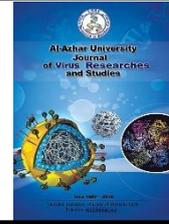




Al-Azhar University Journal for Virus Research and Studies



Umbilical Cord thickness, Interventricular Septum thickness and HbA1c levels in the prediction of Fetal Macrosomia in patients with Gestational Diabetes Mellitus

Hanan Husayin Ali Al subaya¹, Boshra Nasr Ali¹ and Faiza Ahmed Abdel-Hakam¹

¹Department of Obstetrics and Gynecology, Faculty of Medicine for Girls, Al-Azhar University

*E-mail: drfaizafouad@gmail.com

Abstract

Maternity care specialists are still looking for ways to properly anticipate fetal weight in order to reduce the negative consequences associated with traumatic birth. The goal of this study is to see whether assessing umbilical cord thickness, interventricular septum thickness, and HbA1c may help predict fetal macrosomia in gestational diabetes patients. This is prospective case-control research that took place between March 2020 and October 2021 on 80 pregnant women with a gestation of 36 to 37 weeks who visited Al Zahra'a Hospital, Al-Azhar University. After the local hospital ethics and research council accepted the study, the patients were separated into two groups: 40 diabetes pregnant women and 40 non-diabetic pregnant women. The diameter of the umbilical cord was recorded using ultrasound technology. Using ultrasound machine software, the umbilical arteries and veins were measured in a free loop of the umbilical cord. The cross-sectional area of Wharton's jelly was calculated by subtracting the cross-sectional area of the vessels from that of the umbilical cord and the interventricular septum thickness was measured. The HbA1c level was determined. The mean of umbilical cord thickness of study group was (21.55 ± 4.73), umbilical vein (8.85 ± 2.16), umbilical artery (5.18 ± 1.36), Wharton's jelly (54.75 ± 15.85), IVS thickness (5.63 ± 1.55) and HbA1c (6.5 ± 0.92). They had highly statistically significant difference ($P=0.00$) in diabetic group than control group were linked to fetal macrosomia. Using a ROC curve to assess their prediction performance for macrosomia detection, the ideal HbA1c cut-off point > 5.6 percent, with a sensitivity of 100% and a specificity of 68.25 percent (AUC 0.92; $p < 0.00$). Umbilical cord thickness cut-off point > 21.5 where the sensitivity was 100 % and the specificity was (100%), (AUC 1.00; $p < 0.00$) and IVS thickness cut-off point > 4.9 where the sensitivity was 100 % and the specificity was 74.6% (AUC 0.921; $p < 0.00$). The Apgar score of the neonates of study group at (1,5&10) minute was significantly lower than the control group ($P=0.00$). There was a significant very strong positive correlation ($r=0.850$) between NICU duration of admission and IVS thickness ($P=0.00$). In individuals with gestational diabetes, ultrasound measures the diameters of the fetal umbilical cord and interventricular septum thickness, together with HbA1c levels, may help predict fetal macrosomia. Our research found a substantial very strong positive association between interventricular septum thickness and length of stay in the NICU.

Keywords: Gestational Diabetes Mellitus, HbA1c, hemoglobin.

1. Introduction

In According to the American Diabetes Association (ADA), gestational diabetes or (gestational diabetes mellitus, GDM) is diabetes that is diagnosed in the second or third trimester of pregnancy and precludes the possibility of pre-existing type 1 or type 2 diabetes [1]. Gestational diabetes is linked to an increased risk of both maternal and newborn complications. For the mother, there are two types of consequences: short-term consequences those that occur during labor and the early postpartum period (e.g., risk of preeclampsia or instrumental delivery) and those that have longer-term consequences, most notably the risk of type 2 diabetes later in life. Similarly, dangers to the neonate may exist throughout labor and birth, such as macrosomia (a potentially painful birth) and neonatal hypoglycemia, as well as in the long term, such as obesity and type 2 diabetes programming [2].

Fetal hyperglycemia is caused by maternal hyperglycemia, which leads to abnormal fetal hyperinsulinemia. This pathophysiological triggering element induces abnormally high fat tissue deposition and increases overall fetal size, which has been shown by several studies to be the root cause of poor perinatal outcome measures owing to fetal rapid development and macrosomia [3]. Fetal macrosomia affects 20-30% of pregnant women with gestational diabetes [4]. The American College of Obstetricians and Gynecologists (ACOG) defines fetal macrosomia as a birth weight of more than 4000 g, regardless of gestational age. Large for gestational age (LGA) refers to fetuses whose estimated fetal weight (EFW) is in the 90th percentile for their gestational age, which reflects the influence of gestation age on rapid fetal growth [5]. For suspected macrosomia, the purpose of a planned caesarean delivery is to decrease fetal or mother morbidity, or both. The fetus's birth weight is significant in selecting the route of delivery, but pelvic examination should not be overlooked [6]. The evaluation of morphometric variation of the umbilical

