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Association between Glycemic Control and Birth Weight with Glycated Albumin in Women with Gestational Diabetes Mellitus

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ABSTRACT

Background: Gestational diabetes mellitus (GDM) is defined as glucose intolerance that is primarily detected during pregnancy**.**

Objective: To determine the relationship between glycemic control and glycated albumin in women with GDM.

Patients and Methods: This prospective study was carried out in the Department of Obstetrics and Gynecology, Zagazig University Hospitals, Zagazig, Sharkia, Egypt from December 2018 to October 2019. The study included 30 patients suffering from GDM (study group) as well as another matching 30 women (control group)**.** Maternal screening for all cases at 24-28 wks using a 75-gm oral glucose tolerance test (OGTT) which is a fasting blood glucose sample was done.

Results: GA levels were significantly higher after 24 weeks of gestation in the GDM group compared with controls. Elevated GA levels had a positive correlation with birth weight. In the present study, fetal weight was significantly higher among the study group (3850.0±513.7) than controls (3396.6±334) ($p<0.001$). Glycated albumin, HbA1c only showed association with large- for- date status. Also, GA24_28, more than 13.4 had a sensitivity of 82% and specificity of 72% for GDM. ROC curve, as the cut- off point for identifying poor glycemic control in GDM women, and provided the optimal sensitivity (75.93%) and specificity (86.36%).

Conclusion: GDM women, the risk of macrosomia significantly increases when the GA levels are ≥14.45% in the third trimester. The results provide strong support for the use of GA measurements, as a complement to finger stick glucose, for assessing short- term glycemic control and predicting large birth weight in the GDM women.

Keywords: Glycemic Control, Birth Weight, Glycated Albumin, Gestational Diabetes Mellitus.

INTRODUCTION

Gestational diabetes mellitus is defined as glucose intolerance that is primarily detected during pregnancy [(1)].

According to the latest diagnostic criteria of the International Association of Diabetes and Pregnancy Study Groups (IADPSG), the incidence of GDM has increased to 20% [(2)]**.**

Women with pre-gestational diabetes and their fetuses are at increased risk of developing complications compared with the non-diabetic pregnant women, including spontaneous abortion, preterm labor, hypertensive disorders, and delivery by cesarean section [(3)]**.** Women with gestational diabetes mellitus (GDM), although have short disease durations also develop similar complications, though not of the same magnitude. Gestational diabetes mellitus accounts for ~90% of cases where pregnancy is complicated by diabetes, with increasing the risk of subsequently developing type 2 diabetes for both the mother and the child [(4)]**.**

Glycemic control is essential to minimize the maternal and fetal morbidity and mortality of pregnancies with GDM [(5)]**.**

At present, the treatment of GDM is mainly focused on the monitoring and control of blood sugar.

Two types of indicators are monitored, the instant blood glucose (such as fasting blood glucose) and the long-term blood glucose monitoring such as glycosylated hemoglobin (HbAlc). However, the two indicators have their shortcomings. Fasting blood glucose is greatly influenced by previous diet, mental state, and other factors such as stress, and exhibits great fluctuations, making it difficult to control. HbA1c only reflects the blood glucose level during the previous 2–3 months and has a relatively shorter observation period for GDM, thus, it is not sensitive [(6)]**.**

Glycated hemoglobin (HbA1c), the current gold standard marker for glycemic control, reflects blood glucose level but it is affected by an abnormal erythrocyte life span, which may occur in iron deficiency anemia. Pregnant women with gestational diabetes mellitus (GDM) often develop iron deficiency anemia; therefore, HbA1c may be insufficient for assessing glycemic control in them [(7)]**.**

Recent reports have advocated the use of glycated albumin as a marker of glycemic control. [(1)]**.** Glycated albumin is the product of non-enzymatic glycosylation of plasma albumin. GA measurement reflects the blood glucose levels of diabetic patients in the preceding 2–3 weeks [(8)]**.**

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Previous studies have shown that this measurement has a higher sensitivity to glycemic fluctuations than HbAlc, and provides useful information in evaluating blood glucose control in diabetic patients. Compared with HbA1c, GA is more closely correlated with fasting and postprandial glucose, regardless of insulin resistance and blood pressure, and might be a better monitoring index in women with GDM. Thus, GA is likely a more appropriate index for evaluating blood glucose in GDM women [(9)].

