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Retrospective Study For Predicting Perinatal Outcome Using Cerebroplacental Ratio İn Fetal Growth Restricted Pregnancy

İntrauterin Gelişme Kısıtlılığı Olan Hastalarda Serebroplasental Oranın Fetal İyilik Halinin Belirlenmesindeki Etkisinin Gösterilmesine Dair Retrospektif Çalışma

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ÖZ

Amaç: Fetal büyüme kısıtlılığından etkilenen gebeliklerin perinatal sonuçlarını serebroplasental oran kullanarak araştırmak ve öngörmeye çalışmak.

Gereç ve Yöntemler: Doğum öncesi kliniğine başvuran 100 yüksek riskli gebe üzerinde retrospektif bir çalışma yapıldı. 66 hamile kadına ıntra uterin gelişme kısıtlılığı teşhisi kondu. Ve 34 hamile kadına küçük sağlıklı bebek teşhisi kondu. Tüm hastaların temel demografik, geçmiş obstetrik ve tıbbi öyküleri kaydedildi. İntra uterin gelişme kısıtlılığı; sonografik ölçüme dayalı olarak gebelik yaşı için 10 persentilin altındaki tahmini fetal ağırlığı olan gebelere konuldu. 'Küçük sağlıklı bebek' teşhisi ; fetal ağırlığın veya fetal karın çevresi ölçümünün 10. persantilin altında olduğu ancak doppler parametreleri normal olan fetüslere konuldu. Ancak bu fetüslerde beklenen büyüme potansiyeline ulaşmasını engelleyen patolojik faktörler yoktu. Gebelikleri değerlendirmek için orta serebral arter ve umbilikal arterlerin doppler ultrasonografisi kullanıldı. Serebroplasental oran ; Orta serebral arterin persentil indeksinin Umblikal Arterin persentil indeksine bölünmesiyle hesaplanır. Serebroplasental doppler oranının 1'in altında olması anormal kabul edildi. Yenidoğanların bütün olumsuz perinatal sonuçları kaydedildi.

Bulgular: 100 gebe serebroplasental orana göre iki gruba ayrıldı. Grup A' nın serebroplasental oranı 1 den büyüktü (n=87). Grup B' nin serebroplasental oranı 1 den küçüktü (n=13). Grup B'de perinatal morbiditenin istatistiksel olarak anlamlı derecede arttığı izlendi. Anormal serebroplasental orana sahip fetüslerin, daha kötü fetal prognoz ile güçlü bir şekilde korele olduğu izlendi. Respiratuar distres sendromu (p = 0.043; p <0.05), düşük apgar skoru (p = 0.015; p <0.05), mekonyum aspirasyon oranı (p = 0.015; p <0.05) ve yenidoğanlarda hiperbilirubinemi görülme insidansı (p = 0.015) ; p<0.05) Grup B'li yenidoğanlarda anlamlı olarak daha yüksek izlendi (p: 0.022). Yenidoğan yoğun bakım ihtiyacı, prematürite ve perinatal mortalite oranları serebroplasental oran düzeyine göre istatistiksel olarak anlamlı farklılık göstermedi (p> 0.05).

Sonuç: Doppler ultrasonografi intrauterin gelişme kısıtlılığı olan fetüslerin tanı ve tedavisinde en önemli yöntemdir. Parametrelerden biri olan serebroplasental oran klinisyenlere sadece fetal hayatta değil; ayrıca doğum sonrası fetal komorbid durumlar ve riskler hakkında da bilgi verir.

Anahtar Kelimeler: İntrauterin gelişme kısıtlılığı, umbilikal arter, orta serebral arter, doppler ultrason, serebroplasental oran

ABSTRACT

Objective: To investigate and predict perinatal outcomes of pregnancies affected with fetal growth restriction by cerebroplacental ratio.

