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Role Of Fetal Umbılical And Mıddle Cerebral Artery Doppler Indıces In Determınıng Intrauterıne Growth Restrıctıon In Preeclamptıc Pregnancıes

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Abstract

Background: To investigate the utility of the umbilical artery (UA) and middle cerebral artery (MCA) Doppler indicesand the irratios in determining intrauterine growth restriction (IUGR) and unfavorable birth outcomes in preeclamptic pregnancies.

Material and methods: This prospective study included 59 preeclamptic pregnant womenand 63 healthy pregnant women (controls) at a gestational week of 31-40 who were follow edup at the gynecology and obstetrics clinic of a tertiary hospital over a 16-month period. After the evaluation of normal and pre-eclamptic pregnancies using B-Mode ultrasonography, the Doppler indexvalues of the UA and MCA were determine dusing Doppler ultrasonography. By de-termining the velocity-time waves pectraforthe UA and MCA, the systole/diastoleratio (S/D), resistive index (RI), and pulsatility index (PI) values were calculated following the automatical gorithm of thedevice.

Results: The UAS/D (3.47±1.29) and UA RI (0.69±0.13) values of the preeclamptic group statistically significantly differed fromthose of the controls (2.50 ± 0.30 and 0.59 ± 0.06, respectively) (p<0.001). The Doppler indices of the MCA were lower in preeclamptic pregnancies (PI: 1.28±0.34, RI: 0.73±0.09), and this was more prominent in fetuses with IUGR (p<0.001). There were also significant differences between the preeclamptic and healthy control groups in terms of the UA/MCA and MCA/UA Doppler index ratios (p<0.001).

Conclusion: Non-invasive Doppler indicescan be used in combination to increase diagnostic accuracy and prevent fetal Mortality and morbidity.

Keywords: Preeclampsia, intrauterine growth restriction, doppler.

Introduction

Preeclampsia is a specific complication of pregnancy, characterized by high blood pressure, proteinuria, and edema (1-3). It has an incidence of 7-8% in the general population and shows a hereditary tendency. Normal fetal growth and oxygenation depend on the adequate and appropriate perfusion of the intervillous space, which consists of uterine artery branches.An acute or chronic problem that occurs in this area prevents the growth and development of the fetus, resulting in an increase in fetal mortality and morbidity. As a result of the disruption of uteroplacental perfusion in preeclamptic pregnant women, fetal distress and intrauterine growth restriction (IUGR) develop, leading to fetal mortality and morbidity . This condition is defined as a developmental disorder in which the expected fetal weight for gestational age is below the 10% percentile (4). IUGR develops in 6-40% of pregnant women with preeclampsia.

Many methods, such as the non-stress test, biophysical scoring, evaluation of pH in a blood sample taken from the fetal scalp, and Doppler ultrasonography (USG), are used in the diagnosis of IUGR in the fetus. Doppler USG provides information on fetal circulation and/or uteroplacental blood flow dynamics in a non-invasive manner and in a shorter time than other methods (4). In the literature, studies have compared the use of the Doppler parameters of the uterine artery, umbilical artery (UA), and middle cerebral artery (MCA) in determining IUGR and unfavorable birth outcomes (UBOs) that may develop in cases of preeclampsia (5, 6). The current study aimed to investigate the utility of the UA and MCA Doppler indices and their ratios in predicting IUGR and UBOs in preeclamptic pregnancies.

Materıal And Method

This prospective study included 59 preeclamptic pregnant women and 63 healthy pregnant women (controls) at a gestational age of 31-40 weeks who were followed up at

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the gynecology and obstetrics clinic of a tertiary hospital over a 16-month period. After the evaluation of normal and preeclamptic pregnancies using B-Mode USG, the Doppler index values of the UA and MCA were determined by Doppler USG using an EUB 515 (Hitachi -JAPAN) Doppler device anda 3.5-MHz convex probe. Velocity-time wave spectra for the UA and MCA were determined, and the systole/diastole ratio (S/D), resistive index (RI), and pulsatility index (PI) values were calculated following the automatic algorithm of the device.

The preeclampsia group consisted of 59 pregnant women presenting with a blood pressure above 160/110 mmHg, proteinuria (5 g /24 hours), oliguria (≤500 ml /24 hours), cerebral and visual findings, pain in the upper abdominal region, pulmonary edema or cyanosis, elevated liver function parameters, hemolytic anemia, and fetal growth restriction. The control group was formed with healthy pregnant women whose last menstrual period was known, who had normal obstetric and B-Mode examination findings, and who had uncomplicated deliveries through repeat cesarean sections or the cervicovaginal route.In thecontrol group, all deliveries occurred at a gestational age of 37 weeks or above, and the first- and fifth-minute Apgar scores were above 7. None of the fetuses in this group required intensive care.

