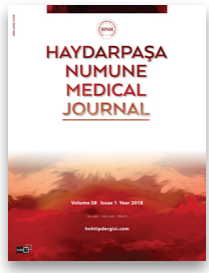
HAYDARPAŞA NUMUNE MEDICAL JOURNAL

DOI: 10.14744/hnhj.2018.95530
Haydarpasa Numune Med J 2019;59(3):229–234



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ORIGINAL ARTICLE

Relationship between Body Mass Index and Ductus Venosus Doppler Measurements at 11-14 Gestational Weeks

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Abstract

Introduction: In this study, we aimed to investigate the possible causative relationship between maternal obesity and flow patterns of ductus venosus.

Methods: One hundred twenty three pregnant women with a body mass index of 25 or higher and 83 pregnant women with body mass index lower than 25 in gestational weeks between 11-14, were included in the present study.

Results: The findings showed that there was no statistically significant difference between the two groups for a combined test, three-component antenatal tests, second-level ultrasonography. In 12% of the women, loss of a wave and/or inverse a wave was noted. In the rest of the women, there were no pathological waves. In 4.8% of women with a BMI less than 25, there was an abnormality in ductus venosus flow pattern, whereas this ratio was 17% in the other group consisted of women with BMI higher than 25; and the difference was statistically significant (p=0.008).

Discussion and Conclusion: We concluded that maternal hyperglycemia and high body mass index might cause abnormal flow patterns in ductus venosus in pregnancies with normal first-trimester scanning and abnormal flow patterns of ductus venosus.

Keywords: Body mass index; ductus venosus doppler; first-trimester screening.

Maternal obesity is a common obstetric problem, with long and short term negative consequences for the mother and fetus which include fetal growth retardation, macrosomia or stillbirth, neural tube defects, and cardiac anomalies [1]. Although the underlying mechanism of these pathologies is not clearly identified, it is thought to develop at the placental level. Studies have found an inverse relationship between maternal obesity and placental villous proliferation and apoptosis [2].

Ductus venosus (DV) is a thin vessel that allows well-oxygenated blood from the placenta to reach the fetal heart. The blood flow pattern in the ductus venosus is important in the detection of fetal acidemia. Fetuses with DV blood flow pattern abnormality that is associated with the increased nuchal thickness (NT) between 11-14 gestational weeks were found to be mostly aneuploid. The findings showed that fetal defects or poor perinatal prognosis may develop in fetuses with normal karyotype and deteriorated DV blood flow pattern [3]. A reverse flow in the ductus venosus is associated with an increased risk of chromosomal anomaly, cardiac defects and sudden fetal death [4].

First-trimester NT screening is an important screening test

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Submitted Date (Başvuru Tarihi): 19.03.2018 **Accepted Date (Kabul Tarihi):** 04.05.2018

for fetal aneuploidy and other risks. Evaluation of DV Doppler in fetuses with increased NT is an important adjunct factor in screening for Down syndrome. However, Prats et al.'s [3] study showed that deterioration of DV blood flow in euploid fetuses with normal nuchal translucency might be the indicative of adverse fetal outcomes. Particularly in the last 10 years, there is a curiosity to investigate the relationship between obesity and abnormal DV Doppler with both maternal and fetal risks. Both parameters were associated with both congenital anomalies and increased poor fetal outcomes. While DV Doppler is included in the first-trimester congenital anomaly screening, many studies have been conducted on the potential negative effects of obesity and insulin resistance on the fetus in early pregnancy [5, 6].

The present study aims to investigate whether there is a relationship between maternal body mass index (BMI) and DV Doppler results, and the potential effects of these variables on pregnancy outcomes.

