advised, to find the association between the dependent and independent variable. A p-value of  $<0.05$  was considered significant.

## Ethical issues

Ethical clearance was obtained from the JNIMS institutional ethical committee.

## RESULTS

**Table 1: Socio-demographic characteristics of the participants**

Characteristics (N = 50)	N	%	
Age (in years)	18 - 24yrs	10	20.0
	25 - 31yrs	23	46.0
	32 - 39yrs	13	26.0
	40 - 45yrs	4	8.0
Socioeconomic Status	Lower	4	8.0
	Upper lower	9	18.0
	Lower middle	22	44.0
	Upper middle	15	30.0
Residence	Urban	29	58.0
	Rural	21	42.0

Majority of the women (n = 23, 46%) fall in the age group of 25-31 years. Twenty six percent (n=13), fall in the age group of 32-39 years. Forty four percent of the women (n = 22), hailed from lower middle class while thirty percent (n = 15), are from upper middle class. Fifty eight percent (n= 29) are from urban area while the rest (n = 21) are from rural areas.

**Table 2: Obstetric history of the participants**

Obstetric history (N = 50)	N	%	
Parity	Primigravida	16	32.0
	Multigravida	32	64.0
	Recurrent Abortion	2	4.0

Majority 64% of the participants are multigravida whereas 32% were primigravidae. 4% had recurrent abortions in the obstetric history of the participants. Eighteen percent (n = 9), had prior medical history.

**Table 3: Presence of Pregnancy-associated Complications in the participants**

Pregnancy-associated Complications (N = 50)	N	%
Absent	29	58.0
Present	21	42.0
Types of Complications Present*		HbA1c $<6.5\%$ HbA1c $>6.5\%$
Previous Caesarean Section	4	1      3
Polyhydramnios	4	1      3
Pre-eclampsia	3	1      2
Oligohydramnios	2	1      1

Placenta Previa	2	1	1
Placenta Accreta Spectrum	2	1	1
Pre-labour Rupture of Membrane	2	0	2
Intrauterine Growth Restriction	1	1	0
Intrauterine Death	1	0	1
Elderly Primigravida	1	0	1
Bad Obstetric History	1	1	0
Hyperemesis Gravidarum	1	0	1
Abruptio Placenta	1	1	0
Preterm labour	1	1	0
Obstructed-handled labour	1	0	1
Threatened pregnancy	1	1	0

\* Multiple complications were present in few of these women.

It was found that forty two percent (n=21), had pregnancy associated complications. They are mainly polyhydramnios (n=4), previous caesarean sections (n=4), preeclampsia (n=3), Placenta accreta spectrum (n=2), placenta praevia (n=2), oligohydramnios (n=2), prelabour rupture of membranes and intrauterine death (n=1).

**Table 4: Ultrasound findings during pregnancy in the participants**

Ultrasound findings during pregnancy (N = 50)		N	%
Presentation	Cephalic	48	96.0
	Breech	2	4.0
Placenta	Normal	48	96.0
	Placenta Previa with Placenta accreta spectrum	2	4.0
Liquor condition	Normal AFI	33	66.0
	Oligohydramnios	7	14.0
	Polyhydramnios	10	20.0
Estimated fetal weight	Less than 2.5kg	10	20.0
	More than 2.5kg	40	80.0

Majority of the participants (n=48), had cephalic presentation. Two of the women had placenta praevia with placenta accreta spectrum. Sixty six percent (n=33) had normal amniotic fluid index. Twenty percent (n=10), had polyhydramnios. Forty percent (n= 20), had low birth weight.

**Table 5: Mode of delivery of the participants**

Mode of Delivery (N = 50)	n	%
Normal Vaginal Delivery	22	44.0
Preterm Vaginal Delivery	5	10.0
Instrumental/ Operative Delivery		
Instrumental Delivery	4	8.0
Elective Caesarean Section	15	30.0
Emergency Caesarean Section	3	6.0
Elective Caesarean Hysterotomy	1	2.0

Forty four percent (n=22) had normal vaginal delivery and 46 (n =23) percent had operative or instrumental delivery and 10 percent (n=5) had preterm vaginal delivery.

**Table 6: Intrapartum Complications present in the participants**

Intrapartum and Postpartum Complications (N = 50)	n	%
Absent	43	86.0
Present	7	14.0
Types of Complications present		
Cardiac arrest leading to maternal death	1	2.0
Obstructed labour	1	2.0
Secondary perineal tear	2	4.0
Shoulder dystocia	2	4.0
Shoulder dystocia with secondary perineal tear	1	2.0

Fourteen percent (n = 7) had intra-partum. One participant had a cardiac arrest leading to maternal death. Four percent had shoulder dystocia (n = 2) and four percent (n = 2) had secondary perineal tear and another participant had both shoulder dystocia and secondary perineal tear.

