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Cerebroplacental ratio assessment after age of fetal maturity in normotensive and hypertensive pregnancies and prediction of perinatal outcome

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Abstract
Background: At or after 37 weeks of pregnancy, the decreased cerebroplacental ratio (CPR) denotes high risk of fetal complication. When low-risk foetuses with lower CPR have intrapartum distress within 72 hours after the start of labour, the prevalence of obstetric intervention is greater. This work aimed to assess CPR as evaluated during term pregnancy and before onset of the labor in normotensive and hypertensive pregnancies and its relationship with perinatal outcomes with reference to intrauterine growth restriction (IUGR), fetal distress, APGAR score, birth weight and admission at Neonatal Intensive Care Unit (NICU).
Methods: This prospective observational study was performed on 40 pregnant cases, their age ranging in years from 20 to 35, singleton living pregnancy, gestational age (37-40) weeks and before onset of labor and cephalic-presenting fetus. Participants were divided into two equal groups: normotensive cases and hypertensive cases.
Results: Significant difference between two studied group regarding abdominal circumference (AC), Amniotic fluid index (AFI), estimated fetal weight (EFW), Umbilical Artery pulsatility index (UAPI), middle cerebral arterial pulsatility index (MCAPI), CPR, APGAR scores at one and five minutes were substantially reduced while rates of cesarean sections and NICU admissions were significantly higher in hypertensive compared with normotensive women. The cutoff value was 1.1 for CPR yielded a sensitivity of 90%, a specificity of 70%, a PPV of 75% and a NPV of 88% with 83% accuracy and with AUC of 0.955.
Conclusions: CPR has high predictive value of perinatal outcome as Apgar score and rate of NICU admission in hypertensive pregnant women.

Keywords: Cerebroplacental ratio, normotensive, hypertensive, perinatal outcome

Introduction
Fetal hypoxia during intrapartum and before onset of labor induces adverse neonate outcomes like cerebral palsy and even death of the fetus [1, 2]. Continuous cardiotocography (CTG) was used during labour but it was shown to have limited specificity for forecasting foetal hypoxia and was not specifically intended to reduce the risk for cerebral palsy or prenatal death [3, 4]. Accordingly, when there is a danger of hypoxia during pregnancy, the continuous CTG is indicated, whereas the intermittent CTG can be used in case of low-risk pregnant women [5-8].
Occurrence of undesirable perinatal outcomes among pregnant women at time of labor admission necessitated the evaluation according to antepartum features and medical history that identify the cases at high risk of intrapartum hypoxia so more fetal monitoring is recommended [9]. Individuals at risk can be found by using Doppler ultrasound in the pregnancy with at term, normal-sized foetuses especially hypertensive pregnant females and normotensive cause with subclinical placental insufficiency.
At or after 37 weeks of pregnancy, the decreased cerebroplacental ratio (CPR) denotes high risk of fetal complication [10, 11]. When low-risk foetuses with lower CPR have intrapartum distress within 72 hours after the start of labour, the prevalence of obstetric intervention is greater. (12).
It is proposed that the of CPR assessment before onset of labor due to fetal distress or fetal hypoxia and the predication of adverse prenatal outcomes [13]. One of the frequent pregnancy problems, hypertension is known to greatly increase the mortality and morbidity of mothers and prenatal ones [14]. Doppler analysis of cerebral vascular blood flow can detect the alternation of cerebral circulation before fetal heart rate changes induced by hypoxia the most accessible

vessel is middle cerebral artery [15]. This work aimed to assess CPR as evaluated during term pregnancy (between 37-40 th week of gestation) and before onset of the labor in normotensive and hypertensive pregnancies and its relationship with perinatal outcomes with reference to intrauterine growth restriction (IUGR), fetal distress, APGAR score, birth weight and admission at neonatal Intensive Care Unit (NICU).

Patients and Methods

This prospective cohort observational work was performed on 40 pregnant cases with age ranging in years from 20 to 35, singleton living pregnancy, gestational age (37-40) weeks and before onset of labor and cephalic-presenting fetus. The research was carried out after obtaining authorization from the Ethics Committee of Tanta University Hospitals' Department of Obstetrics and Gynaecology, Tanta University Hospitals from the first day of October 2020 till 30 September 2021. Each case signed a formal consent with full information.

Patients were split onto two groups at equal: group A (full term normotensive pregnant cases) and group B (full term hypertensive pregnant cases were included, gestational hypertension, preeclampsia, chronic hypertension, superimposed preeclampsia).

