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Value of Glycosylated Hemoglobin at 34 Weeks Gestation in the Prediction of Adverse Neonatal Outcome

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ABSTRACT

Background: Gestational diabetes is diabetes, or high blood sugar levels, that develops during pregnancy. It occurs in about 4% of all pregnancies. It is usually diagnosed in the later stages of pregnancy and often occurs in women who have no prior history of diabetes. **Aim of the Work:** To assess the predictive value of elevated glycosylated hemoglobin at 34 weeks' gestation with adverse fetal outcome as regard fetal macrosomia and neonatal hypoglycemia. **Patients and Methods:** This prospective longitudinal cohort study included 98 pregnant women who were recruited from the obstetric outpatient clinic and department at Al-Galaa Teaching Hospital. **Results:** HbA1c ≥7.9 has sensitivity of 88.1% and specificity of 66.1%, in prediction of macrosomia and a sensitivity of 91.9% and specificity of 63.9% in prediction of Hypoglycemia. **Conclusion:** HbA1c ≥7.9 has moderate diagnostic characteristics in prediction of macrosomia, and hypoglycemia, low diagnostic characteristics in prediction of RDS and NICU. **Recommendations:** Use of HbA1C is recommended for patients with GDM for screening, follow up and prediction of adverse neonatal outcomes.

Keywords: Glycosylated Hemoglobin, gestation, adverse neonatal outcome, fetal macrosomia.

INTRODUCTION

Women with gestational diabetes who receive proper care typically go on to deliver healthy babies. However, if you have persistently elevated blood glucose levels throughout pregnancy, the fetus will also have elevated blood glucose levels. High blood glucose can cause the fetus to be larger than normal, possibly making delivery more complicated. The baby is also at risk for having low blood glucose (hypoglycemia) immediately after birth. Other serious complications of poorly controlled gestational diabetes in the newborn can include a greater risk of jaundice, an increased risk for respiratory distress syndrome, and a higher chance of dying before or following birth. The baby is also at a greater risk of becoming overweight and developing type 2 diabetes later in life. If diabetes is present at any stage of pregnancy, there is an increased risk of birth defects and miscarriage compared to that of mothers without diabetes. Women with gestational diabetes have a greater chance of needing a Cesarean birth (C-section), in part due to large infant size. Gestational diabetes may increase the risk of pre-eclampsia, a maternal condition characterized by high blood pressure and protein in the urine. Women with gestational diabetes are also at increased risk of having type 2 diabetes after the pregnancy [(1)]. Pregnant women with type 1 or type 2 diabetes should receive an individualized insulin regimen and glycemic targets typically using intensive insulin therapy Strive for target glucose values: Fasting PG <5.3 mmol/L1-hour postprandial <7.8 mmol/L2-hour postprandial <6.7 mmol/L, Be prepared to raise these targets if needed because of the increased risk of severe hypoglycemia during pregnancy, Perform SMBG, both pre- and postprandial, to achieve glycemic targets and improve pregnancy outcomes. Women with presentational diabetes may use aspart or lispro in pregnancy instead of regular insulin to improve glycemic control and reduce hypoglycemia, Women should be closely monitored during labor and delivery, and maternal blood glucose levels should be kept between 4.0 and 7.0 mmol/L in order to minimize the risk of neonatal hypoglycemia Metformin and glyburide may be used during breast feeding., women with type 1 diabetes in pregnancy should be screened for postpartum thyroiditis with a TSH test at 6–8 weeks postpartum All women should be encouraged to breastfeed since this may reduce offspring obesity, especially in the setting of maternal obesity [(2)]. There is a statistically significant correlation between HbA1c and BMI, amniotic fluid index, and neonatal outcomes. HbA1c of 7 or higher was found to be a cutoff value for the prediction of prematurity, with area under curve of 91.7%. HbA1c may be a useful marker for prematurity in pregnant diabetic women and may correlate with fetal outcome. For the antenatal care of diabetic mothers, it is recommended is to maintain HbA1c less than 7% decrease fetal adverse outcome [(3)].

