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ORIGINAL ARTICLE

HbA1c as an Early Diagnostic Marker in Gestational Diabetes Mellitus: A Retrospective Study

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ABSTRACT

Aim: To evaluate the efficacy of HbA1c as a single diagnostic marker of Gestational Diabetes mellitus (GDM).
Study Design: A retrospective study
Place and Duration: This study was conducted at Ghulam Muhammad Mahar Medical College Sukkur from June 2021 to June 2022
Methodology: In this retrospective study, a non-probability technique was used. The sample size is 19,065 pregnant women divided into two groups i.e. GDM and Non-GDM.(N=3458 in group 1 and N=15,608 in group 2). This study observes different parameters and tests to evaluate the efficiency of the HbA1c test for the diagnosis of GDM. Inclusion criteria included all pregnant females older than 18 years in their 1st trimester of pregnancy (at the end of 12 weeks of pregnancy).
Results: The number of females suffering from GDM is about 3458(18.1%) of the sample size. The average level of HbA1c in female patients with GDM (Group 1) is approximately higher than in female patients with Non-GDM(Group2). HbA1c-thresholds in %were seen higher in older than 24 years of females. HbA1c is significantly higher in the GDM group than in the Non-GDM group. In a sample size of GDM patients aged 35-39 showed HbA1c levels, 62.4 sensitivity and 58.6% specificity at a cut-off value of 5.% (31 mmol/mol) for GDM diagnosis.

Practical implication: Because of the high sensitivity and low specificity of HbA1c for the diagnosis of GDM in pregnant women, HbA1c may be a straightforward and less invasive screening test alternative for OGTT in GDM patients.
Conclusion: HbA1c test provide assistance for the diagnosis of GDM but it is not used as a measured test to diagnose diabetes in pregnant women, it provides a measured diagnosis for diabetes mellitus type 1.
Keywords: Gestational diabetes mellitus (GDM), HbA1c, Oral glucose tolerance test (OGTT), Diabetes mellitus type 2, Personalized Diabetes Management (PDM)

INTRODUCTION

Gestational diabetes mellitus (GDM) is usually occurring complication observed during pregnancy in females which affects a number of females' nowadays[1]. It is to be considered that pregnant females aged more than 25 years have a higher risk of gestational diabetes[2]. Females having a history of gestational diabetes may get some other complications like shoulder dystonia, fetal birth abnormalities, birth injury, prematurity, preeclampsia, increased C-sections rate and some other consequences related to mother and neonatal complications[1,3,4]. If GDM is not treated in the time span of pregnancy it may lead to diabetes mellitus type 2 which is the severe form of diabetes. There is a directly proportional effect found between maternal and neonatal outcomes with a degree of hyperglycemia. GDM requires exercising, dietary intervention, insulin therapy and plasma monitoring for its control and treatment[5,6.] The basic and accurate diagnosis of GDM in pregnant females requires normalizing the adverse effect of GDM on the mother and fetus. The oral glucose tolerance test(OGTT) is the recommended test procedure in the 24–28 weeks of gestation to diagnose the gestational diabetes mellitus in females, though this test is considered to be complex and challenging to meet the quality standards throughout rural and developed areas[8, 9,10]. This test is time-consuming, labour-intensive and often poorly tolerated by pregnant females. Researchers needed to evaluate some other testing procedures which will be a simple and feasible diagnostic procedure for the detection of gestational diabetes. The World health organization used to recommend testing with glycated hemoglobin (HbA1c) with a cutoff point of 6.5% (48 mmol/mol) for gestational diabetes in female patients in the year 2011 [11].Never the less, it is still under consideration to diagnose GDM via the HbA1c test. Researchers in their studies demonstrated that the level of glycated hemoglobin in the first trimester and mid-pregnancy (23–32 weeks) deficits the sensitivity and specificity in the diagnosis of Gestational diabetes in females, subsequently[14,15.]

Many researchers suggested the usefulness of the glycated hemoglobin (HbA1c) test for the analysis and detection of GDM and proposed different cut-off points for positive cases.

The National Health and Medical Research Council (NHMRC) guidelines 2009 suggested HbA1c as a basis for the diagnosis of diabetes mellitus type 2, with a value of 48 mmol/mol or 6.5% or greater.in comparison with glucose testing, the HbA1c tests have greater reliability and <6% inter-laboratory intervention[12].

The reliability of the HbA1c test for the diagnostic evaluation of GDM patients studied extensively over the past many years but results have been in consistent[13].

