

ORIGINAL RESEARCH

Medicine Science 2020;9(1):136-9

The role of ductus venosus doppler, fetal liver length and placental thickness in gestational diabetes**Murat Cevik¹, Ruya Deveer²**¹*Silopi Public Hospital, Clinic of Obstetric and Gynecology, Sirnak, Turkey*²*Mugla Sıtkı Kocman University, Faculty of Medicine, Department of Obstetric and Gynecology, Mugla, Turkey*

Received 21 August 2019; Accepted 20 October 2019

Available online: 24.02.2020 with doi:10.5455/medscience.2019.08.9153

Copyright © 2020 by authors and Medicine Science Publishing Inc.

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 hyperglycemia 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].

***Corresponding Author:** Ruya Deveer, Mugla Sıtkı Kocman University, Faculty of Medicine, Department of Obstetric and Gynecology, Mugla, Turkey
E-mail: ruyadeveer@hotmail.com

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).

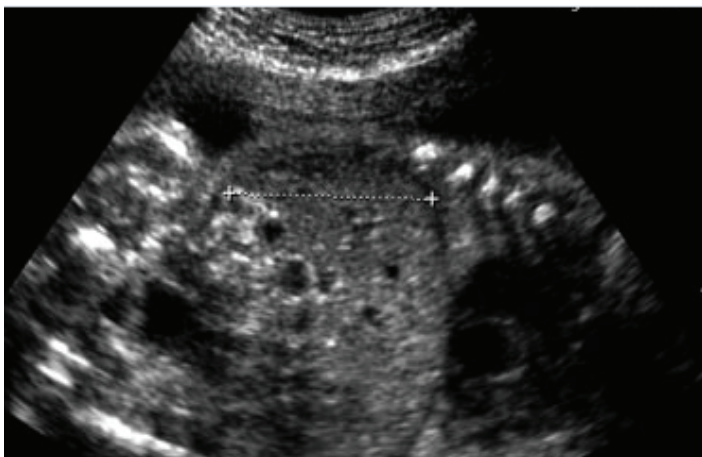


Figure 1. Fetal liver length measurement

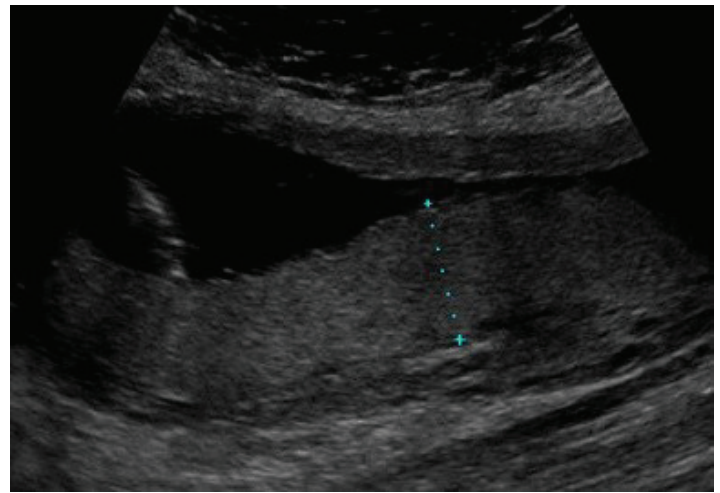


Figure 2. Placental thickness measurement

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

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

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

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

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 techniques 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 pregnant (pregestational 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 scannings, but they had quite a few number of GDM patients. Placental thickness >40mm throughout second trimester and

>60mm throughout third trimester is defined as placentomegaly [21]. In our study, mean placental thickness was 40 mm in GDM group while it was 37 mm in the control group, but the difference was not statistically significant. Berceanu et al. found that 56% of GDM patients had placental thickness more than 40mm throughout weeks 24-28 and that as pregnancy weeks progress the increase in placental thickness becomes more significant [22]. But they had so few patients and all patients had either type 1 DM or GDM, they lacked a healthy control group and patients had no regular glycemic control. Perovic et al suggested placental thickness as one of the ultrasonographic criterion in GDM prediction [23]. Their group consisted solely of patients with GDM risk factors as well. Though there were studies investigating increased placental thickness in GDM patients, they were not methodologically uniform and usually contained limited number of patients. Despite finding the placental thickness in GDM group more than non-GDM group in our study, this difference was not statistically significant. The increase in placental thickness that is detectable with USG, may be a result of long term hyperglycemia; cannot be found at early stages.

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 Kocman University hospital between September 2015-April 2017.