Advise pregnant women with type 1 diabetes to test their fasting pre-meal, one hour post-meal and bed time blood glucose levels daily during pregnancy. Advise pregnant women with type 2 diabetes who are on a multiple daily insulin injection regimen to test their fasting pre-meal, one

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hour post-meal and bedtime blood glucose levels daily during pregnancy. Advise pregnant women with type 2 diabetes to test their fasting and one hour post-meal blood glucose levels daily during pregnancy if they are on diet and exercise therapy, or taking oral therapy (with or without diet and exercise therapy) or single-dose intermediate-acting or long-acting insulin. Measure HbA1c levels in all pregnant women with pre-existing diabetes at the booking appointment to determine the level of risk for the pregnancy. Consider measuring HbA1c levels in the second and third trimesters of pregnancy for women with pre-existing diabetes to assess the level of risk for the pregnancy. The level of risk for the pregnancy for women with pre-existing diabetes increases with an HbA1c level above 48 mmol/mol (6.5%).Do not use HbA1c levels routinely to assess a woman's blood glucose control in the second and third trimesters of pregnancy [(4)].

GDM usually starts between week 24 and week 28 of pregnancy when the body does not produce enough insulin (the hormone that helps convert sugar into energy) to deal with the increased glucose, or sugar, that's circulating in your blood to help your baby grow. One of the most common pregnancy complications, gestational diabetes affects one in 10 expectant women-and because it occurs more often among obese women, rates of GDM in the United States have been rising along with obesity rates [(5)].

People with diabetes should have this test every 3 months to determine whether their blood sugars have reached the target level of control. Those who have their diabetes under good control may be able to wait longer between the blood tests, but experts recommend checking at least 2 times a year. People with diseases affecting hemoglobin, such as anemia, may get abnormal results with this test. Other abnormalities that can affect the results of the hemoglobin A1C include supplements such as vitamins C and E and high cholesterol levels. Kidney disease and liver disease may also affect the result of the hemoglobin A1C test [(6)].

The first step in a changing attitude towards Glycated hemoglobin occurred in March 2016. An International Expert Committee, with members appointed by the American Diabetes Association (ADA), the European Association for the Study of Diabetes (EASD), and the International Diabetes Federation (IDF), had convened in 2008 to consider current and future means of diagnosing diabetes in nonpregnant individuals. In their conclusion, the committee presented its principal finding that the "Glycated hemoglobin assay may be a better means of diagnosing diabetes than measures of glucose levels." The Committee recommended that a glycated hemoglobin diagnostic level of 6.5% be set in order to assist with the ultimate goal of identifying and subsequently treating individuals who are at risk for complications from diabetes [(7)].

In January 2010, the ADA, for the first time, officially recommended the use of Glycated hemoglobin for diagnosis of diabetes based on clinical evidence showing that Glycated hemoglobin was standardized and more reliable than glucose.2 The ADA agreed that an Glycated hemoglobin of 6.5% should be used for diagnosis and additionally suggested a range of 5.7% to 6.4% to be used for the identification of those at risk for diabetes. The ADA stated that the Glycated hemoglobin test "should be performed in a laboratory using a method that is National Glycohemoglobin Standardization Program-certified and standardized to the assay." They further commented that Glycated hemoglobin point-of-care devices were not sufficiently accurate for diagnostic purposes. The current 2014 ADA recommendation contains the warning that "although point-of-care (POC) A1C assays may be National Glycohemoglobin Standardization Program-certified, proficiency testing is not mandated for performing the test, so use of these assays for diagnostic purposes may be problematic." [(8)].

AIM OF THE WORK

To assess the predictive value of elevated glycosylated hemoglobin at 34 weeks gestation with adverse fetal outcome as regard fetal macrosomia and neonatal hypoglycemia.

PATIENTS AND METHODS

This was a prospective longitudinal cohort study including 98 pregnant women. They were recruited from the obstetric outpatient clinic and department at Al-Galaa Teaching Hospital

Inclusion criteria

1-Diabetic patients on insulin treatment
2-Singleton viable fetus
3-Gestational age at time of inclusion 34 week
4-No gross fetal anomalies
5-Maternal age between 18-35 years

Exclusion criteria

1- Diabetic patients on diet control
2- Medical disorders not related to diabetes as thyroid disorders

METHODS

All cases gave an informed written consent
1- Detailed history
2- Physical examination
3- Laboratory investigations once at 34 week

- Glycosylated hemoglobin level
- Fasting and post prandial blood sugar
- Ultrasound fetal biometry, amniotic fluid index and placental maturation

Neonatal evaluation(outcome):

1- APGAR scoring at 1 & 5 minute
2- Adverse neonatal outcome is considered to be one of the following:
   a- APGAR score <7 at 5 minute
   b- Death either intrauterine or early after birth (within 1 week).
   c- Neonatal weight 4 Kg or more
   d- Presence of respiratory distress syndrome
3- Laboratory investigations (1 hour after birth) Blood glucose level <45mg\dl (Hypoglycemia).

