

## The Umbilical Artery Resistive Index and the Cerebro-Placental Ratio as a Predictor of Adverse Foetal Outcome in Patients with Hypertensive Disorders of Pregnancy during Third Trimester.

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**Background:** Hypertensive disorders of pregnancy causes adverse effects both the maternal and faetal circulations. These circulations can be assessed safely and non-invasively by Doppler ultrasound using arterial Doppler indices of umbilical artery alone or combining the umbilical artery with the middle cerebral artery thus attaining the cerebroplacental ratio (ratio of the middle cerebral artery resistive index over that of the umbilical artery). The main objective of this study was to compare the Umbilical Artery Resistive index alone and the cerebroplacental ratio as a predictor of adverse fetal outcome in patients with hypertensive disorders of pregnancy in third trimester.

**Methods:** A prospective cohort study was carried out at the Kenyatta National Hospital (KNH) over a period of nine months. Gravid patients at least 32 weeks gestations by dates were recruited from labor ward. Consecutive sampling method was used. The Umbilical Artery Resistive Index was obtained and the cerebroplacental ratio was also calculated from the Umbilical Artery Resistive Index and Middle Cerebral Artery Resistive index.

**Results:** A total of 160 patients were recruited into the study. Among neonates of mothers with pregnancy induced hypertension with Umbilical Artery Resistive Index  $\leq$  median (0.64), a fetal birth score  $< 7$  was 0.5 (95% CI 0.3, 0.8;  $p < 0.001$ ) times more likely than a score  $> 7$  and 6.6 (Odds Ratio 6.6; 95% CI 2.5, 17.3;  $p < 0.001$ ) times more likely relative to hypertensive mothers with Umbilical Artery Resistive Index  $>$  median (0.64). Combining Umbilical Artery Resistive Index and Middle Cerebral Artery Resistive Index (cerebroplacental ratio) improves the prognostic odds ratio from 6.6 to 82. The Umbilical Artery Resistive Index ( $\leq$ / $>$  median) had 80% (95% CI 63%, 90%) sensitivity, 62.3% (95% CI 54%, 70%) specificity, 33% positive predictive value, and 93.1% negative predictive value for neonatal adaption after birth as seen from the foetal birth score. Among infants of mothers with hypertensive disorder during pregnancy with Umbilical Artery Resistive Index  $\leq$  median (0.64), low birth weight ( $< 10^{\text{th}}$  percentile of expected weight at gestation week) was 0.5 (95% CI 1.9, 7.3) times more likely than normal weight and 9.5 (Odds Ratio 9.5; 95% CI 3.1, 29.2;  $p < 0.001$ ) times more likely relative to infants of hypertensive mothers with Umbilical Artery Resistive Index  $>$  median (0.64). Combining Umbilical Artery Resistive Index and Middle Cerebral Artery Resistive Index (cerebroplacental ratio) does not improve the prognostic odds ratio. The Odds Ratio drops from 9.5 to 5.6. This implies the Umbilical Artery Resistive Index is a better predictor of low birth weight. The Umbilical Artery Resistive Index ( $\leq$ / $>$  median) had 85.2% (95% CI 67.5%, 94%) sensitivity, 62.4% (95% CI 54%, 70%) specificity, 31.5% positive predictive value, and 95.4% negative predictive value for abnormal birth weight.

### Conclusion

- The Cerebroplacental ratio is a better predictor of faetal birth score  $< 7$  as compared to Umbilical Artery Resistive Index.
- The Umbilical Artery Resistive Index is a better predictor of low birth weight as opposed to cerebroplacental ratio.
- Both cerebroplacental ratio and Umbilical Artery Resistive Index can be used in combination to get the best results on faetal birth score and foetal weight.

### Introduction

Hypertensive disorders of pregnancy (HDP) include pre-eclampsia/eclampsia (PE), chronic hypertension, gestational hypertension and chronic hypertension with superimposed pre-eclampsia (1). The Umbilical Artery Resistive Index (UA-RI) is only reflective of placental vascular resistance. The

cerebroplacental ratio is reflective of placental vascular resistance via Umbilical Artery Resistive Index and systemic resistance via Middle Cerebral Artery Resistive Index. A comparison of the Middle Cerebral Artery and Umbilical Artery Resistive Index gives the cerebroplacental ratio (CPR). A ratio >1.0 indicates preferential flow to vital structures like brain, heart and adrenal glands and is therefore considered normal while a cerebroplacental ratio <1.0 is indicative of high resistance in utero-placental circulation and is considered abnormal. This study was aimed at comparing the cerebroplacental ratio to Umbilical Artery Resistive Index as a predictor of adverse foetal outcome in patients with hypertensive disorders of pregnancy at or more than 32 weeks.

