CEREBRAL-UMBILICAL DOPPLER RATIO AS PREDICTOR OF PERINATAL OUTCOME IN PREGNANCIES WITH HYPERTENSION DISORDERS

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BACKGROUND & OBJECTIVES: Doppler velocity study of placental and fetal circulation can provide important information about fetal wellbeing, thus providing an opportunity to improve fetal outcome. The present study was undertaken to evaluate the role of middle cerebral artery and uterine artery pulsatility index as a predictor of perinatal outcome in PIH and hypertensive patients in late third trimester. **METHOD:** 150 Pre-eclamptic and gestational hypertension patients were selected randomly in last weeks of third trimester and were stratified into two groups based on MCA/UA PI ratio. 110 women were in group A (RATIO >1.08) and 40 women in group B (RATIO <1.08). The results of the ratio were evaluated with respect to the perinatal outcome, LSCS for fetal distress, neonatal morbidity and mortality and APGAR SCORE. **RESULTS:** Rate of LSCS was significantly high ($P < 0.001$) in group B than group A. There was a statistically significant increase in perinatal morbidity in group B. APGAR SCORES were found to be lower in group B than group A. In group A 35 (31.8%) were IUGR babies and 37 (92.5%) in group B. Stillbirth were 2 (1.8%) in group A and 3 (7.5%) in group B. **INTERPRETATION AND CONCLUSION:** The MCA/UA PI Ratio is valuable for predicting the perinatal outcome in pre-eclampsia and hypertension pregnancies. When the ratio is <1.08, the fetal prognosis is poor.

KEYWORDS-umbilical artery, middle cerebral artery, perinatal morbidity

INTRODUCTION: Obstetrics concerns not only with the wellbeing of the mother but also the fetus. Hypertension disorders in pregnancy are one of the serious medical disorders during pregnancy affecting both mother and fetus. Doppler is a rapid noninvasive test to know the hemodynamic condition of the fetoplacental unit. In preeclampsia, placental insufficiency due to increased vascular impedance is reflected by raised pulsatility index in the umbilical artery. High flow resistance in the capillaries of the terminal villi lead to low end diastolic flow in the umbilical artery and consequent hypoxia. Vasodilatation of the cerebral arteries as compensatory mechanism to preserve adequate oxygen supply to brain is reflected by decreased pulsatility index in the cerebral arteries. Several studies^{2, 3, 4, 6} have reported higher sensitivities and specificities for MCA/UA doppler ratio compared with umbilical artery alone for the prediction of fetal prognosis. MCA/UA doppler ratio reflects not only the circulatory insufficiency of the umbilical velocimetry of the placenta but also the adaptive changes resulting in the modification of the MCA/UA PI ratio.

The aim of this study was to evaluate the role of MCA/UA PI ratio in predicting perinatal outcome in pregnancies with hypertension disorders. It will help in timely delivery of the hypoxic fetus to prevent IUFD and long term adverse effects.

MATERIAL AND METHODS: It is a prospective study done over a period of three years from August 2009 to August 2012 in GMC Aurangabad. A total of 150 women with singleton cephalic pregnancies

within 31 to 40 weeks of gestation with hypertension disorders of pregnancy were included in our study after obtaining informed consent. Approval for the study was obtained from the ethics committee of the institution. The gestational age of all women was confirmed by last menstrual period and first trimester ultrasonography. Preeclampsia was diagnosed in these women who were normotensive during early pregnancy, but later demonstrated elevated blood pressure with proteinuria. Mild preeclampsia was diagnosed when blood pressure was systolic >140 , diastolic >90 and proteinuria $>1+$. Severe preeclampsia was diagnosed when blood pressure was systolic >160 , diastolic >110 and proteinuria $>2+$. The diagnosis of gestational hypertension was made in women whose blood pressure reached 140/90 mm Hg or greater for the first time during pregnancy but no proteinuria. Women with multifetal pregnancies, medical disorder other than hypertension, congenital anomalies were excluded from the study.

