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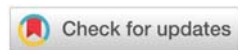
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Research Article

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

Abstract

Objective: To assess and evaluate the role of measuring umbilical cord thickness, interventricular septum thickness and HbA1c level in predictability of fetal macrosomia development in cases having gestational DM

Methods: A prospective case-control research study that recruited 80 pregnant study subjects. They were categorized into two research groups: 40 pregnant women as cases research group having gestational DM and 40 non-diabetic pregnant Study subjects as control research group. Sonographic examination was conducted in which the sonographic cross sectional area of umbilical cord. Umbilical arteries and the umbilical vein measured from a free loop of the umbilical cord, implementing the software of the sonographic machine. The cross-sectional area of Wharton's jelly have been obtained by subtracting the cross sectional area of the vessels from that of the umbilical cord and the interventricular septum thickness was measured. HbA1c level have been assayed for diabetic cases recruited.

Results: Umbilical cord diameter was raised in study subjects with gestational diabetes more than the control group (3.03 ± 1.26) cm. Increase in interventricular septal thickness (0.85 ± 0.51) cm have been correlated and linked with fetal macrosomia in diabetic cases. HbA1c levels in patients with GDM (7.0 ± 1.2) % showed more observed fetal macrosomia cases.

Conclusion: The research study revealed and displayed the sonographic value of measuring umbilical cord thickness, interventricular septum thickness and HbA1c as a prediction tool for fetal macrosomia in cases with gestational DM.

Introduction

Glucose intolerance newly diagnosed during pregnancy despite any degree of severity is clinically defined as gestational DM. Maternal hyperglycemia Cause subsequently fetal hyperglycemia, that triggers pancreatic islet cells in an abnormal manner causing pathological development of fetal hyperinsulinemia . That pathophysiological triggering factor causes abnormally excessive fat tissue deposition and increases total fetal size that is proven by various researchers to be the cornerstone cause of unfavourable perinatal clinical outcomes due to fetal growth acceleration and macrosomia [1-3].

Antenatal detection and predictability of fetal macrosomia is considered one of the major challenging clinical scienarios in every day obstetric practice .Sonographic measurements

such as AC,EFW are extensively researched and are popularly used among obstetricians and fetal medicine specialists .However more sensitive and clinically presenting parameters should be implemented to aid in early detection ,prediction and diagnosis of those case scienarios to hinder or prevent the full developmental pathway of fetal macrosomia with its subsequent maternal and fetal clinical issues such as post-partum hemorrhage and shoulder dystocia .HbA1c a commonly used marker to determine and reflect the glucose levels over a period of 3 months and is used as tool to reveal the risk of anomaly development in diabetic cases within the first trimester .However research efforts should in addition involve other sonographic markers requiring the expertise of fetal echocardiographic specialists such as interventricular septal thickness that is used to determine the functional and

developmental prognosis of the fetal cardiac muscle among other cardiac indices and parameters [4-6].

Sonographic evaluation and assessment of umbilical cord is frequently restricted, To Doppler blood flow studies and counting the number of vessels. However its crucial role in fetal development and physiology denotes that its thickness and components should be thoroughly investigated as a possible sonographic tool reflecting the fetal growth development in integration to biochemical markers such as HbA1c particularly in diabetic gestations that are at high risk of developing fetuses with macrosomic issues [7-9].

Methodology

A prospective case-control research study was carried out at Ain Shams University maternity hospital between April 2015 and October 2015 on 80 pregnant study subjects. Categorized into two research groups: 40 pregnant women as case research group with gestational DM and 40 non-diabetic pregnant women as Research control group after being approved by the local hospital ethical and research committee. A verbal consent have been obtained from each study subject. Inclusive research criteria involved singleton gestation, gestational age above 27 gestational weeks, intact membranes, normal umbilical morphology (two arteries and one vein) and diagnosis of gestational DM Exclusive research criteria was the presence of congenital anomalies, Multifetal gestation, maternal chronic medical diseases (e.g hypertension, renal disease, cardiac and pulmonary disease, etc.) and cases with diagnosis of oligohydramnios, preeclampsia and intrauterine growth retardation.

