Prediction of Fetal Macrosomia in Patients with Gestational Diabetes Mellitus through measuring the umbilical cord thickness and glycated hemoglobin (HbA1c) levels

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Prediction of Fetal Macrosomia in Patients with Gestational Diabetes Mellitus Through Measuring the Umbilical Cord Thickness and Glycated Hemoglobin Levels

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Abstract

Background: Diabetes mellitus, one of the most prevalent medical issues, has emerged as a serious concern to pregnant women. It is linked to a number of maternal and fetal issues, including delivery traumas, perinatal death, shoulder dystocia, macrosomia, and operating room interference. Early prediction of fatal complications will improve outcome and reduce perinatal mortality.

Aim and objectives: To determine whether glycated hemoglobin and umbilical cord thickness in pregnant women with diabetes can accurately predict fetus' macrosomia.

Patients and methods: A 6-month prospective observational research study was performed on 100 women with gestational diabetes who were 28–29-week pregnant at Al-Hussein University Hospital. Patients had a thorough medical history review, an ultrasound assessment, and an ultrasonography examination.

Result: Glycated hemoglobin and Umbilical Cord Thickness (UCT) at 27–28 weeks and 36–37 weeks of gestation were significantly different across the three groups that were examined.

Conclusion: Severe obstetric problems, including shoulder dystocia and postpartum hemorrhage, are caused by macrosomia. There are times when it is difficult to foresee shoulder dystocia. The group most at risk for these issues may be found, however, using macrosomia prediction. There have been documented studies using sonographic measurement for predicting fetal macrosomia. Fetal macrosomia is well predicted by the thickness of the umbilical cord and the fetal fat layer.

Keywords: Diabetes, Glycated hemoglobin, Macrosomia

1. Introduction

The umbilical cord controls the flow of blood between the mother and the fetus. It typically consists of two arteries that carry venous blood and a vein that carries arterial blood, both cushioned by remains of the allantoides and a unique kind of mucous connective tissue called Wharton’s jelly.1

Macrosomia is defined by the American College of Obstetricians and Gynecologists as a birth weight that is more than 4000 g regardless of weeks of gestation, or that is greater than the 90th percentile for gestational age after adjusting for neonatal sex and ethnicity.2 Predictions of the risk of macrosomia during pregnancy have been made by medical experts using glycated hemoglobin (HbA1c) values and estimated fetus weight obtained from ultrasounds.3

Gestational diabetes mellitus (GDM) is associated with several unfavorable pregnancy outcomes, including macrosomia and cesarean section...
delivery. Macrosomia is a well-known sign of maternal diabetes in fetus, which is highly connected with preterm, respiratory distress syndrome, birth trauma, fetal mortality, and bad mother outcome. Overall, 2–6% of pregnant women have GDM, which increases the risk of serious negative perinatal results such as macrosomia and birth injuries. Macrosomia fetal birth has been linked to unfavorable outcomes for both mother and baby. It is possible to have shoulder dystocia during birth and a resulting persistent brachial plexus damage. When compared with babies of normal weight, macrosomic fetuses have greater rates of newborn death and morbidity. A greater incidence of surgical births, postpartum hemorrhages, birth injuries in vaginal delivery, and newborn hypoglycemia are all linked to fetal macrosomia. Only 40% of mothers who give birth to macrosomic kids had known maternal risk factors recognized. Additionally, macrosomia raises the chance of developing some malignancies. The macrosomia morbidity ranges from 7 to 10%. Therefore, monitoring abnormal birth weight and associated risk variables has substantial consequences for public health. According to studies, obesity and metabolic diseases are more likely to occur in newborns who are macrosomic.