Material and Methods: A retrospective study was conducted based on 100 high-risk pregnant who referred to the antenatal clinic. 66 pregnant women were diagnosed with ıntrauterine growth restriction. And 34 pregnant women were diagnosed with small for gestational age. Baseline demographic, past obstetric and medical histories were recorded for all patients. Intrauterine growth restriction was defined that an estimated weight below the 10th percentile for gestational age based on sonographic measurement. The diagnosis of small for gestational age was defined that fetal weight or fetal abdomainal circunference measurement is below 10th percentile. But it was diagnosed in fetuses with normal doppler parameters. And no pathological factors were preventing the fetus from reaching its expected growth potential. Doppler ultrasound of middle cerebral arteries and umbilical arteries were used to assess pregnancies. Cerebroplacental rate ; It is calculated by dividing Middle cerebral artery percentile index to Umbilical artery percentile index. The cerebroplacental doppler ratio less than 1 was accepted abnormal. Adverse perinatal outcomes for newborns were documented for all cases.

Results: 100 pregnant women were classified into two groups according to cerebroplacental ratio. Cerebroplacental ratio ratio of Group A is greater than 1 (n=87). And cerebroplacental ratio ratio of Group B is less than 1 (n=13). Perinatal morbidity statistically significantly increased in Group B. The fetuses with abnormal cerebroplacental ratıo were strongly correlated with worse fetal prognosis. Respiratory distress syndrome rates (p = 0.043; p <0.05), low apgar score of newborns (p = 0.015; p <0.05), meconium aspiration rates (p = 0.015; p <0.05) and incidence of hyperbilirubinemia in newborns (p = 0.015; p <0.05) were significantly higher in the newborns with Group B (p: 0.022). Need for neonatal intensive care, prematurity and perinatal mortality rates did not show a statistically significant difference according to the cerebroplacental ratıo level (p> 0.05).

Conclusion: Doppler ultrasonography is the most important method in the diagnosis and management of fetuses with IUGR. The cerebroplacental ratio, which is one of the parameters, can be explained to clinicians not only in fetal life; ıt also provides information about postpartum fetal comorbid conditions and risks.

Keywords: Intrauterine growth restriction, umbilical artery, middle cerebral artery, doppler ultrasonography, cerebroplacental ratio

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INTRODUCTION

Intrauterine growth restriction (IUGR) is defined as an estimated fetal weight lower than the 10th percentile according the calculated gestational week. Pregnancies affected by IUGR cause a major public health problem related to increased neonatal morbidity and mortality (1,2).

IUGR is the second main cause of perinatal mortality. It is seen in 3-10% of all pregnancies. The fetuses with IUGR have higher perinatal mortality of 6-10 times than fetuses with appropriate weight in a gestational week (3). About 5-10% of fetuses with intrauterine growth restriction are lost in the antenatal or neonatal period, 53% in the preterm period and 26% in the term period (3).

It is usually defined by the statistical deviation of fetal size from a population-based reference, with a typical threshold at the 10th, 5th or 3rd centile; such a threshold is considered better as indicative of a 'small-for-gestational-age' (SGA) fetus. SGA, however, differs from IUGR principally ; because it also encompasses a majority of constitutionally small but healthy fetuses at lower risk of abnormal perinatal outcome. Consensus-based definitions for early and late ıntrauterine fetal growth restriction (IUGR) in absence of congenital anomalies has been shown.(4)

The timing of delivery and determination of intrauterine fetal well-being are important to avoid perinatal morbidity and mortality in fetuses with IUGR. There are many methods for determining fetal well-being. These include maternal fetal movement monitoring, a nonstress test (NST), biophysical profile and fetal doppler ultrasonography evaluation. Among these methods evaluating fetal well-being in fetuses with IUGR, the importance of doppler evaluation stands out. Fetal doppler parameters include middle cerebral artery, ductus venosus, pulmonary artery, umbilical artery and uterine artery examinations. It is accepted that parameters in which two vessels are evaluated, such as the cerebroplacental ratio, give more valuable results (5).

The aim of this study is to evaluate the effectiveness of cerebroplacental ratio (CPR); which is frequently used in the follow-up of pregnant women with growth restriction, and to decide on timing of birth for the patients in our study group. This study aimed to evaluate doppler indices of umbilical, uterine and middle cerebral artery in fetuses with IUGR based on the gestational weeks and determine possible contribution of CPR for evaluating well-being in these fetuses.