## Patients and Methods

This was a prospective cohort study carried out in a tertiary hospital setting of Kenyatta National Hospital in Nairobi. A cohort of women (160) with hypertensive disorders of pregnancy at least 32 weeks by gestation was recruited over the 9 month period after obtaining informed consent. Recruitment took place from the labour ward over a period of 24 hours a day by the principal investigator or research assistant.

After obtaining informed consent from the patient or next of kin, a structured questionnaire was filled out by the principal investigator or research assistant. Blood pressure and urinalysis results recorded. An obstetric ultrasound scan was carried out on request by the clinician and coded for foetal presentation, placental position, foetal heart rate, and approximate ultrasonographic age, BPPS, UA-RI and MCA-RI. The ultrasound machines used were real time machines, the Phillips HD11 and GE Logic 7. The transducer frequency was 3.5 – 5.0 MHz, the Doppler sample volume was 2 mm and the wall filter was 50–100 Hz. The examination was performed with the mother in a semi-recumbent position during relative foetal inactivity and apnoea. This is because the end diastolic flow (EDF) decreases with decreasing foetal heart rate and foetal breathing movements increase variability in the Doppler measurements.

The Umbilical Artery was sampled at the middle of a free loop of umbilical cord. It could also be assessed at the level of the foetal bladder. For Middle Cerebral Artery, a transverse image of the foetal head was obtained at the level of the sphenoid bones. Colour Flow imaging was used to display the circle of Willis. The MCA in the near field was isolated about 1 cm distal to its origin from the internal carotid artery. By using the optimal spectral trace from each artery, the Resistive Index was calculated from the mean of a minimum of five consecutive waveforms on a frozen image. A series of three readings were taken for each artery to avoid errors. The cerebral/placental ratio was calculated from the MCA -RI and UA-RI. The study outcome variables were:

1. The 5 minute APGAR score-5 min ( $< 7$  or  $\geq 7$ )
2. Birth weight – ( $< 10^{\text{th}}$  percentile of the expected weight for gestation was considered as low birth weight)

## Results

Among neonates of mothers with hypertensive disorder during pregnancy with UARI  $\leq$  median (0.64), an APGAR score  $< 7$  was 0.5 (95% CI 0.3, 0.8;  $p < 0.001$ ) times more likely than a score  $> 7$  and 6.6 (OR 6.6; 95% CI 2.5, 17.3;  $p < 0.001$ ) times more likely relative to hypertensive mothers with UARI  $>$  median (0.64). Combining UA-R.I and MCA-R.I (cerebroplacental ratio) improves the prognostic odds ratio from 6.6 to 82. Implying CPR is a better predictor of APGAR score  $< 7$ ] The UARI ( $\leq / >$  median) had 80% (95% CI 63%, 90%) sensitivity, 62.3% (95% CI 54%, 70%) specificity, 33% positive predictive value, and 93.1% negative predictive value for neonatal adaption after birth.

Among infants of mothers with hypertensive disorder during pregnancy with UARI  $\leq$  median (0.64), low birth weight ( $< 10^{\text{th}}$  percentile of expected weight at gestation week) was 0.5 (95% CI 1.9, 7.3) times more likely than normal weight and 9.5 (OR 9.5; 95% CI 3.1, 29.2;  $p < 0.001$ ) times more likely relative to infants of hypertensive mothers with UARI  $>$  median (0.64). Combining UA-R.I and MCA-R.I does not improve the prognostic odds ratio. The prognostic Odds Ratio (OR) however drops from

9.5 to 5.6. This implies that the UA-R.I is a better predictor of low birth weight. The UA-R.I ( $\leq$  median) had 85.2% (95% CI 67.5%, 94%) sensitivity, 62.4% (95% CI 54%, 70%) specificity, 31.5% positive predictive value, and 95.4% negative predictive value for abnormal birth weight.

