VIA MEDICA

An investigation of the effect of placental growth factor on intrapartum fetal compromise prediction in term-induced high risk pregnancies

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ABSTRACT

Objectives: To date, there is no available test to predict the risk of intrapartum fetal compromise (IFC) during labor, either starting spontaneously or induced due to obstetrics indications. The aim of this study was to examine the effectiveness of placental growth factor (PIGF) in identifying cases that develop intrapartum fetal compromise (IFC) in term high-risk pregnancies induced for labor.

Material and methods: This prospective cross-sectional study was conducted on 40 IFC+ cases and 40 IFC- cases with high-risk term pregnancy and labor induction started in the Health Sciences University Gazi Yaşargil Training and Research Hospital, between January 2018 and April 2018. Comparisons were made between the groups in respect of placental growth factor (PIGF) levels, and obstetric and neonatal outcomes.

Results: The PIGF level was found to be statistically significantly lower in the IFC+ cases compared to the IFC- cases. For a PIGF cutoff value of 32 pg/mL for the prediction of IFC+ cases, sensitivity was 74.4%, specificity 73.2%, NPV 75% and PPV 72.5%, with a statistically significant difference determined between the groups. The IFC+ development risk increased 7.91-fold in patients with PIGF ≤ 32 pg/mL.

Conclusions: The PIGF levels in cases of IFC+ high risk pregnancies were found to be statistically significantly lower than those of IFC- cases. However, further, large-scale randomized controlled research is necessary to demonstrate this relationship better.

Key words: term high-risk pregnancy; labor induction; placental growth factor; intrapartum fetal compromise

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INTRODUCTION

Fetal compromise is defined as "hypoxia and acidosis" that develops associated with the accumulation of carbon dioxide together with a reduction in the amount of oxygen in intrauterine life [1]. Although methods such as the neonatal stress test (NST), electronic fetal heart rate monitoring, fetal movements (reduction of frequency and weakening), biophysical profile, fetal scalp blood gas sampling, and cardiotocography (CTG) are used to diagnose fetal compromise in term pregnancies, there is no available test to predict the risk of intrapartum fetal compromise (IFC) during labor, which has either started spontaneously or been induced

due to obstetrics indications [such as preeclampsia, fetal growth restriction (FGR), olighydroamniosis, post-term pregnancy, etc. [1, 2]. However, recent promising studies have suggested that some placental biomarkers may be useful in identifying antepartum and intrapartum fetal compromise [2–4]. Placental growth factor (PIGF), which is a candidate to be one of these placental biomarkers, has a potent angiogenic effect and assists in the formation of low resistant blood flow in the placental bed together with other paracrine and autocrine chemicals and is primarily produced from the placenta [5]. This low placental blood flow in the placental bed plays a vital role in the formation of adequate

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fetoplacental reserve that provides sufficient oxygen flow during uterine contractions in the intrapartum period [2, 5]. However, while it is not possible to exactly clarify the mechanisms that provide this low resistant placental blood flow that is of vital significance to ensure the placental function, it has been asserted that it causes this effect by binding to vascular endothelial growth factor 1(VEGFR-1) receptors that are of vital significance in angiogenesis and vasodilation [5, 6]. At the same time, it has been demonstrated to be at low levels in pregnant women who have FGR, gestational hypertension or are pre-eclamptic, characterized by the inability to provide the low resistant blood flow in the placental bed as a result of abnormal placentation [7–10]. A recent study demonstrated that the PIGF level is lower in term and low risk pregnancies that develop IFC [2]. PIGF was found to be decreased in pregnancies with pre-eclampsia or FGR. However, no study has been conducted concerning PIGF for the identification of IFC development during term labor in such pregnancies [7–12].

The aim of this study was to investigate the effectiveness of the PIGF level in determining IFC+ cases in term high-risk pregnancies induced for labor.

MATERIAL AND METHODS

This prospective, cross-sectional study was conducted between January 20, 2018 and April 20, 2018, at Health Sciences University Diyarbakir Gazi Yaşargil Training and Research Hospital, located in southeast Turkey and serving a large population, where approximately 25,000 babies are delivered annually. Approval for the study was granted by the Ethics Board of the same hospital (January,19, 2018;8). Informed consent was obtained from all the participants before initiation of the study. The manuscript was prepared in accordance with the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines [13] and the principles of the Helsinki Declaration [14].