The care of people with type 2 diabetes includes measures to reduce hyperglycemia, which is a significant aspect of diabetes as a serious public health problem. The HbA1c test determines hyperglycemia by determining the median blood glucose value over the prior 60–120 days. It is advised for diabetic individuals to aim for a HbA1c of 6.5% (48 mmol/mol). Overall, 3.5–5.5% is the range for a nondiabetic normal HbA1c result. A healthy range for diabetics is between 6.5 and 7%. The amount of this HbA1c in those with poorly managed diabetes is much greater than in healthy individuals.

Studies have revealed that HbA1c values and umbilical cord components may be used to predict macrosomia with greater accuracy. Several studies have shown that HbA1c values can be employed to predict macrosomia, nevertheless. The purpose of this research was to evaluate how well HbA1c and umbilical cord thickness predict fetal macrosomia in diabetic pregnant women.

2. Patients and methods

2.1. Ethical considerations

The study protocol was submitted for approval by the Institutional Review Board, Al-Azhar University. Each individual who participated in the research provided informed verbal permission. At every stage of the research, confidentiality, and personal privacy were protected.

In this prospective, observational study conducted over a 6-month period at Al-Hussein University Hospital, 100 pregnant women with gestational diabetes, 28–29 weeks of gestation, received routine prenatal treatment as inpatients or at outpatient clinics. Women who were between 28- and 29-week pregnant, experienced gestational diabetes, and had a singleton pregnancy with normal umbilical morphology met the inclusion criteria. All patients with age over of 40 years, repeated fetal pregnancies, gestational diabetes, maternal chronic illness, multiparity, and drug usage during pregnancy were excluded.

The patients received a comprehensive medical history, a general evaluation, an abdominal examination, and a local clinical diagnosis. The gestational age was established using Negele's rule and confirmed using ultrasonography. Ultrasound with a convex transabdominal probe was used to evaluate umbilical cord thickness beginning at 28–29 weeks of gestation and then every 2 weeks until 36–37 weeks of gestation (mm²).

The fetal anthropometric parameters including biparietal diameter, femur length, and estimated fetal weight, which were automatically computed using Hadlock’s algorithm.

If a pregnant woman had a fasting plasma glucose level of 126 mg/dl (7.0 mmol/l), a random plasma glucose level of 200 mg/dl (11.0 mmol/l), and a HbA1c level of 6.5%, she was diagnosed with gestational diabetes. When the estimated fetal weight was greater than the 90th percentile for gestational age or over 4000 g, macrosomia was considered.

Monitoring of patients during delivery was done, including birth weight, birth method, and fetus sex. Population characteristics such as age, BMI, parity, mode of delivery, ultrasound-estimated birth weight, birth weight, HbA1c, and umbilical cord thickness were noted. The accuracy of the umbilical cord thickness and HbA1c value in predicting fetal macrosomia served as the primary indicators of the study's effectiveness.

Using the SPSS program, data input and analysis were performed (SPSS 20.0 Version, Chicago, USA). We computed the mean, proportion, and percentage. χ² test was used to see if there was a correlation.

3. Results

There was a statistically significant difference in maternal BMI and gravidity between the groups (Table 1).
There was a significant difference between the groups regarding birth weight (Table 2).

Regarding biparietal diameter, belly circumference, and femur length, there was no significant difference between the two study groups (Table 3).

There was no statistically significant difference between the groups in term of mode of delivery (Table 4).

There was a significant difference between the three studied groups regarding HbA1c and Umbilical Cord Thickness (UCT) at 27–28 weeks and 36–37 weeks of pregnancy (Table 5).

Within the macrosomia group, there was a substantial positive connection between birth weight and UCT (Tables 6 and 7).

UCT achieved significance for predicting fetal macrosomia with sensitivity of 91.8%, specificity of 93.6%, positive predictive value of 89%, and negative predictive value of 96%. However, HbA1c did not achieve significance for predicting fetal macrosomia.

4. Discussion

The umbilical cord is in charge of the flow of mother and fetal blood. In the first and early second trimesters of pregnancy, there was a significant difference between fetuses with umbilical cord thickness below the fifth percentile (lean cord) and those with thickness above the fifth percentile (non-lean cord) in terms of average gestation age, mode of delivery, birth weight, and adverse perinatal outcomes.