Materials and Methods

A total of 256 pregnant women who applied to our obstetric clinic between 11-14 weeks of gestation were enrolled in this study. Pregnant women with primary hypertension, type 1 DM, thyroidism, liver or kidney pathologies and fetal aneuploidy detected as a result of screening tests were excluded from this study, and 206 pregnant women were included in the analysis of results. The records of the patients were retrospectively retrieved. Pregnant women were divided into two groups as BMI ≥25 kg/m^2 (n=123) and BMI <25 kg/m^2 (n=83). The gestational week was determined using US and crown-rump length (CRL) measurements. BMI was calculated by dividing the weight by the square of the height in meters (kg/m^2). Pregnant women included in this study were laid in the supine position, and transabdominal ultrasonography was performed within an average of 15 minutes, to search for a wave loss or reverse wave in DV blood flow. Maternal age (year), maternal BMI (kg/m^2), obstetric background, combined test, and triple test results, smoking status, 50 g and 100 g OGTT test results, second-level detailed fetal ultrasonography and fetal results were recorded.

Statistical analyzes were performed using the Statistical Package for Social Sciences (SPSS) version 15. The suitability of the variables to normal distribution was examined using visual and analytical methods. Descriptive analyzes were performed using the median for non-normally distributed variables. Since age, gravida and birth weight did not show normal distribution; the Mann-Whitney U test was used for comparison. Combined, and triple test, 2nd level US, OGTT, additional disease and smoking status, DV abnormality, IUGR, fetal anomaly, presence of miscarriage were expressed using cross-tables. Intergroup differences in the frequencies of these variables were compared using chi-square or Fisher's exact tests where appropriate. The results with p-values less than 0.05 were evaluated as statistically significant.

Results

When the demographic characteristics of the patients included in this study were examined, the mean age of the patients was 27.1 (±4.8) years, and 96% of the patients underwent a combined first-trimester screening test, and 93.3% of them underwent a triple test (Table 1).

In 4.8% of the patients, high risk was detected both in the combined test and triple test. Amniocentesis was performed in two of these patients, and no chromosomal aneuploidy was detected. VSD was found in one of the two patients who underwent amniocentesis, and any patho-

Table 1. Demographic characteristics and antenatal data of the patients

	n=206
Age (year)	
Mean±SD	27.1±4.8
Median	27
Gravida	
Mean±SD	1.98±0.8
Combined test (n,%)	
Yes	199 (96.6)
No	7 (3.4)
Triple tests (n,%)	
Yes	193 (93.7)
No	13 (6.3)
Quad test (n, %)	
Yes	6 (2.9)
No	200 (97.1)
2. Level US (n, %)	
Yes	191 (92.7)
No	15 (7.3)
Smoking (n, %)	
Yes	3 (1.5)
No	203 (98.5)
OGTT (n, %)	
Yes	205 (99.5)
No	1 (0.5)

US: ultrasound; OGTT: oral glucose tolerance test.

logical findings were not detected in the other baby.

Five patients with high risk in the triple test had normal DV blood flow, and one patient had a fetal cardiac anomaly in the postpartum period. The pregnancy of a patient with high risk in the combined test but normal DV flow pattern terminated in miscarriage before 20 gestational weeks. No high risk or anomaly was detected in the patients who underwent detailed fetal ultrasonography and quadruplicate screen tests (Table 2).

Among 206 pregnant women included in this study, BMIs were below 25 kg/m^2 in 83, and above in 123 patients. In 81 pregnant women with BMIs below 25, high risk was not detected in the combined test. Among 123 pregnant women with a BMI ≥25 kg/m^2, 118 underwent a combined test, and 4% of these patients had high risk. Seventy-nine out of 83 pregnant women with BMIs <25 kg/m^2 underwent triple tests, and 3.6% of them had high risk. In addition, 113 of 123 pregnant with BMIs ≥25 kg/m^2 underwent triple test, and 1.6% of them had high risk. There was no statistically significant difference between the two groups in terms of triple test results (p=0.4). Seventy-six of 83 pregnant women with BMIs below 25 kg/m^2, and 115 of 123 pregnant women with BMIs ≥25 kg/m^2 underwent detailed second-level fetal ultrasonography, and none of them had pathologic findings. OGTT was performed in 79 of 83 pregnant women with BMIs below 25 kg/m^2 and all 123 pregnant women with BMIs above 25 kg/m^2. Impaired glucose tolerance was detected in 100 g OGTT test in 6% of the pregnant women, and the patients were referred to the dietician with the recommendation of diet and exercise. In addition, no statistically significant difference was found between the two groups according to OGTT results (p=0.22) (Table 3).

