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ROLE OF HBA1C IN ASSESSING GESTATIONAL DIABETES MELLITUS: A CASE CONTROL STUDY AMONG ANTENATAL CLINIC (ANC) ATTENDEES AT A TERTIARY CARE HOSPITAL IN CENTRAL INDIA

Diabetology

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ABSTRACT

Background: Diabetes in pregnancy or Gestational Diabetes Mellitus (GDM) is defined as carbohydrate intolerance that begins or is first recognized during pregnancy. GDM is a prevalent and potentially serious condition both for mothers and neonates. The objective of this study was to assess the role of glycated hemoglobin A1c (HbA1c) level in assessing gestational diabetes (GDM).

Materials & Methods- A total number of 111 participants, (61 cases and 50 controls) attending ANC clinic of a tertiary care hospital, were recruited. Data on sociodemographic and clinical correlates were collected and fasting and post prandial Blood glucose, and HbA1c estimation was done was done in all participants.

Results- In present study it is observed that HbA1c levels in GDM patients was significantly more than that those of normal pregnancy (6.30±0.587% verses 4.22±0.616%). (p=<0.001).

Conclusion: The results show that HbA1c, in combination with OGTT, may be a useful screening tool for GDM.

KEYWORDS

GDM (Gestational Diabetes Mellitus), HbA1c

INTRODUCTION:

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia which occurs either due to defect in insulin production or effective utilization. This cause abnormal increase in blood sugar (hyperglycemia). Prevalence of Diabetes among adults (aged 20-70 years) in India is about 8.7%. About 10.3 % are prediabetes and there is a huge iceberg with many asymptomatic hyperglycemia individuals. (1)

Gestational diabetes is defined as derangement of blood sugar that first occur during pregnancy. Gestational diabetes increases risk of developing complications both during pregnancy and child birth. It has been reported in the researches that GDM increases the risk of polyhydramnios, preeclampsia (PE), and Cesarean delivery.(2,3) The children born to GDM mothers are prone to developing DM type -2 in adulthood. Diagnosis of gestational diabetes is seldom on the basis of symptoms but during routine ANC screening.(4)Prevalence of GDM varies by the population characteristics and diagnostic test used it ranges from 2.4 to 21 per cent in studies done in India and abroad.(5–7) Opportune move now is screening every single pregnant lady for diabetes, accomplishing normal glucose levels in them and guaranteeing sufficient sustenance of proper nutrition may forestall without a doubt, the endless loop of transmitting diabetes starting with one age then onto the next.Be that as it may, contrasted with high risk screening, widespread screening for GDM identifies more cases and enhances maternal and neonatal forecast. (8,9) Henceforth all-inclusive screening for GDM is basic, as it is commonly acknowledged that women of Asian decadence and particularly ethnic Indians, are at a higher danger of getting GDM and type 2 diabetes post-delivery .

The first blood sample for Ante natal women coming to the OPD is often a post meal/Random blood sample. There is little chance that the women comes in fasting state in the first visit itself therefore she is asked to make a follow up visit fasting which may not have good compliance and one may miss our chance of early detection of a case of glucose intolerance or overt GDM.

There are many screening procedures and diagnostic criteria set by national and international organizations and association for gestational diabetes.

Table 1. Most commonly used guidelines for the diagnosis of GDM (10)

Organisation	Fasting Plasma glucose (mmol/L)	Glucose Challenge	1-h plasma glucose (mmol/L)	2-h plasma glucose (mmol/L)
WHO 2013*	≥ 5.1	75g OGTT	10	≥ 8.5
American Congress of Obstetricians and Gynecologists**	≥5.3	100g OGTT	≥10.0	≥8.6
Canadian Diabetes Association**	≥5.3	75g OGTT	≥10.6	≥8.9
IADPSG***	≥5.1	75g OGTT	≥10.0	≥8.5
ADA(AMERICAN DIABETES ASSOCIATION)	≥5.3	50g OGTT	≥10	≥8.6

*one value is sufficient for diagnosis

** two or more values are required for diagnosis

*** **International Association of the Diabetes and Pregnancy Study Groups**-one value is sufficient for diagnosis

All these diagnostic and screening criteria for GDM most of them are based on estimation of sugar levels in blood at multiple times post oral glucose administration (OGTT).

