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Fetal Cerebral Umbilical Doppler Ratio in Prediction of Adverse Perinatal Outcome in Patient with Preeclampsia

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Abstract

Objectives: *This study was undertaken to evaluate the role of middle cerebral to umbilical artery blood velocity waveform's systolic/diastolic ratio (MCA/UA) and compare with biophysical profile as a predictor of adverse perinatal outcome in a patient complicated with pre eclampsia.*

Methods: *In this prospective cross sectional study 100 gravid women complicated with preeclampsia in 3rd trimester fulfilling the selection criteria was taken for study. Thorough history taking with general, obstetric and pelvic examination & routine and special investigation was done. The periodic follow up was performed using non Stress Test (NST), amniotic fluid index (AFI), umbilical artery resistance index (UARI), middle cerebral artery resistance index (MCARI) and MCA/UA ratio. MCA/UA <1, non reactive NST, AFI <5 were considered abnormal. The results of the ratio, and biophysical profile were evaluated to find out the best predictor of adverse perinatal outcome (APO) defined as perinatal mortality, caesarean delivery for fetal distress, admission to the neonatal intensive care unit (NICU), Apgar score <7 at 5 minute.*

Results: *Among all the antepartum surveillance tests, MCA/UA Doppler ratio had found the highest sensitivity (72.97%),*

specificity 95.24%), Positive Predictive Value (PPV) (90%), Negative Predictive Value (NPV) (85.71%) for prediction of adverse perinatal outcome in pregnancies complicated with pre eclampsia.

Conclusions: *The MCA/UA was found the best predictor of adverse perinatal outcome in patients complicated with pre eclampsia. When the ratio was <1, fetal prognosis was poor.*

Key words: *Doppler, preeclampsia, middle cerebral artery, umbilical artery.*

INTRODUCTION

Preeclampsia is a pregnancy-specific syndrome characterized by reduced organ perfusion secondary to vasospasm and endothelial pathophysiology. The reported incidence of preeclampsia is 5-8%[1]. This condition is a leading cause of maternal mortality and is responsible for considerable perinatal morbidity and mortality [2.]. Abnormal placentation is one of the initial event. Its causes inadequate trophoblastic invasion of the maternal spiral arterioles causes raise of vascular resistances and utero-placental perfusion decrease. As a result of impaired uteroplacental blood flow, manifestations of preeclampsia may be seen in the fetal placental unit. These include intrauterine growth restriction (IUGR), oligohydramnios, placental abruption, and non-reassuring fetal status .[3,4] Antepartum fetal surveillances is based on the idea that identification and timed delivery of the hypoxic fetus can prevent intrauterine fetal death and decrease the risk of long term adverse effect. Test now commonly done for antepartum fetal surveillance are Non-stress test (NST), Amniotic fluid index (AFI), Biophysical profile.(BPP), Doppler study of Umbilical artery (UA), Middle cerebral artery (MCA). Several studies have reported higher sensitivities and specificities for middle cerebral artery/umbilical artery (MCA/UA) Doppler ratio for prediction of fetal prognosis.[5-8]. MCA/UA ratio reflects not only the circulatory insufficiency of the umbilical velocimetry of the placenta manifested by alterations in the umbilical systolic/ diastolic (S/D) ratio but also the adaptive changes resulting in modifications of the middle cerebral S/D ratio.[5] In this study we evaluated the predicting value of the MCA/UA ratio, for fetal prognosis in women with pre eclampsia.

MATERIAL AND METHODS

This prospective cross sectional study was conducted over 1 year period (May 2011 to April 2011) & this trial was approved by the institutional ethical committee. The gravid women attending the antenatal clinic and labour emergency with preeclampsia (mild and severe) with single-tone pregnancy at 3rd trimester of gestation was included in the study. Preeclampsia was diagnosed[9] if –

- BP ≥ 140/90 mm hg after 20 week gestation
- Proteinuria ≥ 300 mg/24 hr or ≥1 | + dipstick

Severe preeclampsia criteria[9] were

- BP > 160 / 110 mm Hg
- Proteinuria > 2 mg/24 hr or > 2 + dipstick

Gestational age was confirmed by a reliable LMP or an early ultrasonography at first trimester or early second trimester. Exclusion factors included:

a) Non cephalic presentation
b) Fetal distress on admission
c) Labour on admission
d) Multiple gestation
e) Post caesarean pregnancy
f) Obstetric complication like antepartum haemorrhage, suspected chorioamnionitis, gross fetal anomalies

g) Medical complication diabetes mellitus.

