

# Ductus Venosus Doppler S/D Value Adjusted Alfa Fetoprotein Levels to Decrease False Positive Rates

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**OBJECTIVE:** Fetal liver is mostly perfused by umbilical vein via ductus venosus and AFP is synthesized and secreted from fetal liver. In this study we tried to determine the effect of ductus venosus and umbilical blood flow on serum AFP levels

**STUDY DESIGN:** Sixty women with 16-20 weeks of gestation were enrolled for the study. Subjects were divided into two: AFP levels lower (n=46) and higher than 2 MoMs (n=14). All participants underwent serum AFP, ductus venosus and umbilical artery Doppler S/D screening. Effect of ductus venosus and umbilical artery blood flow on serum AFP levels were analyzed.

**RESULTS:** Ductus venosus (AUC=0.945, P<0.001) and umbilical artery Doppler S/D (AUC=0.803, P=0.001) values were predictor for low AFP levels. In regression analysis, Ductus venosus Doppler S/D (Beta coefficient= -0.442, P<0.001) and umbilical artery S/D (Beta coefficient= -0.291, P=0.011) values were significantly associated with the AFP levels (R<sup>2</sup>=0.60). DV and umbilical artery Doppler S/D values adjusted serum AFP levels remained significant but mean value of AFP in group with AFP>2 MoM became 1.98 MoM after adjustment.

**CONCLUSION:** Our study revealed that Ductus venosus and umbilical artery S/D value adjusted serum AFP levels may have lower false positive rates.

**Key Words:** Ductus venosus doppler, Alfa fetoprotein, Second trimester screening

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## Introduction

Ductus venosus is a funnel shaped vascular structure that refers umbilical vein blood to fetal liver and plays a major role in venous return flow to the fetal heart with inferior vena cava and hepatic veins. Oxygenated blood from placental unit flows through the ductus venosus to pass toward the left atrium by the foramen ovale.<sup>1</sup> The fetal liver is mostly perfused by umbilical vein via ductus venosus in the fetal circulation.<sup>2</sup> Ductus venosus blood flow shows similar direction to the hepatic veins and the intrahepatic branches of the portal vein. The alterations in the flow resistance ratios show none affection in ductus venosus hence liver. 70% of hepatic blood flow is supplied by umbilical vein and 30% is passing through the ductus venosus.<sup>3</sup>

Doppler velocimetry of umbilical circulation is a noninva-

sive imaging tool in pregnancies. This imaging method easily suggests the fetal circulation in intrauterine growth retardation and hypoxia. Spectral analyses of umbilical artery may demonstrate absent or reversed end diastolic flow that is strongly related with perinatal and neonatal mortality.<sup>4</sup> Absent or reversed end diastolic flow in umbilical artery and occurrence of severe Doppler waveform abnormalities in ductus venosus is both able to predict adverse outcomes.<sup>5</sup>

A recent study concluded that ductus venosus Doppler can be used to increase the effectiveness of the second trimester screening test.<sup>6</sup> From this conclusion we tried to assess whether it is possible to decrease false positive rate of AFP by controlling fetal liver blood supply.

## Material and Method

Sixty women with 16-20 weeks of gestation were enrolled for the study. Subjects were divided into two: AFP levels lower (n=46) and higher than 2 MoMs (n=14). All participants underwent serum AFP, ductus venosus and umbilical artery Doppler S/D screening. Effect of ductus venosus and umbilical artery blood flow on serum AFP levels were analyzed. The cutoff value for AFP level was 2 MoMs. All patients were nonsmoker Caucasians and in normal range of BMI (under 30). We include singleton pregnancies to study. Pregnancies without medical, obstetric or surgical events included. Fetal

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anomalies (autosomal trisomy syndromes, NTD, gastroschisis, omphalocele, esophageal atresia, mole, chorioangioma, and fetal renal diseases), fetal demise, twin gestation, maternal hypertension, cirrhosis, hepatocellular carcinoma and diabetes mellitus were excluded from the study. The participants were healthy and had none risk for NTD. There was no family history for NTD. We also exclude the benign and malign liver conditions that may affect AFP levels. We investigated the DV, UA and UV between 20-24 weeks of gestation. We applied spectral analyses of ductus venosus, umbilical artery and umbilical vein to all patients. The flow velocity waveform is a graph of the frequency shifts present in the sample volume and the alterations over time. The Doppler studies were performed by one radiologist and 1-8 MHz bandwidth convex transabdominal probe with mean 3.5 MHz broadband (Esaote, MyLab60, Geneva, Italy) were used for study. The Doppler signal was optimized with adjustment of probe position, gain measurements and the angle of insonation for accurate determination. All patients have 2 arteries and 1 vein in the umbilical cord. We exclude single UAs. We obtained the proper signal after 4 similar consecutive waveforms for UA and DV. The peak systolic and end diastolic flow velocities were measured for S/D ratios. The S/D velocity ratios are angle independent technique to reflect downstream impedance. The measurement of UA and UV was performed from the midportion of umbilical cord. The DV was identified in an oblique or a midsagittal section of the fetal abdomen. The vessel was identified by its characteristic velocity waveform and audio recognition in the spectral analyses. The measurements of AFP were obtained by using a Beckman automatic analyzer (Abbott-USA).