In India DIPSI (Diabetes in Pregnancy Study Group India) criteria is often used for diagnosis of GDM is a single step procedure irrespective of the last meal. Pregnant women attending the antenatal OPD were given 75g anhydrous glucose in 250-300ml of water and plasma glucose was estimated after 2 hour. A 2-hours plasma glucose ≥ 140 mg/dl is taken as GDM

OGTT is not client friendly as it devours time, the pregnant ladies need to sit for 2 hours and ought to have no less than 3 venipunctures. They likewise have queasiness and retching due the 75 g glucose and deferred gastric purging. Additionally, the all-inclusive screening suggestion has expanded the testing trouble. With these strategies there was a probability of missing patients with strange sugars in first trimester.

There is felt need among doctors for a better screening and diagnostic tool for GDM which can give estimates of long term glycemic status and with better compliance and thus avoiding the danger of non-compliance leading to missing of potential cases and also avoiding

frequent pricks. This particular article explore the potential of use of HbA1C as a screening tool for GDM by correlating the levels HbA1C with the standard blood glucose estimations among Antenatal Females.

MATERIAL & METHODS:

Study Design: The present research findings are from a study comparing the hematological parameters of GDM and non GDM ANCs attending ANC clinic at a tertiary care hospital. The study was a hospital based comparative study.

Study Area: Antenatal clinic in NSCB Medical College & hospital.

Ethical consideration: This study was approved by the research and ethical committee of the University of NSCB Medical College and Hospital, Jabalpur

Sample size: Taking expected proportion exposed in the controls to be 0.05, the assumed odds ratio to be 6, and the desired level of confidence 0.95 and power for the detection of a significant difference between the two groups to be 80%, the sample size per group was found to be 50. Final study was done recruiting 61 cases and 50 controls.

Study Period: The study was conducted over a period of 6 months from 1st march to 31st Aug 2017.

Study population: All antenatal females aged 18-35 years with diagnosed GDM either newly detected or on follow up by DIPSI (Diabetes in Pregnancy Study Group India) criteria, attending ANC clinic of NSCB medical college and hospital, Jabalpur, were included in the study.

Exclusion criteria:

- Women who were known diabetics before pregnancy,
- Patients with known lipid metabolic disorders, Hypothyroidism, Renal disorders were excluded and age above 35 were also excluded to avoid overlap of overt diabetes in above 35years.
- Those with severe anemia (Hb <7 gm%)

Method:

Pregnant females attending ANC clinic at NSCB medical college and hospital irrespective of gestational age who fulfil the inclusion criteria were included in the study after obtaining the written informed consent. Sociodemographic data was taken from cases and controls and about 5ml blood sample was drawn under aseptic precaution from antecubital vein and collected in a sterile tube.

DIPSI (Diabetes in Pregnancy Study Group India) criteria used for diagnosis of GDM. A portion of sampled blood was aliqouted into EDTA tube for measurement of HbA1c. HbA1c was measured using the Randox instruments which includes Rx imola. Randox imola is a compact fully automated bench-top clinical chemistry analyser, capable of handling the workload of a medium to high throughput laboratory.

Statistical analysis: The data were compiled and entered in the Microsoft excel sheet. It was analyzed using statistical software SPSS 20.0 software (IBM USA). The data were represented in tables and charts. The frequency was displayed of all variables. Chi square test was applied to find out the statistical difference between the groups.

RESULTS:

A total of 101 participants (61 cases and 50 controls) were included in the study. The mean age group of cases was 25.16 ± 4.59 and that of controls was 24.70 ±3.71 years. About 30% belonged to rural area and 70% to urban area with significantly more number of GDM cases in urban than in rural area (p>0.05).

More than half of the study participants were 1st time pregnant, about one third were second gravida and rest were 3rd gravida and above.(Figure 1)

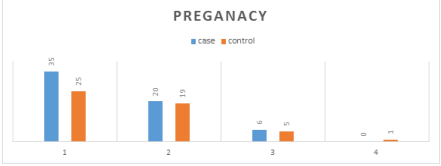

Figure 1: Pregnancy status among cases and control.

