The role of ductus venosus doppler, fetal liver length and placental thickness in gestational diabetes

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Abstract
To detect the possible adaptive changes that may have an impact on placenta and fetus in the presence of gestational diabetes mellitus using ultrasonography. We compared ductus venosus peak systolic flow velocity, fetal liver length and placental thickness between 25 healthy pregnant and 25 pregnant with gestational diabetes mellitus; diagnosed by 75 gram oral glucose tolerance test during their 24–28 weeks of pregnancy. Measurements were conducted with a 2 D transabdominal convex probe. In addition, gravida, parity, type of birth, gestational diabetes mellitus story, diabetes mellitus story in family, body mass index and demographic characteristics were also compared. In the demographic characteristics, family history of diabetes mellitus and personal history of Gestational Diabetes Mellitus were significantly higher in the group with gestational diabetes than the control group. No statistically significant difference was found between other demographic features. The mean ductus venosus peak systolic flow was measured 35 cm/s in group with gestational diabetes mellitus while it was 45 cm/s in the control group, hence significantly lower in the group with gestational diabetes mellitus. The mean fetal liver length was measured 48 mm in group with gestational diabetes mellitus while it was 44 mm in the control group, thus higher in the group with gestational diabetes. The mean placental thickness was measured 40 mm in group with gestational diabetes while it was 37 mm in control group. There was no statistically significant difference in placental thickness between pregnant with gestational diabetes and healthy controls. Ductus venosus peak systolic flow and fetal liver length measurements are different in patients with gestational diabetes than healthy controls.

Keywords: Gestational diabetes mellitus, ductus venosus, placental thickness, fetal liver length

Introduction
Gestational diabetes mellitus (GDM) has been traditionally defined as first detection of abnormal glucose tolerance during pregnancy [1]. It is one of the main complications of pregnancy. Its prevalence diverges among different ethno-racial groups. In our country one of reported prevalence was in the range of 1.2%-9.2% [2]. There is no universal consensus in screening and diagnosis for GDM. Some of the well known risk factors for GDM include older maternal age, higher BMI, being member of a certain ethnic groups (Hispanic, African, Native American, South or East Asian, or Pacific Islands ancestry), polyhydramnios, past history of GDM, macrosomia in a previous pregnancy, history of unexplained stillbirth, type 2 diabetes mellitus in a first degree relative, polycystic ovary syndrome, and metabolic syndrome [3].

Recently, an avoidance has emerged among Turkish society against performing oral glucose tolerance test concerning the potential harms of oral glucose tolerance test (OGTT) for both fetus and mother. This situation led us to seek for easily applied ultrasonographic indicators of gestational diabetes.

In order to predict GDM numerous sonographic markers have been studied including fetal body composition measurements such as subcutaneous fat, liver size, cardiac muscle thickness, placental volumes. Blood flow velocities of different vessels were also investigated [4-6].

In the presence of hyperglysemia various placental changes, especially increase in size has been defined [7,8]. Fetal liver plays an important role in fetal growth by tuning the umbilical venous perfusion. Haugen et Al. suggested that with unbalanced maternal diet fetal liver blood flow increases and the amount of blood shunting from liver through ductus venosus (DV) decreases [9].
So we aimed to study whether measurements of DV peak systolic velocity, fetal liver length and placental thickness are different in patients with GDM.

Material and Methods

After local Ethics Committee approval, this prospective, case-control study was performed on 50 pregnant women attending antenatal polyclinics in the department of Obstetrics and Gynecology at Mugla Sitki Kocman University hospital between September 2015-April 2017. Women of singleton, uncomplicated pregnancy of 24-28 weeks were taken. A 75-g OGTT was performed. Diagnosis of GDM was made if one of the three measurements exceeds the threshold value (92 mg/dl, for fasting, 180 mg/dl for 1 hour, 153 mg/dl for 2 hour). Patients were divided as GDM and control group. All patients were consented. Once taking a comprehensive history, obstetrical and ultrasound examinations were performed. Age of women, parity, family history of diabetes mellitus and history of GDM, body mass index (BMI) before pregnancy and at admission were recorded. All the patients were evaluated prospectively at 4-week intervals from 24 weeks of gestation until delivery. Patients with pregestational diabetes, multiple gestations, hypertension, intra uterine growth restriction, fetal, umbilical cord and placental anomalies were excluded from the study.

Ultrasonographic and doppler examinations were performed transabdominally by the same investigator using a GE Voluson 730 pro with a 3.5-5 MHz transducer with the lowest setting of high-pass filter. DV measurements were performed in the transvers or sagittal sections. The size of the sample volume was in 2-5 mm, adapted to the vessel diameter. The angle between direction of blood flow and the ultrasound beam was held below 60 degrees. At least five heart cycles were used for the measurement of peak systolic velocity of DV.

The fetal abdominal sagittal and coronal sections were employed in order to measure fetal liver length (FLL). After clearing the boundary of the right lobe, measurements were made from the dome of the right hemidiaphragm to the tip of the right lobe (Figure 1). Placental thickness was measured at its greatest thickness. (Figure 2).

