The value of the middle cerebral to umbilical artery Doppler ratio in the prediction of neonatal outcome in patient with preeclampsia and gestational hypertension

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Summary

Objective: To investigate the diagnostic value of MCA/UA pulsatility index ratio for the prediction of adverse perinatal outcome in the fetuses with preeclampsia and gestational hypertension.
Materials and methods: We included in the study 738 patients recovered in our Hospital with the diagnosis of preeclampsia and gestational hypertension, from January 2006 to December 2009. All the patients underwent accurate color Doppler velocimetry examination. The study population was divided into two groups depending on the normal or abnormal values of MCA/UA pulsatility index ratio. Outcome variables were intrauterine and early neonatal death, admission to the neonatal intensive care unit and the duration of treatment, Apgar score below 7 at 5 minutes,cesarean delivery for fetal distress, gestational age at delivery, neonatal birth weight, IUGR.
Results: We divided the study population into two groups depending on normal or abnormal value of MCA/UA pulsatility index ratio. In 314 patients we found abnormal values of MCA/UA pulsatility index ratio. Neonates of mothers with abnormal values of MCA/UA pulsatility index ratio had significantly lower gestational age at delivery (34.8 versus 38.4, P<0.0001), lower birth weight (2174.6 g versus 3215.0g, P<0.001), significantly greater risk for perinatal death (30.8% versus 0.23%, P<0.0001) significantly greater risk of admission to intensive care unit (77.8% versus 47.4%, P<0.0001), longer duration of treatment in NICU (10.6 days versus 6.5 days, P<0.0001), greater rate of cesarean delivery for fetal distress (76.7% versus 62.5%,P<0.0001), a great number of neonates with low Apgar score at 5 minute (61.9% versus 22.4%, P<0.0001) greater rate of cesarean delivery for fetal distress (71.9% versus 62.5%,P<0.0001), a great number of fetuses IUGR (7.18% versus 1.76%,P<0.0001).
Conclusion: ACM/UA pulsatility index ratio is a very good predictor of adverse outcome in the fetuses of women with preeclampsia and gestational hypertension.

Key Words: Doppler, preeclampsia, gestational hypertension.

Introduction

Preeclampsia affects 5-10% of pregnancies and is a major cause of maternal and fetal morbidity and mortality (1,2).
Although there is no proven effective method for the prevention of the preeclampsia, routine antenatal care has the aim to identify women who are at risk for more intensive antenatal care.
Abnormal placentacion is a main preeclampsia characteristic. Its cause is a maternal spiral veins trophoblastic invasion failure, which conditions vascular resistances raise and uterus-placental perfusion decrease.
For the first time Satomura demonstrated that the Doppler technique could evaluate blood flow (3). Nowadays, Doppler ultrasound velocimetry of uteroplacental umbilical and fetal vessels has become established method of antenatal monitoring, allowing the noninvasive assessment of fetal circulation (4). Its indices provide important information on the hemodynamics of the vascular area under study (5). Circulatory changes, reflected in certain fetal Doppler waveforms, predict adverse perinatal outcome (6).
Umbilical arteries are the common vessels assessed by Doppler ultrasound, but recent studies confirm the efficacy of middle cerebral artery (MCA) Doppler assessment and advocate it (7,8). MCA Doppler measurement is a well-known modality for detecting fetal compromise (9). Some studies has showed that MCA blood flow abnormalities were associated with hypoxia (1,8,10) and adverse perinatal outcome (11). Relationship between fetal Doppler findings and perinatal risks have been defined in numerous cross-sectional studies (12).
Several studies have reported higher sensitivities and specificities for middle cerebral artery/umbilical artery (MCA/UA) Doppler ratio compared with umbilical artery velocimetry alone for the prediction of the fetal prognosis (13-16).
MCA/UA ratio reflects not only the circulatory insufficiency of the umbilical velocimetry of the placenta manifested by alterations in the umbilical S/D ratio but also the adaptive changes resulting in modifications of the mid-

dle cerebral S/D ratio (13). In this study we evaluated the predicting value of the MCA/UA ratio, for fetal prognosis in women with gestational hypertension and preeclampsia.

Materials and methods

The study group consisted of 738 singleton pregnancies of women with preeclampsia and gestational hypertension who were recovered at the University Hospital of Obstetric and Gynecology of Tirana and delivered between January 2008-January 2009. The pregnancy outcome and clinical data of all women were collected from Hospital records following delivery.