cord vessels and their relationship to fetal fate at delivery has been aided by advances in ultrasound technology [7]. One of the most difficult clinical circumstances in everyday obstetric practice is detecting and predicting fetal macrosomia before birth [8]. Fetal myocardial muscle changing in fetuses of GDM, revealed the hypertrophic of myocardial changes caused by fetal hyperglycemia and fetal hyperinsulinemia. These changes impact the interventricular septum (IVS) [9]. Cardiac septal overgrowth, also known as Interventricular Septum (IVS) thickness, affects 10–40% of neonates delivered to diabetic mothers [10]. The goal of this study is to see whether assessing umbilical cord thickness, interventricular septum thickness, and HbA1c might help predict fetal macrosomia in GDM patients.

2. Patients and Methods

The design of the study is prospective case-control research and placed of the study at Al Zahra'a Hospital, Al-Azhar University. Duration of the study is from March 2020 to October 2021. Study population was done on 80 pregnant women with gestational ages ranging from 36 to 37 weeks separated into two groups: 40 diabetes pregnant women and 40 non-diabetic pregnant women. Sample Size Justification is IBM© Sample Power version 3 (IBM© Corp., Armonk, NY) was used to compute the needed sample size.

Diagnostic criteria of gestational diabetes mellitus:

- 1- >126 mg/dl (>7.0 mmol/l) fasting plasma glucose.
- 2->200 mg/dl (>11.0 mmol/l) plasma glucose level at random.
- 3-Hemoglobin A1c > 6.5%

Ethical approval is the quality education assurance section of Al Azhar University's Faculty of Medicine granted ethics committee approval (no. RHDIRB201910195). All women who volunteered to participate in the study were fully informed about the nature and

purpose of the research. Any patient who took part in the research had the option to withdraw at any time without affecting the medical care they provided.

2.1 Inclusion Criteria

Participants were as follows: pregnant women with singleton pregnancy, gestational age 36-37 weeks, GDM, normal umbilical morphology (two arteries and one vein), normal amniotic fluid index and intact membrane.

2.2 Exclusion Criteria

There were as follows: fetal congenital abnormalities, multifetal pregnancy, and pregnancy chronic medical conditions (e.g hypertension, diabetes mellitus type 1 or II), preeclampsia, intrauterine growth retardation or Intrauterine fetal death.

2.3. Methodology

After receiving informed consent, all of the women were subjected to a full history taking and thorough general and obstetric exams. The level of HbA1c was measured using an immunoassay approach in venous blood samples obtained from pregnant women in the clinical pathology department of Al Zahra'a Hospital. The ultrasound examination was performed using a LOGIQ V5 with a 3.5 Hz transabdominal probe. Fetal biometry (biparietal diameter, abdomen circumference, femur length) and estimated fetal weight were determined automatically using Hadlock's method during ultrasonography. In addition, the diameters of the umbilical cord, umbilical arteries, and umbilical vein is measured sonographically in the free loop of the umbilical cord, revealing Figure 1. During the measurements, the diameters were measured from the outside to the outside at the widest point of the umbilical cord Figure 2. Using the ultrasound device's software, Subtracting the crosssectional

area of the vessels from that of the umbilical cord yielded the cross-sectional area of Wharton's jelly The IVS must be measured using the four chamber view (which corresponds to the axial view of the chest at the heart).show in Figure 3. Patients were followed till delivery. Mode of delivery, birth weight (fetal macrosomia was identified if fetal weight was 4 kg or higher), fetal sex, Apgar score, NICU admission, and length of stay were all monitored.

2.4 Statistical Analysis

IBM SPSS Statistics version 25 was used to gather, tabulate, and analyze the data (IBM Corp., Armonk, NY). Numerical data with a normally distributed distribution was given as median and SD, whereas data with a skewed distribution was presented as average and range (minimum - maximum). Numbers and percentages were employed to portray qualitative data. The independent t-test was used to compare numerical data that was regularly distributed. The Chi-squared test was used to compare categorical data. The associated distribution tables were examined after each of the test statistics were calculated to get the "P" value (probability value). At a P value of <0.05, statistical significance was accepted (SS). A P value <0.001 was assumed highly substantial (HS), whereas a P value >0.05 was assumed non-significant (NS). The efficacy of ultrasound measurements of umbilical cord thickness and interventricular septum thickness, as well as HbA1c level, for predicting fetal macrosomia, was investigated using receiver-operating characteristic (ROC) curve analysis. An AUROC of 0.75 was selected since it is the smallest AUROC for a diagnostic/predictive test to be clinically relevant.

