



Prognostic accuracy of cerebroplacental ratio for adverse perinatal outcomes in pregnancies complicated with severe pre-eclampsia; a prospective cohort study



Ahmed Alanwar^{a,*}, Ayman Abou El Nour^a, Mohamed El Mandooh^a, Ibrahim A. Abdelazim^a, Luma Abbas^a, Ahmed M. Abbas^b, Ameer Abdallah^c, Wael S. Nossair^d, Shikanova Svetlana^e

^a Department of Obstetrics and Gynecology, Ain Shams Maternity Hospital, Faculty of Medicine, Ain Shams University, Cairo, Egypt

^b Department of Obstetrics and Gynecology, Woman's Health Hospital, Faculty of Medicine, Assiut University, Assiut, Egypt

^c Department of Obstetrics and Gynecology, Minia University, Minia, Egypt

^d Department of Obstetrics and Gynecology, Faculty of Medicine, Zagazig University, Zagazig, Egypt

^e Department of Obstetrics and Gynecology, Marat Ospanov, West Kazakhstan State Medical University, Aktobe, Kazakhstan

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ABSTRACT

Objective: The current study aims to assess the efficacy of fetal middle cerebral artery/umbilical artery pulsatility index ratio (cerebroplacental ratio CPR) in predicting the occurrence of adverse perinatal outcomes in pregnancies complicated with severe pre-eclampsia.

Materials and methods: This cohort study included 100 pregnant women between 34 and 40 weeks of gestation attended the labor ward and diagnosed with severe pre-eclampsia. Doppler evaluation was carried out to measure the CPR. Apgar score and fetal umbilical artery pH were assessed within 5 min of delivery. The rate of neonatal intensive care unit (NICU) admission was obtained.

Results: Apgar score at 5 min > 7 was in 82 cases (82%) and 12 cases (12%) scored < 7. Fetal blood PH was > 7.2 in 67% of cases while 33% of cases had PH < 7.2. As regard the NICU admission; 66% of neonates did not need admission while 34% of neonates were admitted to the NICU. There was a significant association between CPR and low Apgar score at 5 min ($P < 0.001$). The sensitivity of CPR in detection of Apgar score < 7 was 50%, and specificity 88.1%. CPR had a poor predictive value of the low umbilical artery PH < 7.2 ($P = 0.318$) with 43.75% sensitivity and 69.05% specificity. There was a significant association between CPR and NICU admission ($P = 0.009$).

Conclusions: Adding CPR ratio to routine antepartum fetal surveillance from 34 weeks gestation may help with patient counseling regarding adverse neonatal outcomes for women with severe pre-eclampsia as there is a strong correlation between it and adverse neonatal outcomes.

1. Introduction

Pre-eclampsia is a multi-system disorder which was classically characterized by the new onset of hypertension and proteinuria or end-organ dysfunction or both in the last half of pregnancy [1]. The American College of Obstetricians and Gynecologists (ACOG) removed fetal growth restriction (FGR) as a possible feature of severe disease because FGR is managed similarly whether or not pre-eclampsia is diagnosed [1].

However no longer considered as an essential criterion for the diagnosis of severe disease, Pre-eclampsia is known to be associated with

FGR, which is a consequence of placental insufficiency [2,3]. Abnormal spiral artery remodeling in the setting of pre-eclampsia and the development of subsequent FGR shortens the interval to delivery and may adversely affect neonatal outcome [4].

The utilization of umbilical artery (UA) Doppler has been shown to improve the neonatal outcomes in FGR [5,6], but studies evaluating the ability to predict the progression of clinical deterioration by the use of Doppler have demonstrated conflicting results [7,8]. The additional use of middle cerebral artery (MCA), ductus venosus and umbilical vein may have some prognostic value for FGR fetuses, but their use in the aid in the management of FGR is controversial [9].

* Corresponding author at: Obstetrics and Gynecology, Ramses Street (Ahmed Lotfy Elsayed Street), Abbassia, Ain Shams Maternity Hospital, Faculty of Medicine, Ain Shams University, Cairo 11566, Egypt.

E-mail address: ahmed.elanour@med.asu.edu.eg (A. Alanwar).

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The cerebroplacental ratio (CPR), the ratio of the pulsatility index (PI) of the MCA to that of the UA, can detect fetal hypoxemia occurring via two different mechanisms; reduced resistance in the MCA (brain sparing effect) and increasing placental resistance [10]. Recent studies have shown that combining these two parameters in the CPR further improves the prediction [11]. The CPR has been proposed as a better predictor of fetal compromise than either vessel considered alone, even when umbilical resistance index is within the normal range [12].

The CPR abnormal values have been variably described as < 5th percentile for gestational age and less than an absolute measure of 1.08 [13,14]. The latter has been shown to be simpler and similarly efficacious. The CPR is considered to be a marker of centralization of fetal blood flow as an adaptation to placental insufficiency, such as that seen in preeclampsia [15,16]. The CPR has been shown to be correlated with adverse perinatal outcome and impaired long-term neonatal cognitive development [17].

Therefore, the present study was designed to examine the prognostic accuracy of CPR for adverse perinatal outcomes in women with severe pre-eclampsia.