GDM is linked to a number of unfavorable pregnancy outcomes, including macrosomia and cesarean section delivery. A greater prevalence of surgical births, postpartum hemorrhages, birth injuries during natural delivery, and newborn hypoglycemia are all linked to fetal macrosomia. Only 40% of mothers who gave birth to macrosomic infants had known maternal risk factors identified. It has been proposed that one of the potential risk factors for obesity is macrosomia.

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**Table 1. Demographic and clinical features of the examined groups.**

<table>
<thead>
<tr>
<th></th>
<th>No-macrosomia (N = 82)</th>
<th>Macrosomia (N = 18)</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Mean ± SD</td>
<td>30.11 ± 4.73</td>
<td>28.56 ± 4.12</td>
<td>1.29</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>Mean ± SD</td>
<td>26.34 ± 2.39</td>
<td>28.6 ± 2.88</td>
<td>3.49</td>
</tr>
<tr>
<td>Parity</td>
<td>Mean ± SD</td>
<td>2.42 ± 1.15</td>
<td>2.85 ± 1.27</td>
<td>1.41</td>
</tr>
<tr>
<td>Gravidity</td>
<td>Mean ± SD</td>
<td>2.73 ± 1.32</td>
<td>3.51 ± 1.44</td>
<td>2.23</td>
</tr>
</tbody>
</table>

**Table 2. Neonatal characteristics and clinical data between the two studied groups.**

<table>
<thead>
<tr>
<th></th>
<th>No-macrosomia (N = 82)</th>
<th>Macrosomia (N = 18)</th>
<th>t/χ²</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>GA (weeks)</td>
<td>Mean ± SD</td>
<td>37.25 ± 1.86</td>
<td>36.76 ± 2.41</td>
<td>0.957</td>
</tr>
<tr>
<td>Birth weight (kg)</td>
<td>Mean ± SD</td>
<td>3.18 ± 0.609</td>
<td>3.56 ± 0.863</td>
<td>2.21</td>
</tr>
<tr>
<td>Neonatal sex [n (%)]</td>
<td>Male</td>
<td>36 (43.9)</td>
<td>7 (8.9)</td>
<td>0.151</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>46 (56.1)</td>
<td>11 (11.1)</td>
<td></td>
</tr>
<tr>
<td>Apgar at 1 min</td>
<td>Mean ± SD</td>
<td>6.84 ± 2.26</td>
<td>7.2 ± 1.23</td>
<td>0.653</td>
</tr>
<tr>
<td>Apgar at 5 min</td>
<td>Mean ± SD</td>
<td>9.25 ± 1.38</td>
<td>9.7 ± 1.09</td>
<td>1.29</td>
</tr>
</tbody>
</table>

**Table 3. Fetal biometry of the two studied groups.**

<table>
<thead>
<tr>
<th></th>
<th>No-macrosomia (N = 82)</th>
<th>Macrosomia (N = 18)</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biparietal diameter</td>
<td>Mean ± SD</td>
<td>75.42 ± 4.53</td>
<td>77.15 ± 3.86</td>
<td>1.5</td>
</tr>
<tr>
<td>Abdominal circumference</td>
<td>Mean ± SD</td>
<td>24.11 ± 3.92</td>
<td>25.29 ± 3.68</td>
<td>1.17</td>
</tr>
<tr>
<td>Femur length</td>
<td>Mean ± SD</td>
<td>55.18 ± 3.98</td>
<td>56.9 ± 3.49</td>
<td>1.69</td>
</tr>
</tbody>
</table>