MATERİAL AND METHODS

One hundred high-risk pregnant women in third trimester of pregnancy who were referred to the antenatal clinic between 2017 and 2018 were included in the study. The study is a retrospective study. All data of the patients were obtained from the hospital information system (KARMED).

Pregnant women had a single pregnancy ranging between 27-40 weeks of gestation. IUGR was defined as an estimated fetal weight below the 10th percentile (According to the Hadlock Formula). Sixty-six of pregnant women were diagnosed with IUGR. Thirty-four women were diagnosed small for gestational age. Gestational age was calculated according to crown-rump length measurement in first trimester ultrasonography measurement. Pregnant women with a history of serious congenital structural and chromosomal defects were excluded. Pregnant women with renal disease, diabetes mellitus, positive TORCHES, HCV and HIV serology were excluded.(About twenty patients were excluded from study) Baseline demographic, past obstetric and medical histories were recorded for all patients.

Doppler ultrasound parameters of umbilical artery (UA), middle cerebral artery (MCA) and uterine artery were used for the evaluation of pregnancies. Cerebroplacental rate (CPR); It is calculated by dividing MCA percentile index to UA percentile index.

Cerebroplacental doppler ratio less than 1 was accepted abnormal. Adverse perinatal outcome for newborns; such as overall cesarean section rates, fetal distress rates, neonatal unit admission rates, low apgar score, meconium aspiration rates, intraventricular hemorrhage rates, periventricular leukomalacia rates, hypoxic-ischemic encephalopathy rates, necrotizing enterocolitis rates, respiratory distress syndrome rate, sepsis, bronchopulmonary dysplasia rates and death were documented for all cases.

Ethics approval University of Health Sciences, Sakarya Training and Research Hospital Clinical Research Ethics Committee had approved the study on 4 Dec 2017 with 050. 01.04/234 decision no. And the study has clearance regarding ethical and scientific integrity of the study.

Statistical analysis

NCSS (Number Cruncher Statistical System) 2007 software (Kaysville, Utah, USA) was used for data management and statistical analysis. For assessment of study data; in addition to descriptive statistical methods (mean, standard deviation,

frequency), comparison of quantitative data and intergroup comparison of parameters with normal distribution were done by using one-way Anova test. Parameters with normal distribution were compared between two groups by Student t test. Parameters with non-normal distribution were compared between two groups by Mann Whitney U test. Bonferroni test was used for comparisons of normally distributed binary groups. One-way Anova Test was used for comparisons of normally distributed groups of three or more. Kruskal Wallis test was used for comparisons of groups of three or more that did not show normal distribution. And Bonferroni Dunn test was used for pairwise comparisons.Pearson Chi-Square test, Fisher-Freeman-Halton Exact test and Fisher's Exact test were used to compare qualitative data. Significance was evaluated at the $p<0.05$ level at least.

RESULTS

One hundred pregnant women were classified into two groups according to cerebroplacental ratio. CPR of Group A is greater than 1 (n=87). And CPR of Group B is less than 1 (n=13).No significant difference was found between two groups according to demographic data. (Maternal age, body mass index, smoking, gravidity, abortion, number of living children and proteinuria rates)

According to CPR level, there was no statistically significant difference in rates of fetal distress, type of birth and labor induction ($p>0.05$). There was no statistically significant difference between CPR levels according to genders of the fetuses ($p>0.05$).