3 .Results

Table. 1 show there is not statistically significance difference as regard to

maternal age, gravidity, parity, previous miscarriage, previous delivery and gestational age at delivery for study (GDM) group and control group (P-value >0.05). However, there was high statistically significance variance between both groups regarding the BMI (P-value =0.00). Table. 2 shows highly significance statistical difference (P-value=0.00) between both groups. Table 3 shows that there is highly significance statistical difference between both groups as regards fetal weight, macrosomia, NICU admission and duration (P=0.00). About fetal gender there is no statistical significance between two groups. Table. 4 Shows that Apgar score of the neonates of GDM group at (1,5&10) is

significantly lower than the control group. Table. 5 shows that there are highly significance statistical differences between both groups as regards UC diameter, UV diameter, UA diameter, WJ area, IVS thickness and HbA1C. Table. 6 there is a high substantial positive correlation. Table. 7 shows there is significant very strong positive correlation. Table. 8 demonstrates that Large Umbilical cord (UC) diameter, large Wharton's jelly (WJ) area, large inter-ventricular septum (IVS) thickness, HbA1c, Large Umbilical vein (UV) diameter and Large Umbilical Artery (UA) diameter are good predictor for diagnosis of fetal macrosomia.



Figure (1): View of free loop of umbilical cord.



Figure (2): Shows the method of measurement of umbilical cord diameter.



Figure (3): Shows chambers of fetal heart with IVS thickness measurement about 0.83 cm (8.3 mm) in diabetic mother.

Table (1): Comparison between study (GDM) group and the control group as regard to clinical and demographic data.

Studied group. Item	Study (GDM) group. (40)	Control group. (40)	Significance test	P-value	Sig
Age (Years) -Range -Mean \pm SD	20-37 27.65 \pm 4.79	20-43 28.55 \pm 5.48	t-test=0.78	0.4	NS
Gravidity -Range -Median	1-6 3	1-7 3	t-test=0.18	0.9	NS
Parity -Range -Median	0-5 2	0-6 2	t-test=0.15	0.8	NS
BMI (KG/M²) -Range (Mean \pm SD)	22,5-31.6 28.15 \pm 2.06	17.0-31.3 22.67 \pm 3.1	t-test=9.2	0.00	HS
Gestational age (Week)at delivery -Range (Mean \pm SD)	38-39 38.43 \pm 0.5	38-39 38.65 \pm 0.5	t-test=0.22	0.8	NS
Previous miscarriage -Yes -NO	13(32.5%) 27(67.5%)	10(25.0%) 30(75.0%)	X²=0.54	0.45	NS
Previous delivery -Normal delivery -previous Cs -No history of previous delivery	1(2.5%) 28(70.0%) 11(27.5%)	3(7.5%) 29(72.5%) 8(20.0%)	X²=1.5	0.47	NS

P-value > 0.05: Non-Significant; *P-value* \leq 0.05: Significant; *P* \leq 0,001: Highly substantial; Cs: Cesarean section; X²: chi square test; BMI: body mass index.

Table (2): Comparison between study (GDM) group and control group as regard to mode of delivery.

Studied group. Item	Study (GDM) group. (40)		Controls (40)		X ² Chi square test	P- value	Sig.
	No.	%	No.	%			
Mode of delivery: -Caesarean delivery -Normal vaginal deliery	40 0	100 0	31 9	77.5 22.5	10.1	0.00	HS

P-value > 0.05: Non-Significant; *P-value* \leq 0.05: Significant; *P* \leq 0,001: Highly Significant; Cs: cesarean section.

Table (3): Comparison between study (GDM) group and control group as regard to fetal outcome.

Studied group. Item	Study (GDM) group. (40)	Controls (40)	Significance test	P-value	Sig.
Fetal weight (gram) (Mean \pm SD)	3717.5 \pm 716	2842.5 \pm 300	t- test =7.1	0.00	HS
Macrosomia - Yes - No	17 (42.5%) 23 (57.7%)	0 (0.0%) 40 (100%)	X ² =21.5	0.00	HS
NICU admission: - Yes - No	40 (100%) 0 (0.0%)	3 (7.5%) 37 (92.5%)	X ² =68.8	0.00	HS
NICU admission duration (day) (Mean \pm SD)	7.8 \pm 6.7	1.46 \pm 0.4	t- test =6.8	0.00	HS
Fetal gender -Female -Male	14(35.0%) 26(65.0%)	21(52.5%) 19(47.5%)	X ² =2.5	0.11	NS

Table (4): Apgar score to neonates of the study (GDM) group and control group at 1 minute,5 minute and 10 minutes.

