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## The Value of the Cerebroplacental Ratio as an Independent Predictor of Adverse Perinatal Outcome

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### ABSTRACT

**Objectives:** To determine the association between third trimester cerebroplacental ratio (CPR) and adverse perinatal outcomes in appropriate-for-gestational-age (AGA) fetuses.

To know the prevalence of pathological CP Rin low risk term pregnancies.

**Method:** Observational prospective study in low risk singleton pregnancies which delivered over the period of January 201XX to December 201XX, who underwent an ultrasound scan where Doppler parameters were measured between 37 to 42 week of pregnancy. Ethical approval and informed consent of the patients were obtained.

CPR was calculated as the ratio between the umbilical artery pulsatility index (UA-PI) and fetal middle cerebral artery plasticity index (MCA-PI).

Adverse perinatal outcomes were defined as presence of pathological cardiotocography (CTG) trace, arterial cord blood pH < 7.2 and 5-min a pgar score < 7.

Data was analyzed with SPSS 17.0 statistical package.

**Results:** A total of 150 low risk pregnancies were included. Pathological CPR was found in 10.7 % of the cases. The mean age was 31 (range 18-42) and gestational age at ultrasound was 39+3 (37 – 41.3) weeks. The median birth weight was 3390 g

There was no correlation between CPR result and the need of operative delivery for fetal compromise, low neonatal pH or low a pgar and CPR.

**Conclusions:** Our findings in this prospective study demonstrate that lower fetal CPR does not modify delivery route and is not associated with any other perinatal adverse outcome. Calculating the CPR does not add value to assessment in the prediction of adverse perinatal outcome in women with a singleton low risk gestation.

**Keywords:** cerebroplacental ratio, fetal Doppler, fetal compromise, cord pH.

## **INTRODUCTION**

Appropriate for gestational age (AGA) describes a fetus or newborn whose weight is within the normal range for his or her gestational age. To assess fetal growth, four biometric measures are commonly used: biparietal diameter, head circumference, abdominal circumference and femur length. The biometric measurements can be combined to generate an estimated fetal weight<sup>1</sup>. If the ultra soon graphic estimated fetal weight is above the 10th centile and under the 90th centile, we talk about an AGA. Whereas if the ultra soon graphic estimated fetal weight is below the 10th percentile for gestational age, we diagnose a small for gestational age (SGA) fetus and further evaluation should be done, such as amniotic fluid assessment and Doppler blood flow studies of the uterine artery plasticity index (UtA-PI), umbilical artery plasticity index (UA-PI) and cerebral blood flow (CBF) studied by middle cerebral artery plasticity index (MCA-PI). Intrauterine growth restriction is established in all cases that an estimated fetal weight is below the 3th percentile or a Doppler blood flow alteration is found in an SGA fetus<sup>2-4</sup>.

It is well known that fetal growth restriction increases the risk of intrauterine demise, neonatal morbidity and neonatal death<sup>5, 6</sup>. Increased impedance in the UA-PI and reduced impedance in the MCA-PI are considered "early" changes of uteroplacental insufficiency. Late changes included UA absent or reverse end-diastolic flow and abnormal changes in the ductus venosus. Doppler velocimetry abnormalities develop in different vessels of the growth-restricted fetus sequentially. Late changes in vascular adaptation in the severely growth-restricted fetus are the best predictor of perinatal death<sup>8</sup>. Cerebral redistribution showed as an increased CBF has traditionally been regarded as a protective auto regulatory mechanism in order to save main tissues like brain, heart and adrenals under hypoxia situation. A reduction in MCA-PI or in the ratio MCA-PI / UA-PI (cerebroplacental ratio, CPR) below the 5 percentile are most often used to define brain sparing. Recent guidelines recommend delivery of term fetuses with cerebral redistribution as it is predictive of increased risk of adverse neuro developmental outcomes.

The role of CPR as a marker of failure to reach fetus growth potential has recently gained interest among researchers and clinicians. The predictive value of CPR has been shown to be of value in the surveillance of SGA fetuses, but we wonder if it could also be useful in fetus with appropriate weight for gestational age.

Hence the aim of the present study is to test the hypothesis that the CPR is a good predictor of adverse perinatal outcomes in AGA fetuses.

## **METHODS**

Observational prospective study of 150 low risk singleton pregnancies who underwent an ultrasound scan between weeks 37 and 42 of pregnancy.

The inclusion criteria were singleton morphologically normal fetuses born at term ( $\geq 37$  weeks' gestation) in our hospital. Pregnancies complicated by fetal abnormality, aneuploidy and small

for gestational age was excluded from the analysis. Labour was managed according to local protocols and guidelines.

Demographic data collected included maternal age, parity and ethnicity (Caucasian, Asian, South-American and African).