Figure 1. Fetal liver length measurement

Figure 2. Placental thickness measurement

Statistical Analysis

Statistical analysis was performed using SPSS for Windows, v21. Kolmogorov-Smirnov test was used to evaluate normality of the distribution. T test for two independent samples were used provided the distribution of the means was normal. For non-normal distribution, Mann-Whitney U test was performed. The determined level of significance was p<0.05. Categorical data were summarized as frequencies and percentages before being analyzed using the Chi-squared test. For continuous variables, Student’s T test and Mann-Whitney U-test were utilized.

Results

Fifty pregnant women were recruited in the study. Of those, half with GDM (study group) and the other 25 were controls without GDM. Mean age of patients was 30.18 ± 5.85. No statistically significant differences were measured in mean maternal age, parity, or initial visit BMI between the two groups (Table 1). Family history of diabetes mellitus was significantly higher in GDM group (p<0.05). 20 patients in GDM group had diet therapy while the remaining 5 had insulin therapy. Although women in GDM group had therapy after the diagnosis, increase in weight throughout pregnancy and BMI at delivery were measured higher in GDM group (Table 1). The mean birth weight in GDM group was 3430±514 grams, while it was 3230±310 grams in the control group (p=0.105). Previous birth of an infant ≥4000 grams were higher in the GDM group but it was not statistically significant (p=0.104). Personal history of GDM was higher in GDM group and it was statistically significant (p=0.041). Birth weight, mode of delivery and number of neonatal intensive care unit admission were not statistically significant between the two groups.

The mean ductus venosus peak systolic flow was measured 35 cm/s in group with gestational diabetes mellitus while it was 45 cm/s in the control group, hence significantly lower in the group with gestational diabetes mellitus (p=0.001). The mean fetal liver length was measured 48 mm in group with gestational diabetes mellitus while it was 44 mm in the control group, thus higher in the group with gestational diabetes (p=0.030). The mean placental thickness was measured 40 mm in group with gestational diabetes while it was 37 mm in control group. There was no statistically significant difference in placental thickness between pregnant
with gestational diabetes and healthy controls (p=0.171). (Table 2).

Table 1. Characteristics of the study groups

<table>
<thead>
<tr>
<th></th>
<th>GDM (n=25)</th>
<th>Normal (n=25)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age (years)</td>
<td>31.04±6.39</td>
<td>29.32±5.23</td>
<td>0.303</td>
</tr>
<tr>
<td>Parity</td>
<td>1.00 (0-3)</td>
<td>1.00 (0-3)</td>
<td>0.350</td>
</tr>
<tr>
<td>Family history of DM</td>
<td>11 (44%)</td>
<td>3 (12%)</td>
<td>0.025</td>
</tr>
<tr>
<td>BMI (kg/m²) Before pregnancy</td>
<td>25.48±5.44</td>
<td>23.86±3.49</td>
<td>0.211</td>
</tr>
<tr>
<td>BMI (kg/m²) at 24-28 weeks gestation</td>
<td>28.77±5.68</td>
<td>26.13±3.27</td>
<td>0.055</td>
</tr>
<tr>
<td>BMI at delivery (kg/m²)</td>
<td>31.60±5.32</td>
<td>28.81±3.19</td>
<td>0.027</td>
</tr>
<tr>
<td>Weight gain during gestation (kg)</td>
<td>15.92±3.52</td>
<td>13.48±2.48</td>
<td>0.008</td>
</tr>
<tr>
<td>Mode of delivery NSD</td>
<td>8 (32%)</td>
<td>8 (32%)</td>
<td>1.00</td>
</tr>
<tr>
<td>CS</td>
<td>17 (64%)</td>
<td>17 (64%)</td>
<td></td>
</tr>
<tr>
<td>Usg efw (gr)</td>
<td>1048 (734-1466)</td>
<td>922 (653-1370)</td>
<td>0.013</td>
</tr>
<tr>
<td>Gestation at delivery-(weeks)</td>
<td>39 (34-40)</td>
<td>38 (36-41)</td>
<td>0.830</td>
</tr>
<tr>
<td>Birth weight(gr)</td>
<td>3430.00±514.64</td>
<td>3230.80±310.52</td>
<td>0.105</td>
</tr>
<tr>
<td>NICU admission</td>
<td>3 (12%)</td>
<td>2 (8%)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Results are expressed as mean ± SD, median (minimum-maximum), number and frequency (%) BMI, Body mass index; NSD, normal spontaneous delivery; CS, Cesarean section; EFW, estimated fetal weight; NICU, neonatal intensive care unit.