The study aimed to determine the relationship between glycemic control and glycated albumin in women with GDM.

PATIENTS AND METHODS

(1) Technical design:

a) Setting of the Study: This prospective study was carried out in the Department of Obstetrics and Gynecology at Zagazig University Hospitals, Zagazig, Sharkia, Egypt from December 2018 to October 2019.

b) Sample size: A total of 30 women were assigned as the normal (control) group as well as another matching 30 as the GDM (study) group.

c) Target population: pregnant women at 12-16 weeks.

Inclusion Criteria: Pregnant woman at 12w+0 to 16w+0 of gestation with a single living fetus presented for antenatal care.

(2) Operational design:

Type of the study: Prospective Cohort Study.

Steps of performance:

- Full history taking.
- Maternal serum GA level was measured at 12-16 wks, not need fasting, to all cases who met our inclusion criteria in the second and third trimesters at our hospital.
- Maternal screening for all cases at 24-28 wks using 75gm oral glucose tolerance test (OGTT)
- A fasting blood glucose sample had been obtained. It provides a baseline for comparing other glucose values, the patients had been asked to drink a sweet liquid containing a measured amount of glucose. For the glucose tolerance test, she drunk 75 grams.
- Blood samples had been collected at timed intervals of 1, and 2 hours after drinking the glucose.

Values that indicate diabetes: according to the American Diabetes Association [(10)]

Follow up of our patients in the antenatal outpatient clinic: Every 2 weeks till 36 weeks, then every week till delivery, in the 1st visit:

General examination:

Abdominal examination:

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

Investigations:

❖ **Fetal investigations:**

1. Trans-abdominal ultrasound examination for fetal viability, gestational age confirmation, measurement of the fetal abdominal circumference (AC), and calculation of expected fetal birth weight (EFBW) before delivery.
2. CTG was performed in the third trimester of pregnancy (after 28 weeks) as an indicator of fetal well- being.

❖ At 24-28 weeks of gestation, a 75-g oral glucose tolerance test had been carried out, and the GA levels had been determined.

❖ The participants had been divided into two groups (the normal group as the control group and the GDM group as the study group), according to the OGTT results.

❖ GDM women had been referred to an internal medicine clinic for management of case either by diet control, oral therapy, or insulin therapy.

❖ At 36-38 weeks of gestation, the GA levels had been measured.

GA and Plasma Glucose Measurements:

GA was measured using fructosamine level, as GA kits not available in Egypt.

Measurement of Fructosamine and Glycated Albumin:

GA was measured by this equation:

1186 µmol/l fructosamine = 30 mg/ml GA

The amount of glycated albumin had been expressed as an absolute concentration (mg/ml) or as a relative %, determined by the equation below; GA (%) in the sample was then calculated as follows:

% Glycated Albumin (GA) =Glycated Albumin sample divided by

Total albumin sample× 100

Where;

a) Glycated Albumin is in mg /Ml

b) Total Albumin is in mg /mL

- **The mode of delivery** was according to hospital protocol.
- **Ethical consideration**: Ethical approval and consent to the participated women were taken.

Statistical analysis

Data collected throughout history, basic clinical examination, laboratory investigations, and outcome measures coded, entered, and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) (Statistical Package for the Social Sciences) software for analysis. According to the type of data qualitative represent as number and percentage, the quantitative continuous group represented by mean

± SD, the following tests were used to test differences for significance; difference, and association of qualitative variable by Chi-square test (X^2). Differences between quantitative independent groups by t-test, correlation by Pearson's correlation or Spearman's. P-value was set at <0.05 for significant results & <0.001 for high significant result.

RESULTS

There was no significant difference regarding the age or the height or GA. The study group had a significantly higher mean of weight (75.96±10.4) than the control group (65.16±9.19) (p<0.001). Mean BMI was significantly higher among the study group (29.56±4.33) than control (25.23±3.28) (p=0.001) with a significantly higher percentage of obese among the study group (46.7%). 40% of the study group had significantly higher parity ≥3 **(Table 1)**.