Sonographic examination was conducted in all study subjects at 36-37 gestational weeks with Voluson E6 equipped with a 3.5 Hz transabdominal probe. Involving the following parameters and indices fetal biometry (biparietal diameter, abdominal circumference, femur length) and estimated fetal weight calculated according to Hadlock's formula by the sonographic machine software. The sonographic cross sectional area of umbilical cord, the umbilical arteries and the umbilical vein were measured in a free loop of the umbilical cord using the software of the ultrasound device. The cross-sectional area of Wharton's jelly was computed by subtracting the cross-sectional area of the vessels from that of the umbilical cord. The interventricular septum thickness was measured. HbA1c levels was measured for diabetic cases. Cases have been followed up till time of delivery. The neonates were weighed and fetal macrosomia was diagnosed if fetal weight is 4 kg or more.

Results

This study was conducted on 80 pregnant women with their mean age was (31±8) years, mean parity (1-3), mean previous abortions from (0-2) gestational age by LMP ranges from (27 to 39 wks). 17 among the 40 diabetic patients had macrosomic neonates (higher or equal to 4 kg) (42.5%) while there was no macrosomic neonates for the non-diabetic pregnant women (0%) (Figure 2). Large umbilical cord diameter was measured, among the diabetic group with mean (2.77±1.19) cm, among the control group (2.06±0.77) cm with 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. Umbilical artery measures were (0.67±0.47) cm among diabetic group and (0.51 ± 0.16) among non-diabetic group, with specificity, positive and negative predictive values of sonographic. Large umbilical artery diameter in prediction of fetal macrosomia were 33.3%, 25%, 87.5% respectively. Umbilical vein diameter varied from (0.83 ± 0.41) cm among diabetic women and (0.53 ± 0.2) cm among non-diabetic women, with specificity, positive and negative predictive values in the prediction of fetal macrosomia (52.4, 34.8%, 97.1%) respectively. Large Wharton's Jelly area was measured in diabetic group (65.03±17.56) mm² and (44.6±8.99) mm² in non-diabetic group with specificity, positive and negative predictive values of fetal macrosomia (95.2%, 80%, 92.3% respectively). Mean IVS (0.86±0.33) among macrosomic fetuses and (0.65±0.24) among non macrosomic fetuses. IVS has sensitivity, specificity, positive predictive value and negative predictive value 64.7%, 73%, 39.3%, 88.5% respectively. HbA1c is more sensitive (82.4%) than umbilical cord diameter (64.7%) (Tables 1,2 and Figures 1-3).

Table 1: Reveals and displays that there was statistically significant difference between both research groups as regards umbilical cord, artery, vein, wharton jelly area, IVS diameter, HbA1c, birth weight, macrosomic babies (p values = 0.002, 0.050, <0.001, <0.001, <0.001, <0.001, <0.001, <0.001, consecutively).

Variable	Gestational DM group (n=40)	Control group (n=40)	T	df	P-value
Umbilical cord diameter (cm)	2.77 ± 1.19	2.06 ± 0.77	3.186	66.931	0.002¶
Umbilical artery diameter (cm)	0.67 ± 0.47	0.51 ± 0.16	2.011	48.008	0.050¶
Umbilical vein diameter (cm)	0.83 ± 0.41	0.53 ± 0.20	4.114	78	<0.001¶
Wharton Jelly area (mm ²)	65.03 ± 17.56	44.60 ± 8.99	6.548	58.116	<0.001¶
IVS diameter (cm)	0.85 ± 0.29	0.53 ± 0.12	6.557	52.227	<0.001¶
HbA1c (%)	6.6 ± 1.0	5.2 ± 0.5	7.358	58.596	<0.001¶
Birth weight (kg)	3.76 ± 0.61	3.20 ± 0.26	5.340	52.591	<0.001¶
Macrosomic babies	17 (42.5%)	0 (0%)	-	-	<0.001§

Data are mean ± SD or number (%).

t, t-statistic; df, degree of freedom.

¶ Unpaired Student t test.

§ Fisher's exact test.

Table 2: Reveals and displays the outcomes in cases with and without macrosomia revealing statistical significant difference as regards Wharton jelly area, HbA1c, birth weight (p values <0.001).

