

Utility of Cerebroplacental Ratio in IUGR Fetuses from Pregnancy with Preeclampsia in Prediction the Risk for Perinatal Complications

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ABSTRACT: Purpose. The aim of this study was to show that is the incidence of intrauterine growth restriction (IUGR) in women with preeclampsia (PE), assessment of cerebroplacental ratio (CPR) to establish the diagnostic value of CPR in fetuses with preeclampsia with/without IUGR. Material and Methods. We performed an analysis of 49 cases with gestational hypertension and PE and 16 cases with normal pregnancy for control lot, study in Obstetrics and Gynecology Clinic of the Municipal Hospital Filantropia, Craiova, between October 2013 and October 2015. It was performed clinical and laboratory evaluation and management of each case. CPR ratio was measured in the third trimester in all cases, being studied according to the normal and abnormal values obtained, following the evolution of the newborn. Results. Mild PE cases were predominant with 21 cases (19.27%), severe PE accounted for 16 cases (14.68%) and gestational hypertension was found in 16 cases in our study. Distribution of IUGR cases presented interesting and contradictory data, because we met cases of IUGR in pregnancies without PE, at a rate of only 1.54%. The incidence of IUGR was significantly higher in cases with severe early-onset PE (10.20%). Cases of severe PE, but with late-onset, had IUGR in only 2.04% of cases. We found a significant statistical significance ($p < 0.005$) on the incidence of IUGR in cases with severe early-onset PE. CPR identified adverse perinatal outcomes in 18.46% of cases with CPR < 1.08 . Conclusions. This study shows that early onset severe PE and concomitantly IUGR affects a significant proportion of pregnancies. CPR can be used to identify fetuses with an increased risk of intrauterine compromise.

KEYWORDS: *intrauterine growth restriction, preeclampsia, cerebroplacental ratio*

Introduction

Preeclampsia is inconsistently associated with intrauterine growth restriction, but PE and gestational hypertension causes IUGR to occur in 30-40% of cases [1]. Intrauterine growth restriction can be a serious problem in newborns because it is associated with increased morbidity and mortality and long-term neurological sequelae.

From historical point of view, PE was considered that it would lead to some of the worst cases of IUGR. More specifically, there is a lack of evidence demonstrating that IUGR, unless otherwise severe maternal symptoms, should lead to the diagnosis of severe disease and therefore an important impact in clinical

management [2]. Current theories show that the primary cause of IUGR in preeclampsia is abnormal invasion of placental trophoblast. If this theory is correct, we can expect than women with severe preeclampsia to have the highest IUGR risk. Also, according to the same theory, we expected that women with mild preeclampsia would be less likely to have IUGR fetuses [3]. But things are not at all because according to this theory we do not have an explanation for IUGR that occurs also in the absence of preeclampsia. Impaired placental perfusion appears before clinical manifestations of PE and can be followed by Doppler ultrasound [4]. The use of CPR allows the assessment of blood flow disorders in the placenta, umbilical cord, and fetal-cerebral circulation. CPR reflects fetal adaptation to placental chronic hypoxia and

appears to be more sensitive than the Doppler ultrasound of the umbilical and middle cerebral artery by detecting clinically unrecognized fetal compromise [5].

Material and methods

The study was conducted to describe the prevalence of IUGR in women with preeclampsia compared with controls, investigate the relationship between PE and IUGR and investigate the relationship between IUGR, PE and cerebroplacental ratio. To achieve these objectives, we performed a prospective analysis of 49 cases with gestational hypertension and PE and 16 cases with normal pregnancy as controls, studied in Obstetrics and Gynecology Clinic of the Municipal Hospital Filantropia, Craiova, between October 2013 and October 2015. The pregnancies that booked consecutively for pregnancy screening in the first or second trimester were considered eligible for the study. The university and hospital's Ethics Committees approved the utilization of the data for scientific purposes, and written informed consent was obtained from the patients or their caregivers before the evaluations.

We recorded maternal characteristics and medical history of the enrolled pregnant women. For the calculation of CPR, we used the following Doppler indices of middle cerebral

artery (MCA) and umbilical artery (UA): resistance index (RI), pulsatility index (PI) and cut-offs <1.08 to predict the complications [6]. CPR ratio was measured in the third trimester in all cases, being studied according to the normal and abnormal values obtained, following the evolution of the newborn according to a number of parameters: Apgar score <7 at 1 and 5 minutes, admission to the neonatal intensive care department, gestational age at delivery, IUGR diagnosis, neonatal birth weight. It was performed clinical and laboratory evaluation and management of each case.