Table 1: Evaluation of Maternal Demographic Features Accordıng to CPR Levels

		CPR levels		p
CPR ≤ 1 (n=13)		**CPR > 1 (n=87)**		
Maternal age, years	Min-Max (Median)	22-40 (27)	17-43 (27)	[g]**0,746**
	Ort±Ss	28,38±5,06	28,20±6,15	
BMI (kg/m²)(at beginning of pregnancy)	Min-Max (Median)	23,7-41,1 (27,3)	17,1-40,6 (27,7)	[g]**0,854**
	Ort±Ss	28,59±5,26	27,52±4,62	
BMI (at the beginning of pregnancy)	**< 25 kg/m²**	3 (23,1)	28 (32,2)	[b]**0,749**
	25 -30 kg/m²	7 (53,8)	36 (41,4)	
	>30 kg/m²	3 (23,1)	23 (26,4)	
Smoking	**Positive**	2 (15,4)	6 (6,9)	[c]**0,278**
	Negative	11 (84,6)	81 (93,1)	
Gravidity	Min-Max (Median)	1-4 (2)	1-7 (2)	[g]**0,550**
	Ort±Ss	2,08±0,95	2,00±1,19	
Abortion	Min-Max (Median)	0-2 (0)	0-5 (0)	[g]**0,994**
	Ort±Ss	0,31±0,63	0,34±0,78	
Parity	Min-Max (Median)	0-2 (1)	0-3 (0)	[g]**0,587**
	Ort±Ss	0,77±0,73	0,70±0,85	
Number of living children	Min-Max (Median)	0-2 (1)	0-3 (0)	[g]**0,564**
	Ort±Ss	0,69±0,63	0,64±0,81	
Proteinuria	**Negative**	11 (84,6)	81 (93,1)	[c]**0,278**
	Positive	2 (15,4)	6 (6,9)	
Proteinuria	**Negative**	11 (84,6)	81 (93,1)	[b]**0,373**
	+1	0 (0)	1 (1,1)	
	+2	0 (0)	1 (1,1)	
	+3	2 (15,4)	4 (5,6)	
Gestational week at delivery	Min-Max (Median)	28-40 (36)	27-40 (36)	[g]**0,433**
	Ort±Ss	34,94±3,79	35,91±2,73	
Antihypertensive treatment	**positive**	3 (23,1)	8 (9,2)	[c]**0,153**
	negative	10 (76,9)	79 (90,8)	
Corticosteroid for fetal maturation	**Positive**	10 (76,9)	46 (52,9)	[c]**0,004****
	Negative	3 (23,1)	41 (47,1)	
The reason of birth indication	**Maternal causes**	2 (15,4)	49 (56,3)	[c]**0,009****
	Fetal causes	8 (61,5)	33 (37,9)	
	Both of them	3 (23,1)	5 (5,7)	
Oligohidroamnios	**Positive**	7 (53,8)	21 (24,1)	[c]**0,043***
	Negative	6 (46,2)	66 (75,9)	

A statistically significant difference was found between two groups in terms of corticosteroid rates used for fetal lung maturation(p = 0.004; p <0.01); Group B had a higher rate of corticosteroid rates. A statistically significant difference was found between the two groups in terms of oligohydramnios rates (p = 0.043; p <0.05); Group B had a higher rate of oligohydramnios.

Table 2: Displaying Doppler Findings of 13 Patients with CPR Under 1

Patient	Pregnancy week when USG is performed.	MCA PI	UA PI	UA PI Percentile	CPR	CPR percentile
1	37	1,33	1,65	> 95 percentile	0,8	< 5 percentile
2	37	0,95	1,10	> 95 percentile	0,86	< 5 percentile
3	37	0,83	1,17	> 95 percentile	0,70	< 5 percentile
4	38	1,16	1,47	< 95 percentile	0,78	< 5 percentile
5	34	0,79	2,07	> 95 percentile	0,38	< 5 percentile
6	28	1,41	2,60	> 95 percentile	0,54	< 5 percentile
7	28	1,13	2,03	> 95 percentile	0,55	< 5 percentile
8	36	1,11	1,14	< 95 percentile	0,97	< 5 percentile
9	34	0,83	1,35	> 95 percentile	0,61	< 5 percentile
10	39	0,73	1,34	> 95 percentile	0,54	< 5 percentile
11	34+2	1,07	1,10	> 95 percentile	0,97	< 5 percentile
12	32	1,18	1,43	> 95 percentile	0,79	< 5 percentile
13	40	0,93	1,70	< 95 percentile	0,54	< 5 percentile

Note: This table has been prepared using the reference values in the table of the article numbered 17 in the reference list .(26)

(Doppler results of 13 patients are shown in the table above. This patients diagnosed with IUGR have CPR value of less than 1 and have a percentile value of less than 5 percent. Therefore, there is no significant data that can be compared between CPR value and CPR percentile.)