Exclusion criteria were placenta previa or abnormal placentation, any maternal metabolic disordered, morbid obesity with BMI more than 35 kg/m^2, fetal growth restriction and fetal anomaly identified either antenatal or postnatal in previous pregnancies, signs of antepartum hemorrhage, intrauterine infection, premature rupture of membrane and true uterine contraction.

The following tests were performed on the participants that were included: full taking of history, complete general examination, complete abdominal examination, and abdominal ultrasound examination (Fetal biometry, BPD., FL, AC, presentation, fetal well-being and estimate fatal weight and heart rate, amniotic fluid index and estimated fetal weight after delivery of fetus).

Doppler ultrasound

Doppler Ultrasound scanning using (Mindray DC 30 CHINA) by using Middle cerebral artery (MCA) and umbilical artery (UA) pulsatility indexes were assessed. CPR was computed by dividing MCA pulsatility index by UA pulsatility index. The ratio of the MCA-PI and UA-PI was used to determine the CPR. Near the MCA's internal carotid artery origin, in the proximal third, the gate pulsed-wave Doppler of was positioned. As near to 0 degrees as feasible, and no > 15 degrees, were maintained as the angle between the ultrasonic beam with the direction of blood flow. There were recorded at least 3 and no more than ten successive waveforms. Caliper lines were positioned within the vessel's perimeter. When there were at least 3 successive waveforms with a consistent flow velocity with a high signal-to-noise ratio, umbilical artery (UA)Doppler evaluations were carried out in a stationary free loop. The initial fetal blood vessel to be impacted by placental insufficiency is often the UA. Resistance of blood flow in the UA increases retrogradely as a result of the first rise in placental blood flow, or vascular impedance. As placental insufficiency worsens, the descending aorta's blood flow resistance rises, which causes more blood to be diverted across the aortic isthmus shunt to the fetal brain. The second vascular sign in the chain of placental insufficiency, a reduced middle cerebral artery pulsatility index (MCA-PI), reflects that occurrence.

For effective prenatal Doppler monitoring and as part of careful surveillance, early diagnosis of aberrant blood flow redistribution patterns is crucial. This might help to lower fetal mortality and morbidity. The most effective vascular indicator for identifying the aforementioned fetal redistribution patterns has been examined and recommended as CPR.

Knowing the threshold value of CPR, which determines whether it is pathologic or normal, is necessary for effective identification of fetal redistribution of blood flow as an indicator of unfavorable perinatal outcomes.

CPRs over 1.0 are regarded as normal, whereas those below 1.0 are regarded as abnormal. Follow-up on perinatal outcomes, including fetal distress, intrauterine growth restriction (IUGR), stillbirth or live birth, the 5-minute APGAR score, birthweight, and NICU admissions.

Statistical analysis

SPSS v26 (IBM Inc., Chicago, IL, USA) was used for the statistical analysis. The unpaired Student's t-test was used to compare quantitative data between the two groups. The quantitative data were provided as mean and standard deviation (SD). The Chi-square test or Fisher's exact test was used to examine qualitative variables that were reported as frequency and percentage. To determine the overall predictability of the parameter and the appropriate cut-off value with the identification of both specificity and sensitivity at this cut-off value, receiver operating characteristic (ROC curve) analysis was employed. Statistical significance was defined as a two tailed P < value 0.05.

Results

The comparison of (age, gestational age, and BMI) showed no substantial variation among studied groups concerning age, BMI, and Gestational age, but there were significant differences regarding Blood pressure (systolic and diastolic). Table 1

Table 1: Demographic data and blood pressure of the groups under study

	Group A	Group B	P. value
Demographic data			
Age (years)	27.75±3.92	27.90±4.24	0.908
Gestational age (week)	38.45±0.69	38.10±1.1	0.241
BMI	27.76±1.51	28.45±1.81	0.202
Systolic (mmHg)	102.50±8.51	144.0±15.10	0.001*
Diastolic (mmHg)	69.00±6.81	98.25±7.30	0.001*

* Significant p value < 0.05

Significant difference between studied groups as regarding all Ultrasound scanning measurements (AC, EFW and AFI). Table 2

Table 2: Ultrasound scanning of both groups

	Group A	Group B	P. value
FL (mm)	80.94±3.40	79.59±4.87	0.315
AC (mm)	358.10±13.23	340.45±16.93	0.001*
BPD (mm)	94.65±1.96	93.70±2.35	0.173
EFW (kg)	3.41±0.22	2.94±0.30	0.001*
AFI (cm)	14.60±1.19	12.75±1.59	0.001*

* Significant p value < 0.05.

