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Diagnostic Accuracy of HbA1C as Early Prenatal Screening Tool in Gestational Diabetes Mellitus Taking OGTT as Gold Standard

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ABSTRACT

Objective: To assess the diagnostic accuracy of glycated hemoglobin (HbA1c) as early prenatal screening tool in GDM taking oral glucose tolerance test (OGTT) as gold standard.

Methodology: This Cross-sectional study was done at Obstetrics & Gynecology department, CMH Kharian from January 2023 to July 2023. A total of 214 Patients fulfilling the inclusion criteria from gynecology department of CMH Kharian were enrolled in the study after getting permission from ethical committee. HbA1c was done on booking visit and GDM was recorded if it was ≥6%. All patients were called for follow up at 24 weeks of gestation for OGTT to diagnose whether these patients have developed GDM or not.

Results: The mean age of all subjects was 27.29±4.61 years. According to HbA1c, 73(34.11%) females had ≥ 6% and 141(65.89%) females had HbA1C < 6%. According to OGTT, 65(30.37%) cases were positive for GDM. On comparing diagnostic accuracy, 61 cases were positive on both diagnostic methods whereas 137 females were negative on both modalities. 12 females were positive on HbA1c and were negative on OGGT while 4 were positive on OGGT but negative on HbA1c. The sensitivity, specificity, PPV, NPV, and diagnostic accuracy was 93.85%, 91.95%, 83.56%, 97.16% and 92.52% respectively.

Conclusion: Through the findings of this study, it was concluded that HbA1C has high diagnostic accuracy. It can be used to identify such patients in early trimester. So, females with high HbA1c (≥6%) should be enrolled for interventional strategies for better maternal & perinatal outcomes.

Keywords: Gestational diabetes mellitus, oral glucose test, HbA1c, screening, diagnostic accuracy.

Introduction

Gestational diabetes mellitus (GDM) is the most common problem that happens during pregnancy, impacting wellbeing of a large number of pregnant females all around the world.[1] It is identified when the pancreatic function becomes inadequate to cope with the elevated diabetogenic impacts during pregnancy.[2] As the occurrence of diabetes mellitus has reached the levels of pandemic, similarly the proportion of pregnant females getting impacted by GDM is on a rise as well resulting in a high incidence of maternal and fetal complications. [3] As reported by International Diabetes Federation, global prevalence of GDM was 14% in 2021, causing it to be a major public health issue.[4]

GDM is linked with various short as well as long-term maternal and fetal complications. The prompt and accurate

diagnosis of GDM is greatly significant in order to avoid these unwanted conditions.[5] 75g Oral glucose tolerance test (OGTT) is considered as a reference standard by World Health Organization and American Diabetes Association for diagnosing GDM at 24-28 weeks of pregnancy.[6] However, the prerequisites of this test are cumbersome such as at least 8 hours fasting, complex patient preparation, intake of a fixed amount of sugar at once, and multiple blood samples within 2 hours, making it challenging to maintain same standards in the different testing facilities.[7]

Measuring glycated hemoglobin (HbA1c) is an attractive alternative to OGTT, particularly because it is easy to perform, does not require fasting or intake of huge amounts of sugar which can be uncomfortable for pregnant women, can be performed at any time of the day, and show the median blood glucose concentration of the prior 3 months [8]. Despite that, current guidelines by international organizations do not recommend its use for diagnosing GDM yet. Additionally, various studies reporting the capability of HbA1c in diagnosing GDM are inconclusive or controversial.[9-11] A number of studies revealed that concentration of HbA1c is relatively lower during gestation because of the pregnancy-related physiological hydremia, anemia, nutritional deficiencies, and shorter life of red blood cells, which may restrict its importance in diagnosing GDM.[9-11] A study by Valadan et al. reported that HbA1c cannot substitute OGTT for GDM diagnosis owing to the low sensitivity and specificity i.e. 54.8% and 96.8%, respectively.[9] However, few studies have validated that HbA1c is of substantial value in diagnosing GDM and recommended different cut-off values for positive cases.[12,13]

As previous studies showed considerable variations in sensitivity and specificity even in the recent literature and no local study is available on Pakistani population in early prenatal period as of yet. So, this study was designed to assess the diagnostic accuracy of HbA1c for early diagnosis of GDM taking OGTT as a reference standard. The outcomes of this study would be of great help as HbA1c is a cost-effective test for majority of non-affording population and it will reduce the number of unnecessary OGTT, which is relatively an inconvenient test. Furthermore, identifying such patients early will help to develop prompt interventional strategies for better maternal and fetal outcomes.

