Original Article

The Prevalence of Abnormal Cerebro-Placental Doppler Indices Ratio [CPR] in Hypertensive Disorders of Pregnancy

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Objective: 1) To determine the prevalence of abnormal cerebro-placental Doppler indices ratio [CPR] in hypertensive disorders of pregnancy. 2) To analyze the association between abnormal CPR and perinatal outcomes.

Materials and Methods: A cross sectional study was conducted between July 2016 and July 2017 at Bhumibol Adulyadej Hospital. One hundred forty-eight singleton pregnancies with hypertensive disorders during 28 to 40 weeks of gestation were enrolled. Doppler ultrasound analysis of the fetal umbilical and middle cerebral arteries were performed, and the CPR was calculated and interpreted. Patients were followed up until delivery and perinatal outcomes were analyzed.

Results: The present study showed abnormal CPR in 35.62% (52) of the population (148). Pregnancies with abnormal CPR had a significantly increased risk of small for gestational age [SGA] (odds ratio [OR] 3.15; 95% confidence interval [CI] 1.24 to 7.98; p = 0.013), and neonatal intensive care unit [NICU] admission (OR 2.19; 95% CI 1.07 to 4.47; p = 0.030). There was no significant difference in preterm delivery, non-reassuring fetal heart rate pattern, low Apgar score, hypoglycemia, hypothermia, and hyperbilirubinemia.

Conclusion: The prevalence of abnormal CPR in hypertensive disorders of pregnancy was 35.62%. Compared to pregnancies with normal CPR, pregnancies with abnormal CPR were significantly associated with SGA and NICU admission. CPR parameters should be interpreted with caution for assessing the fetal status and prediction of pregnancy outcomes in hypertensive disorders of pregnancy.

Keywords: CPR, Perinatal outcomes, Hypertensive disorders of pregnancy

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Hypertension related to the pregnancy contributes to negative pregnancy outcomes, to both mother and fetus. Fetus can be affected or even die. Pregnancy-induced hypertension [PIH] is the cause 17% of directed obstetric death in developing countries[1]. The prevalence of pregnancy-related hypertension at Bhumibol Adulyadej Hospital between 2005 and 2014 is 0.48%[2]. It can increase risk of super imposed-preeclampsia, cesarean section rate, and fetal growth restriction [FGR][1,2]. The fetal adverse outcomes can be evaluated by ultrasonographic examination of fetal circulation and placenta[3]. The cerebroplacental ratio [CPR], first described in the 1980s, demonstrated the association of abnormal ratio with adverse perinatal outcomes and postnatal neurological deficit. The CPR has been considered as an important predictor of adverse pregnancy outcome and has been used for the assessment of well-being in fetuses diagnosed as small for gestational age [SGA] and appropriate for gestational age [AGA] at near term[4-7]. The CPR is calculated by dividing the Doppler indices of the middle cerebral artery [MCA] by the umbilical artery [UA]. The CPR represents the interaction of alterations in blood flow to the brain as shown by increased diastolic flow from cerebrovascular dilation in hypoxia fetus and increased placental resistance from decreased diastolic flow of the UA. The increased diastolic flow of the MCA results in a decrease in the systolic/diastolic ratio [S/D], resistance index [RI] [(systolic peak velocity/diastolic peak velocity)/systolic peak velocity], and the pulsatility index [PI] [(systolic peak velocity/diastolic peak velocity)/velocity time integral]. In the UA, those measurements are increased as the result of increased resistance to blood flow, which results from placental pathology. The S/D ratio, RI, and PI have been reported for their uses to compute the CPR. The PI CPR is the preferable index reported in their literature[8-10]. The purpose of the present study was to determine the prevalence of abnormal CPR in hypertensive disorders of pregnancy and analyze the association between abnormal CPR and pregnancy outcomes.