Significant difference among studied groups based on Doppler ultrasound scanning (UAPI, MCA PI and Ratio). Table3

Table 3: Doppler ultrasound scanning of umbilical artery and middle cerebral artery

	Group A	Group B	P. value
UA PI	0.72±0.02	1.04±0.10	0.001*
MCA PI	2.61±1.0	1.49±0.36	0.001*
Ratio	3.61±1.37	1.44±0.36	0.001*

* Significant p value < 0.05.

A substantial variation among studied groups based on Mode of delivery and admission at NICU. Table 4.

Table 4: Mode of delivery, causes of cesarean section and admission at neonatal intensive care unit in the studied groups

	Group A (N%)	Group B (N%)	P-value
Mode of delivery			
Vaginal delivery	13 (65.0%)	10 (50.0%)	0.337
Cesarean section	7 (35.0%)	10 (50.0%)	
Cesarean section			
Cephalo pelvic disproportion	2 (28.6%)	2 (20.0%)	
Fetal distress	3 (42.9%)	5 (50.0%)	0.916
Previous cesarean section	2 (28.6%)	3 (30.0%)	
Neonatal outcome			
NICU (Yes)	0 (.0%)	7 (35.0%)	0.004*
Live birth	20 (100.0%)	20 (100.0%)	-
Still birth	0 (.0%)	0 (.0%)	

NICU: neonatal intensive care unit
* Significant p value < 0.05

A substantial variation among studied groups concerning APGAR score 1 minute and 5 minutes. Table 5**.**

Table 5: Comparison between studied groups concerning APGAR score at 1 minute and 5 minutes and fetal weight after delivery

	Group A	Group B	P. value
APGAR 1	8.30±0.66	5.0±0.73	0.001*
APGAR 5	9.30±0.47	6.80±1.28	
Fetal weight after delivery (kg)	3.38±0.24	2.96±0.31	

* Significant p value < 0.05.

Regarding the ROC curve, the cutoff value was 1.1 for CPR yielded a sensitivity of 90%, a specificity of 70%, a PPV of 75% and a NPV of 88% with 83% accuracy and with AUC of 0.955. Figure 1.

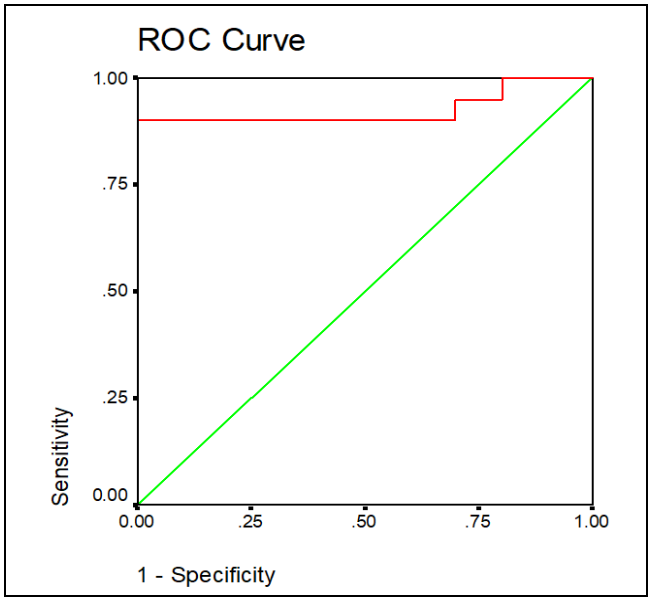
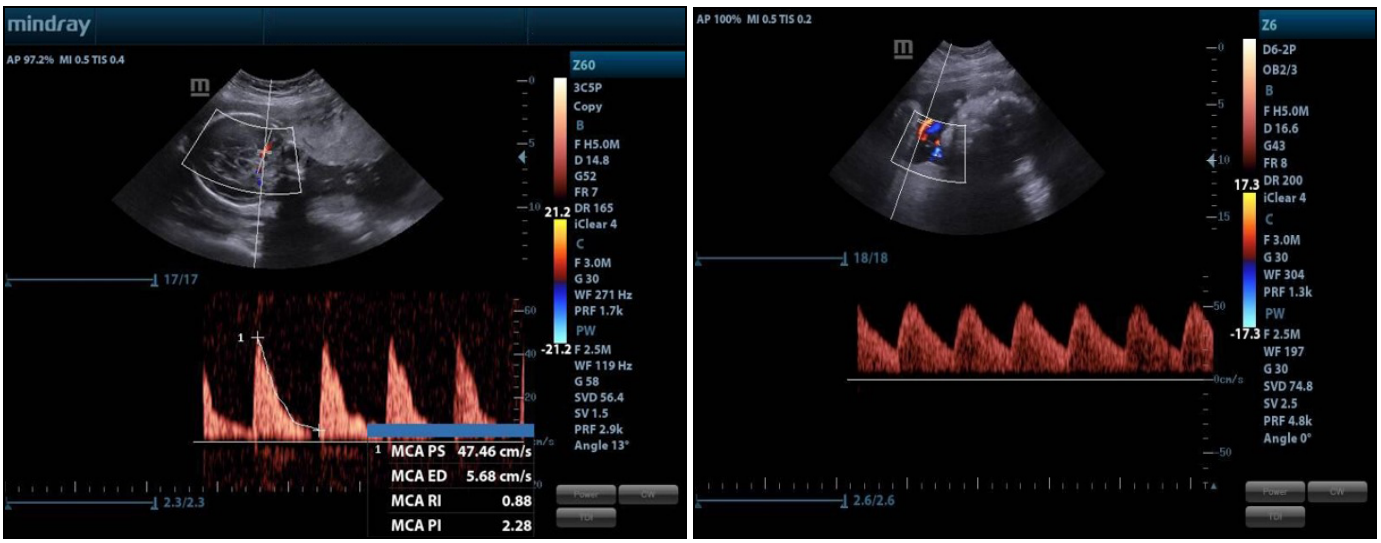


