First trimester Glycosylated Hemoglobin as a Predictor of Gestational Diabetes Mellitus

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Abstract

Background: Gestational diabetes mellitus (GDM) is defined as the development of carbohydrate intolerance during pregnancy, excluding overt diabetes. GDM poses a risk of short-term adverse perinatal outcomes and long-term metabolic morbidity to women and their newborns.

Objectives: The aim of this study was to determine the role of first trimester glycosylated haemoglobin as a predictor of gestational diabetes mellitus.

Patients and methods: The study was carried out at Qena University Hospital, Department of Obstetrics and Gynecology. The glcosylated hemoglob ininvestigation included 200 high risk pregnant ladies from the start trimester taking care of our outpatient facility and in tolerant from May 2019 to May 2020.

Results: Patients who developed gestational diabetes mellitus with HA1c < 5.7% were 12.4% while with HA1c ≥ 5.7% were 47.3%. Also, there is significant statistically difference between both groups (p value= 0.015). ROC curve for HbA1c in 1st trimester as a predictor of gestational diabetes mellitus showed that the cut-off point was ≥6.2%, sensitivity was 93.3% and specificity was 90.0%.

Conclusion: The detection of glycosylated hemoglobin in the first trimester is apromising predictor biomarker for diagnosis of GDM and in the future may replace other basic investigations.

Keywords: Gestational diabetes mellitus; Perinatal outcomes; Metabolic morbidity; HbA1C.

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Introduction

Gestational diabetes mellitus (GDM) is the progression of sugar metabolism during pregnancy in the absence of confirmed diabetes,. GDM poses a risk of short-term antagonistic perinatal outcomes as well as long-term metabolic consequences for women and their children **(Benhalima et al., 2015)**.

Glycosylated hemoglobin (HbA1C) is a three-month average of plasma glucose. It is primarily used for the diagnosis and treatment of diabetes and prediabetes in all individuals **(Larsen et al., 1990)**.

A few studies aimed to estimate of HbA1C fixations, but none of them have identified the diabetic limit in GDM prediction or conclusion **(Fong et al., 2014)**.

While a few rules have suggested that a first-trimester HbA1C fixation of 6.5 percent is a cornerstone for simple diabetes, HbA1C estimate isn't relevant for regular antenatal consideration. The American Diabetic Association and the International Expert Committee on Diabetes recently issued a joint statement recommending the use of (HbA1c) as a method for detecting diabetes rather than the measurement of fasting or postprandial plasma glucose in a nonpregnant population. A determination measure was estimated to be 6.5 percent (48 mmol/mol) (**American Diabetes Association, 2014).**

In non-fasting women, a HbA1c prediction is an appealing option since it is easily applied to the routine early pregnancy testing center checks. There's no doubt that calculating HbA1c is useful, particularly if you've had diabetes before. In either case, multiple studies have shown that HbA1c can be beneficial during diabetes-affected pregnancy, as elevated levels have been consistently linked to unfavorable neonatal outcomes **(Evers et al., 2002)**.

The aim of this study is to determine the role of first trimester glycosylated haemoglobin as a predictor of gestational diabetes mellitus.

Patients and methods

The study was carried out in Qena University Hospital, Department of Obstetrics and Gynecology. The glcosylated Hemoglobin investigation included 200 high risk pregnant ladies from the first trimester attending to our outpatient clinic and in patient from May 2019 to May 2020.

Inclusion criteria: past history of GDM, family background of diabetes, history of IUFD, history of innate peculiarities (heart irregularity and sacral agenesis) and history of macrosomic child

Exclusion standards: pregestational diabetic lady and hypothyroidism

Methodology

All cases who met consideration models had been exposed to the accompanying:

Full history taking including individual, present, past, family, obstetric and menstrual history, gestational age is surveyed by methods for first day of last menstrual period (LMP).