The following cases were accepted as UBOs: deliveries by induction or cesarean section before the estimated date of delivery due to fetal distress according to the physician's evaluation, deliveries that occurred before 37 weeks of gestation, fetal weight below the 10% percentile according to the percentile scale, a fifth-minute Apgar score of less than 7, intensive care admission due to fetal distress, and intrauterine or neonataldeath.

For measurements, the lowest pulse-repetition frequency that would not result inaliasing and a 100-Hz wall filter were used, and the sampling interval was selected as 2 mm. The normal UA diameter in a pregnant woman at term varies between 1.1 and 2.8 mm, and it is normally 2.4 mm. The MCAmeasurement was performed from the proximal section close to the Willis polygon where the thalamus and cavum septum pellucidumwerebest visualized (7).

Statistical Analysis: Statgraf v. 5.0 software was used in the statistical analysis of the data. Student's t-test was used to compare the two groupsfor parametric data, and the Mann-Whitney-U test for non-parametric data. The relationship between the measurement parameters was evaluated using linear regression analysis.

Results

The data of preeclamptic and healthy pregnant women aregiven in Tables 1-3, and the results of the comparative statistical analyses of the cases arepresented in Tables 4 and 5.

Diastolic flow was absent in two cases of IUGR and reversed in a further two cases. The fetuses of two pregnant women with reversed diastolic flow and one pregnant woman with absent diastolic flow died in the intrauterine period. The other pregnant woman with no diastolic flow

Table 1: Clinical and Doppler data of healthy pregnant women included in the study.

n = 63	Mean ± SD	Min-Max
Age (year)	26.58 ± 4.55	19-36
Gravida	2.25 ± 1.27	1-6
Gestational age at birth (week)	38.48 ± 1.70	37-41
Mode of delivery **SVD** **Repeat C/S** **IVD** **C/S**	 46/63 (73%) 7/63 (11%) 2/63 (3%) 8/63 (12%)	
Fifth-minute Apgar score	9.14 ± 0.43	8-10
Fetal weight at birth (g)	3,245.24 ± 560.3	1,800-4,400
UA S/D	2.50 ± 0.30	1.87-3.52
UA RI	0.59 ± 0.06	0.37-0.74
MCA RI	0.79 ± 0.083	0.57-0.96
MCA PI	1.46 ± 0.36	0.85-2.44
UA RI/MCA RI	0.76 ± 0.09	0.58-0.94
MCA RI/UA RI	1.34 ± 0.19	1.06-1.71
UA PI/MCA PI	0.60 ± 0.15	0.31-1.10
MCA PI/UA PI	1.77 ± 0.43	1.08-3.22

SD: standard deviation, SVD: spontaneous vaginal delivery, C/S: cesarean section, IVD: induced vaginal delivery, UA: umbilical artery, S/D: systole/diastole, RI: resistive index, MCA: middle cerebral artery, PI: pulsatility index

Table 2: Clinical and Doppler data of preeclamptic pregnant women included in the study.

n=59	Mean ±SD	Min-Max
Age (year)	28.68 ± 5.71	18-43
Gravida	2.63 ± 2.20	1-10
Gestational age at birth (week)	36.25 ± 3.03	31-40
Mode of delivery **SVD** **Repeat C/S** **IVD** **C/S**	 16/59 (27%) 3/59 (5%) 13/59 (22%) 27/59 (46%)	
Fifth-minute Apgar score	6.67 ± 3.65	0-10
Fetal weight at birth (g)	2,258.81 ± 944.99	800-4,200
NICU admission	22/59 (37%)	
Intrauterine or neonatal death	12/59 (20%)	
UAS/D	3.47 ± 1.29	1.86-6.44
UARI	0.69 ± 0.13	0.48-1.00
MCARI	0.73 ± 0.09	0.58-0.89
MCAPI	1.28 ± 0.34	0.75-2.13
UARI/MCARI	0.97 ± 0.28	0.54-1.73
MCARI/UARI	1.10 ± 0.26	0.58-1.50
UAPI/MCAPI	0.92 ± 0.46	0.40-2.57

SD: standard deviation, SVD: spontaneous vaginal delivery, C/S: cesarean section, IVD: induced vaginal delivery, NICU: neonatal intensive care unit, UA: umbilical artery, S/D: systole/diastole, RI: resistive index, MCA: middle cerebral artery, PI: pulsatility index

Table 3: Comparison of the UA and cerebral Doppler data between pregnancies presenting with IUGR and healthy pregnancies.