Studied group. Item	Study (GDM) group. (40)	Controls (40)	t- test	P-value	Sig.
1 minute Apgar score (Mean \pm SD)	4.25 \pm 1.12	6.95 \pm 1.108	10.8	0.00	HS
5-minute Apgar score (Mean \pm SD)	6.48 \pm 0.93	9.69 \pm 0.82	16.2	0.00	HS
10-minute Apgar score (Mean \pm SD)	6.88 \pm 1.01	9.85 \pm 0.53	16.4	0.00	HS

P-value > 0.05: Non-Significant; P-value \leq 0.05: Significant; P \leq 0.001: Highly Significant

Table (5): Comparison between study (GDM) group and control group as regard to ultrasound measurements and HbA1c.

Studied group. Item	Study (GDM) group. (40) (Mean \pm SD)	Control group. (40) (Mean \pm SD)	t- test	P-value	Sig
UC diameter (mm)	21.55 \pm 4.73	17.95 \pm 18.9	4.46	0.00	HS
UV diameter (mm)	8.85 \pm 2.16	5.32 \pm 2.01	4.113	0.001	HS
UA diameter (mm)	5.18 \pm 1.36	4.51 \pm 1.05	2.45	0.001	HS
WJ (mm)²	54.75 \pm 15.85	37.73 \pm 7.306	6.17	0.00	HS
IVS (mm)	5.63 \pm 1.55	4.19 \pm 0.62	6.17	0.00	HS
HbA1c (%)	6.5 \pm 0.92	4.6 \pm 0.35	12.4	0.00	HS

Table (6): Correlation between fetal weight and HbA1c level.

Variables	fetal weight		
	(r)	P- value	Sig
HbA1c level	0.71	0.00	HS

P-value > 0.05: Non-Significant; P-value ≤ 0.05: Significant; P ≤ 0,001: Highly Significant

Table (7): Correlation between inter-ventricular septum thickness and duration of admission at NICU.

Variables	Duration of admission at NICU		
	(r)	P- value	Sig
IVS mm	0.850	0.00	HS

P-value > 0.05: Non-Significant; P-value ≤ 0.05: Significant; P ≤ 0,001: Highly Significant

Table (8): ROC curve analysis of screening ability of different umbilical cord measurements, inter-ventricular septum thickness and HbA1c level for diagnosis of macrosomia.

Indicator	Sensitivity	Specificity	Positive predictive value	Negative predictive value	AUC	Cut- off point	P- value	Sig
UC (mm)	100	100	100	100	1.00	>21.5	0.00	HS
UV (mm)	94.1	61.9	40.0	97.5	0.757	>8.3	0.00	HS
UA (mm)	82.4	79.4	51.9	94.3	0.874	>5.4	0.00	HS
WJ (mm ²)	94.1	100	100	98.4	0.988	>55	0.00	HS
IVS (mm)	100	74.6	51.5	100	0.921	>4.9	0.00	HS
HbA1c (%)	100	68.25	45.9	100	0.92	>5.6	0.00	HS

P-value > 0.05: Non-Significant; P-value ≤ 0.05: Significant; P ≤ 0,001: Highly Significant

4. Discussion

Gestational diabetes is a long-term metabolic condition that manifests clinically during pregnancy and is defined by metabolic dysfunction that lasts long after the birth of the baby and most often predates it [11]. Macrosomia causes serious difficulties in both the mother and the infant, emphasizing the need for early detection and prevention. In the ACOG Practice Bulletin, this was humorously

described: "Parous mothers, like professionals who utilize ultrasonography or clinical palpation methods, seem to be able to forecast the weight of their babies." [5]. The demographic data of our research found that there was not statistically significance variance as regard to maternal age, gravidity, parity, previous miscarriage, previous delivery and gestational age at delivery for study (GDM) group and

control group (P-value >0.05). Our research revealed high statistically significance difference in the BMI among GDM group and control group. In agreement with that, study identified obesity as a definite risk factor for GDM [12]. Denison et al [13] concluded in their study that Maternal obesity, especially when paired with GDM, should be considered a high-risk pregnancy. Obese pregnant women should be advised to engage in lifestyle changes such as diet and physical exercise. To prevent gaining too much weight during pregnancy, you should keep track of your weight. Obese women of reproductive age should be informed about the dangers of obesity during pregnancy and encouraged to reduce weight before and after their pregnancies.