Gestational age was calculated from the crown-rump length measurement at 11-13 weeks. Routine fetal biometry was performed according to a standard protocol and the estimated fetal weight (EFW) calculated using the formula of Hadlock et al<sup>1</sup>. EFWs were converted into centiles and Doppler indices (UA, MCA and CPR) were converted into multiples of the median (MoM), adjusting for gestational age. CPR, calculated as the simple ratio between the middle cerebral artery pulsatility index (MCA-PI) and the umbilical artery pulsatility index (UA-PI) was also recorded according to a pathological CPR by < 5th centile<sup>2-3</sup>. ICP groups were compared regarding the following intrapartum and neonatal outcomes: pathological Electronic Fetal Monitoring (EFM), emergency delivery (caesarean section or instrumental delivery), Apgar score <7 at 5min and arterial cord blood gases, if performed (arterial pH <7.20).

### **Statistical analysis**

Data were analyzed with the SPSS 17.0 statistical package (SPSS Inc, Chicago, IL). Results are expressed as mean ± standard deviation or proportions. Univariate analysis was conducted with the Student's t-test or Chi-square test.

Differences were considered significant when  $P < 0.05$ .

### **RESULTS**

Over the study period, a total of 150 women fulfilled the inclusion criteria. The mean age was 31 (range 18-42) and gestational age at ultrasound was 39+3 (range 37-42) weeks. Sixty-two percent of the women were primiparous and the most common racial origin was caucasian (76%).

The overall median UA-PI, MCA-PI and CPR of the study cohort were 0.9, 1.6 and 1.9, respectively (± 0.2, 0.5 and 0.9). Doppler was pathological in 2, 25 and 16 cases (1.3, 16.7 and 10.7 % respectively). In our sample, CPR had a prevalence of 10.7% in low risk singleton pregnancies.

The proportion of births that were induced was 31% and the main reason was prolonged gestation followed by premature rupture of membranes. Graphic 1.

The median gestational age at delivery was 40 weeks (range 37-42).

The mean interval between ultrasound and delivery was 2 weeks. Fourteen percent of fetus presented a pathological EFM.

The majority of women (76.7%) had a spontaneous vaginal delivery, 14% an instrumented delivery and 9% a caesarean section. The number of emergency deliveries (instrumental or caesarean section) for fetal compromise was 6%. The median birth weight was 3389.7g (±

390,1g) with a median centile of 51,37. All infants had an A pgar score at 5min of >7, 40% had a cord arterial pH <7,20 and only one required admission to the nursery.

We stratified our results by CPR < 5th centile or CPR ≥5th centile. There are no statistically significant differences neither in the age of the pregnant women or in the weeks of gestation to the childbirth or in the weight of the newborns. The number of induced births does not differ in the CPR groups. Pathological CPR had more pathological EFM but these results were not statistically significant (p=0,18). However, pathological EFM was correlated with cord arterial ph<7.20 , which was statistically significant (p=0,01). There was no correlation between arterial-blood pH and CPR (p=0,31) in neither of the two groups. Infants that required emergency delivery because of fetal compromise had similar CPR (p=0,24). Birth weight does not differ in UA PI, MCA PI and CPR groups. Table1.

## DISCUSSION

As a matter of fact, Doppler indices form an integral component of no invasive evaluation of fetal well-being. Doppler parameters of UA and MCA are integrated in the surveillance of high-risk pregnancies because of the association between its altered PI and perinatal morbidity<sup>7,8,9,10</sup>. Moreover, recent studies have indicated that CPR further improves the prediction. The role of CPR as a marker of failure to reach fetus growth potential has recently gained interest among researchers and clinicians. The predictive value of CPR in the monitoring of fetuses with intrauterine growth defects has been demonstrated, but the role of CPR in low risk gestation with fetuses of adequate weight for gestational age is unknown. In fact, fetal Doppler evaluation could also be useful to detect fetuses with AGA, but complicated by placental insufficiency that fail to reach their genetic growth potential and would present with a higher risk of adverse outcomes.

Authors such as Prior<sup>11</sup> or Khalil<sup>12</sup> have indicated that CPR in the third trimester is an independent predictor of fetal death and perinatal mortality. Dunn<sup>13</sup> in this review on the subject remarked out that although CPR in term fetuses had a strong association with adverse obstetric and perinatal outcomes, there was insufficient evidence to demonstrate its value as an independent parameter. However, comment that twenty-one studies satisfied inclusion with 13 prospective and eight retrospective. Full-term fetuses were included, without discriminating those with intrauterine growth retardation, in which the role of CPR as a predictor of morbidity is already known<sup>14</sup>. According to these results, recent studies showed that, independently of the fetal size, CPR measured in the 72 hours prior to delivery could identify those that probably require obstetric intervention for intra partum fetal compromise<sup>11</sup>.

