Journal of Gynecological Research and Obstetrics

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


Introduction

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy [1]. Maternal hyperglycemia leads to fetal hyperglycemia, which stimulates pancreatic islet cells and consequently fetal hyperinsulinemia. This state results in excessive fat tissue and total body size and the major reason for poor perinatal outcome is accelerated fetal growth and macrosomia [2,3]. Fetal macrosomia complicates 20–30% of pregnancies with gestational diabetes mellitus (GDM) [4]. The presence of hyperglycemia influences biochemical transformation processes in the fetus [5]. The birth of a macrosomic fetus has been associated with adverse outcomes for both mother and fetus. Shoulder dystocia during delivery and related permanent brachial plexus injury may be seen. Both neonatal mortality and morbidity are higher in macrosomic fetuses compared with normal weight fetuses [6]. Maternal complications such as postpartum hemorrhage, infections, as well as third or fourth-degree vaginal lacerations may occur because of operative delivery. Today, cesarean sections performed for fetal macrosomia are not rare at all. Birth weight of the fetus is an important factor in determining the mode of delivery, but pelvic assessment should not be ignored [7]. Ultrasound-based birth weight prediction is still insufficient. Investigators have attempted to improve ultrasound-based prediction of fetal macrosomia by various methods, such as the assessment of fat deposition at different locations. None of these methods have gained wide popularity because of the inability to accurately estimate fetal weight against conventional biometric formulas [8,9]. The umbilical cord is responsible for materno-fetal blood flow. Normally, it is composed of two arteries permeated with venous blood and a vein that transports arterial blood, cushioned by a special type of Wharton’s jelly computed by subtracting the cross sectional area of the vessels from that of the umbilical cord and the interventricular septum thickness was measured. HbA1c level was measured for diabetic patients.

Results: Umbilical cord diameter increased in patients with gestational diabetes more than the control group (3.03±1.26) cm. Increase in interventricular septal thickness (0.85±51) cm was also associated with fetal macrosomia in diabetic patients. HbA1c levels in patients with GDM (7.0±1.2) % showed increased cases of fetal macrosomia.

Conclusion: The results of the study showed the usefulness of sonographic umbilical cord thickness, interventricular septum thickness and HbA1c in prediction of fetal macrosomia in Patients with gestational diabetes mellitus.

Abstract

Objective: To evaluate the role of measuring umbilical cord thickness, interventricular septum thickness and HbA1c level in prediction of fetal macrosomia in patients with gestational diabetes mellitus.

Methods: This prospective case-control study included 80 pregnant women. They were divided into two groups: 40 pregnant women as case group with gestational diabetes mellitus and 40 non-diabetic pregnant women as control group. Ultrasound examination was performed where 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 machine. 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 and the interventricular septum thickness was measured. HbA1c level was measured for diabetic patients.

Results: Umbilical cord diameter increased in patients with gestational diabetes more than the control group (3.03±1.26) cm. Increase in interventricular septal thickness (0.85±51) cm was also associated with fetal macrosomia in diabetic patients. HbA1c levels in patients with GDM (7.0±1.2) % showed increased cases of fetal macrosomia.

Conclusion: The results of the study showed the usefulness of sonographic umbilical cord thickness, interventricular septum thickness and HbA1c in prediction of fetal macrosomia in Patients with gestational diabetes mellitus.

Keywords: Umbilical cord thickness; Interventricular septum thickness (IVS); Gestational Diabetes Mellitus (GDM)
of mucus connective tissue known as Wharton’s jelly and by remnants of the allantois [10]. Ultrasonographic examination of umbilical cord is usually limited to Doppler blood flow and assessment of the number of vessels. Also, the effect of umbilical cord morphology on the fetus and neonates has not been adequately shown [11–13]. Studies that have assessed umbilical cord components to predict fetal weight have shown that there is a correlation between umbilical cord diameter, area and fetal biometric parameters [14]. In addition, some observers have suggested that combination of these two methods should give more reliable results for estimating macrosomic fetuses.

Materials and Methods

This prospective case-control study was carried out at Ain shams University maternity hospital between April 2015 and October 2015 on 80 pregnant women.

They were divided into two groups:

40 pregnant women as case group with gestational diabetes mellitus and 40 non-diabetic pregnant women as control group after being approved by the local hospital ethics and research committee.

A verbal consent was taken from each patient.

Inclusion criteria were singleton gestation, gestational age over 27 weeks, intact membranes, normal umbilical morphology (two arteries and one vein) and Diagnosis of gestational diabetes.

Exclusion criteria were congenital anomalies, Multifetal pregnancy, maternal chronic diseases (hypertension, renal disease, cardiac and pulmonary disease, etc.) and Patients with a diagnosis such as oligohydramnios, preeclampsia and intrauterine growth retardation.

Ultrasound examination was performed at 36–37 weeks of gestation with Voluson E6 equipped with a 3.5 Hz transabdominal probe.