Our current study demonstrated high statistically difference between the two groups as regard to the mode of delivery among the gestational diabetic group and control group. In addition, the caesarean section rate for moms with GDM was 100%, compared to 77.5 percent in the control group. These findings corroborated previous research, which found that the incidence of caesarean section in diabetes women was greater than in the control group [14]. Binbir [15] showed that even if the birth weight was normal, a caesarean section was preferable over a vaginal delivery in diabetes individuals. They hypothesized that the major cause for the increased number of caesarean sections was due to medicolegal issues linked to diabetic fetus dystocia, and that the number of prior caesarean sections was greater in both the GDM and control groups (73.2 percent and 73.2 percent, respectively (32 percent).

Our study demonstrated that, median of fetal weight (3717.5) standard deviation (716) in GDM group and (2842.5±300) in controls with a high statistically significance variance between both groups. The incidence of fetal macrosomia was (42.5%) among cases and equal (0%) among control group. In agreement of our

study Beta [16] who concluded that, Maternal risks connected with macrosomia include a higher likelihood of caesarean delivery. According to studies, the likelihood of caesarean birth for women trying a vaginal delivery with a birth weight of more than 4,000 g is at least twice that of controls.

The present study's fetal outcome data demonstrated a large significant variation in NICU admission between the GDM and control groups. In comparison to babies born to normal women, the number of newborns requiring NICU hospitalization was much greater (100%) for infants born to GDM mothers (7.5 percent).

In line with this findings Ijäs et al [17] study reported that, Infants in GDM groups were more likely to be admitted to the NICU, and this difference was significant, compared to those in the control group.

Furthermore, newborns born to GDM moms had a longer hospital stay (7.8 ± 6.7) than newborn infants born to normal mothers (1.46 ± 0.4) (P value=0.00). Finally, GDM continues to be a serious morbidity for neonates, resulting in increasing NICU admissions and hospital stays. Babies born to GDM moms spent more time in the hospital than newborn infants born to normal mothers (P<03), putting a huge strain on the health-care system [18]. Ijäs [17] found that the higher likelihood of NICU hospitalization may be attributed to regular monitoring of newborns of GDM moms owing to concerns about neonatal hypoglycemia and careful supervision of the infants' blood sugar. Nonetheless, the risk of NISU admission remained elevated in the infants of mothers with GDM after adjustment for neonatal hypoglycemia. In keeping with this, in the first time our research found a substantial very strong positive association between interventricular septum thickness and length of stay in the NICU ($r=0.850$) (P=0.00).

Furthermore, the current study's fetal outcome results revealed a high substantial variation between GDM group and control

group as regard to Apgar score at 1 minute, mean and standard deviation (4.25 ± 1.12), Apgar score at 5 minute (6.48 ± 0.93) and at 10 minute (6.88 ± 1.01) for study and (6.95 ± 1.1080), (9.69 ± 0.82) and (9.85 ± 0.53) for controls. The results of the Hildeñ [19] study indicated that maternal obesity and GDM are important potential risk factors for a poor Apgar score. Similar to other study de Silva [20], neonate of pregnancy complicated by GDM had low Apgar score at 5 minute than those of control. Which reported Apgar score < 7 . Our study different from de Silva [20] that Apgar score was observed also at 1 minute and 10 minute we found Apgar score significantly low < 7 . Based on the results of this research and Hildén [19]; Ijäs [17] GDM is linked to a higher likelihood of a poor Apgar score and NICU admission. Obesity and GDM, on the other hand, are linked to the highest risk of negative pregnancy outcomes.

Our results of umbilical cord measurements of between fetus of GDM mothers and control group in current study there was statistically highly significance difference ($p=0.00$) for umbilical cord (UC), umbilical vein (UV) and umbilical artery (UA). Wharton,s jelly area (mm^2). In similar Rehabe [8] evaluated The role of umbilical cord thickness and interventricular septum thickness in predicting macrosomia in 40 GDM pregnant women and 40 healthy women found a greatly significant relation between umbilical cord area-diameter and fetal estimated weight in the diabetic group at 36–37 pregnancy weeks in the diabetic group ($p < 0.05$).