A total of 100 gravid women with preeclampsia in 3rd trimester of pregnancy were included in this study. Due to the extended scope of our exclusion criteria, the sample size was small. All the eligible and consenting gravid women (Written informed consent was taken from those who were willing to participate in the study) was admitted in the antenatal ward. Thorough history taking with general, obstetric and pelvic examination, routine and special investigation was done. The periodic follow up was performed using NST, AFI. UARI, MCARI and MCA/UA ratio and repeated twice weekly till termination of pregnancy.

The non stress test (NST) by using tococardiographic equipment is widely used for antenatal surveillance of preeclampsia and it is recommended that it should be performed twice weekly or every second day (Schnieder EP 1988).[10] NST was performed on admission and twice weekly to see whether the fetus was reacting or not. The test was considered reactive if baseline heart rate 110-160 per minute and there are two or more fetal heart rate acceleration clearly recorded during a 20 minute period, each of 15 or more beat per minute and lasting for 15 seconds or more.[11] If no spontaneous fetal movement (FM) occurred during the initial 20 minutes, the test was continued for another 20 minutes, during this period FM is provoked by external manipulation. If there was no acceleration with spontaneous or repeated external stimuli during a 40 minute period , the test was considered non reactive.[11]

The amniotic fluid index (AFI) was measured by the four quadrant ultrasonic method. AFI <5 was considered abnormal. 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 cut off value of umbilical artery resistance index (UARI) and middle cerebral artery resistance index (MCARI) were 0.62 and 0.67 respectively. These cut off value taken according to study of Zimmerman et al.[12]. MCA/UA RI<1 was considered abnormal[7].

Periodic follow-up was performed using NST, amniotic fluid measurements, UARI, MCARI and MCA/UA ratio. The patient was given anti hypertensive drug as per requirement. Further management was done depending upon the severity of the preeclampsia, maternal condition, condition of the fetus and condition of the cervix.

Women who were near enough to be managed conservatively until labour commence spontaneously or until cervix become favourable for labour induction. Adverse perinatal outcome were perinatal mortality, caesarean delivery for foetal distress, admission to the neonatal intensive care unit (NICU), Apgar score <7 at 5 minute.

Statistical analysis of categorical variables was performed by chi-square test with continuity correction or Fisher exact test when appropriate and the non paired Student t test to compare continuous variables. Sensitivity, specificity, positive predictive value and negative predictive value of NST, AFI, UARI, MCARI, and MCA/UA ratio calculated in predicting adverse perinatal outcome. All *P* values were two-tailed, and $P < 0.05$ was considered statistically significant. Quickcalcs-GraphPad software was used for all analyses.

RESULTS

100 women carrying pregnancy of third trimester complicated with pre-eclampsia were included in our study. Antenatal surveillance tests were done in all of them & perinatal outcome were noted. Women were divided in two groups according to good perinatal outcome (GPO) and adverse perinatal outcome (APO). Out of these 100 women 63% had good perinatal outcome and 37% had adverse perinatal outcome. There were no significant differences in maternal age, gestational age, parity, but there were statistical significant difference in mean birth weight and mode of delivery between two groups (Table-I).

Table I. Maternal characteristics in the two groups of women (Data are mean±SD)

	Women with GPO (63)	Women with APO (37)	P value
Maternal age	23.27± 3.32	22.45± 3.22	0.2805
Gravidity	1.56± 0.67	1.62±0.70	0.6628
Mean gestational age	37.95 ± 2.55	37.05± 1.20	0.4630
Mean birth wt	2.714± 0.169	2.459± 0.214	0.0001
Mode of delivery			
Vaginal delivery	51 (80.95%)	12(32%)	0.0001
Forceps	0 (0%)	7 (18.92%)	0.0006
Caesarean section	12 (19.05%)	18 (48.65%)	0.0030

Table-II Different types of adverse perinatal outcome found in the study

Adverse perinatal outcome	Total (37)
Fetal distress requiring LSCS	16 (43.24%)
Apgar score < 7 at 5 min	30 (81.08%)
Meconium aspiration syndrome	16 (43.24%)
RDS	15 (40.54%)
NICU admission	37 (100%)
Mechanical ventilation	6 (16.21%)
IUGR	21 (56.75%)
IUFD	1 (2.70%)
Neonatal death	2 (5.40%)

LSCS- Lower segment Caesarean Section, RDS- Respiratory distress syndrome, IUGR- Intrauterine growth restriction, IUFD- Intrauterine Fetal Death.

