Relationship Between Umbilical Artery Doppler Investigations and Perinatal Outcome in Patients with HELLP Syndrome

Mekin Sezik[1], Mehmet Okan Özkaya[1], Hülya Toyran Sezik[2], Elif Gül Yapar[3], Hakan Kaya[2]

[1]*Department of Gynecology and Obstetrics, Faculty of Medicine, Süleyman Demirel University, Isparta*
[2]*Clinics of Gynecology and Obstetrics , Isparta Maternity Hospital, Isparta*
[3]*Zekai Tahir Burak Maternity and Children's Hospital, Ankara*

Abstract

Objective: To investigate the association between umbilical artery Doppler studies and subsequent perinatal mortality in pregnancies with HELLP syndrome.

Methods: Seventy-seven women with HELLP syndrome were retrospectively evaluated regarding systole/diastole (S/D) ratios and presence of absent or reverse end-diastolic flow (AREDF) on umbilical artery Doppler velocimetry. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of S/D ≥5 and AREDF during umbilical artery doppler investigations for the prediction of perinatal mortality were calculated.

Results: Cesarean section rate was 76% (n=57). Indications for cesarean delivery were obstetric causes in 6 women (10.5%) and fetal distress or HELLP syndrome in the remaining patients. Prenatal loss rate was 18% (n=14). There were 4 (6.3%) neonatal deaths out of 63 live-born infants. Sensitivity, specificity, PPV, and NPV of S/D ratio ≥5 on umbilical artery doppler velocimetry for predicting subsequent perinatal mortality was 85.7%, 66.7%, 36.3%, and 95.5%, respectively. Sensitivity, specificity, PPV, and NPV of the presence of AREDV on umbilical artery Doppler velocimetry for predicting subsequent perinatal mortality was 71.4%, 82.5%, 47.6%, and 92.8%, respectively.

Conclusions: Umbilical artery Doppler investigations might be essential for evaluating the risk of perinatal mortality and timing of delivery in patients with HELLP syndrome. Normal umbilical blood flow in HELLP syndrome may demonstrate a low risk for perinatal mortality.

Keywords: HELLP syndrome, umbilical artery, Doppler investigations, perinatal mortality.

HELLP sendromlu hastalarda umbilikal arter Doppler incelemesinin perinatal sonuçlarla ilişkisi

Amaç: HELLP sendromlu hastalarda umbilikal arter Doppler inceleme sonuçlarının, perinatal ve postnatal dönem fetal iyilik hali göstergeleri ile olan ilişkisini belirlemektir.

Yöntem: Yetmiş yedi HELLP sendromlu hasta retrospektif olarak incelendi. Doppler incelemesinde Sistol/Diastol (S/D) oranı ile diastolik akım yokluğu (DAY) ve ters akım (TA) varlığı durumları araştırıldı. Umbilikal arter Doppler incelemesinde S/D ≥5 ve DAY-TA olması durumunun perinatal mortaliteyi belirleyebilmesindeki sensitivite, spesifisite, pozitif prediktif değer (PPD) ve negatif prediktif değeri (NPD) hesaplandı.

Bulgular: Sezaryen oranı %74 (57) idi. Sezaryen ile doğurtulanlardan 6 (%10.5)'sı obstetrik endikasyonlarla sezaryen olurken, geri kalanlarda endikasyonu fetal distress ve HELLP sendromuna bağlı maternal patolojiler oluşturmaktaydı. Toplam 77 hastanın 14'ünde (%18) takip sırasında prenatal kayıp gerçekleşti. Canlı doğan 63 bebekten 4 (%6.3)'ü postpartum dönemde kaybedildi. Umbilikal arter Doppler (UAD) S/D ≥5 olmasının perinatal mortalite riskini belirlemedeki sensitivitesi %85.7, spesivitesi %66.7, PPD'i %36.3 ve NPD'i %95.5, UAD incelemesinde DAYTA olması durumunda ise sensitivite %71.4, spesifisite %82.5, PPD %47.6 ve NPD %92.8 olarak saptandı.

Sonuç: HELLP sendromunun anne ve fetus açısından taşıdığı riskler göz önüne alındığında, bu gebelerde umbilikal arter Doppler incelemesi hem perinatal mortalite riskinin belirlenmesi, hem de doğum zamanın planlanması için önemlidir. Normal umbilikal arter Doppler akımı olması perinatal mortalitenin daha az olmasının göstergesi olabilir.