Murat Cevik ORCID: 0000-0001-6514-4214

Ruya Deveer ORCID: 0000-0002-4445-8086

References

1. Proceedings of the 4th International Workshop-Conference on Gestational Diabetes Mellitus. Chicago, Illinois, USA. 14-16 March 1997. Diabetes Care. United States; 1998. p. B1-167.
2. Ozyurt R, Asıcıoglu O. The Prevalence of Gestational Diabetes Mellitus in Pregnant Women Who were Admitted to İstanbul Teaching and Research. JOPP Derg. 2013;5:7-12.
3. Hartling L, Dryden DM, Guthrie A, et al. Screening and diagnosing gestational diabetes mellitus. Evid Rep Technol Assess (Full Rep). 2012;210:1-327.
4. Dantas AMA, Palmieri ABS, Vieira MR, et al. Doppler ultrasonographic assessment of fetal middle cerebral artery peak systolic velocity in gestational diabetes mellitus. Int J Gynaecol Obstet. 2019;144:174-9.
5. Wong CH, Chen CP, Sun FJ, et al. Comparison of placental three-dimensional power Doppler indices and volume in the first and the second trimesters of pregnancy complicated by gestational diabetes mellitus. J Matern Fetal Neonatal Med. 2019;32:3784-91.
6. Garcia-Flores J, Cruceyra M, Cañamares M, et al. Predictive value of fetal hepatic biometry for birth weight and cord blood markers in gestational diabetes. J Perinatol. 2016;36:723-8.
7. Saha S, Biswas S, Mitra D, et al. Histologic and morphometric study of human placenta in gestational diabetes mellitus. Ital J Anat Embryol. 2014;119:1-9.
8. Edu A, Teodorescu C, Gabriela Dobjanschi C, et al. Placenta changes in pregnancy with gestational diabetes. Rom J Morphol Embryol. 2016;57:507-12.
9. Haugen G, Hanson M, Kiserud T, et al. Fetal liver-sparing cardiovascular adaptations linked to mother's slimness and diet. Circ Res. 2005;96:12-4.
10. Kiserud T. Hemodynamics of the ductus venosus. Eur J Obstet Gynecol Reprod Biol. 1999;84:139-47.
11. Haugen G, Kiserud T, Godfrey K, et al. Portal and umbilical venous blood supply to the liver in the human fetus near term. Ultrasound Obstet Gynecol. 2004;24:599-605.
12. Turan Ş, Turan ÖM. Harmony Behind the Trumped-Shaped Vessel : the Essential Role of the Ductus Venosus in Fetal Medicine. 2018;124-30.
13. Kessler J, Rasmussen S, Hanson M, et al. Longitudinal reference ranges for ductus venosus flow velocities and waveform indices. Ultrasound Obstet Gynecol. 2006;28:890-8.
14. Turan OM, Turan S, Sanapo L, et al. Semiquantitative classification of ductus venosus blood flow patterns. Ultrasound Obstet Gynecol. 2014;43:508-14.
15. Stuart A, Amer-wählin I, Gudmundsson S, et al. Ductus venosus blood flow velocity waveform in diabetic pregnancies. Ultrasound Obstet Gynecol. 2010;36:344-9.
16. Perovic MD, Gojnic M, Arsic B, et al. Relationship between mid-trimester ultrasound fetal liver length measurements and gestational diabetes mellitus. J Diabetes 2015;7:497-505.
17. Hisham Mirghani M, Reem Zayed M. Gestational Diabetes Mellitus: Fetal Liver Length Measurements Between 21 and 24 Weeks' Gestation. J Clin Ultrasound. 2007;35:27-33.
18. İlhan G, Gultekin H, Kubat A, et al. Preliminary evaluation of foetal liver volume by three-dimensional ultrasound in women with gestational diabetes mellitus. J Obstet Gynaecol. 2018;3615:1-5.
19. Tongprasert F, Srisupundit K, Luewan S, et al. Normal length of the fetal liver from 14 to 40 weeks of gestational age. J Clin Ultrasound. 2011;39:74-7.
20. Huynh J, Yamada J, Beauharnais C, et al. Type 1, type 2 and gestational diabetes mellitus differentially impact placental pathologic characteristics of uteroplacental malperfusion. Placenta. W.B. Saunders. 2015;36:1161-6.
21. Dashe JS, BL H. Callen's Ultrasonography in Obstetrics and Gynecology. Philadelphia: Elsevier; 2017;674-703

22. Berceanu C, Tetileanu AV, Ofiteru AM, et al. Morphological and ultrasound findings in the placenta of diabetic pregnancy. *Rom J Morphol Embryol = Rev Roum Morphol Embryol. Romania.* 2018;59:175-86.
23. Perovic M, Garalejic E, Gojnic M, et al. Sensitivity and specificity of ultrasonography as a screening tool for gestational diabetes mellitus. *J Matern Fetal Neonatal Med. England.* 2012;25:1348-53.