**Statistical Analysis**

The statistical analyses were performed using the Statistic Package for Social Sciences (ver. 11.0; SPSS Inc., Chicago, IL). For group comparisons independent samples t test was used. Correlation analysis was used to calculate degree of associations and linear regression analysis was used to determine adjusted associations. ANCOVA was used for statistical adjustment. P value of <0.05 was accepted as statistically significant.

**Results**

Mean age, gravidity, parity and body mass index of the study population was 27.2±3.1 years, 1.7±0.8, 0.7±0.7, 25.1 ± 3.4 kg/m<sup>2</sup> respectively. Mean second trimester AFP level was 1.4±0.6 Moms. Mean S/D of umbilical artery and Ductus venosus Doppler (Figure 1) were 3.5±0.8 and 1.4±0.4. Ductus venosus (1.56 vs. 1.1) and umbilical artery S/D (3.9 vs. 3.3) values were significantly lower in group with high AFP levels (P<0.05). Mean age was significantly lower in group with high AFP levels (25.7 vs. 27.7 years, P<0.05). Mean gravidity (1.8 vs. 1.4), parity (0.7 vs. 0.4) and BMI (25.3 vs. 24.3 kg/m<sup>2</sup>)

were comparable between groups (P>0.05). Mean AFP levels were significantly higher in group with AFP > 2 MoMs (2.13 vs. 1.21 Moms, P<0.05). All umbilical venous flow was non pulsatile. In correlation analysis serum AFP levels were found to be significantly correlated with the umbilical artery (r=-0.415, P=0.001) and ductus venosus Doppler S/D values (r=-0.524, P<0.001). Ductus venosus and umbilical artery Doppler S/D values were significantly correlated (r=0.281, P=0.03). Ductus venosus (AUC=0.945, P<0.001) and umbilical artery Doppler S/D (AUC=0.803, P=0.001) values were predictor for low AFP levels (Figure 2).



Figure 1: Sonographic image of ductus venosus Doppler

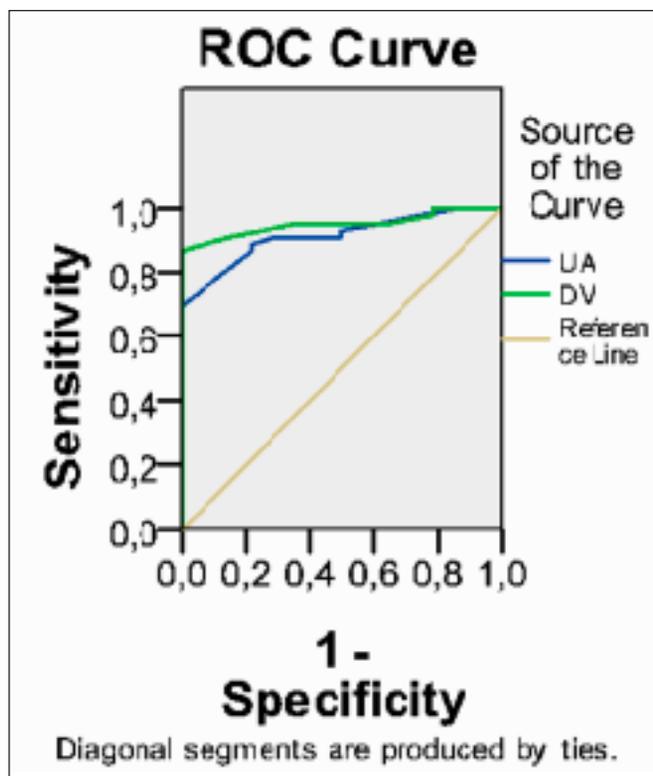


Figure 2: Roc curve of ductus venosus and umbilical artery Doppler S/D values to predict AFP values

In regression analysis, Ductus venosus Doppler S/D (Beta coefficient= -0.442, P<0.001) and umbilical artery S/D (Beta coefficient= -0.291, P=0.011) values were significantly associated with the AFP levels (R<sup>2</sup>=0.60). DV and umbilical artery Doppler S/D values adjusted serum AFP levels remained significant but mean value of AFP in group with AFP>2 MoM became 1.98 MoM after adjustment.