The study population was antenatally assessed by doppler ultrasound at 4 weekly intervals and 48 hours before delivery by senior radiologist (associate professor). Doppler examinations were performed with 3.5 to 5 MHz transducers using Philips medical systems. During the examination, patient was in semirecumbent position and fetus was in quiet resting state. Measurements were obtained from the middle section of the middle cerebral artery (MCA) and the umbilical artery (UA) doppler signal from the free loop. The angle of insonation was maintained as close to 0 degree as possible when interrogating the middle cerebral artery. After technically satisfactory doppler waveforms had been recorded, the pulsatility index of the umbilical artery (UA PI) and the pulsatility index of the middle cerebral artery (MCA PI) was noted and the ratio of MCA PI/UA PI was calculated. The last doppler reports of the study population were used for our analyses. Cerebroplacental doppler ratio measurements were not revealed to treating obstetricians for clinical management.

Considering 1.08 as the lower limit of normal MCA/ UA PI ratio (Gramellini et al¹) study population was divided into two groups-Group A with MCA/UA PI >1.08 and Group B with MCA/UA PI <1.08 . These both groups were followed up and their labour, delivery and neonatal records were studied. Group A and Group B were compared for perinatal outcomes. Perinatal outcomes were considered adverse if any one or more of the major or minor perinatal outcomes occurred:^{2, 3, 4} Major adverse included perinatal death, hypoxic ischemic encephalopathy, intra or periventricular haemorrhage and necrotizing enterocolitis. Minor adverse included caesarean delivery for fetal distress, Apgar score <7 at 5 minutes, respiratory distress syndrome, meconium aspiration syndrome, NICU admission <4 days/ >4 days, sepsis, hyperbilirubinemia, perinatal asphyxia and IUGR. Statistical analysis was performed with the help of the software 'GraphpadPrism5'. For comparing quantitative data between the study groups unpaired 't' test was applied. Comparison of non-parametric (qualitative) data between the study groups was done using "Chi-square test for trend" and "Fisher Exact test" depending on types of data. Also sensitivity, specificity and predictive values of MCA/UA PI ratio <1.08 for major, minor adverse perinatal outcomes and IUGR were calculated using software.

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RESULTS:

Maternal characteristics	Group A n=110	Group B n=40	p value
Mean Maternal age (mean+/-2S.D)	23.27+/-3.563	23.50+/-3.644	0.7318
Body mass index(kg/m2) (mean +/-2S.D)	24.15+/-1.487	24.48+/-1.505	0.2377
Gravidity Primigravida Multigravida	50% 50%	47.5% 52.5%	0.5229
Pregnancy induced hypertension Mild preeclampsia Severe preeclampsia Gestational hypertension	55.5% 42.7% 1.8%	7.5% 92.5% -	<0.0001 <0.0001 1.0000
Mean gestational age at the time of delivery(weeks)	36.66+/-1.939	34.80+/-2.080	<0.0001
Delivery Vaginal LSCS	81.8% 18.2%	62.5% 37.5%	0.0337 0.0172

Table no.1

Neonatal characteristics	Group A n=110	Group B n=40	p value
Birth weight(grams) Mean+/-2S.D	2203+/-574.1	1521+/-366.3	<0.0001
Preterm	50%	75%	<0.0001
Apgar <7 at 5 minutes	0.9%	10.8%	0.0152
NICU admissions	38.18%	87.5%	<0.0001
NICU stay>4 days	26.36%	70%	<0.0001
IUGR(Birth weight<10 th percentile)	31.8%	92.5%	<0.0001
Perinatal deaths Still births +neonatal deaths	3.6%	30%	<0.0001
LSCS for fetal distress	25%	86.7%	0.0248

Table no. 2

Mean PI	Mild preeclampsia	Severe preeclampsia	p value
MCA PI Mean+/-S.D	1.363+/-0.2440	1.400+/-0.3145	0.4354
UA PI Mean +/-S.D	0.9253+/-0.0808	1.238+/-0.3282	<0.0001

Table no. 3

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Umbilical artery		Middle cerebral artery			C/U ratio	Fetal outcome	Birth weight(g)	Apgar at 1 and 5 min	NICU admission
PI	RI	PI	RI	SD					
2.9	REDV	1.3	0.66	2.9	0.45	IUD at 31.2 wks	1000 g		
1.94	AEDV	1.16	0.52	2.4	0.59	IUD at 32 wks	1100 g		
1.32	AEDV	1.3	0.7	3.2	0.98	LSCS at 36.4 wks	1600 g	6 and 7	>4 days

Table no. 4

Diagnostic accuracy	Major adverse	Minor adverse	IUGR
Sensitivity	75%	44.32%	51.39%
Specificity	79%	98.39%	96.15%
Positive predictive value	30%	97.5%	92.5%
Negative predictive value	96.36%	55.45%	68.18%