2. Materials and methods

2.1. Study type, settings and duration

The present study was a prospective cohort study conducted in a tertiary University hospital between January and November 2017. The institutional Ethical Review Board approved the study protocol. All participants signed a written informed consent before inclusion in the study.

2.2. Study participants

All pregnant women between 34 and 40 weeks of gestation attended the labor ward of the aforementioned hospital during the study period were clinically evaluated and those diagnosed as severe pre-eclampsia were invited to participate in the study.

Severe pre-eclampsia was diagnosed if one of the following symptoms or signs are found in the presence of preeclampsia according to the ACOG guidelines 2013 [1]: systolic blood pressure (SBP) ≥ 160 mmHg or diastolic blood pressure (DBP) ≥ 110 mmHg on two occasions at least 4 h apart while the patient is on bed rest and heavy proteinuria ≥ 5 g in 24 h urine.

Patients with multiple pregnancy, preexisting renal disease, diabetes mellitus, gestational hypertension, FGR, fetal congenital anomalies and those who had hemodynamic instability were excluded from the study. Moreover, women presented with clinical emergencies necessitating immediate termination of pregnancy were also excluded.

2.3. Study tools & intervention

At the time of recruitment, one of the study investigators approached all eligible participants for obtaining detailed history taking; maternal age, gestational age, parity and previous miscarriages. Additionally, they subjected to clinical examination; blood pressure (BP) measurement and assessment of protein in urine. BP was measured by mercury sphygmomanometer in patients with pre-eclampsia in their right arm while lying in the supine position.

Then, all patients were evaluated by level II sonographer using Sono-Ace X4 machine (Medison, Korea). All sonographic examinations were performed *trans*-abdominally using a 4.0 MHz probe at the Fetal Care Unit of our hospital. UA Doppler evaluation was performed by a sampling of a free-floating loop of umbilical cord and the PI was obtained. MCA-PI measurement was taken during fetal quiescence; the MCA was sampled near the point of bifurcation from the Circle of Willis, at an angle of insonation as near to 0° as possible, with angle correction performed if 0–10° degrees, and without measurement if an

angle of insonation < 10° could not be obtained. Multiple MCA measurements were obtained and the average PI was used. The CPR was calculated as $CPR = (MCA-PI/UA-PI)$. An abnormal CPR is defined as a CPR of less than 1 or a CPR below the 5th percentile for gestational age on the basis of the nomogram by Baschat and Gembruch [10].

2.4. Follow-up

Women were managed according to the standard, single-institution protocol. Mode of delivery was at the discretion of the primary obstetrician either by vaginal delivery or cesarean section (CS). After delivery, all neonates had been assessed by Apgar scoring system at 5 min after birth. Fetal blood pH was measured within 5 min of delivery. Neonatal morbidity was established if: Apgar score < 7 at 5 min, neonatal acidemia of pH < 7.2 or newborn was admitted to the neonatal intensive care unit (NICU).

2.5. Sample size

Sample size had been calculated using PASS® version 11 program. It was estimated that a total sample of 100 women according to inclusion criteria, was required to achieve a power of 80% (accepted margin of error 5%) and confidence level 95%, for detection of statistical significance as regards the correlation between 3rd trimester MCA/UA Doppler parameters and neonatal outcome. The equation used: $\frac{Z_{\alpha} \times P \times 1 - P}{(Alfa)^2}$.

2.6. Statistical analysis

The collected data was revised, coded, tabulated and introduced to a PC using Statistical Package for Social Science (SPSS 20 for Windows; SPSS Inc, Chicago, IL, 2001). Quantitative variables were expressed as mean and standard deviation (SD). Qualitative variables were expressed as frequencies and percent. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of CPR were calculated for prediction of each adverse perinatal outcome. P-value < 0.05 was considered statistically significant.

3. Results

The total number of cases included in the study was 100 women. The mean age of the study participants was 28.62 ± 4.27 years and the mean gestational age at inclusion was 36.24 ± 1.66 weeks. Twenty four cases (24%) were nullipara and 36% of cases had a history of previous miscarriage. As regard the mode of delivery, 86 cases (86%) were delivered by CS versus 14 cases (14%) delivered vaginally.

As regards the Doppler indices; the mean (SD) of the MCA-PI was 1.22 (0.52), mean (SD) of UA-PI was 0.80 (0.28), and the mean (SD) of MCA/UA-PI ratio was 1.60 (0.61) (Table 1). Eighty four cases (84%) of the study population had normal (≥ 1.0) CPR while 16 cases (16%) had abnormal (< 1.0) CPR

In our study, Apgar score at 5 min > 7 was in 82 cases (82%) and 12 cases (12%) scored < 7. Fetal umbilical artery PH was > 7.2 in 67% of

Table 1
Doppler indices in the study participants.

| | | |
|--------|----------------|-------------|
| MCA-PI | Range | 0.5–2.67 |
| | Mean ± SD | 1.22 ± 0.52 |
| UA-PI | Range | 0.4–1.91 |
| | Mean ± SD | 0.80 ± 0.28 |
| CPR | Range | 0.6–3.18 |
| | Mean ± SD | 1.60 ± 0.61 |
| CPR | Normal (≥ 1.0) | 84 (84%) |
| | Low (< 1.0) | 16 (16%) |

MCA: middle cerebral artery, UA: umbilical artery, CPR: cerebroplacental ratio, PI: pulsatility index.

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