A wave loss and/or inverse a wave were observed in DV in 12% of the pregnant women included in this study. Ductus venosus flow pattern abnormalities were found in 4.8% of patients with BMIs below 25 kg/m^2, whereas 17% of pregnant with BMI ≥25 kg/m^2 had impaired ductus venosus flow pattern and this difference was statistically significant (p=0.008) (Table 4).

Table 2. Risk distribution in antenatal monitorization

	High risk (n, %)	Low Risk (n, %)
Combined Test	5 (2.4)	194 (94.2)
Triple Test	5 (2.4)	187 (90.8)
Quad Test	0 (0)	6 (2.9)
2. Level US	0 (0)	191 (92.7)

US: ultrasound.

Table 3. Intergroup comparisons of demographic features

	BMI <24.9 kg/m^2 (n=83)	BMI ≥25 kg/m^2 (n=123)	p
Age (year, Median, Mean±SD)	27 26.7 (±4.9)	27 27.4 (±4.7)	0.35*
Gravida (Median, Mean±SD)	2 1.9 (±0.8)	2 2.02 (±0.8)	0.22*
Combined Test (n,%)			
Low risk	81 (97.5)	113 (91.8)	0.8¥
High risk	0	5 (4.0)	
Triple test (n,%)			
Low risk	76 (91.5)	111 (90.2)	0.4¥
High risk	3 (3.6)	2 (1.6)	
2. Level US (n,%)			
Normal	76 (91.5)	115 (93.4)	0.6ψ
Abnormal	0	0	
OGTT (n,%)			
High	5 (6)	14 (11.3)	0.22¥
Low	77 (92.7)	109 (88.6)	
Smoking (n,%)			
Yes	0	3 (2.4)	0.27¥
No	83 (100)	12 0 (97.5)	

BMI, body mass index; US, ultrasound; OGTT, oral glucose tolerance test. *Mann- Whitney U test; ¥Fisher exact test; ψPearson Chi Square; p<0.05, level of statistical significance.

Table 4. Intergroup comparisons of ductus venosus pathologies

	BMII <24.9 kg/m^2 (n=83)	BMI≥25 kg/m^2 (n=123)	p
Ductus venosus abnormaliites (n,%)			
Yes	4 (4.8)	21 (17)	0.008*
No	79 (95.2)	102 (83)	

*Pearson chi-square test; p<0.05,level of statistical significance.

The average birth week was 37 weeks in patients with and without normal flow pattern. While IUGR was observed in 4.2% of pregnant women with normal ductus venosus flow pattern, and in 8.2% of the patients with impaired ductus venosus flow pattern. This difference was not found to be statistically significant (p=0.48). Fetal anomaly was seen in 0.7% of the patients with normal ductus venosus flow patterns and in 4.1% of those with abnormal ductus venosus flow pattern withoutany statistically significant difference between the two groups. There were two miscarriages in the group with normal ductus venosus flow pattern and one miscarriage in the group with abnormal ductus venosus flow pattern (p=0.63) (Table 5).

Table 5. Comparison between ductus venosus pathologies and fetal outcomes

	DV normal (n=179)	DV abnormal (n=24)	p
Birth week (Mean±SD)	37.7 (±1.9)	37.1 (±2.1)	0.5¥
Presence of IUGR (n,%)	6 (4.2)	2 (8.2)	0.48*
Presence of Fetal anomaly (n,%)	1 (0.7)	1 (4.1)	0.44*
Miscarriage (n,%)	2 (1.4)	1 (4.1)	0.63*

DV: ductus venosus; IUGG: intrauterine growth retardation; ¥ Mann Whitney U test; *Fisher exact test; p<0.05; level of statistical significance.