The gestational age of all women was confirmed, either by menstrual dates or by first trimester ultrasonography. Preeclampsia was diagnosed in those women who were normotensive during early pregnancy, but later demonstrated elevated blood pressure. All of them had a mild (systolic blood pressure > 140 mmHg, diastolic >90 mmHg and proteinuria 300 mg/24 h or = + 1 dipstick) or severe preeclampsia (systolic blood pressure > 160 mmHg, diastolic > 100 mmHg and severe proteinuria 2 g/24 h or +2 dipstick). The diagnosis of gestational hypertension was made in women whose blood pressure reached 140/ 90 mmHg or greater for the first time during pregnancy but in whom proteinuria was not developed (17.) Women with twin pregnancies, chromosomal abnormalities, gestational diabetes, were excluded from the study. Those included were followed by periodical Doppler flow measurements at least one time per week measurements until delivery.

The UA color Doppler waveforms were obtained from a free floating portion of the umbilical cord during minimal fetal activity and the absence of fetal breathing. All measurements were performed in the semi recumbent positions with the head and chest slightly elevated. For measurement of the MCA, an axial view of the fetal head was obtained at the level of cerebral peduncles, then the color Doppler was used to visualize the circle of Willis, and Doppler sample volume was placed within 1 cm of the origin of the MCA that was easily identified as a major branch running anterolateral from the circle of Willis toward to the lateral edge of the orbit. The angle between the ultrasonographic beam and direction of blood flow was always <30 degrees. The Doppler signals were recorded with a 3.5 mHz curved array duplex transducer.

The UA pulsatility index were considered abnormal when the values were >2SD,the MCA pulsatility index was considered abnormal when the values were <5th percentile. MCA/UA PI<1 was considered abnormal (18). The reference values are according to Gramellini et al. (19).

Major adverse perinatal outcome were stillbirth and neonatal death. Minor adverse perinatal outcome were cesarean delivery for fetal distress, admission to the neonatal intensive care unit, Apgar score below 7 at 5 minutes, IUGR fetuses.

Statistical analysis included the χ^2 test to compare proportions and the non paired Student t test to compare continuous variables.Also we used the test of sensitivity specificity, positive and negative predictive values and likelihood ratios. P values less than 0.05 were considered statistically significant.

Table I - Maternal characteristics in correlation with normal or abnormal MCA/UA ratio.

	MCA/UA>1 (n=424)	MCA/UA<1 (n=314)	Statistical Tests values	P value
Maternal age	27.3+/-5.0	31.1+/-7.2		
Gestational age at delivery (week)	38.4	34.8	t-13.86	<0.0001
Gravidity	2.5+/-3.2	3.6+/-2.1		
Proteinuria	323 (76.1%)	281 (89.4%)	+0.17 (χ^2)	<0.0001
Cesarean delivery	265 (62.5%)	241 (76.7%)	+0.15 (χ^2)	<0.0001
Vaginal delivery	159 (37.5%)	73 (23.2%)	-0.15(χ^2)	<0.0001

Results

The 738 women underwent Doppler sonography until delivery. The results of the last Doppler sonography examination before delivery were collected for the statistical analyzes. The study population was divided into 2 groups based on the MCA/UA ratio. Group A, MCA/UA ratio>1 (n=424); group B MCA/UA ratio <=1 (n=314). There were no significant differences in maternal age and gravidity. There is a statistical significant difference in gestational age at delivery between two groups, route of delivery and proteinuria between two groups (P<0.0001) (Table I).

The characteristics of the neonates are summarized in table 2 from the total of 738 delivery there were 481 (65.18 %) term babies. There were 54 (7.3%) stillbirths and 684 livebirths 44 (5.96%) neonates died within neonatal period. Of the 684 livebirths, 457 (66.81%) were admitted to the neonatal intensive care unit, 310 (45.32%) neonates have Apgar score less than 7 at 5 minute. There were 506 (73.97%) cesarean delivery for fetal distress. IUGR was diagnosed in 8.94% of cases.

As showed in table III, a statistically significant difference in neonatal weight and gestational age at delivery was found between the two groups (P<0.0001). There was a significant increase in perinatal deaths in cases with abnormal MCA/UA PI ratio, 97 cases (30.8%) versus 1 case (0.23%) (P <0.0001). All the stillbirths were

Table II - Neonatal characteristics of the study population.