1-History

A- Personal data (age, residence, occupation, smoking or drug abuse)
B- Past history of medical and \or obstetric complications
C- Family history of consanguinity, medical diseases that run in families
D- Preconception menstrual history and the date of last menstruation
E- Obstetric history clarifying the parity, the mode of previous deliveries, the antepartum complications

2-Examination:

A- General examination included general conditions (height and weight) for calculation BMI, vital signs, pallor, edema of extremities
B- Clinical chest and heart examination
C- Full obstetric examination included:
   - Inspection of the abdominal contour
   - Palpation of fundal level and grip, umbilical and pelvic grips

3-Investigations

A-Conventional ultrasound

Technique: Abdominal ultrasound was performed over all patients while they were in a slightly tilted position with the head of the bed raise 30 degrees. aim to:

- Detect of fetal viability
- Exclude multiple pregnancy and major congenital anomalies
- Estimation of gestational age and fetal weight to screen for large for gestational age fetuses
- Estimation of placental maturation
- Estimation of AFI

B-Fasting and postprandial blood glucose level is measured at 34 wk gestation.

C-Glycosylated hemoglobin.

4-Pregnancy outcome estimation

Fetal adverse effects was assessed as follow:

A-Low Apgar score <7 at 5th min:

Sign	0 points	1 point	2point
Heart rate	Absent	<100	>100
Resp-effort	Absent	Slow, irregular	Good crying
Muscle tone	Flaccid	Some flexion of extremities	Active motion
Reflex irritability	No response	Grimace	Vigorous cry
Color	Blue, pale	Bodypink, extrimities blue	Completely pink

B-Neonatal weight:

Macrosomia was defined as birth weight greater than 4000 g regardless of gestational age or as birth weight greater than the 90th percentile for gestational age. Large for gestational age (LGA) was defined as birth weight greater than the 90th percentile for sex and gestational age Fetal macrosomia was defined as abdominal circumference >90th percentile for gestational age as measured by ultrasound .

C- Age of delivery: less than 37 wks is considered prematurity

D- Presence signs of respiratory distress syndrome

E- Neonatal hypoglycemia : if blood sugar after 1 hour of delivery is < 45mg\dl

F- Mode of delivery : either normal vaginal delivery or caesarian section**.**

Smoothed percentiles of birth weight (g) for Gestational age in the United States based on 3, 134, 879 singleton live births

The study was approved by the Ethics Board of Ain Shams University.

Sample Size Justification

The required sample size has been calculated using the Power Analysis and Sample Size Software (PASS©) version 11.0.10 (NCSS©, LLC. Kaysville, Utah, USA).

The primary outcome measure is the accuracy of HbA1C for prediction of macrosomia and neonatal hypoglycemia. A previous study reported that HbA1C had an area under the receiver-operating characteristic (ROC) curve (AUC) of 0.726 or 0.983 for prediction of macrosomia or neonatal hypoglycemia, respectively. In that study the incidence of macrosomia or neonatal hypoglycemia was 38% and 40%, respectively [(9)]**.** So, it is estimated that a sample size of 98 patients would yield 37 (38%) patients with macrosomic babies and 39 (40%) with babies suffering from neonatal hypoglycemia. This sample size of 98 patients would have a power of 91% (type II error, 0.09) to detect a difference of 0.226 between a null AUC of 0.5 and

an alternative AUC of 0.726 for prediction of macrosomia using a two-sided binomial test with a confidence level of 99% (type I error, 0.01), and assuming that the rate of macrosomia is 38% (i.e., positive group: negative group ratio = 0.62). As regards neonatal hypoglycemia, this sample size would have a power exceeding 99.9% (type II error, <0.001) to detect a difference of 0.483 between a null AUC of 0.5 and an alternative AUC of 0.983 for prediction of macrosomia using a two-sided binomial test with a confidence level of 99% (type I error, 0.01), and assuming that the rate of neonatal hypoglycemia is 40% (i.e., positive group: negative group ratio = 0.67).