Over the past three decades, a great deal of research has been done on the reliability of the HbA1c test as a pregnancy screening tool, but the results have been mixed [16].The current study is conducted to evaluate the efficacy of HbA1c as a single diagnostic marker of Gestational Diabetes mellitus (GDM)

METHODOLOGY

It is retrospective study design using a non-probability sampling technique for sample collection. The permission was taken from the ethical review committee of the institute. The sample size which is taken to evaluate the results are 19,065 pregnant female patients which are divided into two groups. Group 1 has female patients suffering from GDM while in group 2 female patients have no history of GDM.(Non-GDM).In group 1 we have a sample size of about N=3458 (18.13%)while in Group 2 N=15,608(81.86%). Inclusion criteria included all pregnant females older than 18 years in their 1st trimester of pregnancy (at the end of 12 weeks of pregnancy). Exclusion criteria included all pregnant female patients having diabetes mellitus type 1 and type 2, spontaneous abortions or elective termination of pregnancies were excluded.

For taking the results out of the number of samples we have taken information regarding patient age, Weight in BMI, patient's BP levels (both systolic and diastolic), their previous history of diabetes in a family, the occurrence of multiple pregnancies, Hb

level, serum ferritin plasma level, fasting glucose level, levels of glucose in body after an hour and HbA1c levels.

In this study, pregnant female patients were the first monitored with oral glucose (quantity 50 gram) for the oral glucose tolerance test (OGTT).and also noticed their HbA1c levels. This study was directed to detect the association between HbA1c levels and glucose levels of OGTT and further conducted to evaluate the performance of glycated hemoglobin test in the detection of gestational diabetes in pregnant females.

After observing all the important levels in a number of samples, for analyzing the effect of HbA1c in the diagnosis of gestational diabetes, we have calculated all the sample values in mean and standard deviation (by using SPSS), so that we can easily elaborate on results in the form of average values. Receiver Operator Curve (RO CURVE) is used for sensitivity, specificity, positive (PPV) and negative (NPV) and the Youden index for calculation of HbA1c cut-off.

RESULTS

In this study, we have identified 19,065 pregnant women, Group 1 contains 3458 female patients who are suffering from GDM while group2 has 15,608female patients who have no history of GDM (Non-GDM). 5.08+0.4 vs 4.84+0.45).Almost all the parameters are higher in GDM patients as compared to Non-GDM patients, i.e. serum ferritin, Hb level, fasting glucose, and random glucose levels.

On average, the patients in group 1 are aged and have an increasing body mass index and also have a history of multiple pregnancies than patients in the group 2 without GDM diagnosis. (5% vs 3.2%) Data are expressed in the form of mean ± standard deviation (SD). P-value is less than 0.05 between GDM and Non-GDM groups.

The most important aspect is that the average glycated hemoglobin levels of pregnant female patients with the GDM (Group 1) are approximately higher than in the female patients having the Non-GDM group(Group2). (5.08+0.4 vs 4.84+0.45).

Female patients suffering from gestational diabetes have a history of increasing levels of fasting glucose, higher 1-h Glucose levels than patients in the Non-GDM group.Gestational diabetic females' patients have slightly increasing levels of hemoglobin than other patients having no history of gestational diabetes and also having higher levels of Serum ferritin levels. . (87.2+52.2 vs 67.3+48.1)

Patients in group 1 having GDM have a prior family history of diabetes than patients in group 2 i.e. Non-GDM patients. (18.1% VS 6.5%).

The glycated hemoglobin test(HbA1c test) has lesser levels of sensitivity and specificity for the detection of gestational diabetes in female patients. A ROC curve (As shown in Figure 1) analyzes the detection of gestational diabetes in females with the use of glycated hemoglobin(HbA1c test), for which we have observed an area under the curve having the value of 0.664(95%m P is less than 0.01) exhibit specificity, sensitivity, and the Youden index at various cut-off points on the curve.

We have divided all the patients into different age groups to analyze the prevalence of GDM in older age females(As shown in table2).We have observe that patients aged more than 24 years have greater prevalence of GDM. There are more patients we have seen in age groups between 25-29,30-34 and 35-39. About 3205 patients we have observed in the age group between 35-39 which is the higher number of patients seen in any other age group.

We have evaluated the performance of the glycated hemoglobin tests in the diagnosis of gestational diabetes in female patients of various age groups. HbA1c-thresholds % seen higher in older than 24 years of females. That is 5%in all the other age groups of GDM patients. Although age groups older than 24 years of age also have low sensitivity and specificity for diagnosing GDM.

HbA1c is significantly higher in the GDM group than in the Non-GDM group. A sample size of GDM patients having aged 35-39 showed HbA1c levels, 62.4sensitivity and 58.6% specificity at a cut-off value of 5.% (31 mmol/mol) for GDM diagnosis. The prognostic value of HbA1c for GDM was evaluated by ROC curve analysis.