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Materials and Methods

A cross-sectional study was conducted. The present study was approved by the Bhumibol Adulyadej Hospital Ethic Committee. The hypertensive pregnant women that attended antenatal care between July 1, 2015 and July 31, 2016 were recruited. The inclusion criteria were singleton pregnancy, corrected pregnancy dating by confirmed LMP or first trimester ultrasound, and diagnosed as gestational hypertension or preeclampsia or chronic hypertension and delivered at the hospital. Exclusion criteria were women with fetal abnormalities or lost follow-up. Sample sized was calculated from the incidence of abnormal CPR in neonates with SGA[11]. One hundred forty-eight patients were recruited for estimated population prevalence with 95% confidence and acceptable error within 8%. Ultrasound scanning for Doppler parameters of MCA and UA of fetus for CPR were done only one time during gestational 28 to 40 weeks. To measure MCA and UA related parameters, the Doppler range-gate was placed on the middle portion of MCA and over the free loop of umbilical cord, respectively. The angle of insonation was kept almost always less than 10 degrees, as recommended by Abuhamad[12]. The SPSS software (SPSS 16.0, SPSS Inc., USA) was used for statistical analysis to summarize mean and proportion where appropriated. Chi-square test, relative risk with 95% confidence interval [CI] was used to compare between categorical variables. A *p*-value of less than 0.05 was considered as significant. All patients provided written informed consents approved by the Bhumibol Adulyadej Hospital, Royal Thai Air Force's Ethic Committee (IRB 59/60).

Results

One hundred forty-eight hypertensive pregnant women were enrolled into the study, two cases were lost follow-up, thus, 146 cases were studied. There were 51 primigravida and 95 multigravidas. Out of 146 women with hypertensive disorders of pregnancy, 52 cases (35.62%) had abnormal CPR, and 94 cases (64.38%) were normal. Demographic data of the study population is shown in Table 1. There were no significant differences between women with normal CPR and abnormal CPR in term of maternal age, height, gestational age [GA] at examination, GA at delivery, and birth weight of the baby. Mean maternal weight of women with normal CPR (85 kg) was significantly higher than mothers with abnormal CPR (76 kg). The mean height was 160 and 158 cm. The mean maternal ages were 33.38 and 32.46 years. The mean of GA at examination were 33.88 weeks and 33.85 weeks. The mean of GA at delivery were 37.37 weeks and 37.25 weeks. The mean of birth weight were 3,024 and 2,813 grams, respectively.

Abnormal CPR and normal CPR in prediction of perinatal outcomes are compared in Table 2. Significant differences were found in SGA newborns (25% versus 9.57%, 95% CI 1.24 to 7.98) and neonatal intensive care unit [NICU] admission (44.23% versus 26.60%, 95% CI 1.07 to 4.47). However, there was no significant difference in preterm, non-reassuring fetal heart rate pattern, low Apgar score, hypoglycemia, hypothermia, and hyperbilirubinemia.

Discussion

Ultrasound has an important role in current medical practice, especially Doppler sonography in obstetrics to predict perinatal outcomes. Doppler ultrasound of blood vessels and fetal vessels have been practiced worldwide. Abnormal Doppler waveforms in various vessels have been studied in pregnancy with hypertensive disorders. Abnormal umbilical Doppler indices and CPR are strong predictors of FGR and adverse perinatal outcomes. Recently, several studies showed that comparing with umbilical or MCA Doppler indices alone, CPR have better sensitivity and improved accuracy in predicting the placental abnormality in high-risk pregnancies liked preeclampsia[13,14].

Table 1. Demographic data of the study population

	Normal CPR (n = 94), mean ± SD	Abnormal CPR (n = 52), mean ± SD	*p*-value
Height (cm)	160.04±6.74	158.71±5.54	0.227
Weight (kg)	85.01±16.35	76.38±14.31	0.002
Age (year)	33.38±6.25	32.46±7.41	0.426
GA at examination (weeks)	33.88±2.95	33.85±3.27	0.945
GA at delivery (weeks)	37.37±1.69	37.25±1.96	0.693
BW(g)	3,024.66±611.77	2,813.19±751.20	0.068

GA = gestation age; BW = birth weight, CPR = cerebro-placental Doppler indices ratio

Table 2. Fetal outcomes in relation to abnormal CPR and normal CPR

Perinatal outcomes	Abnormal CPR (n = 52), n (%)	Normal CPR (n = 94), n (%)	Odd ratio	95% CI
Preterm	12 (23.07)	21 (22.34)	1.04	0.47 to 2.34
Non-reassuring fetal heart rate	1 (1.92)	4 (4.26)	0.44	0.05 to 4.05
SGA	13 (25.00)	9 (9.57)	3.15	1.24 to 7.98*
Low Apgar	0 (0.00)	1 (1.06)	1.01	0.99 to 1.03
NICU	23 (44.23)	25 (26.60)	2.19	1.07 to 4.47*
Hypoglycemia	22 (42.31)	37 (39.36)	1.13	0.57 to 2.25
Hypothermia	13 (25.00)	18 (19.15)	1.41	0.64 to 3.17
Hyperbilirubinemia	14 (26.92)	21 (22.34)	1.28	0.59 to 2.80
Mode of delivery			0.69	0.32 to 1.47
C/S	36 (69.23)	72 (76.60)		
Normal delivery	16 (30.77)	22 (23.40)		