Results

We did not have major adverse perinatal outcome as stillbirth and neonatal death. The minor adverse perinatal outcome was admission to the neonatal intensive care department, Apgar score ≤ 7 at 5 minutes, cesarean delivery for fetal distress, low birth weight.

Distribution of cases by diagnostics groups of PE showed us that mild cases of PE were predominant, 21 cases (19.27%), followed by cases of severe PE, 16 (14.68%), characterized by systolic blood pressure ≥ 160 mmHg and/or DBP ≥ 110 mmHg and proteinuria ≥ 300 mg/l in a collection of urine/24h with or without systemic general symptoms or fetal distress (Fig. 1).

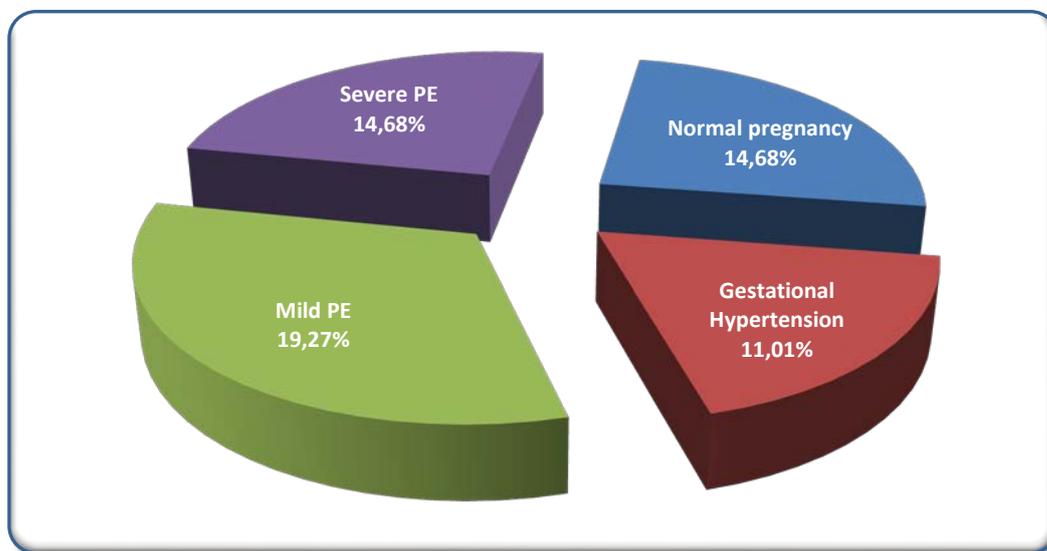


Fig. 1. Distribution of cases with PE

We have studied the implication of the onset of PE on the development of the fetus. Distribution of IUGR cases presented interesting and contradictory data because we met cases of

IUGR in pregnancies with normal evolution, is true that a low percentage, 1.54%.

The IUGR percentage was increased in severe and in mild PE, 9.23% and 7.69% respectively (Fig. 2)