Table no. 5: Diagnostic accuracy of MCA/UA PI in predicting major and minor adverse perinatal outcome and IUGR

The characteristics of the study population are shown in table no.1. There was no statistical significant difference in both groups A and B with respect to the maternal age, body mass index and gravidity. There was statistically significant difference in the incidence of severity of preeclampsia. Mild preeclampsia was found to be statistically significant higher in group A (55.5%) Vs group B (7.5%) while severe preeclampsia was statistically significant higher in group B (92.5%) Vs group A (42.7%).No statistical significant difference was found in both the groups with respect to gestational hypertension. The mean gestational age at the time of delivery was significantly lower in group B (34.80+/-2.080 weeks) Vs group A (36.66+/-1.939 weeks).In both the groups majority delivered vaginally but percentage of cesarean deliveries was significantly higher in group B (37.5%) Vs group A (18.2%).

Table no.2 shows mean UA PI in study population with mild pre-eclampsia was 0.9253+/-0.0809 and in those with severe pre-eclampsia was 1.238+/-0.3282 with statistically significant higher mean UA PI in those with severe pre-eclampsia (p value<0.0001).Mean MCA PI in those with mild preeclampsia was 1.363+/-0.2440 and in those with severe preeclampsia was 1.400+/-0.3145 with no statistical significant difference in mild and severe preeclampsia.

In table no.3, both the groups, group A with normal MCA/UA PI > 1.08 and group B with abnormal MCA/UA PI<1.08 were compared for perinatal outcomes. It was found that the perinatal outcome was adverse in group B than in group A with the mean birth weight significantly lesser in group B(1521+/- 366.3 grams) Vs group A(2203+/-574.1 grams), greater number of neonates with IUGR defined as birth weight less than 10th percentile in group B(92.5%) Vs group A (31.8%) and more preterm babies in group B (75%) Vs group A (50%). It was found that greater number of babies in group B had lower Apgar scores <7 at 5 minutes (10.8%) Vs group A (0.9%), statistically

significantly more NICU admissions in group B (87.5%) Vs group A (38.18%), longer NICU stay of more than 4 days in group B (70%) Vs group A (26.36%) and statistically greater number of perinatal deaths in group B (30%) Vs group A (3.6%). Also significantly higher percentage of LSCS for fetal distress in group B (86.7%) Vs group A (25%) lead to adverse perinatal outcome in group B than in group A.

Table no.4 shows subjects with absent end diastolic velocity and reversed end diastolic velocity in umbilical artery had MCA/UA PI<1.08. One with REDV had IUD and among two with AEDV, one with low MCA values had IUD and one with normal MCA values had LSCS for fetal distress with the baby requiring NICU admission for more than 4 days.

In table no.5, the sensitivity, specificity, positive predictive value and negative predictive value of MCA/UA PI <1.08 to predict major and minor adverse perinatal outcomes as well as IUGR was calculated. The ratio had high negative predictive value (96.36%), moderate sensitivity (75%) and moderate specificity (79%) to predict major adverse perinatal outcome. It had high specificity (98.39%) and high positive predictive value (97.5%) to predict minor adverse perinatal outcome. Also, specificity and positive predictive value to predict IUGR was high-96.15% and 92.5% respectively.

DISCUSSION: In this study, MCA/UA PI 48 hours before delivery was evaluated to predict perinatal outcome. The mean UA PI was statistically significantly higher in those with severe preeclampsia than in mild preeclampsia stressing the fact that there is increased uteroplacental resistance in severe preeclampsia. There was no statistical difference in the mean MCA PI in those with mild preeclampsia and severe pre-eclampsia. It can be explained as MCA PI decreases with the compensatory mechanism of brain sparing effect, it again goes on increasing with increasing cerebral oedema due to hypoxia as the brain sparing effect goes on decreasing.

The findings in our study correlate with the studies done by Rozela Shahinaj et al², Shahina Bano et al⁶ and Harneet Narula et al⁷ with statistically significant higher rate of LSCS for fetal distress, greater number of babies with birth weight<10th percentile and Apgar score<7 at 5 min in group with abnormal MCA/UA PI. Also, significantly greater number of neonates requiring NICU admission with long hospital stay in group with abnormal MCA/UA PI correlates well with these studies. Severe degree of uteroplacental insufficiency in group B than in group A could be the reason for greater number of IUGR babies in group B. The fetuses are already compromised with the brain sparing effect in group B with more risk of fetal distress during labour.