Anahtar Sözcükler: HELLP sendromu, umbilikal arter, Doppler inceleme, perinatal mortalite.

Correspondence: Dr. Mekin Sezik, Süleyman Demirel Üniversitesi, Kadın Hastalıkları ve Doğum Anabilim Dalı, Isparta
e-mail: msezik@yahoo.com

Introduction

Preeclampsia is one of the most important complications of the pregnancy. Increase in the blood pressure and proteinuria in the preeclampsia is a rule.[1] HELLP syndrome is a multi system illness with hemolysis, raised liver enzyme level and low thrombocyte count.[2] HELLP syndrome is generally followed by preeclampsia and sometimes sporadic. Although define etiopathogenesis is not known, genetic closure, abnormal placentation, immunological pathologies and mother vascular endothelium dysfunction can play a role.[3,4] It is known that HELLP syndrome has a relationship between raised perinatal mortality and fetal growth retardation (FBG).[5]

It is shown that in the examination of umbilical artery Doppler (UAD), in the case of the absent or reverse end-diastolic flow (AREDF) , some undesired consequences can happen such as intrauterine growth retardation or perinatal mortality.[6,7] But there is not acidosis in all of the fetuses that AREDF is detected.[8] Today, evaluation of umbilical blood stream plays an important role for the detection of feto-placental deficiency.[9] Although there are some studies evaluating umbilical blood changes for pregnant with FBG and preeclampsia, this parameter is not studied efficiently for the patients with HELLP syndrome.

The objective of our study is to investigate the association between UAD investigation results and determinants of perinatal and postnatal period fetal well being.

Methods

77 patients with HELLP syndrome who hospitalized and cured in Department of Gynecology and Obstetrics of Isparta Süleyman Demirel University and Clinics Gynecology and Obstetrics of Maternity Hospital Isparta, and Ankara Zekai Tahir Burak Maternity and Children's Hospital were investigated retrospectively. Some of the patients were affected by HELLP syndrome while they were monitored for preeclampsia or hypertension reasoning from pregnancy and some other patients were diagnosed as HELLP syndrome in their first time (AST≥ 70 U/L, thrombotic count < 150000/≥ and LHD > 150 U/L). All of the patients had the routine physical examination and obstetric ultrasonography, routine bio chemistry examinations, complete urine analysis, hemogram, hematocrit, thrombosis count examinations. UAD examinations were practiced by the same ultrasonography devices (Medison Sonace 8800 and Kretz Technic Combison 420) for the patients diagnosed HELLP syndrome or developed HELLP syndrome while their monitoring. In the Doppler examination, Sistol/Diastol (S/D) ratio and absent of diastolic flow (ADF) or reverse flow (RF) were searched. It was examined whether there was chronic hypertension or diabetes in anamnesis, abortion history and chronic illness in family history. Patients were closely monitored beginning from the time hospitalized to the time they were discharged from hospital after birth. Non-stress test (NST) results, intrauterine fetal loss and post partum fetal loss ratios, convulsion ratios were determined while the monitoring.

In UAD investigation, sensitivity, specificity, positive predictive value (PPD) and negative predictive value (NPD) according to perinatal mortality of detected S/D ≥5 and AREDF were calculated. In addition, sensitivity, specificity, PPD and NPD in determining the probability of non-reactive NST for being S/D ≥5 in UAD investigation were calculated. Sensitivity, specificity, PPD and NPD for NST to determine perinatal mortality were determined. Student's t-test was used for statistical analysis.

Results

Average age of the patients included in the study was 28.0≥ 6.5 years, gravida was 2.4≥1.8 and parity was 1.1 ≥1.4. Demographical characterizes of the patients and laboratory and Doppler results are shown in the Table 1.

For 14 of the total 77 patients (18%), intrauterine fetal loss was seen while monitoring. 38 of the patients (49.3%) of the patients had female fetus, 39 of the (50.3%) of the patients had male fetus. 7 patients (9%) were diagnosed eclampsia. When anamneses were examined, 10 of the patients (13%) had abortion history, 4 of the patients (5.2%) had chronic hypertension and 9 of the patients (11.7%) had hypertension history in the family. 50 patients (65%) in total were cured with antihypertensive treatment and magnesium sulfate treatment. 20 of the patients (26%) had vaginal delivery and the other had cesarean section. 6 of the patients (10.5%) having cesarean section reasoned

Table 1. Demographical characteristics, laboratory and Doppler results of the patients.