General assessment: - vital signs (beat, Blood Pressure and Temperature). - Maternal BMI had been estimated by dividing the weight in kilograms by square of the height in meters.

abdominal assessment: It was performed at each antenatal visit from 24 weeks to determine fetal size and from 36 weeks growth to assess fundal height, presentation, position and station/engagement of the presenting part.

Examinations

1. Trans-abdominal ultrasound assessment for fetal viability, gestational age confirmation.

2. Maternal serum GA level was estimated to all cases in the first and second trimesters.

 GDM ladies had been referred to internal medicine center for the management of case either by diet control, oral treatment or insulin treatment.

Ethical consideration

Ethical approval and consent to paticipate:

 Ethical approval was gotten from Institutional Review Board (IRB) at Qena University and the

head of Obstetric and Gynecology Department at Qena University Hospital.

 All ladies were guaranteed that their information would be kept secret, that their interest was deliberate and that they could pull out from the examination whenever. They were educated regarding the reason and the system of the examination and all ladies gave composed assent before incorporation.

 Women were given composed data about the examination and this data was evaluated with them orally.

Results

This study included 200 pregnant women who consistently went to the outpatient facility in the primary trimester for antenatal consideration.

Patients with HA1c < 5.7% were 72.5% while with HA1c ≥ 5.7% were 27.5%.(**Table.1)**

Age of patients with HA1c < 5.7% ranged from 20-36 years and mean was 27.06 years while with HA1c ≥ 5.7% ranged from 20-37 and mean was 28.09 years, also BMI mean was 2.14 and 32.16 respectively. There is significant statistically difference between both groups as regard to BMI (p < 0.001).

However there is no significant statistically difference between both groups as regard their parity, and gestational age and result of 1st and 2nd trimester HA1c screening. **(Table .2)**

Patients who developed gestational diabetes mellitus with HA1c < 5.7% were 12.4% while with HA1c ≥ 5.7% were 47.3%. Also, there is significant statistically difference between both groups (p value= 0.015). **(Table .3)**

ROC curve for HbA1c in 1st trimester as a predictor of gestational diabetes mellitus showed that the cut-off point was ≥6.2%, sensitivity was 93.3% and specificity was 90.0%. **(Table .4)**

Table 1. Studied patients according to Glycated hemoglobin value

Glycated hemoglobin value	No (%)
< 5.7%	145 (72.5%)
≥ 5.7%	55 (27.5%)

Table 2. Comparison between women with glycated hemoglobin value (<5.7% vs. ≥5.7%) according to age , BMI , Parity,gestational age and mean of HbA1c.

Variables	Glycated hemoglobin value		t test	P value
	<5.7% (N=145)	≥5.7% (N=55)		
Age (years)				
Range	20–36	20–37	0.559	0.269
Mean±SD	27.06±7.58	28.09±8.29		
BMI (kg/m2)				
Range	22–32	24–37	3.972	<0.001**
Mean±SD	23.14±2.86	32.16±4.46		
Parity			**χ2 test**	**P value**
One No (%)	55 (37.9%)	22 (40%)	1.645	0.428
Two No (%)	75 (51.7%)	27 (49.1%)		
≥ Three No (%)	15 (10.4%)	6 (10.9%)		
Gestational age at 1st trimester screening				
Range	6–14	6–12	2.185	0.274
Mean ±SD	9.25±2.22	8.64±1.59		
Gestational age at 2nd trimester screening				
Range	23–30	22–29	1.274	0.072
Mean±SD	27.10±1.91	25.75±2.07		
HbA1c at 1st trimester screening				
Range	4.5–5.5	5.7–7.4	5.364	0.037*
Mean ±SD	5.17±2.43	7.24±3.47		
HbA1c at 2nd trimester screening				

Range	4.7–5.6	5.7–7.8	4.165	0.018*
Mean±SD	5.49±1.28	7.53±3.19		
P value [1]	0.429	0.615		

1 comparison between HbA1c in 1st and 2nd trimester
P value more than 0.05, nonsignificant.
*P value less than 0.05, significant.