SGA = small for gestational age; NICU = neonatal intensive care unit'; C/S = cesarean section; CPR = cerebro-placental Doppler indices ratio

* Statistical significant

Of the 146 women, we found that the prevalence of abnormal CPR in hypertensive disorders of pregnancy was 35.62%, in the range of previous reports, from 22% to 46%. This was also comparable with the study of the CPR as a prognostic factor of fetal outcome in pregnancy with hypertension and the study of abnormal CPR in preeclamptic and hypertensive women, they found the abnormal CPR were 29% and 32%, respectively[15,16]. The prevalence of 35.62% of the present report and the results from other reports have shown approximately one-third of hypertensive disorder pregnant women would have abnormal CPR, which might be at risk for adverse perinatal outcomes. The difference of prevalence reported, which ranged from 22% to 46%, depended upon the maternal conditions and the severity of hypertensive disorders. The mean GA at examination in the present study was 33 weeks. Reports from the study at GA 34 weeks had the prevalence of abnormal CPR 29%, at GA 37 weeks 32%[15,16]. Early detection of abnormal CPR would give the obstetrician time to plan for appropriate management to prevent adverse pregnancy outcomes.

Concerning the cut-off value for CPR, several studies reported the use of a single cut-off value for CPR such as 1 or below, or 1.08 or below[15-17]. Some reports had used other cut-off value as below the fifth centile, below the 2.5 centile, below the 0.05 MoM, or below the 0.6765 MoM[18]. The cut-off values used for the CPR at the authors' hospital and in the present study were the reference ranges according to GA. A study showed that the use of uniform cut-off of CPR for the second half of pregnancy predicted adverse outcome equally well compared with using reference ranges according to GA. The results of CPR performed before and after 34 weeks of gestation were different. This probably reflects differences in physiologic responses of vascular system of the fetus. CPR allows clinician to detect early the small changes in blood flow of particular vessels, detect fetuses at early onset of SGA, and predict the risk of adverse outcomes.

The result of 52 cases of abnormal CPR was compared with 94 cases of normal CPR for the fetal outcomes. SGA and NICU admission were significantly associated with abnormal CPR. Compared to other studies, they found statistically significant higher rate of babies with birth weight below the tenth percentile and Apgar score lower than 7 at 5 minutes in abnormal CPR. In addition, significantly greater number of neonates required NICU admission with abnormal CPR, and low Apgar score[19-21]. Low Apgar score was not significant in our study.

Limitation of the present study is small sample size, and some other confounding factors liked GA at examination, maternal conditions, and the types and severity of hypertensive disorders. CPR for fetal assessment and prediction of adverse pregnancy outcome is suggested in hypertensive pregnancies. CPR may be used for decision-making for appropriate intervention in obstetrical care and prevent the adverse pregnancy outcomes. Further studies are needed to validate our findings.

Conclusion

The prevalence of abnormal CPR in hypertensive disorders of pregnancy was 35.62%. Compared to pregnancies with normal CPR, pregnancies with abnormal CPR was significantly associated with SGA and NICU admission. CPR parameters should be interpreted with caution for assessing the fetal status and prediction of pregnancy outcomes in hypertensive

disorders of pregnancy.

What is already known on this topic?

Hypertension related to the pregnancy contributes to negative pregnancy outcomes, to both mother and fetus. Fetus can be affected or even die. Abnormal umbilical Doppler indices and CPR are strong predictors of FGR and adverse perinatal outcomes. Several studies showed statistically significant higher rate of babies with birth weight below the tenth percentile and Apgar score lower than 7 at 5 minutes in abnormal CPR. In addition, a significantly greater number of neonates are requiring NICU admission with abnormal CPR, and low Apgar score.

What this study adds?

Doppler ultrasound studies play an important role in the management of a pregnancy complicated by a diagnosis of FGR. CPR is not significantly related to Apgar score below 7 at 5 minutes. When using Doppler ultrasound studies of CPR for management of hypertensive pregnancies, the clinician should be aware that normal Doppler findings might relate to abnormal pregnancy outcomes. Further studies are needed to validate our findings. Our findings should be interpreted with caution for assessing the fetal status and prediction of pregnancy outcomes in hypertensive pregnancies.

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Potential conflicts of interest

The authors declare no conflict of interest.

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