The sensitivity, specificity, positive and negative predictive values of cut off level of biophysical profile, umbilical artery and middle cerebral artery resistance indices, and the MCA/UA RI were calculated for the prediction of adverse perinatal outcome.

Table- III. Relationship between adverse perinatal outcome and AFI < 5

AFI	APO (37)	GPO (63)
AFI< 5 (25)	12 (32.43%)	13 (20.63%)
AFI ≥ 5 (75)	25 (67.56%)	50 (79.36%)

Table- III shows out of 100 women 25 had AFI < 5 among which 12 had adverse perinatal outcome. 75 had AFI ≥ 5, out of them 25 had adverse outcome. So,

- Sensitivity- 32.43%
- Specificity- 79.37%
- PPV- 48%
- NPV- 66.67%

Table IV: Relationship between adverse perinatal outcome and non reactive NST

Non stress Test	APO (37)	GPO(63)
Nonreactive (30)	13 (35.13%)	17 (26.98%)
Reactive (70)	24 (64.86%)	46 (73.01%)

Table IV shows out of 100 women 30 had Non Reactive NST among which 13 had adverse perinatal outcome. Rest (70) had Reactive NST, out of them 24 had adverse outcome. So

- Sensitivity- 35.14%
- Specificity- 73.02%
- PPV- 43.33%
- NPV-65.71%

Table V: Relationship between adverse perinatal outcome and umbilical artery RI (UARI) in the two groups-

UARI	APO (37)	GPO (63)
≥ 0.62 (50)	24 (64.86%)	26 (41.26%)
<0.62 (50)	13 (35.13%)	37 (58.73%)

Out of 100 women 50 had UARI ≥ 0.62, among which 24 (64.86%) had adverse perinatal outcome. Rest 50 had UARI < 0.62, out of them 13(35.13%) had adverse outcome. .

- Sensitivity- 64.86%
- Specificity- 58.73%
- PPV- 48%
- NPV- 74%

Table-VI: Relationship between adverse perinatal outcome and MCA RI value

MCA RI	APO(37)	GPO (63)
<0.67 (54)	24 (64.86%)	30 (47.61%)
≥0.67 (46)	13 (35.13%)	33 (52.38%)

Out of 100 women 54 had MCA RI < 0.67 among them 24 had adverse perinatal outcome. 46 had MCA RI ≥ 0.67, of them 13 had adverse outcome.

- Sensitivity- 64.86%
- Specificity- 52.38%
- PPV- 44.44%
- NPV- 71.74%

Table-VII: Relationship between adverse perinatal outcome and MCA/UA ratio < 1

MCA/UA	APO (37)	GPO (63)
<= 1 (30)	27 (72.97%)	3 (4.76%)
>1 (70)	10 (27.02%)	60 (95.23%)

Out of 100 women 30 had MCA/UA ratio <=1, among them 27 had adverse perinatal outcome . Rest 70 had MCA/ UA ratio >1, of them only 10 had adverse perinatal outcome.