As regards to Interventricular septum thickness, our result found that the mean of IVS was thicker among GDM group than the controls with high statistically significance difference ($P\text{-value} = 0.00$). Pawel [21] investigated the relation between umbilical cord diameter, IVS thickness, HbA1c and fetal weight to predict fetal macrosomia in 102 study group divided to 80 GDM and 24 type 1

diabetes mellitus(T1DM) pregnant women at 37–39 weeks of pregnancy. reported that IVS was significantly greater in patients with GDM as compared to control group ($p < .01$). This is in line with Jose-Gracia Flores [22] who reported that the most useful marker for determining the impact of diabetes management on the fetal heart is IVS thickness; nevertheless, the presence of a hypertrophic IVS should be followed by a systemic systolic and diastolic functional examination. Jose-Gracia-Flores [22] reported that despite capillary glycemic control, diabetic women' babies are at danger of cardiac hypertrophic alterations owing to fetal hyperglycemia and hyper insulins. The interventricular septum is most affected by these ostensibly temporary alterations. Rehabe [8] reported that in patients with GDM, IVS was substantially higher than in controls. The lack of any aberrant function in a hypertrophy IVS does not rule out fetal danger; it might be linked to increased perinatal mortality as part of diabetes fetopathy, or it could be an indication of undetected poor mother glycemic control. As regards to HbA1c levels of the our result the mean of HbA1c% was higher among gestational diabetic group (6.5 ± 0.92) than the controls (4.6 ± 0.35) with statistically highly substantial variance ($P=0.00$). Also, there was a substantial strong positive association between fetal weight and HbA1c level ($r= 0.71$, $P=0.00$). In agreement with our result Pawel et al [21] reported when comparing women with GDM to controls, there was a significant rise in HbA1c concentration ($P < .05$). Furthermore, a correlation analysis of the whole study group revealed that there were positive associations between fetal birth weight(FBW) and HbA1c concentration in the third trimester ($r=0.48$, $P < .001$). In contrast to our study Mahmoud et al [14] observed on 100 GDM pregnant women, the association between umbilical cord thickness, HbA1c, and macrocosmic fetal birth weight revealed that glycated hemoglobin had neither a strong nor

substantial association with birth weight, measured at 36 – 37 weeks.

The results of our study used of ROC curve to predict macrosomia as regard to Large umbilical cord diameter was an excellent predictor for macrosomia, with sonographic sensitivity (100%), specificity (100%), positive predictive value (100%), and negative predictive value (100%) and we detected Cut-off point > 21.5 with a strong statistically significant difference (P value=0,00). As regard to Umbilical vein diameter measures was a good predictor for macrosomia with Sensitivity (94.1%), Specificity (61.9%), Positive predictive value (40%), Negative predictive values (97.5%) and we detected Cut-off point > 8.3 with high statistically significance difference. Also, as regard to Umbilical artery measures was a good predictor for macrosomia with Sensitivity (82.4%), Specificity (79.4%), Positive predictive values (51.9%), Negative predictive values (94.3%) of sonographic and we detected Cut-off point > 5.4. And as regard to Large Wharton's Jelly area was an excellent classifier for diagnosis of fetal macrosomia with Sensitivity (94.1%), Specificity (100%), Positive predictive values (100%), Negative predictive values (98.4%) and were detected Cut-off point > 55 with high statistically significance difference (P value=0.00) between study and control groups. Similar to Rehabe [8] was reported that Large umbilical cord diameter, Specificity, positive and negative predictive values of sonographic large umbilical cord in the prediction of birth weight > 4000 g were 82.5%, 50%, 89.7% respectively, and cut-off point >23.0. And they reported that in the prediction of fetal macrosomia, umbilical vein diameter has specificity, positive and negative predictive values (52.4, 34.8 percent, and 97.1 percent, respectively) and cut-off point >6.6. Also reported, Positive and negative sonographic prognostic values for the umbilical artery, with specificity. Large umbilical artery diameter is associated with 33.3 percent, 25%, and

87.5 percent of cases of fetal macrosomia, respectively and cut-off point > 4.1. And reported that Large Wharton's Jelly region with specificity, positive and negative fetal macrosomia prognostic values (95.2 percent, 80 percent, 92.3 percent respectively) and cut-off point > 50. According to Rehabe et al (2018), in the diabetes group at 36–37 pregnancy week, there was a strong substantial link between umbilical cord area-diameter and fetal estimated weight.