Comparable number of antenatal females in cases and control group with no statistical difference in distribution (p>0.05)

Since the study involve estimation of HbA1c levels that may confound the results of our study, so we estimated he hemoglobin levels of all study participants to look for comparibity .(Table 2)

Table 2-Distribution of study participants with grading of anemia

ANEMIA GRADING	GROUP (ANC)		Total (%)
	Cases (%)	Controls (%)	
7-9 (Moderate)	20 (32.8)	23 (46.0)	43 (38.7)
10-12 (Mild)	41 (67.2)	27 (54.0)	68 (61.3)
Total (%)	61 (100)	50 (100)	111 (100)

x^2=2.021; p>0.05

All participating females were anemic. The distribution of cases and controls for mild and moderate anemia was not found statistically significant (P>0.05) rendering better comparability of HbA1c status among the two groups.(Table 2)

The present study shows that mean HbA1c level in cases are 6.30 +/- 0.587 while in control group it is 4.22+/-0.616. Taking a standard cut of 6.5 for Hba1c about 24.6% of the cases shows abnormal (>6.5%) level of HbA1c.Since p value is less than 0.0001 , so that the difference of HbA1c levels in cases and controls is significant.(Table 3)

Table 3: HBA1c levels among cases and controls

HbA1C level	GROUP		Total (%)
	Cases (%)	Controls (%)	
Normal (<6.5)	46 (75.4)	50 (100.0)	96 (86.5)
Abnormal (>=6.5)	15 (24.6)	0 (0.0)	15 (13.5)
Total (%)	61 (100)	50 (100)	111 (100)

x^2=14.216; p<0.0001

The unpaired t tests was then applied to test the null hypothesis that the population means related to two independent samples from two groups ,namely cases (ANCs with GDM) and controls (ANCs without GDM) ,are equal or not (Table 4)

Table 4. Mean values of concerned parameters (FBS, RBS, Hb, HbA1C) among cases (n1=61) and controls (n2=50)

Characteristics	Cases (N=61)	Controls (N=50)	Significance
FBS	161.93 ±52.578	75.28 ±7.177	t=11.557; p<0.0001*
PPBS	190.41 ±61.255	103.68 ±13.597	t=9.808; p<0..0001*
HB	9.70 ±0.972	9.38 ±1.244	t=1.545; p>0.05
HbA1c	6.30 ±0.587	4.22 ±0.616	t=18.122; p<0..0001*

*Significant

As it is clear from Table 4 the mean HbA1C level distribution among cases and controls are in line with the mean blood glucose estimation with statistical significance (p<0.05).

This highlights the potential of use of HbA1c as a screening tool for GDM

DISCUSSION:

In this study, it was found that mean glycosylated hemoglobin level was significantly higher in cases than in controls. This parameter provides the level of blood glucose 8-12 week period prior to determination. So, by estimating this parameter, we can avoid further deterioration of the disease process by early detection and prompt treatment. Significantly elevated levels of glycosylated hemoglobin in gestational diabetes were also reported by researchers in several studies such as Baxi L et al.(11) and Metzger et al(12) supporting our hypothesis. In comparison with glucose measurements, the use of HbA1c as a diagnostic test has advantages including: convenience, as fasting is not needed for assessment, less day-to-day variability, and greater pre-analytical stability with international standardization not inferior to a glucose assay. However, HbA1c measurement also has certain limitations, such as being more costly than plasma glucose.

Some hemoglobin traits such as HbS, HbC, and HbF interfere with some HbA1c assays and any condition that changes red cell turnover, such as hemolytic anemia, chronic malaria, major blood loss, or blood transfusions, will lead to spurious HbA1c results and a lack of concordance between fasting/ 2-hour plasma glucose and HbA1c. Although HbA1c is now recommended for the diagnosis of diabetes, there are no recommendations available for the use of HbA1c as a diagnostic tool for GDM. In present study it is observed that HbA1c in GDM patients are more than that of normal pregnancy (6.30±0.587% Vs 4.22±0.616%) which is statistically significant (p=<0.001).

The finding is similar to the another study done by Vijayam Balaji,MD.et al.(13)

Higher amounts of glycated hemoglobin, indicating poorer control of blood glucose levels, have been associated with cardiovascular disease, nephropathy and retinopathy. The HbA1c strongly associated with the risk of development & progression of microvascular and nerve complications. High HbA1c (>9.0-9.5%) is associated with very rapid progression of microvascular complications.(14)

As HbA1C levels are closely correlate to blood sugar level in GDM. It is therefore a reliable indicator of overall glycemic control among the patients of diabetes in pregnancy[80]. Levels of HA1c are not influenced by daily fluctuations in the blood glucose concentration, reflect the average glucose level over the prior 6 to 8 weeks. Therefore HbA1c is a useful indicator of blood glucose controlled in the recent past & may be used to monitor the effect of drug therapy on blood glucose level. (15) HbA1c on other hand, is a spot test with no requirement for prior preparation, no risk of misinterpretation owing to recent meal or drug. (16) So by monitoring HbA1c we can reduce the complications both in mother & fetus due to GDM.

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