Table 2. Comparison of OGTT values and ultrasonographic markers in women with and without GDM

<table>
<thead>
<tr>
<th></th>
<th>GDM (n=25)</th>
<th>Normal (n=25)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting Glucose (mg/dl)</td>
<td>89 (72-126)</td>
<td>77 (68-89)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>OGTT 1hour(mg/dl)</td>
<td>196 (145-266)</td>
<td>128 (90-178)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>OGTT 2 hour (mg/dl)</td>
<td>156 (110-240)</td>
<td>111 (65-149)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DV Peak Systolic Velocity (cm/s)</td>
<td>35 (25-40)</td>
<td>45(30-60)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fetal liver length (mm)</td>
<td>48.32±6.88</td>
<td>44.16±6.36</td>
<td>0.031</td>
</tr>
<tr>
<td>Placental Thickness (mm)</td>
<td>40 (27-65)</td>
<td>37 (20-77)</td>
<td>0.171</td>
</tr>
</tbody>
</table>

Results are expressed as mean ± SD, median (minimum-maximum)

Discussion

It is important to detect gestational diabetes mellitus during pregnancy, because women with gestational diabetes mellitus are at increased risk of developing adverse obstetrical outcome. Yet there is no consensus regarding screening and diagnostic testing for gestational diabetes even in the same clinic. In the present study we aimed to study some possible sonographic markers which may be useful in the diagnosis of gestational diabetes besides conventional tests. The study group and the control group had patients with similar age, gravida, parity and BMI. Although family history of diabetes mellitus and personal history of GDM were higher in the GDM group, most of our patients had no risk factors for GDM.

According to our results, the GDM group had lower DV peak velocity and higher FLL than those of the control group. As far as we know, our study is the first involving peak systolic velocity of DV, FLL, and placental thickness in comparing GDM with healthy controls. DV is a small fetal vessel that shunts oxygenated blood from umbilical vein to the left side of inferior vena cava towards the foramen ovale [10]. Approximately 25% of the umbilical venous blood flow goes through DV and bypasses the hepatic circulation, whereas 55% goes to the left and 20% goes to the right liver lobes, respectively [11]. DV doppler measurement has multiple clinical uses including DV assessment of first trimester screening, twin-to-twin transfusion syndrome and fetal growth restriction [12]. DV waveform consists of two peak and two trough phases. The first peak is S wave and represents systole in the cardiac cycle. Three different measurement technics can be used including Semi-quantitative analysis of the pulsatility index for the vein, visual assessment, [13] and velocity ratios assessments [14]. We used the peak systolic velocity measurement for DV doppler and found it lower in the group with gestational diabetes. In previously conducted studies, Stuart et al. discovered that diabetic pregnancies (gestational vs gestational diabetics) had increased pulsatility index of DV blood flow than non-diabetics had [15]. Their study consisted of more pregestational than gestational diabetics and retrospective in design. They associated the change they found with a possible fetal cardiac effect. We, on the other hand, did not include pregestational diabetes in our study and believe that the low systolic blood flow we found is originated from umbilical liver perfusion in presence of hyperglycemia. There are a lot of studies investigating the relationship between gestational diabetes and fetal liver length. Perovic et al. found FLL as a predictor of GDM in population with high risk for GDM. They measured a cut-off value for FLL as 39mm on the USG they performed in the 23rd gestational week [16]. We measured FLL as 48 mm for the GDM group and 44 mm for the control group. Mirghani et al measured FLL as 36 mm for patients with gestational diabetes and 31 mm for non-GDM patients between weeks 21-24 [17]. A recent publication by Ilhan et al. suggested that FLL evaluation throughout the second-trimester ultrasound scanning by three dimensional USG may predict GDM [18]. Due to the fact that 3D USG is not widespread in our country, using it will not be a useful method. Tongprasert et al established the nomogram of fetal liver length in a Thai population from 14 to 40 weeks of gestation and they claimed that it would be a useful tool in predicting pathologic conditions [19]. We also believe that for FLL value, measuring FLL after reference values are determined based on pregnancy weeks would be more accurate concerning GDM.

Another commonly inquired topic for GDM is placental thickness. Various functional and structural pathological changes occur in the placenta of patients with diabetes[20]. In their study, Edu A et al. found that sizes of placentas in patients with gestational diabetes did increase [8]. They discovered that throughout the weeks 24-28, patients with GDM had placental thickness of 33 mm; while the patients not having GDM had placental thickness of 27 mm. They recommended that increased placental size can be used in GDM scanings, but they had quite a few number of GDM patients. Placental thickness >40mm throughout second trimester and
Performing ultrasound tests on 50 pregnant women attending antenatal polyclinics in the department after local Ethics Committee approval, this prospective, case-control study was conducted. Ethical approval was given, and the authors declare that they have no competing interest. The authors received no financial support for this study.

Limitation of our study is that being a case control study with a small sample size and lack of nomograms of fetal liver length and placental thickness of our population. We believe that simple measurements of DV peak systolic flow and FLL may be helpful in the evaluation of GDM. These sonographic parameters may further be useful for monitoring the efficacy of the treatment in future studies.

Conclusion

In conclusion, ultrasonographic findings may help scan tests due to the fact that there is no consensus between GDM methods and their ratios of diagnosing the disease. Broader studies with more number of patients are needed.

Competing interests
The authors declare that they have no competing interest.

Financial Disclosure
The authors received no financial support for this study.

Ethical approval
After local Ethics Committee approval, this prospective, case-control study was performed on 50 pregnant women attending antenatal polyclinics in the department of Obstetrics and Gynecology at Mugla Sıtkı Koçman University hospital between September 2015-April 2017.

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References