## Discussion

In this study we tried to analyze the ductus venosus and umbilical artery Doppler S/D value adjusted AFP values with reference to the previous study by Demirturk et al.<sup>6</sup> Our study revealed that adjustment for ductus venosus Doppler S/D values lead to decrease in false positive rates of this screening method. Doppler US is a safe, noninvasive, rapid imaging tool to assess the physiology and pathophysiology of the fetomaternal circulations. Thus it may have a role in increasing the predictive power of some screening tests during pregnancy.

Neural tube defect (NTD) is one of the most common malformations. Its prevalence is 1-3/1000 live births worldwide. They are caused by failure of closure of neural tube during neurulation in 21-28 embryonic days. Closure failure of cranial pole and spinal part of neural tube named as anencephaly and spina bifida are the most common types of NTD, respectively.<sup>7</sup>

Development of the neural tube is a multi-factorial process controlled by genes and modulated by a host of environmental factors. Gene-gene, gene-environment and gene-nutrient interactions can be listed roughly as etiology. The exact etiology of NTD remains rather complex despite years of intensive epidemiological, clinical and experimental research.<sup>8</sup>

Due to Early diagnosis of affected pregnancies allows couples the option of pregnancy termination or an opportunity to prepare for the birth of a child, The American College of Medical Genetics recommends use of maternal serum alpha-fetoprotein and/or ultrasound for detection of neural tube defects between 15 and 20 weeks of gestation.<sup>9</sup> The flow of nutrient-rich blood from the placenta divides as it enters the fetus, either to perfuse the fetal liver, or to bypass it via the ductus venosus. Blood flow through ductus venosus is directed preferentially through the foramen ovale to the left atrium, then to the left ventricle and ascending aorta to supply the coronary and cranial vascular beds.<sup>10,11</sup> Our hypothesis was based on this data that this highly nourished blood passing through liver may affect synthetic function of the fetal liver. In a previous study it was shown that false positive rate of first trimester screening test may be decreased by combining ductus venosus Doppler.<sup>12</sup> Recently published study assessed the value of ductus venosus Doppler in second trimester screening

and study revealed that ductus venosus Doppler can be used to increase the effectiveness of the second trimester screening test.<sup>6</sup> False positive rate of AFP is accepted to be up to 5 % if the cut off value is accepted as 2.5 MoM which is expected to be higher when cut off point is accepted to be 2 Moms.<sup>13</sup>

This is a study assessing the ductus venosus and the umbilical artery Doppler findings with serum AFP levels. Although the AFP screening is the preferred test to determine NTDs, adjustment of these factors may increase predictive value of AFP in detecting NTD. Our study revealed that Ductus venosus S/D adjusted serum AFP levels may have lower false positive rates.

## Duktus Venozus S/D Oranına Göre Düzeltilmiş Alfa Fetoprotein Düzeyinin Yalancı Pozitiflik Oranını Azaltması

**AMAÇ:** Fetal karaciğer çoğunlukla duktus venozus aracılığıyla umbilikal venden beslenmektedir. Alfa Fetoprotein (AFP) fetal karaciğerde üretilip, salgılanmaktadır. Çalışmamızda, serum AFP düzeyine duktus venozus ve umbilikal kan akımının etkisi incelendi.

**GEREÇ VE YÖNTEM:** Çalışmaya 16-20 hafta gebeliği olan 60 kadın alındı. Olgular AFP seviyeleri 2 MoM üzeri (n=46) ve altı (n=14) olarak ikiye ayrıldı. Tüm olgular serum AFP ölçümü ile Doppler görüntüleme duktus venozus ve umbilikal arter S/D oranı değerlendirilmesine yönlendirildi. Duktus venozus ve umbilikal arter kan akımının serum AFP seviyesi üzerine olan etkisi araştırıldı.

**BULGULAR:** Umbilikal arter ve duktus venozus kan akımının serum AFP seviyesi ile ilişkili olduğu saptandı (p<0.05). Yüksek AFP seviyesi olan olgularda, umbilikal arter ve duktus venozus S/D oranları belirgin olarak düşüktü (p<0.05).

**SONUÇ:** Çalışmamızda duktus venozus ve umbilikal arter kan akımının serum AFP seviyesini etkileyebileceği ön görülmektedir. AFP düzeyinin bu faktörlere göre yeniden düzenlenmesi, Nöral Tüp Defekti teşhisinde prediktif değerini artırabilir.

**Anahtar Kelimeler:** Duktus venozus, Umbilikal arter, Alfa fetoprotein

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