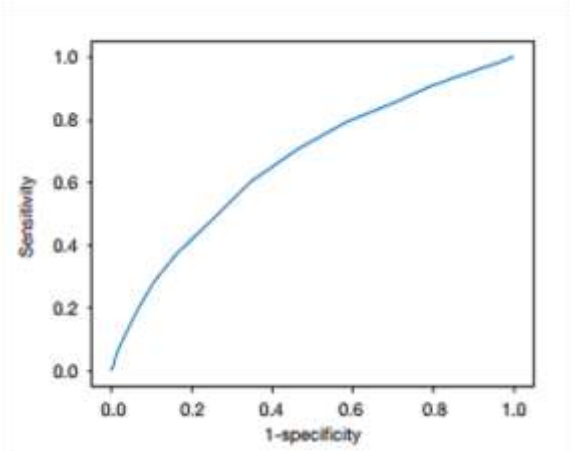

FIG 1: ROC curve analysis of glycated hemoglobin (HbA1c) for detection of gestational diabetes in female patients.

Table 1: Parameters observe in female pregnant patients having history of gestational diabetes/ or no history of gestational diabetes. (GDM/Non-GDM) (Total number of patients 19,065)

Characteristics	GDM group (n=3,458)	Non-GDM group (n=15,608)
Age (years)	31.08+4.12	30.45+4.02
Body mass index (kg/m2)	21.31±2.58	20.83±2.66
Blood pressure, systolic (mmHg)	118+12.4	112+11.7
Blood pressure, Diastolic (mmHg)	75+10.9	68+9.8
Previous history of diabetes in family(%)	18.1%	5.9%
Multiple pregnancies (%)	5%	3.2%
Hb levels (g/L)	121.16+3.4	120.17+3.8
Fasting glycaemia (mmol/L)	4.87+0.49	4.45+0.28
Glycaemia one hour after glucose load	9.68±1.48	7.25±1.33
Serum ferritin (µg/L	87.2+52.2	67.3+48.1
HbA1c (%)	5.08+0.4	4.84+0.45

Table 2: Optimal cut-off points of glycated hemoglobin (HbA1c) for gestational diabetes mellitus in the different age group of female pregnant patients.

Groups of age in years	Number of patients	Prevalence of Gestational diabetes(%)	HbA1c-thresholds, % [mmol/mol]	Sensitivity, %	Specificity, %	Positive predictive value (PPV), %	Negative predictive value (NPV), %	Youden index
20-24	805	7.5	4.9[30]	72	61.4	13	96.6	0.32
25-29	7150	14.32	5 [31]	57	69	22	90.8	0.25
30-34	7315	18.9	5 [31]	62	65.2	29.2	88	0.265
35-39	3205	24.8	5 [31]	62.4	58.6	33.8	80.7	0.196
>40	590	32.1	5 [31]	70.3	55.7	42.6	79.5	0.257

DISCUSSION

In this research paper, we have analyzed the detective performance ofthe HbA1c test in gestational diabetes mellitus in females and to detect whether it is helpful to provide evidence for the diagnosis of gestational diabetes mellitus. We are expecting that this study is become beneficial to detect the diagnostic

property of the HBA1c test to detect gestational diabetes in females.

This study shows the differential distribution of the HbA1c test in pregnant female patients having gestational diabetes or no gestational diabetes. This Study briefs the idea that HbA1c level is higher in female patients of group 1 having GDM than in group 2 Non-GDM patients. This study evaluates the mean HbA1c levels in the large number of individuals suffering from gestational diabetes. This study also provides evidence that Asians are more susceptible to getting gestational diabetes during pregnancy than any other race of patients.

On the contrary, we have analyzed the poor detective value of HbA1c for the detection of gestational diabetes in female patients. The Area under the curve for the glycated hemoglobin levels for detecting gestational diabetesis 0.664 (95% P-value is less than 0.01).

HbA1c was a possible predictor of PDM and showed high sensitivity with somewhat low specificity for the diagnosis of GDM in pregnant females (Integrated personalized diabetes management). HbA1c may be a straightforward and less invasive screening test alternative for OGTT in GDM patients. But it is not considered to be a diagnostic measure for the detection of gestational diabetes. It works best to provide support, detection and management of diabetes mellitus type 1.

Several studies conducted previously, examined the use of the HbA1c test is used for the diagnostic measure of gestational diabetes however it is concluded by such studies that it is not currently recommended to diagnose gestational diabetes at any point of pregnancy. The HbA1c test is a simple, less invasive and supportive marker for the diagnosis of diabetes type 1, in several studies, researchers observed that the HbA1c test is not used for the diagnosis of gestational diabetes but the oral glucose tolerance test is the measuring element for the diagnosis of gestational diabetes in females.

CONCLUSION

HbA1c test provide assistance for the diagnosis of GDM but it is not used as a measured test to diagnose diabetes in pregnant women, it provides a measured diagnosis for diabetes mellitus type 1.\

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