**Table 1 : Logistic regression for the correlates of Infant’s APGAR (5 minutes) Score among mothers with hypertensive disorder during the index pregnancy**

Characteristics	Infant’s APGAR score		Prognostic Odds Ratio			
	APGAR score (< 7)/n	Odds (95% CI)	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Cerebral/Placental Ratio						
• < 1.0	28/47 (59.6%)	1.47 (0.8, 2.6)	82 (18, 372)	< 0.001	66 (13, 340)	< 0.001
• $\geq$ 1.0	2/113 (1.8%)	0.018 (0.005, 0.07)	ref		ref	
UARI						
• $\leq$ median (0.64)	24/73 (32.9%)	0.5 (0.3, 0.8)	6.6 (2.5, 17.3)	< 0.001		
• > median (0.64)	6/87 (6.9)	0.07 (0.03, 0.2)	ref			

**Table 2. Logistic regression for the correlates of Infant’s birth weight among mothers with hypertensive disorder during the index pregnancy**

Characteristics	Infant’s birth weight		Prognostic Odds Ratio			
	% Low birth weight	Odds (95% CI)	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Cerebral/Placental Ratio						
• < 1.0	37/47 (78.7%)	3.7 (1.9, 7.3)	5.6 (2.5, 12.4)	< 0.001	4.7 (2, 11.1)	< 0.001
• $\geq$ 1.0	45/113 (39.8%)	0.66 (0.45, 0.96)	ref		ref	
UARI						
• $\leq$ median (0.64)	23/73 (31.5%)	0.5 (0.3, 0.75)	9.5 (3.1, 29.2)	<0.001		
• > median (0.64)	4/87 (4.6%)	0.05 (0.02, 0.13)	ref			

### Discussion

In this study that studied a total of 160 patients with hypertensive disorders in pregnancy, the aim was to compare the prediction value on the adverse foetal outcome of the Umbilical Artery Resistive Index versus the cerebroplacental ratio. Combining Umbilical Artery Resistive index and Middle Cerebral Artery Resistive Index (cerebroplacental ratio) improves the prognostic odds ratio from 6.6 to 82. This implies the cerebroplacental ratio is a better predictor of foetal birth (APGAR) score < 7]. This is in contradiction to the study by Lakhkar which found the umbilical S/D ratio as a sensitive indicator and the Middle Cerebral Artery P.I as a specific indicator<sup>2</sup>. It is also in contradiction to a study by Fong Katherine which found the Umbilical P.I to be a better predictor of adverse foetal outcome<sup>3</sup>. This could be explained by the differences in sample size which was 58 in Lakhkar et al and 293 in Fong Katherine et al though randomized control trials may be needed to confirm this. It could also be due to the other studies using P.I which is a measurement of variability of blood velocity in a vessel equal to the difference between PSV and EDV divided by the mean velocity during one cardiac cycle. It is a more accurate indicator of vascular resistance as it continues to show change even with no diastolic flow as compared to R.I that was used in this study which is a measure of resistance of an organ to perfusion. It is measured by subtracting end- diastolic velocity (EDV) from peak systolic velocity (PSV) and dividing that by peak- systolic velocity and with vascular compliance, RI is dependent on resistance of

the vessel and it therefore increases with increase in vascular resistance. It approaches one when the diastolic velocity reaches zero.

This finding was in keeping with Gramellini et al<sup>4</sup> which showed the diagnostic accuracy for the cerebral-umbilical ratio was 90%, compared with 78.8% for the middle cerebral artery and 83.3% for the umbilical artery. Combining the Umbilical Artery Resistive Index and Middle Cerebral Artery Resistive Index (cerebroplacental ratio) does not improve the prognostic odds ratio for low birth weight which dropped from 9.5 to 5.6. This implies that the Umbilical Artery Resistive Index is a better predictor of low birth weight. This was in keeping with Khanduri Sachin et al<sup>5</sup> found that the Umbilical Artery Resistive Index was more sensitive at 75% for intrauterine growth restriction resulting in low birth weight.

### Conclusion

1. The Cerebroplacental ratio is a better predictor than Umbilical Artery Resistive Index of low foetal birth (APGAR) score (less than 7) thus the cerebroplacental ratio should be used to determine degree of intrauterine foetal distress.
2. The Umbilical Artery Resistive Index is a better predictor than cerebroplacental ratio of low birth weight. Thus the Umbilical Artery Resistive Index should be used to determine intrauterine growth restriction as an indicator of low birth weight
3. Both the cerebroplacental ratio and the Umbilical Artery Resistive Index should be used in combination as one is a better predictor of foetal birth (APGAR) score <7 while the other is a better predictor of low birth weight.

### References

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