A statistically significant difference was found between two groups in terms of cause of birth indication (p = 0.009; p <0.01). (Reasons of birth indication ; maternal causes: history of previous cesarean section, non-progressive labor, gestational hypertension. Fetal causes: fetal distress, cephalopelvic disproportion,fetal presentation anomalies) . Rates of both maternal and fetal causes in terms of birth indication were high in those with Group B. But rate of maternal cause was higher in those with Group A than Group B in terms of delivery indication.

Table 3: Evaluation of Newborn Outcomes According to CPR Levels

CFR ≤ 1 (n=13)		**CPR levels**		
CFR > 1 (n=87)				**p**
Fetal stress diagnosed during labor	**Positive**	10 (76,9)	46 (52,9)	[c]**0,103**
	Negative	3 (23,1)	41 (47,1)	
Gender of fetuses	**Female**	6 (46,2)	59 (67,8)	[c]**0,210**
	Male	7 (53,8)	28 (32,2)	
Way of birth	**Vaginal delivery**	4 (30,8)	34 (39,1)	[c]**0,761**
	Cesarean section	9 (69,2)	53 (60,9)	
Delivery weeks	Min-Max (Median)	28-40 (37)	29-41 (38)	[g]**0,031***
	Mean ± Ss	35,38±3,80	37,63±2,04	
Birthweight (gram)	Min-Max (Median)	690-3030 (2270)	670-3450 (2580)	[g]**0,008****
	Mean ± Ss	1977,69±734,95	2520,33±509,73	
Apgar score (at 1 min)	Min-Max (Median)	0-9 (8)	4-9 (9)	[g]**0,021***
	Ort±Ss	7,15±2,58	8,48±0,97	
Apgar score (at 5 min)	Min-Max (Median)	0-10 (9)	5-10 (10)	[g]**0,015***
	Mean ± Ss	8,15±2,82	9,56±0,95	
Birth induction	**positive**	4 (30,8)	32 (36,8)	[c]**0,765**
	negative	9 (69,2)	55 (63,2)	
Newborn comorbid conditions				
Neonatal unit admission		5 (38,5)	22 (25,3)	[c]**0,329**
Duration of stay in the intensive care unit (days)	Min-Max (Median)	8-64 (24)	1-91 (4)	[g]**0,014***
	27,60±22,20	11,90±21,94		
Mean ± Ss				
Prematurity		5 (38,5)	15 (17,2)	[c]**0,129**
Respiratory Distress Syndrome		5 (38,5)	12 (13,8)	[c]**0,043***
Meconium stained liquor		4 (30,8)	5 (5,7)	[c]**0,015***
Hyperbilirubinemia		3 (23,1)	2 (2,3)	[c]**0,015***
Perinatal mortality		1 (7,7)	0 (0)	[c]**0,130**

Fisher-Freeman-Halton Exact Test [c]Pearson Chi-square Test [c]Fisher's Exact Test

[g]Mann Whitney U Test **p<0.01 *p<0.05

A statistically significant difference was found between two groups in terms of birth weeks of the newborns during delivery(p = 0.031; p <0.05). Birth weeks of Group B were lower than Group A. The birth weeks of Group B were lower than Group A (p=0.031; p<0.05). Group B had a lower birth weight of newborns than Group A. In Group B, apgar score of newborns at first minute (p = 0.021; p <0.05) and at 5th minute (p = 0.015; p <0.05) were lower than Group A. Group B (p: 0.022) had statistically significant higher rates of respiratory distress syndrome rates (p = 0.043; p <0.05), meconium aspiration rates (p = 0.015; p <0.05) and incidence of hyperbilirubinemia in newborns (p = 0.015; p <0.05).