Fig 1: ROC curve

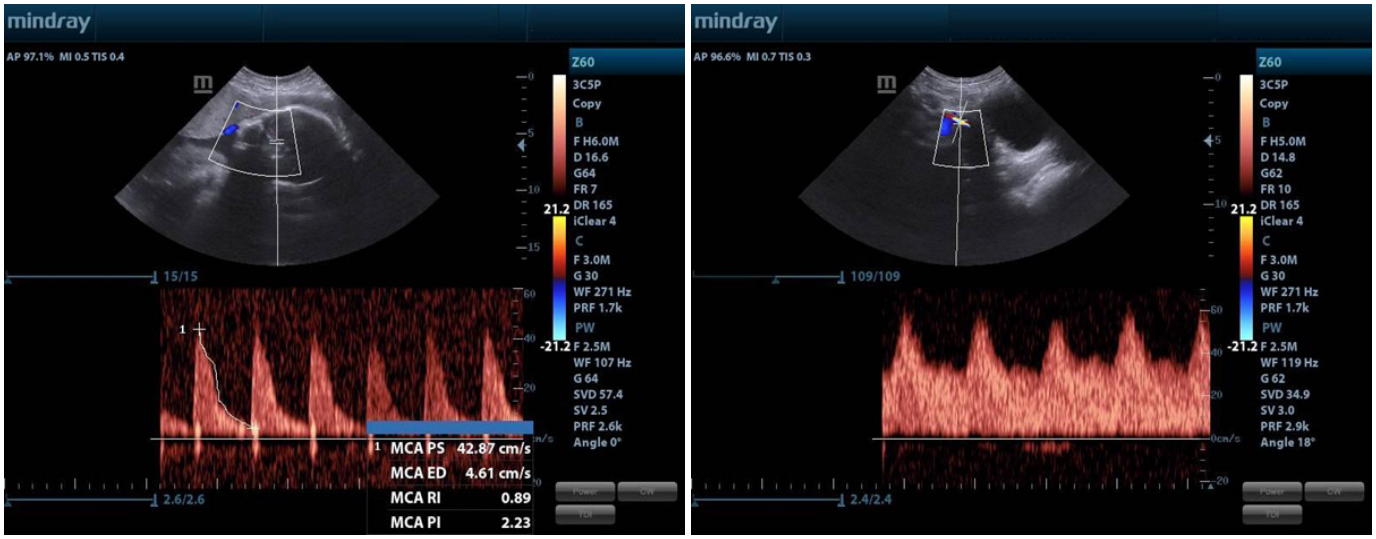
Examples of middle cerebral artery (MCA PI) and umbilical artery (UA) pulsitilty index at 38 weeks of gestation in normotensive patients. Figure 2.



A B

Fig 2: Doppler of (A) middle cerebral artery pulsitilty index measurement (MCA PI) and (B) umbilical artery (UA) in 38 week of gestation in normotensive patients

Examples of umbilical artery (UA) and middle cerebral artery (MCA) pulsitility index at 40 weeks in a hypertensive patient. Figure 3.