The findings in the present study correlate with the studies by Rozela Shahinaj et al², Shahina Bano et al⁶ and Mehmet Ozeren et al⁵ with significantly more perinatal deaths in group with abnormal MCA/UA PI than in group with normal MCA/UA PI.

Those with absent end diastolic velocity and reversed end diastolic velocity in umbilical artery had poor perinatal outcome correlating well with the study by Narula Harneet et al⁷. One with REDV had IUD and among two with AEDV, one with low MCA values had IUD and one with normal MCA values had LSCS for fetal distress with the baby requiring NICU admission for more than 4 days.

In the present study, 38.18% of neonates in group A and 87.5% neonates in group B required NICU admission for various neonatal complications-hypothermia, hypoglycemia, hyperbilirubinemia, RDS, meconium aspiration syndrome, NEC, sepsis, perinatal asphyxia and others.

In the present study, diagnostic performance of MCA/UA PI 1.08 to predict major adverse perinatal outcome that is perinatal deaths, HIE, intra/ periventricular haemorrhage, NEC was calculated. The results were, sensitivity-75%, specificity-79%, positive predictive value-30% and negative predictive value-99.36%.

In the studies by Rozela Shahinaj et al (2010)² and B N Lakhtar et al (2006)³ sensitivity, specificity, positive predictive value (PPV) and the negative predictive value (NPV) of the MCA/UA PI ratio to predict major adverse perinatal outcome are 98%, 66%, 30.8%, 99.7% and 66.6%, 73.9%, 40%, 89.4% respectively.

In the studies by Katherine W. Fong et al (1999)⁴ and Gramellini et al (1992)¹, sensitivity, specificity, positive predictive value (PPV) and the negative predictive value (NPV) of the MCA/UA PI ratio to predict major adverse perinatal outcome are 62.5%, 75.5%, 18.5%, 95.8% and 68%, 98.4%, 94.4%, 88% respectively.

In the present study, diagnostic performance of MCA/UA PI 1.08 to predict minor adverse perinatal outcome that is LSCS for fetal distress, RDS, meconium aspiration syndrome, NICU admission, sepsis, hyperbilirubinemia, perinatal asphyxia, IUGR was calculated. The results were, sensitivity-44%, 32%, specificity-98.39%, positive predictive value-97.5% and negative predictive value-55.45%.

In this study, performance of MCA/UA PI 1.08 to predict IUGR was calculated. The results were, sensitivity-51.39%, specificity-96.15%, positive predictive value-92.5% and negative predictive value-68.18%.

In the study by Rozela Shahinaj et al (2010)², sensitivity, specificity, positive predictive value (PPV) and the negative predictive value (NPV) of the MCA/UA PI ratio to predict IUGR is 80.3%, 61.1%, 16.8% and 96.9%.

In the studies by Shahina Bano et al (2010)⁶ and Mehmet Ozeren et al (1999)⁵ sensitivity, specificity, positive predictive value (PPV) and the negative predictive value (NPV) of the MCA/UA PI ratio to predict IUGR are 44.4%, 100%, 100%, 64.3% and 84%, 89%, 84%, 89% respectively.

CONCLUSION: The use of Doppler ultrasound in pregnancies with hypertension disorders appears to be useful in improving perinatal outcome and in reducing perinatal deaths.

In the present study, study population with MCA/UA PI <1.08 had significantly high incidence of LSCS for fetal distress, lower gestational age at delivery, less mean birth weight, greater number of neonates with IUGR, Apgar score <7 at 5 minutes, NICU admissions and with longer hospital stay and more perinatal deaths.

In our study. sensitivity and specificity of MCA/UA PI to predict major adverse perinatal outcome was modest with 75% & 79% respectively while negative predictive value was high (99.36%).

Specificity and positive predictive value of MCA/UA PI to predict minor adverse perinatal outcome was quite high with 98.39% & 97.5% respectively.

Also, specificity & positive predictive value of MCA/UA PI to predict IUGR was quite high at 96.15% & 92.5% respectively.

Diagnostic accuracy of MCA/UA PI to predict major adverse perinatal outcome was better (78.67%) than to predict minor adverse perinatal outcome (66.67%) & IUGR (74.67%).

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Because the cerebroplacental ratio incorporates data not only on the placental status, but also on fetal response, it was felt to be potentially advantageous in predicting outcome.

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