Statistical Methods

Data were collected, tabulated, then analyzed using IBM© SPSS© Statistics version 22 (IBM© Corp., Armonk, NY). Normally distributed numerical data were presented as mean and SD, and skewed data as median and interquartile range. Qualitative data were presented as number and percentage. Comparison of normally distributed numerical data will be done using the unpaired t test. Skewed data will be compared using the Mann-Whitney test. Categorical data will be compared using the chi-squared test. Receiver-operating characteristic (ROC) curve analysis will be used to examine the predictive value of HbA1C.

A two-sided p-value <0.05 will be considered statistically significant.

RESULTS

Table (1): Glycemic findings of the studied cases

	Mean±SD		**Range**
FBG (mg/dL)	98.9±11.0		74.0–129.0
PPBG (mg/dL)	184.9±29.5		126.0–257.0
HbA1c	8.0±0.9		5.9–10.8
	N		**%**
HbA1c grade	**Very good**	2	2.1
	Good	15	15.3
	Poor	66	67.3
	Bad	15	15.3

Total=98

Table (3): Mode of delivery among the studied cases

		N	**%**
Mode of delivery	**CS**	59	60.2
	VD	39	39.8
Indications of CS	**Macrosomia**	40	67.8
	Fetal distress	12	20.3
	Post CS	4	6.8
	Others	3	5.1

Total=98

Table (4): Gestational age and maturity at delivery

		Mean±SD	**Range**
GA (weeks)		37.6±0.8	36.0–38.0
		N	**%**
Maturity	**Premature**	16	16.3
	Mature	82	83.7

Total=98

Table (5): Birth weight and macrosomia at delivery

	Mean±SD	**Range**
Birth weight (gm)	3774.6±474.2	3121.0–5012.0
	N	**%**
Macrosomia	42	42.9

Total=98

Table (6): Neonatal condition at delivery

	Mean±SD	**Range**
APGAR 1	7.5±1.2	3.0–9.0
APGAR 5	8.3±1.4	4.0–10.0
	N	**%**
Hypoglycemia	37	37.8
RDS	27	27.6
NICU	10	10.2
Death	2	2.0

Total=98

Table (7): Comparison between modes of delivery regarding glycemic findings

Findings		**CS (N=59)**	**VD (N=39)**	**P**
FBG (mg/dL)		100.2±11.0	97.0±10.9	^0.161
PPBG (mg/dL)		187.9±29.4	180.4±29.5	^0.216
HbA1c		8.3±0.8	7.5±0.8	**^<0.001***
HbA1c grade	**Very good**	0 (0.0%)	2 (5.1%)	**#<0.001***
	Good	3 (5.1%)	12 (30.8%)	
	Poor	43 (72.9%)	23 (59.0%)	
	Bad	13 (22.0%)	2 (5.1%)	

^Independent t-test, *Significant

Table (7) and figure (6) show that: **HbA1c** was significantly higher among CS cases.

Table (8): Comparison between maturity conditions at delivery regarding glycemic findings

Findings		Premature (N=16)	Mature (N=82)	P
FBG (mg/dL)		99.3±12.6	98.8±10.8	^0.870
PPBG (mg/dL)		186.1±34.9	184.7±28.6	^0.862
HbA1c		7.7±1.5	8.1±0.8	^0.151
HbA1c grade	**Very good**	2 (12.5%)	0 (0.0%)	# **<0.001***
	Good	6 (37.5%)	9 (11.0%)	
	Poor	4 (25.0%)	62 (75.6%)	
	Bad	4 (25.0%)	11 (13.4%)	

^Independent t-test, *Significant

Table (8) and figure (7) show that: **HbA1c** was significantly lower among premature cases.

Table (9): Comparison between sizes at delivery regarding glycemic findings

Findings		Macrosomia(N=42)	Non-macrosomia(N=56)	P
FBG (mg/dL)		101.9±10.7	96.7±10.8	^0.020
PPBG (mg/dL)		192.6±28.6	179.2±29.2	^0.025
HbA1c		8.6±0.7	7.6±0.8	**^<0.001***
HbA1c grade	**Very good**	0 (0.0%)	2 (3.6%)	# **<0.001***
	Good	0 (0.0%)	15 (26.8%)	
	Poor	31 (73.8%)	35 (62.5%)	
	Bad	11 (26.2%)	4 (7.1%)	

^Independent t-test, *Significant

Table (9) and figure (8) show that: **HbA1c** was significantly higher among macrosomic cases.