Variable	Macrosomia (n=17)	No macrosomia (n=63)	t	df	P-value ¶
Umbilical cord diameter (cm)	3.03 ± 1.26	2.25 ± 0.94	2.797	78	0.006
Umbilical artery diameter (cm)	0.75 ± 0.56	0.55 ± 0.27	1.470	17.969	0.159
Umbilical vein diameter (cm)	0.90 ± 0.55	0.62 ± 0.26	2.958	78	0.004
Wharton jelly area (mm ²)	76.24 ± 14.62	49.03 ± 12.82	7.534	78	<0.001
IVS diameter (cm)	0.86 ± 0.33	0.65 ± 0.24	2.401	20.609	0.026
HbA1c (%)	7.0 ± 1.2	5.6 ± 0.8	5.351	78	<0.001
Birth weight (kg)	4.22 ± 0.62	3.28 ± 0.29	9.047	78	<0.001

Data are mean ± SD.

t, t-statistic; df, degree of freedom.

¶ Unpaired Student t test.

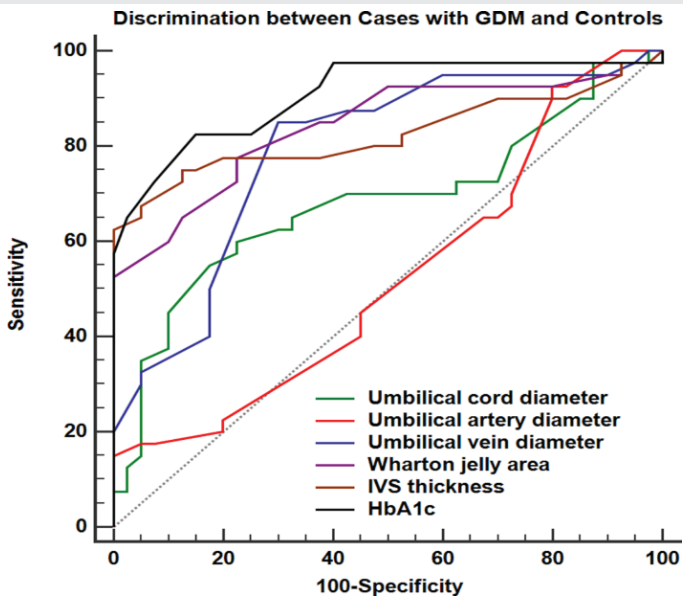


Figure 1: Receiver-operating characteristic (ROC) curves for discrimination between patients with GDM and normal controls using various sonographic measures or HbA1c level.

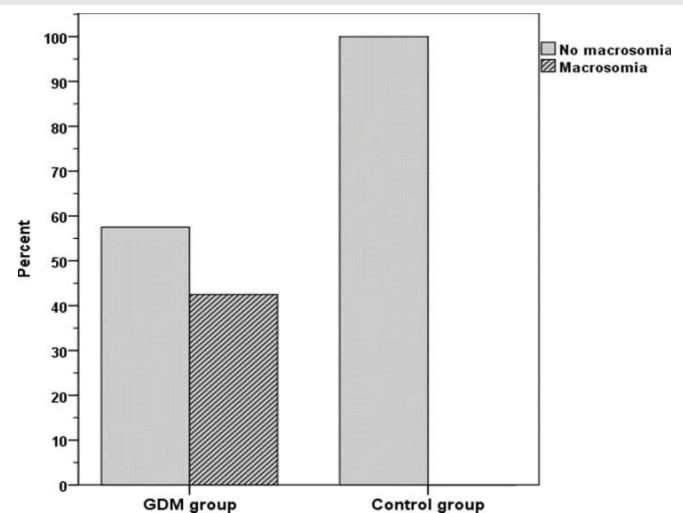


Figure 2: Incidence of fetal macrosomia in patients with GDM or normal controls.