Table 3. Comparison between women with glycated hemoglobin value (<5.7% vs. ≥5.7%) according development of gestational diabetes mellitus

Variables	Glycated hemoglobin value		χ2 test	P value
	<5.7% (N=145)	≥5.7% (N=55)		
Development of gestational diabetes mellitus No (%)	18 (12.4%)	26 (47.3%)	1.295	**0.015***

Table 4. HbA1c in 1st trimester as a predictor of gestational diabetes mellitus

Test Result Variable(s)	Cut off*	P-value	95% C. I.		Sensitivity	Specificity
HbA1c	≥6.2%	0.000	0.938	1.00	93.3%	90.0%

p value: Probability value
CI: Confidence Intervals
*: Statistically significant at p ≤ 0.05
#Cut off was choose according to Youden index

Discussion

Gestational diabetes mellitus is related with a high risk of perinatal morbidity and mortality, and the main complication is macrosomia or large for gestational age (LGA) fetuses. Macrosomia is characterized as birth weight > 4,000 g; nonetheless, this definition neglects to think about gestational age (GA). large for gestational age compares to birth weight ≥ 90th percentile for the relating GA **.(Mitanchez et al., 2015).**

Regarding HbA1C assessment, it is not basically needed for routine antenatal procedures; thought, albeit a couple of decides have upheld that a first-trimester HbA1C center ≥6.5% is fundamental for clear diabetes **(Khalafallah et al., 2016).**

The primary aim of this study was to determine the role of first trimester glycosylated hemoglobin as an indicator of gestational diabetes mellitus.

A cohort study was conducted at Qena University Hospital, obstetrics and gynecology department during the time frame between April 2019 till April 2020 including 200 pregnant ladies who consistently went to the outpatient clinic in the first trimester for antenatal visit.

Glycosylated hemoglobin was found in 72.5 percent of the sampled group (5.7 percent). Glycosylated hemoglobin was found in 27.5 percent of them (5.7 percent). There was a significant difference in BMI for women with high glycated hemoglobin levels (5.7 percent vs 5.7 percent). Nonetheless, there was no discernible difference in age for women with high glycated hemoglobin levels (5.7 percent vs 5.7 percent).

Our findings were backed up by an analysis by **Arbib et al. (2019),** who reported that the mean HbA1C focus (percentage) for all samples collected up to 12 weeks after conception was 5.43 0.42 percent.

These results were in line with those of **Huh et al. (2014),** who discovered a backwards relationship between HbA1C and BMI as a result of the effects of different components on glucose resilience status.

Furthermore, these findings were in agreement with a report by **Fong et al. (2014),** which discovered that women in the high hemoglobin esteem group (HbA1C 5.7–6.4%) had a higher pre-pregnancy BMI and, for the most part, had high HbA1C esteems.

Although, in the study of **Punnose et al. (2020),** the age and BMI of the GDM participants were both increased (p 0.05 for all). In women with and without GDM, the mean standard deviation of HbA1c–FT (HbA1c testing in the first trimester) was 5.04 0.04 percent (31 0.44 mmol/l) and 4.9 0.37 percent (30 4 mmol/l), respectively (p 0.001).

Few analytic approaches have backed alternative screening measures including fasting plasma glucose and glycated hemoglobin (HbA1c) to reduce the number of OGTTs done for GDM determination. HbA1c estimation has a few advantages over OGTT, including the need for only one non-fasting measure, higher pre-insightful dependability and reproducibility, and the absence of obstruction from severe distressing situations. The accuracy of HbA1c as a GDM screening tool has been extensively debated in recent years, but the results have remained unclear **(Paula et al., 2015)**.

The current examination showed that there was no genuinely huge distinction between ladies with glycated hemoglobin esteem (<5.7% versus ≥5.7%) as per equality.

Our outcomes were in concurrence with investigation of **Fattah et al. (2020)** as they exhibited that no genuinely huge distinction between ladies with a HbA1C esteem (<5.7% versus 5.7–6.4%) as indicated by equality.