Need for neonatal intensive care, perinatal mortality rates of newborns and prematurity rates did not differ significantly in terms of the CPR level (p> 0.05). This may be due to the low number of patients. Perinatal mortality was seen in one fetus with Group B.

DISCUSSION

Ultrasound examination is the basic diagnostic tool to evaluate fetal growth (4). The Hadlock Formula is the most widely used and accepted method to estimate fetal weight using sonographic measurements of fetal abdomen, fetal head and femur length (1,6). Doppler ultrasonography allows non invasive examination of vessels for evaluating blood flow velocity profile. When doppler sonography is done concurrently with other tests; it provides very useful information about fetal well-being.

Abnormalities in doppler flow indicate transition of severe fetal growth restriction from fetal adaptation to failure. Early changes in fetal growth restriction due to placental factors detected in peripheral vessels such as middle cerebral and umbilical arteries. Late changes in fetal growth restriction can be detected by ductus venous, aortic, pulmonary flows abnormalities and reverse flow in the umbilical artery (6). Due to progressive placental dysfunction; diastolic velocity of middle cerebral arteries increase (brain sparing). Brain sparing means that vasodilatation of cerebral arteries to response for hypoxemia (7).

The compensatory mechanism starts against placental insufficiency. The purpose of redistribution is to increase blood flow of brachiocephalic circulation and myocardium. This condition is defined as brain sparing effect. The systolic downslope of middle cerebral artery waveform is smoothed so that waveform is almost similar to the umbilical artery at advanced levels of placental faılure. Doppler index is considerably decreased with increasing mean velocity (6).

One of most used parameters in doppler ultrasound monitoring is CPR. CPR is calculated by dividing middle cerebral artery pulsatility index to umbilical artery pulsatility index (MCA-PI / UA-PI). The limit value of cerebroplacental ratio; It is accepted to be less than 5th percentile for the gestational week or less than 1, 1.08, 0.05, 2.5. It can be more easily applied in clinical practice as a limit of values of 1 or 1.08 (7,8).

Systematic review of seven studies involving 1428 fetuses reported that fetuses with abnormal CPR values have higher cesarean section rates, lower APGAR scores and neonatal complication rates due to fetal distress than normal CPR values (9). Grammellini et al showed that a CPR value below 1.08 is important for fetuses with placental insufficiency (9,10). PORTO study conducted on pregnant women with abnormal brain protective effect; showed an eleven-fold increase in perinatal morbidity compared to those with abnormal umbilical artery doppler results. They also observed an increase in rate of neonatal mortality due to abnormal umbilical arteries doppler parameters(11).

Doppler parameters have prognostic significance for diagnosis and management of IUGR. MCA doppler and UA doppler assessment alone are not enough to evaluate these patients. If evaluated together; its diagnostic value will be higher in determining severity of fetal hypoxia and predicting neonatal outcomes. Figueras conducted a study in 2015 with 509 fetuses who had late-onset developmental restriction . He observed that urgent cesarean requirement, low umbilical cord venous ph value and newborn intensive care requirement were higher in fetuses with abnormal CPR value (12).

Khalil AA conducted a study in 2015 on delayed developmental restriction of 8382 fetuses with abnormal CPR values (≥37 weeks) . They observed that urgent cesarean need, low Apgar score, operative delivery and newborn intensive care requirement were higher in group with a CPR less than 1 (13).

Vollgraff Heidweiller-Schreurs et al; ın 2018, they showed that cerebroplacental ratio was more effective than middle cerebral artery in predicting negative perinatal outcomes and neurodevelopmental outcomes which including low apgar score and perinatal death in fetuses with intrauterine growth restriction. [13] However; according to the next meta-analysis conducted by Vollgraff Heidweiller-Schreurs et al In 2020; they argued that measuring CPR did not add any predictive value beyond UA PI for predicting perinatal outcomes. Although they state that they do not support its use outside the study in the meta-analysis; they suggested that personalized prediction models should be developed for pregnancies who have high risk of placental insufficiency (15).