**Table 7: Perinatal outcome of the neonates born to the participants**

Perinatal Outcomes (N = 50)		n	HbA1c < 6.5%	HbA1c above 6.5%
Weight of the baby	Low Birth Weight	10	6	4
	Normal	23	23	0
	Macrosomia	17	1	16
APGAR Score	7 - 10	41	23	18
	4 - 6	8	3	5
	0 - 3	1	0	1
Admission in NICU	Present	14	8	6

	Absent	36	19	17
Types of Perinatal Complications present	Macrosomia	16	1	15
	Respiratory distress syndrome	7	4	3
	Hypoglycemia	1	0	1
	Meconium aspiration syndrome	2	0	2
	Intra-uterine death	1	0	1
	Both macrosomia and meconium-stained liquor	1	0	1

Thirty four percent (n= 17) had macrosomia (more than 3.5 kg) and twenty percent (n=10) had low birth weight (less than 2.5 kg). Eighty two percent (n=41) had a good Apgar score of 7-10. Twenty eight percent (n=14) were admitted in NICU. Fifty six percent (n=28) had perinatal complications. Thirty two percent (i.e. 16) had macrosomia and 12 percent (n=6) had respiratory distress syndrome. One neonate was both macrosomia and had meconium-stained liquor.

**Table 8: Association between HbA1c level of the pregnant participants with its outcomes, complications and others**

Outcomes Characters		Hba1c		Total	$\chi^2$ -value	P-value
		< 6.5	≥ 6.5			
Pregnancy Associated Complications	Present	7	14	21	4.023	0.045*
	Absent	18	11	29		
Mode of Delivery	Normal Vaginal Delivery	14	8	22	6.958	0.031*
	Preterm Vaginal Delivery	4	1	05		
	Other types of delivery	7	16	23		
Weight of the baby born	Low Birth Weight	6	4	10	15.602	0.000*
	Normal	17	6	23		
	Macrosomia	2	15	17		
presence of perinatal complications in the baby born	Present	7	22	29	18.473	0.000*
	Absent	18	3	21		
Different types of perinatal complications	NA	19	3	22	30.172	0.000*
	Macrosomia	1	15	16		
	RDS	5	2	7		
	Hypoglycemia	0	1	1		
	MAS	0	2	2		
	IUD	0	1	1		
	Both macrosomia and MSL	0	1	1		

\*p-value < 0.05, Significant.

Pregnancy associated complications were present in seven participants whose HbA1C was less than 6.5 % and in fourteen women with values more than 6.5 %. P Value is 0.045. It can be interpreted that HbA1C value of more than 6.5 is significantly related with pregnancy associated complications. Out of the women whose value of HbA1c was more than 6.5%, 8 had normal vaginal delivery, 16 had instrumental or operative delivery and 1 had preterm vaginal delivery. P Value is 0.031. There is statistical association between HbA1C and type of delivery. Most of the neonates (n=15) born to mothers with HbA1C values more than 6.5, had macrosomia weighing more than 3.5 kg and out of those with less than 6.5% value, two had macrosomia. P value is 0.000. It can be interpreted that there is a high statistical correlation between HbA1C level and weight of the baby. Among women with HbA1c values less than 6.5%, 7 had perinatal complications and they were found in 22 women with values more than 6.5%. P value was found to be at 0.000. Statistically, there is correlation with HbA1C and perinatal complications. Among the women with HbA1c values more than 6.5%, 15 had macrosomia, two had respiratory distress syndrome, one had hypoglycaemia, one had meconium aspiration syndrome, one was intrauterine death and one had both macrosomia and meconium-stained liquor. P value is 0.000. There is statistical significance.

## DISCUSSION

In the present observational study, majority of the women (i.e., 23) fall in the age group of 25-31 years. Twenty six percent (n=13), fall in the age group of 32-39 years. Anna V et al states that, compared with women aged 20–24 years, women aged 35–39 years had an approximately four times higher risk of GDM. In women aged >40 years, the risk of GDM was more than six times that of those aged 20–24 years.<sup>[1,2,3,4]</sup> Forty four percent of the women (n=22), hailed from lower middle class while thirty percent (n=15), are from upper middle class. Fifty eight percent (n= 29) are from urban area while the rest (n=21) are from rural areas. In a study done by Anna V et al, they found that socioeconomic status was inversely associated with risk of GDM.<sup>[5]</sup> Majority of the participants are multigravida in the study (n=32). Thirty two percent (n=16), are primigravidae. Four percent (n=4) had recurrent abortions. In clinical studies such as Ben-Haroush A, parity has been described as a risk factor for GDM. However, although epidemiological studies have also demonstrated this relationship. Berkowitz GS et al highlights that it may not persist after adjustment for other risk factors such as age and obesity.<sup>[6]</sup> Our study showed that forty two percent (n=21), had pregnancy associated complications. In the Hyperglycaemia and adverse pregnancy outcome