Table (10): Comparison between hypoglycemia conditions regarding glycemic findings

Findings		Present(N=37)	Absent (N=61)	^P
FBG (mg/dL)		101.1±9.9	97.6±11.5	^0.123
PPBG (mg/dL)		191.2±27.4	181.1±30.3	^0.101
HbA1c		8.6±0.7	7.6±0.8	**^<0.001***
HbA1c grade	**Very good**	0 (0.0%)	2 (3.3%)	# **<0.001***
	Good	0 (0.0%)	15 (24.6%)	
	Poor	26 (70.3%)	40 (65.6%)	
	Bad	11 (29.7%)	4 (6.6%)	

^Independent t-test, *Significant

Table (10) and figure (9) show that: **HbA1c** was significantly higher among hypoglycemic cases.

Table (11): Comparison between RDS conditions at delivery regarding glycemic findings

Findings		Present(N=27)	Absent (N=71)	P
FBG (mg/dL)		100.6±11.5	98.3±10.9	^0.361
PPBG (mg/dL)		188.7±30.2	183.5±29.4	^0.439
HbA1c		8.6±0.8	7.8±0.9	**^<0.001***
HbA1c grade	**Very good**	0 (0.0%)	2 (2.8%)	# **0.009***
	Good	0 (0.0%)	15 (21.1%)	
	Poor	20 (74.1%)	46 (64.8%)	
	Bad	7 (25.9%)	8 (11.3%)	

^Independent t-test, *Significant

Table (11) and figure (10) show that: **HbA1c** was significantly higher among RDS cases.

Table (12): Comparison between NICU conditions at delivery regarding glycemic findings

Findings		Present (N=10)	Absent (N=88)	P
FBG (mg/dL)		98.6±12.5	98.9±10.9	^0.929
PPBG (mg/dL)		184.0±34.7	185.0±29.1	^0.916
HbA1c		8.6±0.8	7.9±0.9	**^0.038***
HbA1c grade	**Very good**	0 (0.0%)	2 (2.3%)	# 0.346
	Good	0 (0.0%)	15 (17.0%)	
	Poor	7 (70.0%)	59 (67.0%)	
	Bad	3 (30.0%)	12 (13.6%)	

^Independent t-test, *Significant

Table (12) and figure (11) show that: **HbA1c** was significantly higher among **NICU** cases.

Table (13): Correlation between glycemic characteristics and other variables

Variables	FBG		PPBG		HbA1c	
	r	p	r	p	R	p
GA	0.081	0.430	0.079	0.439	0.192	0.058
APGAR1	0.032	0.754	0.029	0.774	-0.218	**0.031***
APGAR5	0.020	0.846	0.019	0.855	-0.245	**0.015***
BW	0.171	0.092	0.170	0.094	0.764	**<0.001***

Total=98, Pearson correlation, *Significant

Table (13) and figure (12): There were significant positive correlation between HbA1c anmd BW& negative correlations with APGAR scores.

Table (14): Comparison between HbA1c grades outcomes

Findings	Very good/good (N=17)	Poor/Bad (N=81)	P
CS	3 (17.6%)	56 (69.1%)	^**<0.001***
Prematurity	8 (47.1%)	8 (9.9%)	^**<0.001***
Macrosomia	0 (0.0%)	42 (51.9%)	^**<0.001***
Hypoglycemia	0 (0.0%)	37 (45.7%)	^**<0.001***
RDS	0 (0.0%)	27 (33.3%)	**#0.003***
NICU	0 (0.0%)	10 (12.3%)	#0.226

^Chi square test, #Fisher's Exact test, *Significant

Poor outcomes were more frequent in poor/bad grades, the difference were significant except in NICU.