The results of ROC curve in our study to predict macrosomia, as regard to third trimester HbA1c level was excellent predictor for fetal macrosomia (AUC= 0.92) and cut -off point is > 5.6% (38 mmol/ mol) with sensitivity (100 %), specificity (68.25%), positive predictive value (45.9%) and negative predictive value (100%). In line with our result found Liliana [23] third trimester HbA1c. Using a ROC curve to assess the predictive capacity of third trimester HbA1c for large for gestational age (LGA) identification, the best HbA1c cut-off value for LGA identification was 5.4 percent (36 mmol/ mol), with a sensitivity of 77.4 percent and a specificity of 71.7 percent (AUC 0.782; P < 0.001). Wong [24] showed that HbA1c levels that were high at the time of GDM diagnosis or at 36 weeks of pregnancy were both independent predictors of LGA offspring and neonatal hypoglycemia. After diagnosis, they reported HbA1c cut-offs of 5.4 percent (36 mmol/mol) and 5.5 percent (37 mmol/mol) and at 36 weeks, they reported HbA1c cut-offs of 5.5 percent (37 mmol/mol). Our findings also show that women with GDM who had a third trimester HbA1c of more than 5.6 percent (37 mmol/mol) between 36 and 37 weeks of pregnancy were more likely to have an LGA child. Our findings are consistent with those of previous research that have shown HbA1c to be useful in predicting LGA or macrosomia. Our ROC curve findings for IVS show that it is a potential macrosomia predictor, with a cut-off point of 4.9 mm or (AUC = 0.921; P = 0.00) as

the best cut-off point. To demonstrate its predictive capabilities, the following statistical performance indicators were created: Sensitivity of 100 percent, negative predictive value (NPV) of 100 percent, specificity of 74.6 percent, and positive predictive value of 51.5 percent (PPV). In line with Szmyd [25] was studied the optimum cut-off point for macrosomia prediction was 4.7 mm (AUC = 0.644; P = 0.0177). It has a predictive capacity of 71.43 percent sensitivity, 95.40 percent negative predictive value (NPV), 61.25 percent specificity, and 16.00 percent positive predictive value (PPV). When LGA/hypertrophy is indicated, IVS measurement seems to be superior to Sono graphically derived fetal biometry. When the two techniques (IVS \geq 4.7 mm and/or LGA/hypertrophy) are combined, they have a sensitivity of 78.57 percent, an NPV of 96.27 percent, a specificity of 57.20 percent, and a PPV of 15.94 percent. Rather than improving current methods, they set out to discover a new parameter.

References

1. American Diabetes Association (2020): Standards of medical care in diabetes; Diabetes care 43 (suppl.1):514-531/https://doi.org/10.2337/dc20-5002.
2. Sofia N, Jas-mine S, Alexis S, Christine H, Elif I (2018): Biomarkers for Macrosomia Prediction in Pregnancies Affected by Diabetes Front. Endocrinol.,31July2018https://doi.org/10.3389/fendo.00407.
3. Ahmed H, Abushama M, Khraisheh M, Dudenhausen J, (2015): Role of ultrasound in the mangement of diabetes in pregnancy . J. Maternal Fetal Neonatal Med . 28:1856-1863.
4. De Onis M, Blossner M and Borghi E (2010): Global prevalence and trends of overweight and obesity among preschool children. Am J Clin Nutr92:1257–1264.
5. American College of Obstetricians and Gynecologists (2020): Macrosomia. ACOG Practice Bulletin No. 216. American College of Obstetricians and Gynecologists. Obstet Gynecol ;135:e18–35.
6. King JR, Korst LM, Miller DA, Ouzounian JG (2012): Increased composite maternal and neonatal morbidity associated with ultrasonographically suspected fetal macrosomia. J Matern Fetal Neonatal Med ;25: 1953–9.

6. Conclusion

The HbA1c level, fetal IVS, and umbilical cord ultrasound-derived parameters all increased significantly in pregnancy with GDM, according to our findings.

The thickness of the umbilical cord, the thickness of the fetal IVS, and HbA1c are all strong predictors of fetal macrosomia.

We highlight the role and benefit of a third-trimester HbA1c test, since it may alert clinicians to this risk and help them better treat these pregnant women.

Our research found a substantial very strong positive association between interventricular septum thickness and length of stay in the NICU.

Funding Sources: There was no support for this study from any governmental, private, or non-profit organization.

Conflicts of interest: no competing interests.