(HAPO) study, a large-scale (25,000 pregnant women) multinational epidemiologic study, majority of the analyses of secondary outcomes showed significant positive associations with maternal glycemia, after adjustment for confounders. The strongest associations were found for preeclampsia, for which the odds ratio for each 1-SD increase in each glucose measure ranged from 1.21 to 1.28; corresponding odds ratios for shoulder dystocia or birth injury were approximately 1.20.<sup>[7]</sup>

In this study, pregnancy associated complications were present in seven participants whose HbA1C was less than 6.5 % and in fourteen women with values more than 6.5 %. P Value is 0.045. It can be interpreted that HbA1C value of more than 6.5 is significantly related with pregnancy associated complications. Forty four percent (n=22) had normal vaginal delivery and 46 (n=23) percent had operative or instrumental delivery and 10 percent (n=5) had preterm vaginal delivery. Fourteen percent (n= 7) had intrapartum and post-partum complications. One participant had a cardiac arrest leading to maternal death. Four percent had shoulder dystocia (n=2) and four percent (n=2) had secondary perineal tear and another participant had both shoulder dystocia and secondary perineal tear.<sup>[8]</sup>

Out of the women whose value of HbA1c was more than 6.5% (n=25) in this study, 8 had normal vaginal delivery, 16 had instrumental or operative delivery and 1 had preterm vaginal delivery. P Value is 0.031. There is statistical association between HbA1C and type of delivery. Other studies have confirmed the correlation between GDM and adverse outcomes of the pregnant mothers such as preeclampsia and C-section delivery.<sup>[9]</sup>

In hospital-based study in North India, by Saxena P et al, hypertension, polyhydramnios, macrosomia, foetopelvic disproportion, and caesarean sections were more (P<0.001) among diabetic pregnancies. Boriboonhirunsarn D et al states maternal complications were found in 35 cases (21.6%) and the most common complications were postpartum haemorrhage (17 cases, 10.5%), mild preeclampsia (6 cases, 3.7%) and severe preeclampsia (3 cases, 1.9%).<sup>[10]</sup>

Most of the neonates (n=15) born to mothers with HbA1C values more than 6.5, had macrosomia weighing more than 3.5 kg and out of those with less than 6.5% value, two had macrosomia. It can be interpreted that there is a high statistical correlation between HbA1C level and weight of the baby. Among women with HbA1c values less than 6.5%, 7 had perinatal complications and they were found in 22 women with values more than 6.5%. P value was found to be at 0.000. Statistically, there is correlation with HbA1C and perinatal complications.<sup>[11]</sup>

Person B et al states that the most frequent and significant morbidity is fetal macrosomia, which in turn is associated with increased risk of birth injuries and asphyxia. In a nationwide study in Sweden (1991-1993) of a large series (n = 3322) of treated GDM pregnancies, perinatal mortality rate was not

increased; but the rate of preeclampsia was doubled, and the rate of emergency caesarean section was 1.6 times higher than in the background population. The rates of fetal macrosomia (> or = 4,500 g), asphyxia, and transient tachypnoea were two to three times higher than normal Erb's palsy was 0.7 and 5% in vaginally delivered infants weighing < 4,500 and  $\pm$ 4,500 g, respectively. Balaji et al says that there is growing data to suggest that HbA1c can be used for predicting adverse pregnancy outcomes in women with GDM.<sup>[12]</sup>

In Lowe et al 's HAPO study, it was found that in pregnant women, who are not overtly diabetic, association is found between increasing glucose levels and fetal outcomes such as birth weight, need for intensive care, hypoglycaemia, and hyperbilirubinemia as also with obstetrical outcome like caesarean sections.<sup>[13]</sup>

## CONCLUSION

The study shows that the parity and the socioeconomic condition of the pregnant women are closely associated with the risk of deranged GCT. Among the participants with deranged GCT, the risk of complications during pregnancy like fetal macrosomia, polyhydramnios are high if the hyperglycaemia is not controlled. There is significant risk of association of intrapartum complications like instrumental deliveries, perinatal tear, shoulder dystocia, meconium stained liquor, fetal asphyxia in the group with Hb1Ac >6.5% in compared with those <6.5%.

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