Discussion

Blood flow in the ductus venosus is indicative of cardiac function. Major cardiac anomalies and Down syndrome are the leading causes of abnormal fetal ductus venosus blood flow pattern in pregnant women; however, hyperglycemia also leads to deterioration of DV flow pattern. Studies investigating the effect of maternal uncontrolled hyperglycemia on the fetal heart discuss this effect over increased insulin resistance as well as changes in DV flow pattern produced by hyperglycemia. When pregnant women with uncontrolled diabetes were compared with pregnant women without diabetes, a marked difference was detected in fetal diastolic myocardial function in the first-trimester [7]. Umbilical artery, descending aorta and ductus venosus pulsatility indices of pregnant women with maternal hyperglycemia increased significantly [8].

In a study by Stuart et al., [9] the authors investigated whether there was a difference in DV blood flow patterns between fetuses of diabetic and non-diabetic mothers and in the first group there was a statistically significant increase in the deterioration of DV blood flow pattern and cardiac defects. Hyperinsulinemia, hyperglycemia, insulin-like growth factors and increased insulin resistance were thought to play a role in the pathogenesis of this condition. Similarly, according to a study by Girsen et al., [10] fetuses of diabetic mothers showed significantly increased deterioration in DV blood flow patterns compared to fetuses of non-diabetic mothers, even in the presence of good glycemic control and normal placental hemodynamic parameters.

In our study, we compared DV flow patterns in pregnant women with BMIs ≥25 kg/m^2 and pregnant women with BMIs <25 kg/m^2. Concomitant increases in BMIs and incidence of deterioration in DV flow patterns may suggest the presence of a relationship between them. As indicated in the literature, this hypothesis may be explained by increased hyperglycemia in obese patients. One of the limitations of our study is that we did not evaluate insulin resistance in pregnant women, and as glycemic control, only OGTT was performed. Down syndrome is one of the leading causes of abnormalities in fetal ductus venosus blood flow pattern in pregnant women. In the literature, deterioration of DV flow pattern has been evaluated by keeping various confounding factors, such as neck thickness, constant.

In a case-control study by Oh et al., [11] 47 (1.9%) nuchal translucency and DV Doppler measurements showed the deterioration of the DV flow pattern, while nuchal translucency was within normal limits and two of these 47 patients had isolated IUGR (intrauterine growth retardation). Aneuploidy was detected in three, and other anomalies in six patients. In the remaining 36 pregnant women, DV a wave returned to normal after the first-trimester. In our study, only one out of 19 pregnant women with abnormal DV blood flow had high risk in a combined test, resulting in miscarriage at 16 weeks of gestation, and any negative fetal outcomes were not detected in the remaining 18 pregnant women.

In a study by Matias et al., [12] six cases with nuchal translucency measured within normal limits but with impaired DV blood flow patterns were examined and three of six cases had karyotype abnormality, and one of the remaining three cases had major cardiac defects. Murta et al. [13] reported that abnormal DV flow pattern could detect 93% of chromosomally abnormal fetuses and chromosomal abnormality was found in four out of 10 fetuses with nuchal translucency at normal margins but with impaired DV flow patterns. As a result of their studies, karyotype analysis was recommended to fetuses with DV flow pattern deterioration even if the NT measurements were within normal limits. According to a study by Toyama et al., [14] fatal aneuploidy was not detected in pregnant women with NT measurements within normal range but with impaired DV.

In a study by Yolanda et al., [15] DV blood flow pattern was evaluated in 181 pregnant women with normal, and 117 pregnant women with abnormal nuchal translucency measurements, and it was observed that DV pulsatility index increased in the second group compared to the first group without statistically significant intergroup difference (p=0, one). Cardiac defects and heart failure are thought to play a role in the pathophysiology of DV blood flow pattern deterioration and an increase in nuchal translucency. In addition, impaired endothelial development and differentiation and lymphatic abnormalities have been reported to play a role in the disorder.