Table (1): Basic demographic data distribution between both groups at the beginning of the study

			Study (N=30)	Control (N=30)	t/X^2	P-value
Age			32.25±9.91	29.1±8.78	1.352	0.113[1]
Weight			75.96±10.4	65.16±9.19	4.256	**<0.001****[1]
Height			160.8±4.16	160.53±2.9	0.287	0.775[1]
Gestational Age			13.46±1.35	13.4±1.32	0.192	0.848[1]
BMI group	**Average**	**N**	4	20		
		%	13.3%	66.7%		
	Overweight	**N**	12	8	20.46	**<0.001****[2]
		%	40.0%	26.7%		
	Obese	**N**	14	2		
		%	46.7%	6.7%		
	Mean ±SD		29.56±4.33	25.23±3.28	3.121	**0.001****[1]
Parity	**1**	**N**	6	17		
		%	20.0%	56.7%		
	2	**N**	12	13		
		%	40.0%	43.3%		
	≥3	**N**	12	0	17.3	**0.001****[2]
		%	40.0%	0.0%		

Abbreviations: **BMI,** body mass index (calculated as weight in kilograms divided by the square of height in meters); **GDM,** gestational diabetes mellitus; **SD**, standard deviation.

In this table study group had significantly higher contraception percentage (83.3%) than controls (46.7%) (p=0.003). Also, the study group had a higher family history of diabetes than controls (p<0.001) **(Table 2)**.

Table (2): Clinical characters distribution between both groups

			Group		X^2	P-value
			Study (N=30)	**Control (N=30)**		
Abortion	**-VE**	**N**	24	24		
		%	80.0%	80.0%		
	+VE	**N**	6	6	0.0	1.0
		%	10.0%	16.7%		
Contraception	**-VE**	**N**	5	16		
		%	16.7%	53.3%		
	+VE	**N**	25	14	8.86	**0.003***
		%	83.3%	46.7%		
Medical history	**-VE**	**N**	28	26		
		%	93.3%	86.7%		
	+VE	**N**	2	4	0.74	0.38
		%	6.7%	13.3%		
Surgical history	**-VE**	**N**	24	22		
		%	80.0%	73.3%		
	+VE	**N**	6	8	0.37	0.54
		%	20.0%	26.7%		
Family history diabetes	**-VE**	**N**	7	22		
		%	23.3%	73.3%		
	1ST degree	**N**	17	5	15.3	**<0.001****
		%	56.7%	16.7%		

	Relative	**N**	6	3		
		%	20.0%	10.0%		

Table 3 showed that fetal weight was significantly higher among the study group (3850.0±513.7) than controls (3396.6±334) (p<0.001). Fetal complications LGA, premature, and shoulder dystocia were significantly higher among the study group than controls. NICU admission was significantly higher among the study group (43.3%) than controls (10%) (p=0.004).

Table (3): Fetal outcome distribution between the two groups

			Group		**t/X²**	**P-value**
			Study (N=30)	**Control (N=30)**		
Fetal weight Mean ±SD			3850.0±513.7	3396.6±334.7	4.049	**<0.001***
Fetal sex	**Male**	**N**	13	14		
		%	43.3%	46.7%		
	Female	**N**	17	16	0.067	0.79
		%	56.7%	53.3%		
Fetal complication	**No**	**N**	17	29		
		%	56.7%	96.7%		
	LGA	**N**	10	0		
		%	33.3%	0.0%	31.32	**0.00****
	Premature	**N**	1	0	17.13	**0.002***
		%	3.3%	0.0%	1.66	**0.21**
	Neonatal death	**N**	0	1		
		%	0.0%	3.3%	1.66	**0.21**
	Shoulder dystocia	**N**	2	0		
		%	6.7%	0.0%	4.88	**0.02***
NICU admission	**Yes**	**N**	13	1		
		%	43.3%	3.0%		
	No	**N**	17	27	8.52	**0.004***
		%	56.7%	90.0%		

Abbreviations: **LGA**, large for gestational age; **NICU**, neonatal intensive care unit.

GA (24-28 weeks) was significantly higher among the study group than the controls **(Table 4)**.

Table (4): Marker distribution between both groups

	Study (N=30)	**Control (N=30)**	**t**	**P-value**
GA (24-28 weeks)	13.84±0.89	13.2±1.01	2.587	**0.012***

GA, glycated albumin.