The current investigation showed that there was no genuinely critical distinction between ladies with glycated hemoglobin esteem (<5.7% versus ≥5.7%) as per gestational age in first and second trimester.

Arbib et al. (2019) found that there was a significant direct and negative relationship between first trimester HbA1C fixation and gestational age at conveyance (r=0.317, P0. 001): the higher the HbA1C fixation, the shorter the gestational age.

In the examination in our grasp, there was genuinely critical distinction between ladies with glycated hemoglobin esteem (<5.7% versus ≥5.7%) as per mean of HbA1c first and second trimester. There was genuinely critical contrast between ladies with glycated hemoglobin esteem (<5.7% versus ≥5.7%) as regard advancement of gestational diabetes mellitus.

Arbib et al. (2019) confirmed our findings, stating that there was a significant difference in primary trimester HbA1C concentration between women with and without GDM (5.74 0.33 percent versus 5.31 0.40 percent, P0.001).

Fong et al. (2014) investigated the association between a specific HbA1C cutoff prior to 20 weeks of development and the progression of GDM in 526 women. They discovered that women with HbA1C values of 5.7–6.4% had a nearly twofold increased risk of developing GDM than women with HbA1C values of 5.7 percent. The risk of GDM remained the same in a subanalysis of 413 women who had their HbA1C levels measured before 14 weeks of incubation, which is more like the new examination companion. Other outcomes, such as cesarean section, birth weight, macrosomia, and neonatal adverse effects, were not found to be profoundly linked to HbA1C levels.

In a study by **Osmundson et al. (2016),** they compared 189 prediabetic women with a HbA1C value of 5.7–6.4% to 2623 women with a HbA1C of less than 5.7 percent and found that they were more likely to develop GDM than women with a HbA1C of less than 5.7 percent.

In a proposed follow-up investigation of 250 women enrolled at 11 + 0 to 14 + a month and a half after pregnancy, **Berggren et al. (2017)** investigated the predictive function of early HbA1C in the absence of sex chemical restricting globulin (SHBG). Neither factor, despite being considered alternative markers for insulin obstruction, accurately predicted the later improvement of GDM. Women with GDM had a higher first-trimester HbA1C fixation than women without GDM (5.4 0.4 percent vs 5.2 0.3 percent), but HbA1C was not linked to GDM in a multivariate analysis. The disparities between these investigations and the current study's findings are most likely due to differences in the specific cutoffs used and the populations' varying risks.

According to **Mukherjee and Sudha (2018),** women with higher HbA1c (>5.7) are more likely to develop GDM than women with lower HbA1c (5.7). HbA1c testing should be available early in pregnancy (first trimester). Women that have a high HbA1c level (>5.7) will benefit from early intervention in pregnancy to avoid GDM and unfavorable perinatal and pregnancy outcomes.

According to **Amylidi-Mohr et al. (2015), pregnant** women with a HbA1c of 5.7–6.4 percent in the first trimester are more likely to have gestational diabetes. Pre-diabetes should therefore be considered a risk factor, and further research should focus on determining whether early intervention versus normal GDM review rules is associated with better short and long-term maternal and neonatal outcomes.

The current examination showed that utilizing ROC bend for HbA1c in first trimester as an indicator of gestational diabetes mellitus, the cut-off point was ≥6.2%, affectability was 93.3% and particularity was 90.0%.

Furthermore, **Arbib et al. (2019)** discovered that HbA1C in the first trimester was profoundly linked to the progression of GDM, with a region under the curve of 0.809 (95 percent CI 0.737–0.882, P0.001). An HbA1C level of 5.45 percent or higher predicted GDM with 83.3 percent affectability and 69 percent explicitness, with a positive predictive value of 53 percent and a negative predictive value of 90.8 percent.

Conclusion

The detection of glycosylated hemoglobin in the first trimester is apromising predictor biomarker for diagnosis of GDM and in the future may replace other basic investigations.

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