Table (15): Diagnostic performance of glycemic findings in predicting outcomes

Factors	AUC	SE	P	95% CI	Cut off
CS					
FBG	0.570	0.060	0.240	0.453–0.688	--
PPBG	0.570	0.060	0.243	0.453–0.687	--
HbA1c	0.804	0.047	**<0.001***	0.712–0.896	≥7.9
Prematurity					
FBG	0.511	0.086	0.889	0.343–0.679	--
PPBG	0.510	0.086	0.897	0.342–0.679	--
HbA1c	0.658	0.098	**0.047***	0.466–0.849	--
Macrosomia					
FBG	0.629	0.056	**0.029***	0.518–0.740	--
PPBG	0.626	0.057	**0.033***	0.516–0.737	--
HbA1c	0.844	0.039	**<0.001***	0.767–0.921	≥7.9
Hypoglycemia					
FBG	0.605	0.058	**0.081**	0.492–0.719	--
PPBG	0.602	0.058	**0.091**	0.488–0.716	--
HbA1c	0.829	0.040	**<0.001***	0.750–0.908	≥7.9
RDS					
FBG	0.547	0.065	0.469	0.421–0.674	--
PPBG	0.546	0.064	0.479	0.420–0.673	--
HbA1c	0.758	0.048	**<0.001***	0.664–0.852	≥7.9
NICU					
FBG	0.526	0.100	**0.787**	0.330–0.722	--
PPBG	0.529	0.100	**0.765**	0.333–0.725	--
HbA1c	0.714	0.063	**0.027***	0.589–0.838	≥7.9

AUC: Area under curve, SE: Standard error, CI: Confidence interval, *significant

Table (15) and figure (13): Only **HbA1c** had significant moderate diagnostic performance in predicting **CS, macrosomia** and **hypoglycemia**. Only **HbA1c** had significant weak diagnostic performance in predicting **prematurity**, **RDS** and **NICU**.

Table (16): Diagnostic characteristics of HbA1c ≥7.9 in prediction of outcomes

	CS		Macrosomia		Hypoglycemia		RDS		NICU	
	Value	95% CI	Value	95% CI	Value	95% CI	Value	95% CI	Value	95% CI
Sensitivity	78.0%	65.3%–87.7%	88.1%	74.4%–96.0%	91.9%	78.1%–98.3%	88.9%	70.8%–97.6%	90.0%	55.5%–99.7%
Specificity	74.4%	57.9%–87.0%	66.1%	52.2%–	63.9%	50.6%–	54.9%	42.7%–	46.6%	35.9%–

				78.2%		75.8%		66.8%		57.5%
DA	76.5%	66.9%–84.5%	75.5%	65.8%–83.6%	74.5%	64.7%–82.8%	64.3%	54.0%–73.7%	51.0%	40.7%–61.3%
Youden's index	52.3%	35.0%–69.6%	54.2%	38.4%–70.0%	55.8%	40.9%–70.7%	43.8%	27.3%–60.4%	36.6%	15.3%–57.9%
PPV	82.1%	69.6%–91.1%	66.1%	52.2%–78.2%	60.7%	46.8%–73.5%	42.9%	29.7%–56.8%	16.1%	7.6%–28.3%
NPV	69.0%	52.9%–82.4%	88.1%	74.4%–96.0%	92.9%	80.5%–98.5%	92.9%	80.5%–98.5%	97.6%	87.4%–99.9%
LR+	3.04	1.75–5.28	2.60	1.77–3.80	2.55	1.80–3.61	1.97	1.48–2.63	1.69	1.27–2.24
LR-	3.37	2.02–5.64	5.55	2.39–12.91	7.89	2.62–23.71	4.94	1.67–14.67	4.66	0.72–30.31
LR	10.26	3.98–26.44	14.41	4.87–42.66	20.09	5.53–73.06	9.75	2.69–35.35	7.85	0.95–64.63
Kappa	0.52	0.34–0.69	0.52	0.36–0.68	0.51	0.35–0.66	0.33	0.18–0.48	0.12	0.02–0.22

CI: Confidence interval, DA: Diagnostic accuracy, PPV: Positive Predictive value, NPV: Negative Predictive value, LR+: Positive likelihood ratio, LR-: Negative likelihood ratio, LR: Diagnostic odd ratio.

HbA1c ≥7.9 had moderate diagnostic characteristics in prediction of **CS**, **macrosomia** and **hypoglycemia**, low diagnostic characteristics in prediction of **RDS** and **NICU**.

DISCUSSION

The chronic metabolic disorder (diabetes mellitus) is a fast-growing global problem with huge social, health, and economic consequences. It is estimated that in 2010 there were globally 285 million people (approximately 6.4% of the adult population) suffering from this disease (10).

This number is estimated to increase to 430 million in the absence of better control or cure (11).