Ultrasound examination included fetal biometry (biparietal diameter, abdominal circumference, femur length) and estimated fetal weight were calculated automatically according to hadlock’s formula additionally.

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 patients.

These patients were followed up till delivery.

The neonates were weighed and fetal macrosomia was diagnosed if fetal weight is 4 kg or more.

Sample size justification

A sample size of 40 diabetic and 40 non-diabetic pregnant women is enough to predict if there is a correlation between umbilical cord thicknesses, inter ventricular septum thickness, the HbA1c level and fetal macrosomia.

Statistical analysis

Statistical analysis will be performed using Microsoft Excel 2007 and Statistical Package for Social Science (SPSS®) version 17.0. Data will be presented as range mean and standard deviation (for parametric variables), range, median and quartile range (for non-parametric variables) and number and percentage (for categorical variables). Differences between variables of two groups will be analyzed by using student’s T-Test (for quantitative parametric measures). Mann-Whitney's test V-test (for quantitative non-parametric measures). Person’s correlation coefficient (for parametric values) and Spearmann’s correlation coefficient (for rank variables). A receiver-operating characteristic (ROC) curve “cutoff” between two variables will be estimated in terms of sensitivity, specificity, positive and negative predictive values and accuracy as well as likelihood ratios.

Statistical methods

Data were analyzed using IBM® SPSS® Statistics version 23 (IBM® Corp., Armonk, NY, USA). Normality of numerical data distribution was examined with the Shapiro–Wilk. Continuous numerical variables were presented as mean ± SD and inter–group differences were compared using the unpaired Student t test. Discrete numerical variables were presented as median and interquartile range and between–group differences were compared using the Mann–Whitney U test. Categorical variables were presented as number (%) and inter–group differences were compared using Fisher’s exact test. Receiver–operating characteristic (ROC) curve analysis was used to examine the value of umbilical cord dimensions, IVS thickness, or HbA1c level for discrimination between cases with gestational DM and normal controls, and for discrimination between women with or without macrosomic babies. The DeLong method was used to compare the area under different ROC curves. A two–sided p-value <0.05 was considered statistically significant.

Results

This study was conducted on 88 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 macromesonic neonates (higher or equal to 4 kg) (42.5%) while there was no macromesonic neonates for the non-diabetic pregnant women (0%) (Figures 1–3). 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).

**Discussion**

Fetal macrosomia affects 20–30% of gestational diabetes pregnancies. Delivery of a macrosomic fetus is correlated to unfavorable clinical outcomes at maternal and fetal levels. Brachial plexus injuries and shoulder dystocia issues could be experienced in gestations affected by fetal macrosomia particularly when causative gestational DM exists. Macrosomic fetuses have higher incidence of morbidity and mortality in

---

**Table 1:** Outcome measures in patients with GDM and normal controls.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Gestational DM group (n=40)</th>
<th>Control group (n=40)</th>
<th>t</th>
<th>df</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Umbilical cord diameter (cm)</td>
<td>2.77 ± 1.19</td>
<td>2.06 ± 0.77</td>
<td>3.186</td>
<td>66.931</td>
<td>0.002*</td>
</tr>
<tr>
<td>Umbilical artery diameter (cm)</td>
<td>0.67 ± 0.47</td>
<td>0.51 ± 0.16</td>
<td>2.011</td>
<td>48.008</td>
<td>0.050*</td>
</tr>
<tr>
<td>Umbilical vein diameter (cm)</td>
<td>0.83 ± 0.41</td>
<td>0.53 ± 0.20</td>
<td>4.114</td>
<td>&lt;78</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Wharton Jelly area (mm²)</td>
<td>65.03 ± 17.56</td>
<td>44.60 ± 8.99</td>
<td>6.548</td>
<td>58.116</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>IVS thickness</td>
<td>0.85 ± 0.29</td>
<td>0.53 ± 0.12</td>
<td>6.557</td>
<td>52.227</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>6.6 ± 1.0</td>
<td>5.2 ± 0.5</td>
<td>7.358</td>
<td>58.596</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Birth weight (kg)</td>
<td>3.76 ± 0.61</td>
<td>3.20 ± 0.26</td>
<td>5.340</td>
<td>52.591</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Macrosomic babies</td>
<td>17 (42.5%)</td>
<td>0 (0%)</td>
<td>-</td>
<td>-</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