	IUGR (n=21)	Healthy (n=63)	
	Mean ± SD	Mean ± SD	p
Fetal weight at birth (g)	1,515.29 ± 464.80	3,245.24 ± 560.3	0.03
UA S/D	4.20 ± 1.42	2.50 ± 0.30	0.03
UA RI	0.75 ± 0.14	0.59 ± 0.06	0.09
MCA RI	0.72 ± 0.09	0.79 ± 0.083	0.66
MCA PI	1.20 ± 0.36	1.46 ± 0.36	0.37
MCA RI/UA RI	1.01 ± 0.30	1.34 ± 0.19	0.20
MCA PI/UA PI	1.11 ±0.57	1.77 ± 0.43	0.153

IUGR: intrauterine growth restriction, SD: standard deviation,UA: umbilical artery, S/D: systole/diastole, RI: resistive index, MCA: middle cerebral artery, PI: pulsatility index

Table 4: Comparison of the clinical and Doppler artery index parameters between healthy and preeclamptic pregnancies

	Healthy (n = 63) Mean ± SD	Preeclamptic (n = 59) Mean ± SD	p
Age (year)	26.58 ± 4.55	26.68 ± 5.71	0.02
Gravida	2.25 ± 1.27	2.63 ± 2.20	0.24
Gestational age at birth (week)	38.48 ± 1.70	36.25 ± 3.03	**< 0.001**
Fifth-minute Apgar score	9.14 ± 0.43	6.67 ± 3.65	**< 0.001**
Fetal weight at birth (g)	3245.24 ± 560.3	2258.81 ± 944.99	**< 0.001**
UA S/D	2.50 ± 0.30	3.47 ± 1.29	**< 0.001**
UA RI	0.59 ± 0.06	0.69 ± 0.13	**< 0.001**
MCA RI	0.79 ± 0.06	0.73 ± 0.09	**< 0.001**
MCA PI	1.46 ± 0.36	1.28 ± 0.34	0.003
UA RI/MCA RI	0.76 ± 0.09	0.97 ± 0.28	**< 0.001**
MCA RI/UA RI	1.34 ± 0.19	1.10 ± 0.26	**< 0.001**
MCA PI/UA PI	1.77 ± 0.43	1.31 ± 0.54	**< 0.001**

SD: standard deviation, UA: umbilical artery, S/D: systole/diastole, RI: resistive index, MCA: middle cerebral artery, PI: pulsatility index

had a premature delivery. Intracerebral hemorrhage was detected in one of the fetuses that died in the intrauterine period.Among the 21 cases with IUGR , the S/D ratio of the UA was pathological in 16 cases, and the RI and PI values of the MCA were pathological in nine cases each.

Discussion

Preeclampsia is a specific complication of pregnancy, characterized by high blood pressure, proteinuria, and edema (3). Doppler USG is used in the evaluation of normal pregnancies and high-risk pregnant women, such as those with preeclampsia.Doppler evaluations of the uterine artery, UA, ductus venosus , and MCAare frequently undertaken due to the widespread clinical use of this imaging modality and the importance of the results in terms of fetal-placental hemodynamics (8). The current study was conducted with healthy pregnant women and preeclamptic pregnant women at a gestational age of over 31 weeks, considering that UA values show high variations before the 30th gestational week.

It has been reported that placental vascular resistance decreases, end-diastolic flow velocities increase, and the UA index decreases in the advancing weeks of gestation in normal pregnancies. However, in preeclamptic pregnant women, due to the increase in vascular resistance, end-diastolic flow decreases, and the UA index increases (4,8). Divon et al. accepted a UAS/D value of greater than 3.00 to be pathological in women at a gestational age of 30 weeks and above.In our study, the mean S/D value of the UA was calculated to be 2.50±0.30 for the healthy control group and higher than normal (3.47±1.29)for pregnant women with preeclampsia. In addition, the increase in the UAS/D value was higher in cases of IUGR (4.20±1.42). Incontrast, parallel with the decrease that occurs in vasodilation and vascular resistance as the gestational week progresses, the UA RI valuedoes notdecrease.

Zimmerman et al. (8) accepted the mean UA RI value of healthy pregnant women as 0.62 and pathological at above 0.62. In the current study, the mean UA RI value was (0.59 ± 0.06) for the healthy control, consistent with the commonly used cut-off value of 0.62 in the literature.We determined the UA RI value to be 0.69 in pregnant women with preeclampsia and 0.75 in cases of IUGR.

Sekizuka (9) reported the sensitivity and specificity of the UA RI value to be 61.8% and 84.6%, respectively, in the detection of IUGR. In our study, the UA RI value had higher diagnostic accuracy and sensitivity(75% and 73%, respectively) than the UAS/D value (70% and 64%, respectively) in thedetermination of UBOs . However, despite the higher sensitivity of the UA RI valuein the detection of IUGR (80 % vs. 71% , respectively), both the UA RI and the UAS/D had the same diagnostic accuracy (64%)in determining IUGR.