Methodology

This Cross-sectional study was done at Obstetrics & Gynecology department, CMH Kharian, from 10th January 2023 to 9th July 2023. Sample size was estimated as n=214, that was calculated utilizing 95% confidence interval, 10% desired precision with expected sensitivity of HbA1c as 87.1% [14], expected specificity as 98.3% [15] and expected prevalence of GDM as 31.9% [16], by taking OGTT as a reference standard. Data was gathered utilizing consecutive sampling technique. All pregnant women aged between 20-35 years with any parity or gravidity having viable singleton pregnancy confirmed by ultrasound, females with gestational age 6-12 weeks calculated by first day of last menstrual periods (LMP) in patients who were sure of dates and presented for their routine antenatal checkup were included in this study. Patients who were already diagnosed with DM or fasting plasma or random serum glucose level > 7.0mmol/L, patients having history of treatment with any hyperglycemic drugs like glucocorticoids as determined on history or females having body mass index ≥ 35 kg/m^2 were excluded.

After taking acceptance from the institutional review committee and consent from the patients, samples were taken from outdoor department of CMH Kharian. Demographic details were taken from each patient. HbA1c was done on booking visit and GDM was recorded if the value was $\geq$ 6%. All patients were called for follow up at 24 weeks of gestation for OGTT, which was done after an overnight fasting of $\geq$8 hours while subjects were on an unrestricted diet and unlimited physical activity for at least 3 days, to diagnose whether these patients have developed GDM or not. The diagnosis of GDM was validated if any 2 of the following were found [17]

- On fasting: 5.3 mmol/l or 95 mg/dl
- At one hour after taking glucose solution: 10 mmol/l or 180 mg/dl
- At two hours after taking glucose solution: 8.6 mmol/l or 155 mg/dl
- At three hours after taking glucose solution: 7.8 mmol/l (140 mg/dl)[17]

All the collected data was analyzed with SPSS version 20. Frequency and percentages was computed for categorical data. Mean $\pm$ Standard Deviation was presented for numerical data. Sensitivity, specificity, PPV, NPV and diagnostic accuracy of HBA1c taking OGTT as gold standard.

Results

The current study included 214 participants with mean age as 27.29±4.61 years having minimum and maximum ages of 18 and 35 years. There were 102(47.66%) females with ages between 18-27 years and 112(52.34%) females were 28-35 years of age. A total of 171(79.91%) females had parity between 1-3 and 43(20.09%) of females had parity > 3. Mean gestational age was 8.92 ± 2.01 weeks [ranged as 6 - 12 weeks]. There were 123(57.48%) cases with gestational age of 6-9 weeks and 91(42.52%) had gestational age of 10-12 weeks. The mean weight, height and BMI were 63.36±10.58 kg, 1.40 ± 0.08 m and 24.78±3.82 kg/m². A total of 36(16.82%) females were obese and 178(83.18%) were non-obese as elaborated in table I.

Table I: Baseline parameters of study participants. (n=214)

Parameters	N	%
Age of the patients (years)		
Mean ± S.D	27.29±4.61	
18-27	102	47.66
28-35	112	52.34
Parity		
1-3	171	79.91
>3	43	20.09
Gestational age (weeks)		
Mean ± S.D	8.92 ± 2.01	
6-9 weeks	123	57.48
10-12 weeks	91	42.52
Weight (kg) (Mean ± S.D)	63.36±10.58	
Height (m) (Mean ± S.D)	1.40 ± 0.08	
BMI (kg/m²) (Mean ± S.D)	24.78±3.82	
Obesity		
Yes	36	16.82
No	178	83.18

Descriptive statistics of HbA1c and OGTT are illustrated in table II. Mean HbA1c was 4.8±5.5%. 73(34.11%) females had HbA1c ≥ 6% while 141(65.89%) females had HbA1C < 6%. According to final OGTT, 65(30.37%) cases were positive for GDM and 149(69.63%) cases were negative.