The estimated lifetime risk of developing diabetes for individuals born in 2000 is 32.8% for males and 38.5% for females. Females have higher residual lifetime risks at all ages. The highest estimated lifetime risk for diabetes is among Hispanics (males, 45.4% and females, 52.5%). Individuals diagnosed as having diabetes have large reductions in life expectancy. For example, we estimated that if an individual is diagnosed at age 40 years, men will lose 11.6 life-years and 18.6 quality-adjusted life-years and women will lose 14.3 life-years and 22.0 quality-adjusted life-years (12). This study assessed the accuracy of maternal level HbA1C at 34 weeks in predicting fetal macrosomia and hypoglycemia in diabetic pregnant women.

This was a prospective longitudinal cohort study including (98) pregnant women who were recruited from the obstetric outpatient clinic and department at Al-Galaa Teaching Hospital. According to the results of this study, it was found that, HbA1c ≥7.9 had moderate prognostic characteristics in prediction of macrosomia, and hypoglycemia, low prognostic characteristics in prediction of RDS and NICU.

The study results showed that the cut off value of HbA1C ≥ 7, 9 had moderate prognostic value in prediction of macrosomia with p-value was <0.001, sensitivity was 88.1% and specificity 66, 1%. This result similar with that reported by ***Helen et al.*** [13] who reported that, Continuous glucose monitoring during pregnancy is associated with improved glycemic control in the third trimester, lower birth weight, and reduced risk of macrosomia. This prospective, open label randomized controlled trial included (71) women with type 1 diabetes (n=46) or type 2 diabetes (n=25) allocated to antenatal care plus continuous glucose monitoring (n=38) or to standard antenatal care (n=33), Women randomized to continuous glucose monitoring had lower mean HbA1C levels from 32 to 36 weeks' gestation compared with women randomised to standard antenatal care: 5.8% (SD 0.6) versus 6.4% (SD 0.7). Compared with infants of mothers in the control arm those of mothers in the intervention arm had decreased mean birth weight standard deviation scores (0.9 versus1.6; effect size 0.7 SD, 95% confidence interval 0.0 to 1.3), decreased median customized birth weight centiles (69% versus 93%), and a reduced risk of macrosomia (odds ratio 0.36, 95% confidence interval 0.13 to 0.98).

On the other hand, ***Ingrid et al.*** [14] showed that prediction of birth weight HbA1c at pregnancy weeks 32–36 was included (β 137, 95 % CI −10 to 283, p = 0.07). However, the association was only borderline statistically significant, and in an evaluation of the stability of the model [15]. It was only selected in 23 % of the replicates. The difference in the result may be due to Ingrid et al included 677 women in their study. The hyperglycemia and adverse pregnancy outcomes (HAPO) study found that associations with birth weight were significantly stronger for glucose than for HbA1c [16]. That difference may be due to the

study of Lowe et al was based to compare if HbA1C measurement can provide an alternative to an oral glucose tolerance test (OGTT) in the prediction of adverse neonatal outcomes.

Hou et al. (2014) found no significant difference in HbA1c at pregnancy weeks 28–37 in non-diabetic women having newborns appropriate-for-gestational age compared to large-for-gestational age [(17)]. In contrast, Karcaaltincaba and co-workers (2014) found a positive and independent association between second trimester HbA1c and birth weight and none between fasting plasma glucose and birth weight in non-diabetic pregnancies [(18)]. ***Hughes et al.*** found that a high HbA1c before pregnancy week 20 was associated with an increased risk of large-for-gestational age newborn, but not macrosomia. However, a high HbA1c was associated with an increased risk of major congenital anomaly, preeclampsia, shoulder dystocia, and perinatal death [(19)]. The results of this study showed that the cut off value of HbA1C ≥ 7, 9 had moderate prognostic value in prediction of hypoglycemia with p-value was < 0.001, sensitivity was 91, 9% and specificity 63, 9%. These results coincided with that ***Arumugam and Abdul Majeed*** [(20)] reported in a prospective analysis of 150 pregnant mothers with either pre-existing or gestational diabetes. Found that single reading of HbA1C is very good in prediction of neonatal hypoglycemia..