Age (years)	28.0 ± 6.5	Thrombosis (/μL)	141.2 ± 65.9
Gravida	2.4 ± 1.8	Sodium (mmol/dl)	138.4 ± 4.0
Parite	1.1 ± 1.4	Potassium (mmol/dl)	4.35 ± 0.5
Estimated fetal weight by the ultrasonography (g)	1606 ± 699	Calcium (mmol/dl)	8.45 ± 0.8
Systolic blood pressure (mmHg)	151.5 ± 15.3	Prothrombin Time (sec)	11.9 ± 1.04
Diastolic blood pressure (mmHg)	97.9 ± 10.0	Activity partial thromboplastin time (Sec)	34.2 ± 4.7
Hemoglobin (g/dl)	13.0 ± 2.02	Urine protein for 24 hours (g)	341 ± 193
Hemotocric (%)	39.0 ± 6.3	24 saatlik idrar protein (g)	2.85 ± 1.7
Fibrinojen (g/L)	455 ± 120.5	Serum protein (g/dl)	6.08 ± 0.8
AST (U/L)	102.5 ± 131.6	Serum albumin (g/dl)	2.98 ± 0.5
ALT (U/L)	75.6 ± 93.1	Serum creatinine (mg/dl)	0.92 ± 0.4
Serum bilirubin (mg/dl)	0.7 ± 0.5		

Table 2. Values for determining perinatal mortality in the study.

	Perinatal mortalite			
	Sensitivity	**Specificity**	**PPD**	**NPD**
Umbilical artery Doppler S/D ≥5	%85.7	%66.7	%36.3	%95.5
Umbilical artery DAYTA	%71.4	%82.5	%47.6	%92.8
NST non-reactive	%100	%71.4	%43.8	%100

Sensitivity: %72.2, **Specificity:** %82.9, **PPD:** %78.8, **NPD:** %72.3

Table 3. Values to determine non-reactive NST for being S/D ≥5 umbilical artery Doppler.

		NST non -reactive		
		+	**–**	**Total**
Umbilical Doppler S/D ≥5	+	26	7	33
	–	10	34	44
	Total	**36**	**41**	**77**

from obstetric inductions and the other from fetal distress and maternal factors of HELLP syndrome (thrombocytopenia, increase of hepatic enzyme). 9 of the patients (11.7%) gave the birth after the 36th pregnancy week, other infants (88.3%) were preterm delivery. 4 of the 63 live births (6.3%) were lost after postpartum period in the 2nd, 7th and 15th days.

Sensitivity, specificity, PPD and NPD to determine perinatal mortality in cases of UAD S/D ≥5 and non-reactive NST is given in the table 2. Sensitivity in determining the perinatal mortality for being UAD S/D ≥5 is 87.5%, specificity is 66.7%, PPD is 36.3% and NPD is 95.5 %, In case of AREDF in UAD investigation, sensitivity is 71.4 %, specificity is 82.5%, PPD is 47.6% and NPD is 92.8%. Sensitivity, specificity, PPD and NPD to determine probability of non-reactive NST is given in the Table 3.

Discussion

Doppler investigations are an important method to evaluate fetal well being in the intrauterine period.[10] Abnormal Doppler results or AREDF detection is related with bad perinatal results.[10] Perinatal mortality ratios reaching 80% was informed for AREDF developed cases.[10] In the Doppler investigation in intrauterine period, besides umbilical artery, investigations of middle cerebral artery and uterine artery can also be made. In the studies of Lacin et al emphasized that UAD investigation results are better than middle cerebral artery in order to show perinatal results.[11] Nevermore, it is stated that joint investigation of bilateral uterine artery, middle cerebral artery and umbilical artery is better for the estimation of the results of perinatal.[12] Joern et al investigated parameters of umbilical artery and bilateral uterine artery Doppler for FBG and/or preeclampsia or HELLP syndrome patients in their studies.[13] They detected that average birth week and birth weight decrease significantly with a Doppler distortion in one of these veins. In the same study, in the cases of Doppler distortion of double side uterine artery, 90% problem can develop for risky pregnancies, and this ratio is 72% for umbilical artery.