Table II: Descriptive statistics of HbA1c and OGTT in study participants. (*n* =214)

Variables	n	%
Glycated hemoglobin (HbA1c)		
≥6%	*73*	*34.11*
<6%	141	65.89
Oral Glucose Tolerance Test (OGTT)		
Positive	65	30.37
Negative	149	69.63
Total	**214**	**100**

On comparing diagnostic accuracy, 61 cases were positive on both diagnostic methods while 137 cases were negative on both modalities. 12 females were positive on HbA1c and were negative on OGGT while 4 were positive on OGGT but negative on HBA1c (Table III). The sensitivity, specificity, PPV, NPV and diagnostic accuracy was 93.85%, 91.95%, 83.56%, 97.16% and 92.52%, respectively.

Table III: Diagnostic Accuracy of HbA1c in comparison with OGTT.

		Result on the basis of OGTT			P-value*
		Positive	Negative	Total	
HbA1c	≥6%	61	12	73	<0.0001
	<6%	4	137	141	
	Total	65	149	214	

Discussion

GDM is the glucose intolerance first identified during gestation resulting in various maternal and fetal complications if not taken into account timely.[18] Prevalence of GDM has a wide range across the world. Global prevalence of gestational hyperglycemia caused negative effects on 16.2% of all live births in 2017, with GDM accounting for 86.4% cases.[19] Early and accurate diagnosis is crucial in order to avoid maternal and fetal complications. Diagnosis varies according to the tools used for assessment as well as in different populations. So, this study was carried out to evaluate the diagnostic accuracy of HbA1c for early diagnosis of GDM taking OGTT as a reference standard. The current study reported that HbA1c had sensitivity as 93.85%, specificity as 91.95%, PPV as 83.56%, NPV as 97.16% and diagnostic accuracy was found as 92.52%.

For the diagnosis of GDM, a study reported a specificity of 95%, sensitivity of 27% and NPV of 91% utilizing an HbA1c concentration of 5.4% on ≥26 weeks. When the cut-off value of HbA1c was lowered to 5.1%, the sensitivity was enhanced to 55% whereas the specificity was reduced to 80%. The positive relation between HbA1c and OGTT is of great value, however the reduced sensitivity of HbA1c is cumbersome in standardizing this test in gestation.[20] Another study reported that the females with GDM and normoglycemia had mean HbA1c levels of 6.2 ± 0.6% and 5.4 ± 0.5%, respectively. Diabetic females reported an increased occurrence of gestational complications juxtaposed to females with normoglycemia. For diagnosis of GDM, an HbA1c cutoff of 5.3% had a

sensitivity and specificity of 95.6% and 51.6% respectively.[21]

One study reported the similar statistics to the current study, documenting sensitivity and specificity of 100% each. [22]. One more study reported lower diagnostic accuracy with 45% sensitivity and 92% specificity. For HbA1c ≥5.7%, sensitivity, specificity, and PPV were 30%, 97%, and 91%, respectively.[23]

However, some studies contradicted the findings of the current study. A study by Lai et al. documented that HbA1c test was weakly correlated with OGTT during gestation, and it provides little insight in detecting GDM [8]. Another study revealed that HbA1c level doesn't substitute OGTT for diagnosing GDM but it can be utilized in addition to OGTT to preclude the requirement of OGTT in a lot of pregnant women [24]. A study reported that at a cut-off value of 5.8% of HbA1c, Sensitivity was only 17.1%. However, specificity, PPV, NPV, and accuracy were 17.1, 100, 100, 73.2, and 74.6%, respectively.[25]

Conclusion

Through the findings of this study, it was concluded that HbA1C has high diagnostic accuracy. It can be used to identify such patients in early trimester. So females with high HbA1C (≥6%) should be enrolled for interventional strategies for better maternal & perinatal outcomes.

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