Neonatal characteristics	No	%
Term babies	481	65.18
Stillbirth	54	7.31
Neonatal deaths	44	5.96
Perinatal deaths	98	13.27
Admission to NICU	403	58.91
Apgar at 5 min <7	256	37.42
Cesarean delivery for fetal distress	506	73.97
IUGR	66	8.94

in the group of abnormal MCA/UA PI ratio.There is a statistically significant difference in neonatal deaths between two groups, 43 (13.6%) versus 1 (0.23%) (P<0.0001).

Perinatal morbidity is increased significantly in the group with abnormal MCA/UA pulsatility index comparing to the group with normal MCA/UA pulsatility index ratio; 202 neonates (77.6%) versus 201 neonates (47.4%) were admitted to neonatal intensive care unit (NICU) (P<0,0001). There is a significant difference between the duration (in days) of treatment at neonatal intensive care unit (10.6 days versus 6.5 days) (P<0.0001).

It was found to be more neonates with Apgar scores less than 7 at 5 minute in the group with abnormal MCA/UA PI ratio than in group with normal MCA/ UA PI ratio 161 (61.9%) versus 95 (22.4%) (P<0.0001).

It was found a statistically difference between two

Table III - Minor and major adverse perinatal outcome in correlation with two groups of MCA/UA pulsatility index ratio.

	Normal MCA/UA (n=424)	Abnormal MCA/UA (n=314)	Statistical tests value	P - value
Average birth weight (grams)	3215.0	2174.6	-18.8 (t)	<.0001
Gestational age(weeks)	38.4	34.8	-13.86 (t)	<.0001
Perinatal deaths	1 (0.23%)	97 (30.8%)	+0.45 (χ^2)	<.0001
Stillbirths	0 (0%)	54 (17.1%)	+0.33 (χ^2)	<.0001
Neonatal deaths	1 (0.23%)	43 (13.6%)	+0.32 (χ^2)	<.0001
Need for NICU	201 (47.4%)	202 (77.6%)	+0.3 (χ^2)	<.0001
Duration of treatment to NICU	6.5 (days)	10.6 (days)	-10.49 (t)	<.0001
Apgar < 7 at 5 minute	95 (22.4%)	161 (61.9%)	+0.4 (χ^2)	<.0001
Cesarean delivery for fetal distress	265 (62.5%)	187 (71.9%)	+0.1 (χ^2)	0.01
IUGR	13 (1.76%)	53 (7.18%)	+0.24 (χ^2)	<.0001

Table IV - Diagnostic performance of MCA/UA pulsatility index ratio for major and minor adverse outcome.

Perinatal outcome	TP	FN	FP	TN	Sensitivity	Specificity	Predictive value Positive	Predictive value Negative	Likelihood ratio Positive	Likelihood ratio Negative
Perinatal deaths	97	1	217	423	98% (93.6, 99.9)	66% (62.2, 69.7)	30.8 (25.8, 36.3)	99.7 (98.4, 99.9)	2.9 (2.61, 3.25)	0.01 (0.002, 0.108)
Stillbirths	54	260	0	424	100 (91.7, 1.00)	61 (58, 265.6)	17.1 (13, 221.9)	100 (98.8, 1.00)	2.6 (2.93, 2.89)	0 (0,None)
Neonatal deaths	43	1	217	423	97.7 (86.4, 99.8)	66.0 (62.2, 69.7)	16.5 (12.3, 21.7)	99.7 (98, 499.9)	2.88 (2.56, 3.24)	0.03 (0.004, 0.239)
Need for NICU	202	201	58	223	50.1 (45.1, 55.1)	79.3 (74.0, 83.8)	77.6 (72.o, 82.5)	52.5 (47.7, 57.4)	2.42 (1.89, 3.11)	0.62 (0.56, 0.69)
S/c for fetal distress	187	265	73	159	41.3 (36.8, 46.0)	68.5 (62.0, 74.3)	71.9 (65.9, 77.2)	37.5 (32.9, 42.3)	1.31 (1.05, 1.63)	0.85 (0.78, 0.92)
Apgar < 7 at 5 min	161	95	99	329	62.8 (56.6, 68.7)	76.8 (72.5, 80.7)	61.9 (55.6, 66.7)	77.5 (73.2, 81.4)	2.71 (2.23, 3.30)	0.48 (0.41, 0.56)
IUGR	53	13	261	411	80.3 (68.3, 88.6)	61.1 (57.3, 64.8)	16.8 (13.0, 21.5)	96.9 (94.6, 98.2)	2.06 (1.77,2.40)	0.32 (0.19, 0.52)