A B

Fig 3: Doppler study of middle cerebral artery (MCA) (A) and umbilical artery (UA) (B) pulsitility index at 40weeks in a hypertensive patient

Discussion

Doppler ultrasonography detected individuals at risk, particularly hypertensive pregnant females and normotensive with subclinical placental insufficiency, in pregnancies with normal sized babies at term [16].

At or beyond 37 weeks of pregnancy, a decreased CPR increases the chance of fetal problem. Regarding fetal biometry, statistical analysis of current results showed that AC, EFW and AFI were significantly lower in hypertensive compared with normotensive women.

Abdelwahid *et al*., [17] agreed with current study and stated that EFW (mean ± SD and range) grams was substantially reduced in hypertensive women contrasted to the control group 1019 ± 1.9 (657-3461) vs. 3181 ± 2.1 (876-3742).

In order to evaluate the fetus at higher risk of a poor perinatal outcomes, Patil *et al*. [18] research was focused on determining the function of CPR in pregnant women with hypertension conditions. This cohort research was carried out at the Mysore Hospital in India. For the study, 128 antenatal women who were more than 32 weeks along were chosen, and initial information was gathered and exposed to the ultrasound scan. They agreed with current study and stated that average fetal weight was significantly restricted in hypertensive women (34.3%) ranged between 1.5-2.5 kg. Also, A strong correlation was existed between the ultrasound gestational age and CPR, with aberrant CPR (value <1) being seen in gestations longer than 32 weeks..

Regarding Doppler indices, statistical analysis of current results showed that UA PI, MCA PI and CPR were substantially decreased in hypertensive contrasted to normotensive women.

Abdelwahid *et al*., [17] agreed with current study and stated that After adjusting for gestational age, MCA-PI, the UA-PI, and CPR were significantly lower and related with poor perinatal outcomes in the gestational hypertension group. For UA-PI, MCA-PI, and CPR, the risk of a higher rate of elective cesarean delivery, less weight at birth, and preterm birth increased in a way that was statistically substantial.

Patil *et al*., [18] was in line with present study and stated that UA-PI, MCA-PI and CPR values were significantly lower in hypertensive cases; UA PI exhibited a mean value of 1.34 (with a range 0-2.6) and the MCA PI exhibited a mean value of 1.22 (scores ranged from 0 to 1.96). When the CPR was determined, it exhibited a mean value of 0.92 and a range of 0 to 1.63; anything below 1.0 was deemed abnormal, while anything over 1.0 was also deemed abnormal.

Abdelrazik *et al*., [19] evaluated the MCA-PI and UA-PI ratio role in forecasting neonatal outcomes in pregnancy-induced hypertension. The reliability of the MCA/UA PI ratio for forecasting acidemia, admission to the NICU, and poor Apgar scores at 5 minutes after delivery in neonates of severe preeclamptic pregnant women was assessed in this research, which comprised 100 women with severe preeclampsia. The MCA/UA PI ratio was having poor predictive value for a minimal UA PI as p value =0.318 which is not statistically substantial, which may be due to different sample size and population criteria compared with current study. They agreed with the current study and stated that there was a significant association between CPR ratio and poor Apgar score at five minutes and CPR ratio was lower in hypertensive cases.

According to Alalfy *et al*. [20] who supported the findings of the present investigation, MCA PI, UA PI, CPR, birth weight, and fetal weight were statistically substantially greater in the control research group than in the hypertensive pregnancy research group (p values <0.001).

Regarding the ROC curve, the cutoff value was 1.1 for CPR yielded a sensitivity of 90%, a specificity of 70%, a PPV of 75% and a NPV of 88% with 83% accuracy and with AUC of 0.955.

In disagreement with our study, Guo, Chai *et al*. 2019 found that CPR cutoff values in 37 to 41+6 weeks was 1.29, 1.36, and 1.22, respectively [21].

In contrast to our study, DeVore 2015 found that CPR cutoff value in 37 to 41+6 weeks was 0.67 [22].

Limitations: More clinical studies with greater sample sizes and more data are required for further evaluation and detection of cutoff value of CPR with proper sensitivity and specificity

Conclusions

CPR is an important predictor of adverse perinatal outcomes as APGAR score, small for gestational age and rate of NICU admission in hypertensive pregnant women with a cutoff value is 1.1.

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Conflict of Interest: Nil

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