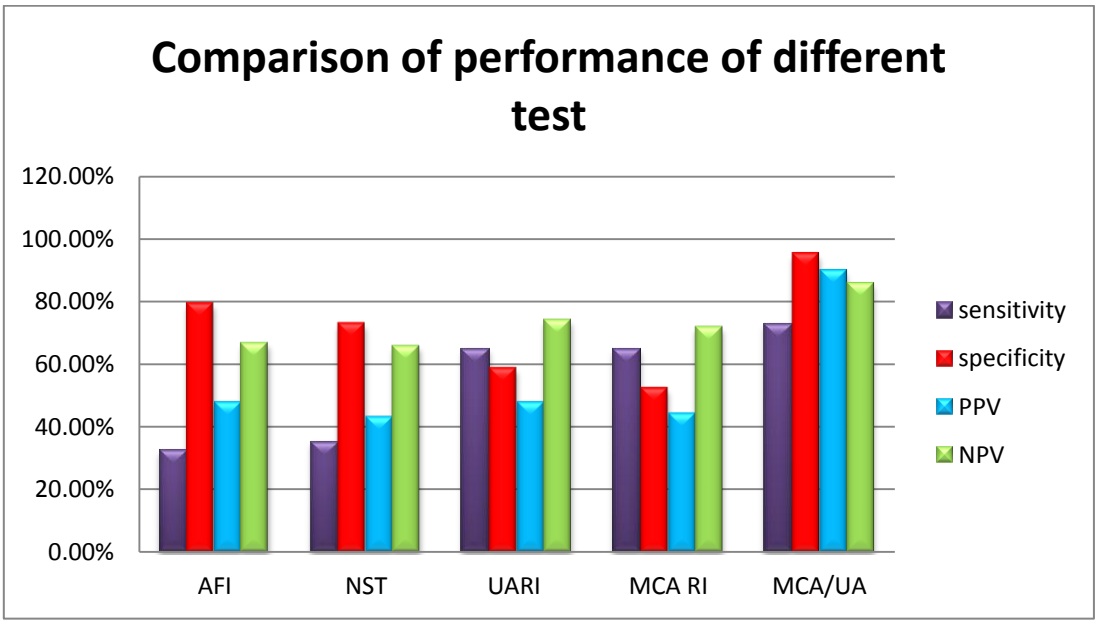
- Sensitivity- 72.97%
- Specificity- 95.24%
- PPV- 90%
- NPV- 85.71%

Table- VIII: Comparison of different antenatal surveillance test result for prediction of adverse perinatal -outcome

Test	Sensitivity	Specificity	PPV	NPV
AFI	32.43%	79.37%	48%	66.67%
NST	35.14%	73.02%	43.33%	65.71%
UA RI	64.86%	58.73%	48%	74%
MCA RI	64.86%	52.38%	44.44%	71.74%
MCA/UA	72.97%	95.24%	90%	85.71%

Table- VIII compares the results of different surveillance tests. MCA/UA ratio shows the maximum sensitivity (72.97%), specificity (95.24%), PPV (90%) and NPV (85.71%) in predicting adverse perinatal outcome.

Figure -1



DISCUSSION

Management of pregnancies complicated with preeclampsia is always a challenge to the obstetricians. It's having significant impact on perinatal outcome. Advances in Doppler ultrasonography have improved access to the fetal

circulation. There has been a great deal of interest in the fetal intracranial vessels.[13] Knowledge of Doppler flow velocimetry of the fetal MCA may assist in perinatal diagnosis and management of complicated pregnancies. 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.[14]

Fetuses with abnormal Doppler MCA/UA RI ratio in our study had a significantly lower birth weight, higher incidence of perinatal deaths, increase rate of caesarean section, higher incidence of admission to NICU and lower Apgar score at 5 minute. In fetuses with abnormal MCA/UA ratio are 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 cerebro-placental ratio is greater than 1. The index becomes less than 1 if the flow distribution is in favour of the brain in pathological pregnancies. This phenomenon, called the brain sparing effect, is supposed to compensate for foetal hypoxia and is associated most of the time with fetal growth retardation with low umbilical artery *p*H.[15]

In our study among all the antepartum surveillance test (NST, AFI, UARI, MCARI, MCA/UA RI) , we found MCA/UA ratio having highest sensitivity (72.97%), specificity (95.24%), PPV (90%) and NPV (85.71%) in predicting adverse perinatal outcome.

Table- IX. Comparison of our results of the sensitivity, specificity, positive predictive value, negative predictive value of MCA/UA ratio with other studies.

	Sensitivity	Specificity	PPV	NPV
Our study	72.97%	95.24%	90%	85.71%
Rozeta S. et al[16]	98%	66%	30.08%	99.70%
Gramellini et al[17]	68.0%	98.4%	94.4%	88%
BN Lakhkar[18]	66.6%,	73.9%	40%	89.4%
Katherine W. Fong[19]	62.5%	75.5%	18.5%	95.8%
Alaa Ebrashy[20]	64.1%	72.7%	89.3%	36.4%

From Table- IX. it was found that others authors finding regarding predictive power of MCA/UA ratio to predict adverse perinatal outcome is almost similar.

So in conclusion, Doppler velocimetry studies of placental and fetal circulation can provide important information regarding fetal well-being, yielding an opportunity to improve fetal outcome[21]. Although the sample size of our study was small, our results suggested that the MCA/UA Doppler ratio of less than 1 was a good predictive tool for neonatal outcome in pre eclamptic women and could be used to identify fetuses at risk of morbidity.

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