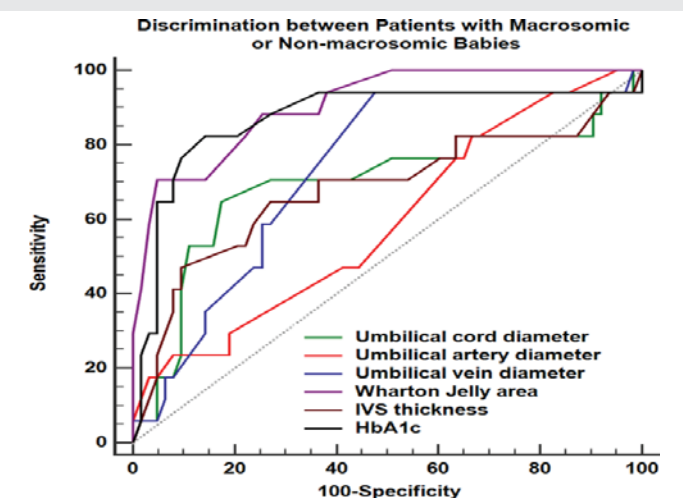


Figure 3: Receiver-operating characteristic (ROC) curves for discrimination between patients with or without fetal macrosomia using various sonographic measures or HbA1c level.

Discussion

Fetal macrosomia exists in around 20–30% of gestational DM pregnancies. Delivery of a macrosomic fetus is correlated various unfavourable clinical issues as regards fetal clinical wellbeing e.g shoulder dystocia causing brachial plexus injuries with raised rates of morbidity and mortality of macrosomic fetuses in comparison to normal weight fetuses. Operative vaginal delivery interventions required in some case scenarios could result in post-partum haemorrhage, third and fourth degree vaginal lacerations [10–12].

In the current research study conducted, the recruited 80 gestations have been assessed and evaluated that there was statistically significant difference between both research groups (normal cases versus Gestational DM) as regards umbilical cord, artery, vein, wharton jelly area, IVS diameter, HbA1c, birth weight, macrosomic babies (p values = 0.002, 0.050, <0.001, <0.001, <0.001, <0.001, <0.001, <0.001, consecutively). Furthermore the current research study revealed that the outcomes in cases with and without macrosomia had statistical significant difference as regards Wharton jelly area, HbA1c birth weight (p values <0.001).

A prior research study performed prospectively investigated the correlation and linkage between umbilical cord thickness (diameter or area) and HbA1c in the predictive value for development of macrosomic fetus, 103 gestations in the study group and 57 gestations in the control group. Percentage of fetal macrosomia observed was 14% in the study research group and 10% in the control research group. The relative risk statistical estimation of fetal macrosomia in the study research group was 1.5 times more than in the control research group. The preliminary assessment and examination at 27–28 gestational weeks, the mean surface area of the umbilical cord was 214 mm² for the study research group and 210 mm² for the control research group. Whilst comparison between macrosomic fetuses with normal weight fetuses in both research groups, have displayed that the umbilical cord and Wharton’s jelly surface area indices have been statistically significantly variable by comparing between study group and control group [13–15].

Another issue revealed by investigators in a prior similar research study to the current research is that by comparing between macrosomic fetuses with non macrosomic fetuses have shown that umbilical artery area, vein and diameter indices are not different statistically those findings show great contradiction to the current research study findings [1,4,7].

Another research group of investigators have revealed and displayed that HbA1c serum levels were statistically significantly greater in macrosomic fetuses in comparison to non macrosomic fetuses furthermore the investigators have shown that HbA1c indices are more statistically sensitive (82.4%) than umbilical cord diameter indices (64.7%). There was strong correlation between HbA1c serum levels and development of fetal macrosomia [3,8,9].

Interestingly a prior research study performed observing fetal myocardial muscle changes have revealed and displayed

that fetuses of diabetic gestations are at risk of developing hypertrophic myocardial changes due to fetal hyperglycemia and hyper insulinism regardless of glycemic control. These apparently temporary changes chiefly impact the fetal cardiac interventricular septum furthermore another research group revealed and displayed that IVS thickness is the most crucial sonographic measurement mirroring tightness of glycemic control and its influence on the fetal cardiac development [10,11].

Conclusions and recommendations

The current research denotes that there is great value to integrate the IVS thickness, glycosylated HbA1c and umbilical cord thickness indices to predict possible pathological macrosomia development in gestational DM. However future research studies are recommended to be conducted in multicentric fashion with larger sample sizes to determine the normal and abnormal ranges of values according to racial and ethnic differences that could affect those parameters. Future guidelines could be innovated by extensive research to determine the possible effective algorithm to detect those cases before full development and to enhance the level of care offered to cases with gestational DM.

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