Consequently, it is emphasized that investigation of bilateral uterine artery is an indispensable method to determine fetal risk.[13]

In our study, UAD results, perinatal results and NST were evaluated for the patients hospitalized for HELPP syndrome or developed HELLP syndrome while monitoring. We detected that AREDF detection in the UAD investigation or S/D ≥5 have high sensitivity and specificity in order to determine perinatal mortality.

Spirilla et al searched umbilical artery S/D ratio and short term neonatal complications and neurological developments for the first two years for 582 monomer pregnancies (between 24-35 weeks). 45.7% of the patients had also FBG diagnosis. In this group of patients, neonatal death or cerebral palsy (p: 0.001) was seen at the ratio of 3.4% when S/D ratio is below 95 percent, 4.9% when it is 95 percent and above and 17.3% when AREDF develops.[7] In our study, 18% fetus of the mothers with HELLP syndrome is lost in intrauterine period. 10 of them (71.4%) had S/D ratio of ≥5.74% of the patients had cesarean section, 89.5% of these had cesarean induction reasoned from fetal distress or maternal problems from HELLP syndrome.

Venous Doppler investigations were done in the literature. Ductus venosus is one of the most used veins for that. For 35 patients that AREDF was detected in UAD, short term results of ductus venosus and effect to birth timing were investigated. Short term results (such as artery pH, intraventricular bleeding, and mortality) showed that evaluation of ductus venosus Doppler pulsality index is important. In the study, it is also important ductus venosus Doppler evaluation in order to determine fetal results and pregnancy timing for the pregnancies with AREDF in umbilical artery current.[14]

In the literature generally patients with preeclampsia or FBG are studied in arterial Doppler investigations.[15,16] UAD examinations are not commonly used for the HELLP syndrome cased in order to evaluate perinatal results. High sensitivity (83%) and high specificity (80%) for the fetuses whose Doppler results is FBG to determine bad fetal condition is stated in the literature.[17]

In our study, fetal loss in intrauterine group with AREDF is 47.6% (10 of the total 21 patients); neonatal mortality is 18.2% (2 fetuses from total 21 patients). 12 of the fetuses in 32 patients with UAD S/D≥5 (37.5%) was lost in the intrauterine period, 3 of 20 live born fetuses (15%) was lost in the neonatal period. All of the 4 fetuses lost in the neonatal period were born in the 32nd pregnancy week. Similar to our study as in our study, for patients with AREDF in UAD investigation, high ratios of neonatal death was informed.[16,18] In our study, prematurity should be effective for neonatal deaths, not the deficiency in Doppler examination. Indeed, AREDF detection in umbilical artery blood current may not have a separate effect on perinatal mortality after the chances such as FBG and premature is checked.[19] The objective of the conservative approach to the cases with HELLP syndrome is to decrease perinatal mortality by gaining time with fetal maturation but in our study, 14 of the fetuses (18%) were lost during the conservative treatment. The reason for that can be the low pregnancy week of the cases and thus the insistence for continuing conservative treatment.

In the literature, it is stated that UAD result are not efficient to determine fetal well being and the seriousness of the preeclampsia (thrill, hypertension level and other) but in the cases of deficient Doppler, ratio of FBG and cesarean increases.[20,21]

HELLP syndrome is an important obstetric problem that can cause bad results both for the mother and the infant. Umbilical artery S/D ratio is ≥5 for approximately half of the pregnancies with HELLP syndrome. When umbilical artery S/D ratio is ≥5, high sensitivity and NPD ratios are detected for the determination of perinatal mortality. When AREDF is monitored in UAD examination, high specificity and NPD ratios are detected for the determination of perinatal mortality. Pregnancies with pathologic UAD examinations, pregnancies result earlier.

When the risks of HELLP syndrome are considered for mother and infant, UAD investigation of these pregnancies are important both for the determination of perinatal mortality risk and the timing of birth. We believe that when not only the evaluation of umbilical artery but also bilateral uterine artery and middle cerebral Doppler evaluation is made, perinatal and postnatal mortality and morbidity can be better determined.

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