In a study by Özlem et al., [16] maternal age, nuchal translucency, DV Doppler findings were examined in 213 pregnant women between 11-14 gestational weeks. DV PI was >95 p in 12 of 213 patients and in fetuses of two of these pregnants IUGR was detected.

A relationship between abnormal blood flow and fetal aneuploidy has been suggested in DV. It has been indicated that measurement of the nuchal translucency along with DV flow pattern may increase the sensitivity in detecting trisomy 21 [17–22]. In fetuses with cardiac defects or fetal hypoxia, some abnormal patterns have been observed in the DV a wave [23]. Murta et al. [13] detected a wave loss or reversed a wave in cases with DV during atrial contraction in 93% of non-euploid fetuses. However, abnormal DV blood flow was found in 5.2% of euploid fetuses and 70.8% of fetuses with trisomy 21 [17]. It has been reported that even if nuchal translucency is normal, the reverse current seen during atrial contraction in DV has a strong association with adverse fetal outcomes, such as IUGR, cardiovascular anomalies and renal anomalies [24].

Favre et al. [25] found an increase in nuchal translucency and abnormal DV blood flow in 36% of fetuses with normal chromosomes but with major cardiac anomalies. In chromosomally normal fetuses with increased nuchal translucency, the measurement of DV blood flow is considered to have an important role in predicting underlying cardiac disease. However, in this study, no pathological changes were detected in the DV blood flow pattern in two cases with cardiac anomalies.

In our study, high risk was found in the combined test of five patients. Only one of these fetuses had deterioration in DV blood flow, and this pregnancy resulted in miscarriage in less than 20 gestational weeks, and no other fetal outcomes were observed. Five patients with high risk in the triple test had normal DV blood flow, and one patient had a cardiac anomaly in the postpartum period. In our study, the incidence of anomalies in fetuses with impaired DV blood flow pattern did not increase compared to the control group.

Toyama J.M. investigated 1217 singleton pregnancies between 11-14 gestational weeks and performed DV and NT measurements. DV flow pattern was abnormal in 84 cases (7.7%) and NT value was higher than 95p in 41 cases (48.8%) ($p<0.0001$) [14]. The relationship between abnormal DV flow pattern and increased NT was also described by Zoppi et al. [26]. Abnormal DV current was detected in 39% of cases above NT of 95p, although DV current deteriorated in only 1% of the cases with normal NT. However, Borrell et al. [27] and Antolin et al. [21] stated in their studies that there is no relationship between these two parameters.

In conclusion, studies in the literature showed that maternal hyperglycemia and increased BMI might lead to deterioration in DV flow pattern in fetuses whose first-trimester prenatal screening is normal and the only abnormal finding is impaired ductus venosus flow pattern. In addition, in most of the studies performed to investigate chromosomal anomaly risk, further examination and follow-up were required for these patients.

Many studies suggested that maternal obesity may be associated with negative fetal and maternal outcomes during pregnancy. To our knowledge, in the literature, there are no studies evaluating the effects of maternal obesity and ductus venosus on fetal anomaly and pregnancy outcomes in combination. In our study, it was observed that DV flow pattern abnormality was seen more frequently in pregnant women with BMIs ≥25 kg/m^2 compared to pregnant women with BMIs <25 kg/m^2, but the incidence of cardiac or chromosomal abnormalities did not increase in patients with abnormal DV blood flow pattern. We think that this observational study could raise curiosity about the relationship between obesity and DV flow pattern and will be the source of studies to investigate this relationship on the basis of causal correlation.

Ethics Committee Approval: The study was approved by the Local Ethics Committee.

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: Z.A.; Design: Z.A., C.T., H.S.; Data Collection or Processing: Z.A.; Analysis or Interpretation: Z.A., C.T., H.S.; Literature Search: S.A.A., C.T.; Writing: S.A.A., Z.A.

Conflict of Interest: None declared.

Financial Disclosure: The authors declared that this study received no financial support.

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