On the other hand, using mean HbA1c levels throughout pregnancy as a marker for neonatal hypoglycemia, [(21)]. Indicated that there was no correlation between neonatal hypoglycemia and HbA1c levels at any point in pregnancy or with the mean pregnancy HbA1c levels. The difference in the results may be due to the study of ***Taylor et al***. included women with (T1DM). However, they found a significant negative correlation between neonatal blood glucose levels and maternal blood sugars during labor [(22)]. 12 monitoring maternal glycemic levels in 59 mothers with insulin-treated diabetes, showed that neonatal hypoglycemia could still occur despite well controlled diabetes.

The study results showed that the cut off value of HbA1C ≥ 7, 9 has low prognostic value in prediction of RDS with p-value was <0.001, sensitivity was 88.9% and specificity 54, 9%.

These results coincided with that reported by ***Ye et al.*** [(23)] reported that women with singleton pregnancies, who completed a 2h oral glucose tolerance test (OGTT) and HbA1c test at gestational week 24-28 were enrolled in this retrospective study. Clinical information was obtained and statistical analyses were performed to assess the diagnostic value of HbA1c for GDM and the association of HbA1c with adverse pregnancy outcomes. Of the 1959 pregnant women enrolled in the study, 413 were diagnosed with GDM. HbA1c cutoff value <4.8% showed adequate sensitivity to exclude GDM (85.0%) but low specificity (31.8%). While HbA1c cutoff value ≥5.5% presented adequate specificity (95.7%) but low sensitivity (14.8%) in diagnosing GDM. Adoption of HbA1c as a screening test for GDM could eliminate the need for an OGTT in 34.7% women in our study, however, with 6.5% being wrongly diagnosed. HbA1c level was significantly associated with the risk of preterm delivery, neonatal hyper - bilirubinemia, and neonatal asphyxia. Whether adoption of HbA1c as a screening test for GDM would benefit pregnant women remains to be determined. However, HbA1c might be a useful tool to predict patients at increased risk of several adverse pregnancy outcomes.

The study results showed that the cut off value of HbA1C ≥ 7, 9 has low prognostic value in prediction of NICU with p-value was 0.027, sensitivity was 90.0% and specificity 46.6%.

These results confirmed with what ***Ho et al.*** [(24)] reported that conducted a prospective study enrolled 1, 989 pregnant Taiwanese women. A two-step approach, including a 50-g, 1-h GCT and 100-g, 3-h oral glucose tolerance test (OGTT), was employed for the diagnosis of GDM at weeks 23-32.

The mid-pregnancy HbA1c level was measured at the time the OGTT was performed. A receiver operating characteristic (ROC) curve was used to determine the relationship between the mid-pregnancy HbA1c level and GDM. Multiple logistic regression models were implemented to assess the relationships between the mid-pregnancy HbA1c level and adverse pregnancy outcomes. An ROC curve demonstrated that the optimal mid-pregnancy HbA1c cut-off point to predict GDM, as diagnosed by the Carpenter-Coustan criteria using a two-step approach, was 5.7%. The area under the ROC curve of the mid-pregnancy HbA1c level for GDM was 0.70. Compared with the levels of 4.5-4.9%, higher mid-pregnancy HbA1c levels (5.0-5.4, 5.5-5.9, 6.0-6.4, 6.5-6.9, and >7.0%) were significantly associated with increased risks of gestational hypertension or preeclampsia, preterm delivery, admission to the neonatal intensive care unit, low birth weight, and macrosomia (the odds ratio [OR] ranges were 1.20-9.98, 1.31-5.16, 0.88-3.15, 0.89-4.10, and 2.22-27.86, respectively).

So the mid-pregnancy HbA1c level was associated with various adverse pregnancy outcomes in high-risk Taiwanese women. However, it lacked adequate sensitivity and specificity to replace the two-step approach in the diagnosis of GDM. The current study comprised a single-center prospective study; thus, additional, randomized control design studies are required.

CONCLUSION AND RECOMMENDATIONS

HbA1c ≥7.9 has moderate diagnostic characteristics in prediction of macrosomia, and hypoglycemia, low diagnostic characteristics in prediction of RDS and NICU.

We recommended the use of HbA1C with patients with GDM for screening, follow up and prediction of adverse neonatal outcomes.

Further confirmation studies are required to justify the above mentioned results and conclusions , just by increasing the numbers of the experimental diabetic women.

It is recommended to carry out further research on HbA1C level at different gestational age and its relation to fetal and maternal outcomes.

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