**Table 2:** Outcome measures in patients with or without fetal macrosomia.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Macrosomia (n=17)</th>
<th>No macrosomia (n=63)</th>
<th>t</th>
<th>df</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Umbilical cord diameter (cm)</td>
<td>3.03 ± 1.26</td>
<td>2.25 ± 0.94</td>
<td>2.797</td>
<td>78</td>
<td>0.066</td>
</tr>
<tr>
<td>Umbilical artery diameter (cm)</td>
<td>0.75 ± 0.56</td>
<td>0.55 ± 0.27</td>
<td>1.470</td>
<td>17.969</td>
<td>0.159</td>
</tr>
<tr>
<td>Umbilical vein diameter (cm)</td>
<td>0.90 ± 0.55</td>
<td>0.62 ± 0.26</td>
<td>2.958</td>
<td>78</td>
<td>0.026</td>
</tr>
<tr>
<td>Wharton jelly area (mm²)</td>
<td>76.24 ± 14.62</td>
<td>49.03 ± 12.82</td>
<td>7.534</td>
<td>78</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>IVS diameter (cm)</td>
<td>0.86 ± 0.33</td>
<td>0.65 ± 0.24</td>
<td>2.401</td>
<td>20.609</td>
<td>0.026</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>7.0 ± 1.2</td>
<td>5.6 ± 0.8</td>
<td>5.351</td>
<td>78</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Birth weight (kg)</td>
<td>4.22 ± 0.62</td>
<td>3.28 ± 0.29</td>
<td>9.047</td>
<td>78</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

Data are mean ± SD or number (%). t, t-statistic; df, degree of freedom. * Unpaired Student t test. § Fisher’s exact test.
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. In the current research study conducted, the recruited 80 gestations have been assessed and evaluated by abdominal sonography and expected fetal weight calculated by obtained fetal parameters was tabulated in addition to neonatal weight. Forty gestations were in diabetic research group and 40 subjects were in research control group (i.e. non-diabetic). 17 Within the 40 diabetic gestations (42.5%) had macromesonic neonates (neonatal weight greater or equal to 4 kg) whereas there was no macromesonic neonates in the control research group. The measured umbilical cord diameter, within the gestational DM research group has specificity, positive and negative predictive values in predictability of birth weight > 4000 g of 82.5%, 50%, 89.7% consecutively. On the other hand large umbilical artery diameter, showed specificity, positive and negative predictive for prediction of macromesonic fetus of 33.3%, 25%, 87.5%, and for the umbilical vein diameter (52.4%, 34.8%, 97.1%) consecutively while Large Wharton’s Jelly area showed specificity, positive and negative predictive values for macromesonic fetus of 95.2%, 80%, 92.3%. 

A prior research study conducted in a prospective manner investigated the correlation between umbilical cord thickness (diameter or area) and HbA1c in the predictability value for macromesonic fetus, 103 gestations in the research study group and 57 gestations in the research control group. Percentage of fetal macromesia observed was 14% in the study research group and 10% in the control research group. The calculated relative risk of fetal macromesia in the study research group was 1.5 times greater than in the control research group. At the initial 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 macromesonic 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 different (in the study research group compared to the control research group). On the other hand comparison between macromesonic fetuses with non macromesonic fetuses in both research groups, revealed that umbilical artery area, vein and diameter indices are not different statistically. At the subsequent evaluation and assessment at 36–37 gestation the umbilical cord surface area, Wharton’s Jelly surface area, umbilical cord diameter in addition to umbilical artery and vein surface area indices were found to be statistically significant for both research groups when comparing between macromesonic fetuses and non-macromesonic fetuses at the subsequent assessment and evaluation. HbA1c levels were not statistically significant when macromesonic fetuses have been compared with non-macromesonic fetuses. There was a highly statistically significant correlation between umbilical cord area–diameter indices and expected fetal weight in the research diabetic group at 36–37 gestational weeks. There was a strong positive correlation between umbilical cord thickness indices, umbilical artery diameter parameters, umbilical vein diameter values, Wharton’s Jelly surface area and fetal macromesia. The current research study is contradictory from Birol et al. research study findings in which HbA1c serum levels were statistically significantly greater in macromesonic fetuses in comparison to non macromesonic fetuses. In that research study, HbA1c indices was revealed to be more sensitive (82.4%) than umbilical cord diameter indices (64.7%). There was strong correlation between HbA1c serum levels and development of fetal macromesia. Gracia–Flores et al. research group concluded that fetuses of diabetic gestations are at risk of developing hypertrophic myocardial changes due to fetal hyperglycemia and hyperinsulinism in spite of good capillary glycemic control. These apparently temporary changes chiefly impact the fetal cardiac interventricular septum. In the current study mean IVS value was 0.86±0.33 within fetuses with macromesia and 0.65±0.24 within non macromesonic fetuses. IVS had a calculated sensitivity, specificity, positive predictive value and negative predictive value 64.7%, 73%, 39.3%, 88.5% consecutively. Our results displayed that prenatal interventricular septal thickness is considered a reliable parameter in predictability of macromesonic fetus pathological development with cut off value > 0.71. This is in agreement with Gracia–Flores et al research group. As they concluded that IVS thickness is the most sonographically important parameter to reveal the impact of glycemic control on the fetal heart development, the observation of a hypertrophic IVS requires evaluation of systolic and diastolic functional flow and parameters. Nonexistence of functional abnormalities in fetuses with hypertrophic IVS could not exclude fetal risk, since it could be correlated with greater perinatal mortality due to pathological development of diabetic fetopathy, and may point to a hidden and poor maternal glycemic control.

References