7. Elghazaly EA, Ali QM, Babikir HH (2016): Umbilical cord abnormalities. *Sudan Med Monit*;11(1):1.
8. Rehab M, Salma MM (2018): The role of Umbilical Cord thickness, Interventricular Septum thickness and HbA1c levels in the prediction of fetal Macrosomia in patients with Gestational Diabetes Mellitus. *J.Gynecol Res Obstet* 4(3): 039-043.
9. El-Ganzoury MM, El-Masry SA, El-Farash RA (2012): infants of diabetes mother: echocardiographic measurements and cord blood IGF-I and IGFBP-1. *Pediatric Diabetes* 13: 189-196. Link: <http://tinyurl.com/y55gdgfr>.
10. Aman J, Hansson U, Ostlund I, Wall K, and Persson B (2011): "Increased fat mass and cardiac septal hypertrophy in newborn infants of mothers with well-controlled diabetes during pregnancy," *Neonatology*, vol. 100, no. 2, pp. 147–154.
11. Retnakaran R, David R. McCance, Michael Maresh and David A. Sacks (2018): *Metabolic Abnormalities in Gestational Diabetes. A Practical Manual of Diabetes in Pregnancy*, Second Edition; © 2018 John Wiley & Sons Ltd. Published by John Wiley & Sons Ltd.
12. Eman M Alfadhli (2021): Maternal obesity influences birth weight more than gestational diabetes. *BMC Pregnancy and Childbirth* 21:111 <https://doi.org/10.1186/s12884-021-03571-5>.
13. Denison FC, Aedla NR, Keag O, Hor K, Reynolds RM, Milne A, Diamond A (2019): Care of Women with Obesity in Pregnancy. *BJOG An Int J Obstet Gynaecol*; 126(3): e62 –106.
14. Mahmoud Fayez Mohamed Fathi, Taher Mohammed Moustafa, and Ibrahim Ramadan Alsawy Rady (2020): The role of umbilical cord thickness and glycated hemoglobin (hba1c) levels for prediction of fetal macrosomia in patients with gestational diabetes mellitus. *Al-Azhar Med. J. (Surgery)* 1741 - 1752 DOI: 10.12816/amj.120632 https://amj.journals.ekb.eg/article_120632.html.
15. Binbir B, Yeniel AO, Ergenoglu AM, Kazandi M, Akercan F (2012): The role of umbilical cord thickness and HbA1c levels for the prediction of fetal macrosomia in patients with gestational diabetes mellitus. *Arch Gynecol Obstet* 285: 635–639. Link: <http://tinyurl.com/y23nagoj>.
16. Beta J, Khan N, Khalil A, Fiolna M, Ramadan G, Akolekar R (2019): Maternal and neonatal complications of fetal macrosomia: systematic review and meta-analysis. *Ultrasound Obstet Gynecol* ;54:308–18. (Systematic Review and Meta-Analysis).
17. Ijäs H, Koivunen S, Raudaskoski T, Kajantie E, Gissler M, Väärasmäki M (2019): Independent and concomitant associations of gestational diabetes and maternal obesity to perinatal outcome: A register-based study. *PLoS One*.14(8): e0221549.
18. Al-Khalifah A Al-Subaihin, Al-Kharfi S, Khalid M (2012): Neonatal Short-Term Outcomes of Gestational Diabetes Mellitus in Saudi Mothers: A Retrospective Cohort Study. *J Clin Neonatol*.doi:104103/2249-4847.92241.
19. Hildén K, Hanson U, Persson M, Magnuson A, Simmons D, Fadl H (2019): Gestational diabetes and

- adiposity are independent risk factors for perinatal outcomes: a population-based cohort study in Sweden. *Diabet Med*; 36(2):151–7.
20. de Silva A, Auguosta R, Daniela S, de Oliveira S (2017): Neonatal outcomes according to different therapies for gestational diabetes mellitus. <https://doi.org/10.1016/j.jpeds>.
21. Paweł J Stanirowski , Agata M, Michał L, Dorota Bomba-Opoń , Mirosław W (2021) : Ultrasound evaluation of the fetal fat tissue, heart, liver and umbilical cord measurements in pregnancies complicated by gestational and type 1 diabetes mellitus: potential application in the fetal birth-weight estimation and prediction of the fetal macrosomia. Stanirowski et al. *Diabetol Metab Syndr* 13:22 <https://doi.org/10.1186/s13098-021-00634>.
22. Gracia-Flores J, Jan~ez M, Gonzalez MC, Martinez N, Espada M (2011): Fetal myocardial morphological and functional changes associated with wellcontrolled gestational diabetes. *European Journal of Obstetrics, Gynecology and Reproductive Biology* 154: 24-26. Link: <http://tinyurl.com/y5xxc8s>.
23. Liliana F, Miguel Saraiva Ana Amado, Sílvia Paredes (2021): Third trimester HbA1c and the association with large-for-gestational-age neonates in women with gestational diabetes. DOI: 10.20945/2359-3997000000366.
24. useful, W, Chong S, Mediratta S, Jalaludin B (2017): Measuring glycated haemoglobin in women with gestational diabetes mellitus: How useful is it? *Aust N Z J Obstet Gynaecol*.57(3): 260-5.
25. Szmyd B, Biedrzycka M, Karuga F.F, Rogut M, Strzelecka I, Respondek-Liberska M (2021): Interventricular Septal Thickness as a Diagnostic Marker of Fetal Macrosomia. *J. Clin. Med.* 10, 949. <https://doi.org/10.3390/jcm10050949>.