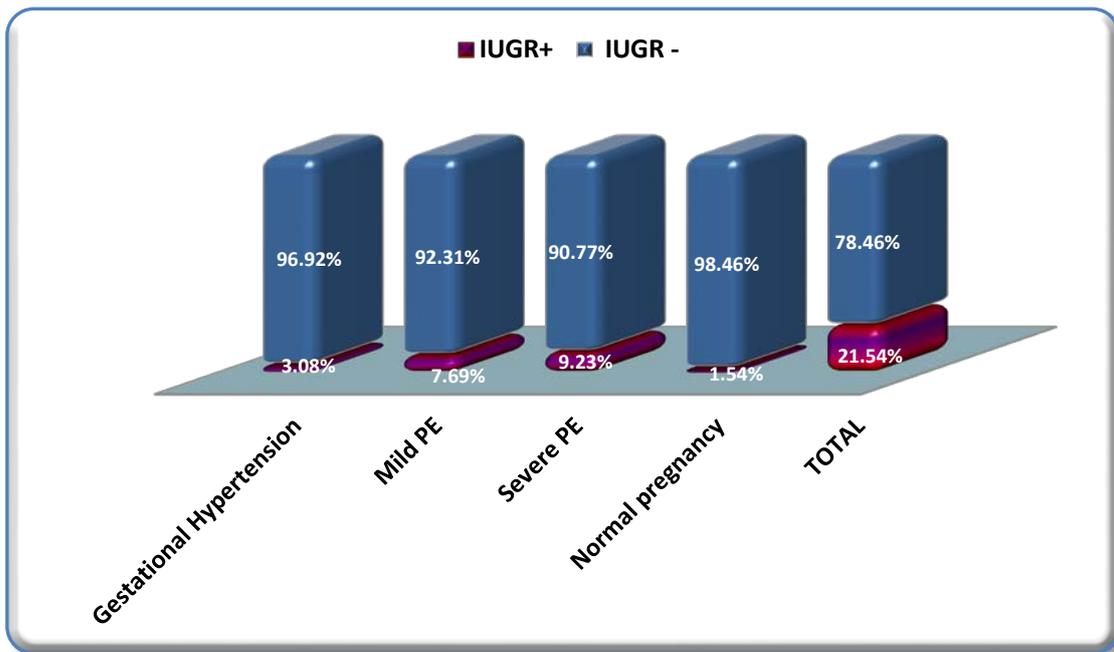


Fig. 2. The distribution of IUGR

Early onset of PE, is frequently associated with IUGR and maternal and neonatal complications. In contrast, late-onset PE, after 34 weeks, is mostly associated with a low rate of fetal involvement and favorable perinatal outcomes.

We found in our study, a higher distribution of IUGR cases with early onset PE, especially in cases with severe PE, 5 of 6 cases (10.20%) with early onset severe preeclampsia <34 weeks, and 1 case (2.04%) with late-onset severe PE >34 weeks developing IUGR. (Fig. 3).

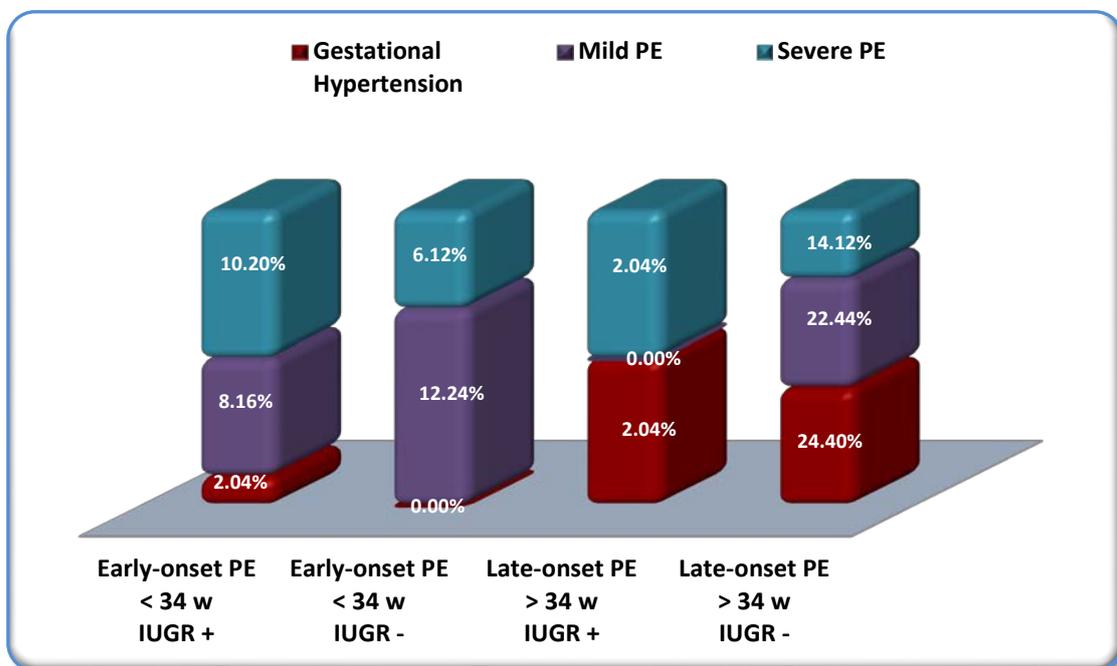


Fig. 3. Repartition of IUGR following the onset of PE

CPR that reflects fetal adaptation to placental chronic hypoxia appears to be more sensitive than the Doppler ultrasound of the umbilical and cerebral artery assessed separately, by detecting

clinically unrecognized fetal compromise [5]. We used this concept to see the implication of CPR in detecting the fetus with a risk of antenatal compromise (Table 1).