**Table 4. Mode of delivery distribution among the studied groups.**

<table>
<thead>
<tr>
<th></th>
<th>No-macrosomia (N = 82)</th>
<th>Macrosomia (N = 18)</th>
<th>χ²</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cesarean section</td>
<td>48 (59.5%)</td>
<td>13 (72.2%)</td>
<td>1.16</td>
<td>0.282</td>
</tr>
<tr>
<td>Vaginal delivery</td>
<td>34 (41.5%)</td>
<td>5 (27.8%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 5. Glycated hemoglobin and the umbilical cord area of the two studied groups.**

<table>
<thead>
<tr>
<th></th>
<th>No-macrosomia (N = 82)</th>
<th>Macrosomia (N = 18)</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c (%)</td>
<td>Mean ± SD</td>
<td>6.42 ± 0.418</td>
<td>6.15 ± 0.322</td>
<td>2.57</td>
</tr>
<tr>
<td>UCT (mm²)</td>
<td>Mean ± SD</td>
<td>202.24 ± 2.68</td>
<td>211.8 ± 3.19</td>
<td>13</td>
</tr>
</tbody>
</table>

**Table 6. Correlation of birth weight with glycated hemoglobin and UCT among macrosomia group.**

<table>
<thead>
<tr>
<th></th>
<th>Birth weight</th>
<th>r</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macrosomia group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UCT</td>
<td>0.654</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>HbA1c</td>
<td>0.281</td>
<td>0.092</td>
<td></td>
</tr>
</tbody>
</table>

HbA1c, glycated hemoglobin.
There was a significant difference between the groups (no-macrosomia and macrosomia) regarding maternal BMI and gravidity.

Our results were in agreement with a study of Fayez Mohamed Fathi et al.\[15\] as they reported that there was a significant difference between their investigated groups (no-macrosomia and macrosomia) regarding maternal BMI and gravidity.

Similarly, Ismail et al.\[16\] revealed that both groups varied considerably in terms of gravidity, where in group 1 (macrosomia), women had a mean of $3.6 \pm 1.3$ compared with $2.5 \pm 1.2$ for group 2 (non-macrosomia), although neither group varied in terms of parity. Five (33%) women of the 15 patients who delivered macrosomic fetuses were obese, eight (54%) were overweight, and two (13%) were normal, with a significant difference between the two groups.\[16\]

The present study showed that there was no significant difference between the groups in terms of mode of delivery.

In contrary to our results, a study by Ismail et al.\[16\] reported that there was significant difference between their studied groups regarding mode of delivery.

The current study showed that there was a significant difference between the groups regarding birth weight. There was no significant difference among the three studied groups regarding biparietal diameter, abdominal circumference, and femur length.\[16\]

In accordance with our results, a study by Fayez Mohamed Fathi et al.\[15\] reported that both groups' delivered fetuses had different birth weights; group 1 (macrosomia) had a mean birth weight of $3924.9 \pm 418.3$ gm for 15 delivered fetuses, which was significantly higher ($P < 0.0001$) than that in group 2 ($3332.3 \pm 296.1$ g) for 85 delivered fetuses.\[15\]

Furthermore, Ismail et al.\[16\] revealed that there was a significant difference between the groups regarding birth weight.\[16\]

In our study, there was a significant difference between the two investigated groups regarding HbA1c and UCT at 27–28 weeks and 36–37 weeks of gestation.

Our results were in accordance with Ismail et al.\[16\] who assessed the association between umbilical cord components, HbA1c, and baby macrosomia at 27–28 weeks of gestation. Fetuses with and without macrosomy were compared. The median umbilical cord area of macroomic fetuses was $213.1 \pm 2.8$ mm$^2$ compared with $204.2 \pm 2.1$ mm$^2$ for the non-macrosomic group, and there were statistically distinct results for Wharton's jelly for each group. At this gestational stage, there were no statistically significant differences in the cord diameter, umbilical artery, or vein area measurements between groups. When compared with the levels obtained at 27–28 gestational weeks, neither group's HbA1c levels differed substantially. Although the macrosomic group had a greater HbA1c than group 2 at 36–37 weeks of gestation ($6.4 \pm 0.3$ vs. $5.8 \pm 0.4\%$, respectively), this difference was extremely statistically substantial.\[16\]

Furthermore, Fayez Mohamed Fathi and colleagues, demonstrated that HbA1c and UCT were substantially different between the two study groups at 27–28 weeks and 36–37 weeks of pregnancy, respectively.