Daphne Moreta, Samuel V, Guy D Eslick and Ronald Benzie compiled 47 studies in 2019. And they made a meta-analysis with 66,392 patients with intrauterine growth restriction . Of these 47 studies; 17 were retrospective, 25 were prospective and 5 were case-control studies. Their results showed that neonatal unit care admission (NICU), low apgar score, stillbirth, neonatal morbidity and neonatal death rates could be identified using CPR (16).

Anca Ciobanu, Ranjit Akolekar, Emilie Zingler, Argyro Syngelaki and Kypros H. Nicolaides conducted a study in 2019. This was a prospective observational study in 47,211 pregnant women with singleton pregnancies. Their results showed that low cerebroplacental ratio (<10th percentile) was associated with higher risk of adverse perinatal outcome, urgent cesarean rates and perinatal hypoxia rates(17).

Limitations of the study: This study is a retrospective study and has less number of patients with cerebroplasental ratio lower than 1. Umbilical arterial or venous cord blood pH which gives information about fetal hypoxia, had not been studied.

DISCUSSION

Doppler ultrasonography is the most important method in the diagnosis and management of fetuses with IUGR. The cerebroplacental ratio, which is one of the parameters, can be explained to clinicians not only in fetal life; ıt also provides information about postpartum fetal comorbid conditions and risks.

There are a lot of causes of IUGR . They can be fetus-related or mother-related. Oldest known causes that there are chromosomal anomalies, genetic syndromes and infections.

Among maternal conditions ; the most common are clinically relevant conditions such as autoimmune disorders, clinically relevant conditions such as autoimmune disorders, hypoxemic conditions (such as severe anaemia, congenital cyanotic heart diseases), cardiovascular diseases (such as hypertension) or the exposition to environmental toxins. (18) The mechanism leading to IUGR involves an abnormal tophoblast invasion of the maternal spiral arteries during pregnancy, which results in an incomplete remodelling of these vessels and in the persistence of a high-resistance and low-flow uteroplacental circulation;

which on its turn determines, insufficient gaseous and nutrient exchange for optimal fetal growth. (18,19) This results in a cascade of events that including reduced placental perfusion and imbalance in angiogenic factors (such as releasing vascular endothelial growth factor and placental growth factor). And this situation may lead to placenta-mediated complications of pregnancy such as IUGR, preeclampsia, placental abruption and late pregnancy loss. (18,20,21).

The management of IUGR is based on the prolongation of pregnancy long enough for fetal organs to mature while avoiding irreversible fetus sufferance. (18,22) If we have to talk

about pharmacological management for prevention of IUGR; most guidelines recommend treatment with low-dose aspirin (Preferred up to 16 weeks of pregnancy) (23) .Although this

approach is not universally accepted (18,24).The use of heparin is also controversial. The Canadian guideline recommends that heparin should be offered in selected women (18,23).

Although recent evidence shows that enoxaparin is not effective in preventing IUGR;It is recommended for women with pre-existing severe or early-onset IUFGR or trombophilia. (18,25). Furthermore, several other encouraging therapies are under investigation.

Cerebroplacental ratio used by clinicians in intrauterine period; one of most important parameters of doppler ultrasonography in diagnosis and management of fetuses with IUGR. And also it gives information about postpartum fetal comorbid conditions. My results showed that the cerebroplacental ratio could be a good predictive tool for neonatal outcomes in pregnancy with IUGR.

Cerebroplacental ratio has an important place in the follow-up and delivery of the fetus, especially in the management of late-onset IUGR. Fetuses who found CPR value less than 1; have low 1st and 5th minute birth Apgars scores. Apgars scores are more likely to be less than 7. And neonatal intensive care needs and comorbid conditions are more is known to be.

These results have implications for monitoring pregnancies at risk. We aim to express reduced evidence of danger bias. The group which CPR rate was below 1 has negative fetal results compared to the other group. We can use CPR as a doppler parameter to predict fetal prognosis, if we want fetal outcomes to be even more unfavorable. Conflict of Interest: The authors declared no conflict of interest.

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