Abnormal UA waveforms have been described in 60% of fetuses with developmental delays. In these pregnancies, a significant decrease is observed in the end-diastolic flow velocity due to the increase in placental resistance. Diastolic flow may disappear or be reversed.In such cases, if the fetus is not delivered, fetal deathmay occur within the 12-24 hour period (10).

The first Doppler study in cerebral arterieswas undertaken by Bada et al. in 1979, and the Doppler index values were found to be lower than normal in cases of hypoxia.During hypoxia, vasodilation develops in cerebral arteries, and the amount of blood flowing to the brain increases, which is known as the brain protection effect (11). As a result of vasodilation in cerebral arteries, vascular

Table 5: Diagnostic value of the fetal Doppler indices in detecting cases of IUGR among preeclamptic pregnant women.

	Sensitivity	Specificity	PPV	NPV	Diagnostic accuracy
UA S/D >1 SD	15/21 (71%)	23/38 (61%)	15/30 (50%)	23/29 (80%)	38/59 (64%)
UA RI >1 SD	17/21 (81%)	21/38 (55%)	17/34 (50%)	21/25 (84%)	38/59 (64%)
MCA RI >1 SD	10/21 (48%)	19/38 (50%)	10/29 (34%)	19/30 (63%)	29/59 (49%)
MCA PI >1 SD	10/21 (48%)	29/38 (76%)	10/19 (53%)	29/30 (73%)	39/59 (63%)
UA RI/MCA RI >1 SD	16/21 (76%)	21/38 (55%)	16/33 (48%)	21/26 (81%)	37/59 (63%)
MCA RI/UA RI >1 SD	15/21 (71%)	22/38 (58%)	15/31 (48%)	22/28 (79%)	37/59 (63%)
UA PI/MCA PI >1 SD	15/21 (71%)	22/38 (58%)	15/31 (48%)	22/28 (79%)	37/59 (63%)
MCA PI/UA PI >1 SD	15/21 (71%)	21/38 (55%)	15/32 (47%)	21/27 (78%)	36/59 (61%)

PPV: positive predictive value, NPV: negative predictive value, SD: standard deviation, UA: umbilical artery, S/D: systole/diastole, RI: resistive index, MCA: middle cerebral artery, PI: pulsatility index

resistance decreases and end-diastole flow increases.This results in a decrease in Doppler index values (RI and PI). Sekizuka (9) also found that the UA RI value increased, and the MCA RI value decreased in preeclamptic pregnant women.In the healthy pregnant group included in our study, the mean MCA RI value was 0.79 ± 0.083, with one standard deviation (SD) below the mean being calculated as 0.71, and the mean MCA PI value was 1.46 ± 0.36, with one SDbelow the mean being calculated as 1.10. While the UA Doppler index values are observed to be pathological in some fetuses in pregnancies with severe preeclampsia, the cerebral artery Doppler index values may be normal.In the literature, this situation is explained by the failure of the brain protection effect in fetuses affected by hypoxia (11). In our study, of the 21 casesthat developed IUGR as a result of severe hypoxia, 16 had a pathological UAS/D value, nine patients had a pathological MCA RIvalue, and 10 cases had a pathological MCA PI value .

It is stated that the ratio of the fetal cerebral artery and UA indices is more effective than other indices in determining poor perinatal outcomes and is more related to IUGR (5).The MCA RI/UA RI ratio is above 1 in normal pregnancies and below 1 in preeclamptic pregnancies. We determined the MCA/UA RI ratio to be lower than normal in pregnant women with preeclampsia (1.10±0.26).This decrease was even more prominent in cases that developed IUGR (1.01±0.30).The MCA RI/UA RI ratio was found to be pathological in 12 of the 21 pregnancies presenting with IUGR. In our study, one SD of the mean MCA PI/UA PI ratio (1.77±0.43) was calculated to be 1.33. The MCA PI/UA PI ratio was found to be lower than normal in preeclamptic pregnancies (1). The decrease in the ratio was more pronounced in cases of IUGR (1, 9). The MCA PI/UA PI ratio was pathological in 12 of the 21 pregnancies that developed IUGR. In our study, there was no significant difference in the sensitivity of the MCA RI/UA RI and MCA PI/UA PI ratios in determining IUGR; however, the MCA RI/UA RIratiohad higher diagnostic accuracy (63%, 61%, respectively). No statistically significant difference was detectedin the sensitivity or diagnostic accuracy of the Doppler indices in determining UBOs.

In conclusion, the umbilical and cerebral artery Doppler indices were found to be high in preeclamptic pregnant women. This elevation was more pronounced in cases of IUGR. The combined use of umbilical and cerebral Doppler indices in determining UBOs increased their sensitivity, specificity, and diagnostic accuracy. Lastly, umbilical and cerebral Doppler indices had lower diagnostic accuracy in determining IUGR, and the combined use of these indices did not result in an increase in diagnostic accuracy.

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