Lower umbilical cord blood pH has been one of the main findings associated with pathological CPR, better than birth weight. This result was not correlated in our population where AGA fetuses with low CPR presented the same neonatal cord pH and a pgar as normal CPR group.

Pathological CPR has also been associated with other adverse pregnancy outcomes such as operative delivery for presumed fetal compromise, neonatal unit admission, stillbirth, and neonatal morbidity<sup>12</sup>. We did not find association between CPR and the need of operative delivery for presumed fetal compromise and CPR value did not modify the delivery route.

Despite of Khalil<sup>12-13</sup> mortality results in pathological CPR fetuses were consistent, the association between CPR-Mo M and neonatal unit admission, stillbirth and perinatal death in our sample could not be demonstrated due to only one case that required neonatal unit admission and there were not any case of stillbirth or perinatal death.

In our study, CPR results are not associated with adverse neonatal results because AGA fetuses with low CPR present the same neonatal cord pH and a pgar than normal CPR.

We feel same as Dunn<sup>13</sup>, that there is insufficient evidence to demonstrate CPR as an independent parameter for predicting adverse perinatal outcomes in AGA fetuses.

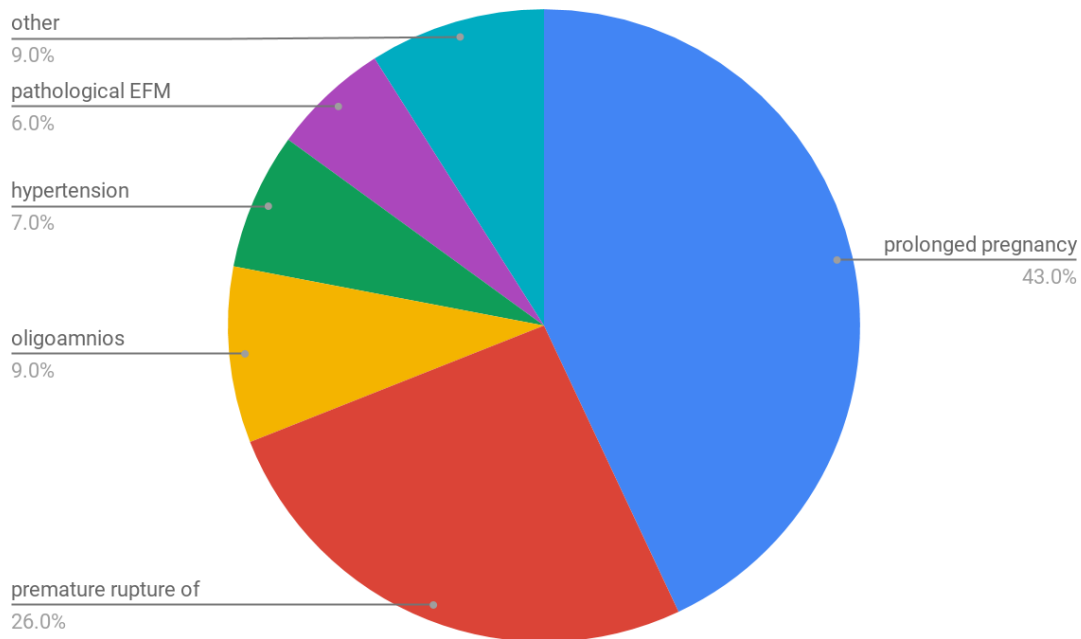
Evaluating our results, we agree with Kalafat<sup>15</sup> that the role of CPR in predicting adverse perinatal outcomes in AGA fetuses is yet to be determined and more studies are required.

### CONCLUSION

The findings of this prospective study demonstrate that calculating the CPR does not add value to assessment in the prediction of adverse perinatal outcome in women with a singleton AGA gestation. The role of CPR in predicting adverse perinatal outcomes, such as acidosis or low a pgar scores in fetuses with AGA, has not yet been determined.

More methodologically well-conducted studies that delve into the true role of CPR in low-risk pregnancy, if it exists, would be lacking.

### Graphic 1. Reasons for induction



**Table1. Intrapartum and neonatal outcomes stratified by ICP result**

	<b>CPR ≥ 5th centile N=134</b>	<b>CPR &lt; 5th centile N=16</b>	<b>p value</b>
Newborns weight (percentil)	3389 (54)	3390 (54,1)	0,7 (0,4)
Induced births	33,6	12,5	0,08
Pathological EFM (%)	12,7	25	0,18
Emergency delivery (%)	0,05	12,5	0,2
Apgar score <7 at 5min	0	0	--
Arterial cord blood gases	7,2	7,1	0,1
Admission to the nursery	1	0	--

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