In our research, macrosomic babies were delivered by six (14.6%) of 41 women with GDM or pre-GDM, compared with five (10%) of 50 individuals who were not diabetic. The diabetic group's relative risk of macrosomia was found to be 1.5 times greater.

Naylor et al.\[17\] reported that in individuals with GDM, the frequency of macrosomia was 16–29% compared with 10% in the general population. In those with diabetes, the relative risk of macrosomia might be 1.5 to three times greater. Additionally, Naylor et al.\[17\] reported that moms with GDM had a $30\%$ cesarean section rate compared with a $20\%$ rate in the control group.

Our results showed that among the macrosomia group, there was a substantial positive connection between birth weight and UCT. Using ROC curve, UCT achieved significance for predicting fetal macrosomia with sensitivity of 91.8% and specificity of 93.6%, with positive predictive value of 89% and negative predictive value of 96%.

However, a study by Ismail et al.\[16\] reported that the umbilical cord area was shown to be more accurate in predicting fetal macrosomia at the correct criteria when the ROC curves of both the umbilical cord area and the HbA1c were compared. It was determined that the difference in predicting effectiveness between the two factors was statistically very substantial. The HbA1c did not significantly or

### Table 7. Validity of glycated hemoglobin and UCT.

<table>
<thead>
<tr>
<th>Variables</th>
<th>AUC</th>
<th>SE</th>
<th>Significance</th>
<th>95% CI</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>UCT</td>
<td>0.928</td>
<td>0.034</td>
<td>&lt;0.001*</td>
<td>0.861–0.995</td>
<td>91.8%</td>
<td>93.6%</td>
<td>89.2%</td>
<td>96%</td>
</tr>
<tr>
<td>HbA1c</td>
<td>0.615</td>
<td>0.074</td>
<td>0.126</td>
<td>0.471–0.761</td>
<td>58.1%</td>
<td>87.2%</td>
<td>33%</td>
<td>89%</td>
</tr>
</tbody>
</table>

AUC, area under the curve; CI, confidence interval; HbA1c, glycated hemoglobin; NPV, negative predictive value; PPV, positive predictive value.
strongly correlate with birth weight, nor did measurements taken at 27–28 weeks of gestation or 36–37 weeks of gestation.\textsuperscript{16}

In the study by Fayez Mohamed Fathi et al.,\textsuperscript{15} when the umbilical cord area and birth weight in group 1 (macrosomic fetuses) were correlated, it was discovered that there was a strong, dependent, and positive (direct) connection between the two parameters, whether measurement at 27–28 weeks or measurement at 36–37 weeks of gestation ($r = 0.7340$ and $0.7483$, respectively). Additionally, it was discovered that these connections were statistically very substantial ($P = 0.0002$ and 0.0001, respectively). HbA1c measurements at 27–28 weeks of gestation and 36–37 weeks of gestation did not significantly or strongly correlate with birth weight.\textsuperscript{15}

4.1. Conclusion

Severe obstetric problems, including shoulder dystocia, delivery hypoxia, and postpartum hemorrhage, are caused by macrosomia. There are times when it is difficult to foresee shoulder dystocia. The group most at risk for these issues may be found, however, using macrosomia prediction. There have been documented studies using sonographic measurement for predicting fetal macrosomia. Fetal macrosomia is well predicted by the thickness of the umbilical cord and the fetal fat layer.

The clinical risk factors must be taken into account in addition to the ultrasonographic data when determining the risk of macrosomia. Further research is required to assess the therapeutic utility of using these soft tissue measures in fetal weight estimate algorithms.

Conflict of interest

There are no conflicts of interest.

References