Table 1. Adverse perinatal outcome in correlation with CPR

Parameter	Birth weight in grams (Mean±SD)	Gestational age at birth in weeks (Mean±SD)	Apgar score		Admission to NICD (%)	CS for fetal distress (%)	IUGR (%)
			Apgar ≤ 7 at 1 min. (%)	Apgar ≤ 7 at 5 min. (%)			
CPR>1.08	3100±504.09	38±0.96	12.30	3.07	7.69	15.46	4.61
CPR<1.08	2405±241.07	36.3±0.80	18.46	10.76	18.46	44.44	16.92

In 21.53% of cases we had CPR<1.08 according to Gramellini [6]. In these cases, we noticed a birth weight of 2405±241.07g compared to a birth weight of 3100±504.09g in fetuses with CPR>1.08. Gestational age at birth was lower for CPR <1.08 (36.3±0.80 w) versus fetuses with CPR>1.08 (38±0.96 w).

Apgar score in fetuses with CPR<1.08 was ≤7 at 5 minutes in 10.76% of cases, compared with 3.07% in fetuses with CPR>1.08.

Admission to NICD was higher by 18.46% vs. 7.69% in fetuses with low CPR compared to those with CPR>1.08.

Also increased the percentage of cesarean section for fetal distress in fetuses with CPR <1.08, which was 44.44% of all cesarean section, compared to 15.46% in fetuses with CPR>1.08. In our study, we found 16.92% fetuses with IUGR who presented a CPR deterioration.

Discussion

IUGR and PE is an obstetric complication, which has an incidence of 10% and 3-10% respectively of all pregnancies [7]. It is important to identify the IUGR-affected pregnancy in order to be able to apply an intervention to reduce the morbidity and mortality caused by this pathology [8].

While early onset PE appears to be due to poor trophoblastic invasion and failure of spiral artery remodeling, late PE is due to the maternal inflammatory vascular status of normal pregnancy or placental atherosclerosis at baseline normal placental development [9].

A study from 2015 [12], showed that the late onset of severe preeclampsia had no effect on the incidence of IUGR.

In our study, the most important statistical significance on IUGR was found just in cases with early onset severe PE. Villar et al. [1] suggest that the inexplicable IUGR, even if it

has a similar PE etiology, appears to be biologically separated, even though PE and IUGR have probably a similar pathophysiologic spectrum.

The complexity of the entire system is well documented, with similar placental changes in IUGR pregnancy without PE coexistence.

In our study, we had, indeed, a small number of cases with IUGR pregnancies without PE, only 1.54%.

Several studies have proposed that a combination PE+IUGR is associated with a phenotype of severe PE, compared to women with PE and without IUGR [11,12].

Fetal hypoxia represents one of the causes of perinatal morbidity and mortality rates [13]. CPR determination is used to evaluate fetal response to hypoxia in utero.

There is a decrease of resistance in fetal circulation once the pregnancy progresses to term. But resistance in middle cerebral artery should remain higher than in the umbilical artery. Therefore, CPR should be greater than 1-1.1 in an uncomplicated pregnancy [14].

In our study, the decrease of CPR<1.08 determined a lower birth weight at a lower gestational age, and consequently an increase in the cesarean section for fetal distress.

The Apgar score was lower than in cases with CPR>1.08, which led to an increase in admission to NICD.

It seems that one of the risk factors for intrapartum fetal distress would be the installation of cerebral redistribution before labor rather than the degradation of fetal biometric status.

Thus, CPR can be used to identify fetuses that have a higher risk of hemodynamic damage before birth, CPR being considered as a marker of placental underperfusion and placental reserve [15].

Conclusion

Integrating CPR in clinical management may help to better identify fetuses at risk for adverse perinatal events, since abnormal CPR has been associated with an increased risk of perinatal complications, especially in IUGR fetuses from PE pregnancy.

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