groups for the elective cesarean delivery for fetal distress (P=0.01).
There are more IUGR cases in the group with MCA/UA <1 (7.18% versus 1.76%), there is a significant difference between two groups (P<0.0001).
Table IV show the sensitivity, specificity, positive predictive value, negative predictive value, and likelihood ratios positive and negative of MCA/UA PI ratio for major and minor adverse outcome. MCA/UA PI ratio <1 has the higher sensitivity (100%) for stillbirth, higher specificity and positive predicted value for admission to neonatal care unit (79.3% and 77.6%). The likelihood positive ratio for th MCA/UA PI ratio<1 was higher in perinatal deaths (2.9). Table 5 show a comparation of densitivity, specificity, positive predictive value negative predictive value of MCA/UA in our study and in those of Gramellini et al. (19).

Table V - Comparation of our results of the sensitivity, specificity, positive predictive value, negative predictive value of MCA/UA ratio with those of the study of Gramellini et al.

	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Gramellini D	68.0%	98.4%	94.4%	88.0%
Our study	98%	66%	30.8%	99.7%

Discussion

Advances in Doppler ultrasonography have improved access to the fetal circulation. There has been a great deal of interest in the fetal intracranial vessels (20). Knowledge of Doppler flow velocimetry of the fetal MCA may assist in perinatal diagnosis and management of complicated pregnancies. A low index of pulsatility in the middle cerebral artery associated with fetal compromise has been described (21-24). Because the MCA/UA ratio incorporates data not only on placental status but also on fetal response, it is potentially more advantageous in predicting perinatal outcome. Doppler data combining both umbilical and cerebral velocimetry provide additional information on fetal consequences of the placental abnormality (25).
Abnormal MCA/UA PI Doppler ratio is strongly correlated with worse fetal prognosis. In normal pregnancies the diastolic component in the cerebral arteries is lower than in the umbilical arteries at any gestational age. Therefore, the cerebro-vascular resistance remains higher than the placental resistance and the MCA/UA ratio is greater than 1. The index becomes less than 1 if the flow distribution is in favor of the brain in pathological pregnancies. We observed reduction in placental perfusion and an increase in flow towards the brain. This phenomenon, called the brain sparing effect, is supposed to compensate for fetal hypoxia and is associated most of the time with fetal growth retardation with low umbilical artery pH. The cerebrovascular index decreases progressively, as in the normal fetuses so the hypoxia to be compensated by the brain hyperperfusion (26).
Fetuses with abnormal Doppler MCA/UA PI ratio in our study had a significantly lower birth weight, lower gestational age at delivery, l significantly higher incidence of perinatal deaths, higher incidence of admission to NICU and longer duration of treatment there, lower Apgar score at 5 minute (22).
Brar et al. (23) recognized that Doppler studies of the internal carotid artery or a ratio of cerebral to umbilical resistance could be used to identify pregnancies with a compromised post date fetus. The fetuses in our study with adverse outcome had a lower middle cerebral artery PI index, supporting the finding of Brar et al. (27). According to Gramellini et al. and Arduini et al, assessment of MCA/UA PI index provide better information in predicting perinatal outcome when compared with umbilical or middle cerebral artery Doppler indices alone (19,28). In our study we found high sensitivity of the MCA/UA PI ratio in predicting stillbirth (100%). Also we found a high specificity and positive predicting value in need for treatment in neonatal intensive care unit.
Arduini and Rizzo (14) studied the test characteristics of the pulsatility index from UA, MCA and RA to predict adverse perinatal outcome in 120 SGA fetuses. In 46.7% (56 of 120) of fetuses there was at least one of the following adverse outcomes: perinatal deaths, cesarean delivery for fetal distress, asphyxia that necessitate admission to the neonatal intensive care unit for more than 48 hours. The author found that UA/MCA PI index ratio was the best test when compared with MCA, UA, and RA PI indices (sensitivity 89%, specificity 94%).
Doppler velocimetry studies of placental and fetal circulation can provide important information regarding fetal well-being, yielding an opportunity to improve fetal outcome. Our results suggested that the MCA/UA PI Doppler ratio of less than 1 was a good predictive tool for neonatal outcome in preeclamptic and hypertensive pregnant women and could be used to identify fetuses at risk of morbidity and mortality.
The use of Doppler ultrasound in high risk pregnancies appears to improve a number of obstetric care outcomes and promising in reducing perinatal deaths (20).

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