Mean HbA1c distribution was significantly higher among the study group than the control group **(Fig. 1).**

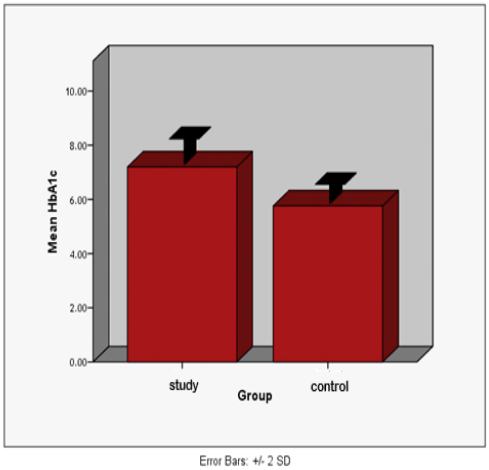

Fig. (1): Mean HbA1c distribution between both groups

Table 5 showed that GA was significantly higher among complicated cases in the study group at 24-28 weeks and 36-38 weeks.

Table (5): Relation between fetal complication and GA at each time

	Study Group	**Study Group**		
	No complication	Fetal complication	**t**	P-value
GA 24_ 28	**13.27±0.89**	**14.33±0.93**	**-3.809**	**0.00****

GA 24-28 weeks more than 13.4 had a sensitivity of 82% and specificity of 72% for GDM **(Table 6)**.

Table (6): Validity of marker cutoffs regards the study group

Test Result Variable(s)	**Area**	**Cutoff**	**P-value**	**95% Confidence Interval**		**Sensitivity**	**Specificity**
				Lower Bound	**Upper Bound**		
GA (24-28 weeks)	**0.683**	**13.400**	**0.015***	**0.548**	**0.819**	**82.0%**	**72.0%**

GA, glycated albumin.

DISCUSSION

The present retrospective analysis of prospectively collected data has shown that the GA levels were significantly higher after 24 weeks of gestation in the GDM group compared with controls. We also observed that elevated GA levels had a positive correlation with birth weight.

This is in agreement with **Li *et al.*** [9] study which found a significant positive correlation between GA levels and the incidence of babies with birthweights ≥3,500 g, and macrosomia in GDM women with poor glycemic control.

In the present study, fetal weight was significantly higher among the study group (3850.0±513.7) than controls (3396.6±334) ($p<0.001$).

In the present investigation, however, and contrary to what was found with glycated albumin, HbA1c only showed association with large- for- date status.

Swierzewska *et al.* [11] reported HbA1c concentration in late pregnancy (36–38 weeks) to be a good predictor of neonatal hypoglycemia in pregnant women with overt diabetes and GDM.

In a similar study, **Yang *et al.*** [12] showed that HbA1c >6.5% in the 3rd trimester had a stronger association with neonatal care unit admission and intravenous glucose requirement.

In our study GA24_28, more than 13.4 had a sensitivity of 82% and specificity of 72% for GDM. GA 36_38 weeks more than 13.9 had a sensitivity of 97.5% and specificity of 87.7% for GDM.

In agreement with **Mendes *et al.*** [13] study in which the performance of glycated albumin and fructosamine as predictive factors of at least one neonatal complication and respiratory disorders in infants of mothers with GDM was quite similar.

They were also similar in their association with LGA newborns. Glycated albumin and fructosamine performed better than HbA1c for these purposes.

Li *et al.* [9] study further identified the value of a GA ≥11.60% level, which was derived from the ROC curve, as the cut- off point for identifying poor glycemic control in GDM women, and provided the optimal sensitivity (75.93%) and specificity (86.36%).

Few studies have assessed the validity of GA in GDM management. The primary utility of the GA cut-off level of 11.60% is to detect approximately 80% of subjects with poor glycemic control, to positively affect GDM management largely, and to permit the early identification of subjects who are at imminent risk of disease development, and who can then be referred for further evaluation and appropriate management. Also, GA use could be more sensitive to short-term glycemic variations than HbA1c and also relegate SMBG testing. Thereby, increasing compliance and improving GDM women empowerment, which might result in significant healthcare cost savings [14].

CONCLUSION

GDM women, the risk of macrosomia significantly increases when the GA levels are ≥14.45% in the third trimester. The results reported in the present study provide strong support for the use of GA measurements, as a complement to finger stick glucose, for assessing short- term glycemic control and predicting large birth weight in the GDM women.

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