The study included pregnant women with a gestational age of 37 weeks or more. Gestational age was calculated using either the first trimester ultrasound measurements or the last menstrual date. Following admission to the delivery unit with any obstetrics indications, labor induction was started with 10 mg dinoprostol (Propess™, Ferring, Germany). The obstetrics indications defined for labor induction were oligohydroamniosis (amniotic fluid index < 5 cm [15]), FGR (estimated fetal weight < 10th percentile [2]), pre-eclampsia and post-term (pregnancy week ≥ 42 weeks). The cases were divided into two groups as 40 pregnant women who were admitted with the above indications, diagnosed with IFC by intrapartum continuous fetal monitoring during labor and underwent emergency cesarean section, and 40 pregnant women who were not diagnosed with IFC and gave birth vaginally. When designing the study, there were planned to

be 40 pregnant women in each group and the study was stopped when the number of pregnant women reached 40 in both groups. During intrapartum continuous fetal monitoring, IFC+ cases were diagnosed based on The International Federation of Gynecology and Obstetrics (FIGO) 2015 guidelines criteria (*Baseline heart rate*: < 100 beats per minute, *Variability*: Reduced variability for > 15 minute, increased variability for > 30 minutes or sinusoidal pattern for > 30 minutes, *Decelerations*: Repetitive late or prolonged deceleration for > 30 minutes or 20 minutes if reduced variability or one prolonged deceleration was > 5 minutes) [16]. The venous blood samples taken from all pregnant women during admission to the delivery unit were withdrawn into 10 mL *ethylenediaminetetraacetic acid* (EDTA) plasma tubes, rapidly centrifuged for 20 minutes (2000–3000 rpm) and stored at -80°C. In addition, the age, gravida, parity, systolic-diastolic blood pressure, pregnancy week, admission indication, type of delivery, infant birth weight, 1 and 5-minute APGAR scores, pH value of the infant umbilical cord, ratio of hospitalization in the neonatal intensive care unit (NICU) and placental weight were recorded. Comparisons were made between the IFC+ and IFC- cases in respect of all the parameters. A cut-off point was determined for PIGF in the venous blood samples and the sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) were calculated for the prediction of IFC+ cases. Patients were excluded from the study if they were diagnosed with fetal anomaly, had twin pregnancies, non-vertex presentation, previous uterine surgery, a diagnosis of pre-gestational diabetes mellitus or gestational diabetes mellitus, a chronic disease, or contraindications for vaginal delivery.

PIGF Analysis

After reaching 40 pregnant women in both study groups, the venous blood samples that had been taken and stored at -80°C were assayed for PIGF levels using the *enzyme-linked immunosorbent assay* (Rel Assay Diagnostics®, Mega Tıp, Gaziantep, Turkey) according to the manufacturer's instructions.

Statistical Analysis

Descriptive statistics (mean, standard deviation, minimum, median, maximum, interquartile range) were used to define continuous variables. The comparison of two independent variables not conforming to normal distribution was made using the Independent Samples t-test. The Chi-Square test (or, when appropriate, the Fisher Exact test and Mann-Whitney U test) was used to determine the relationship between categorical variables. Receiver operator characteristic (ROC) curve analysis was applied to determine the most compatible cut-off point for the PIGF level (according to the Youden Index). The specificity, sensitivity,

area under the ROC curve (AUC), NPV and PPV of the test in predicting IFC+ values were determined according to the PIGF cut-off point. The statistical significance between these values was determined with the Chi-Square test. Logistic regression analysis (backward condition method) was used to investigate the relationship between PIGF levels and IFC in induced high-risk term pregnancy

RESULTS
Clinical and laboratory characteristics of the study population

The characteristics of the cases are summarized in Table 1. In the comparison between the IFC+ cases and IFC- cases, there was no statistically significant difference in terms of age, gravida, parity, systolic blood pressure, diastolic blood pressure, pregnancy week, oligohydroamniosis, FGR, preeclampsia, post-term pregnancies, 1-minute APGAR score, 1-minute APGAR score < 7.5-minute APGAR score. However, there was a statistically significant difference in terms of infant birth weight, placenta weight, 5-minute APGAR score < 7 and NICU hospitalization ratio (Tab. 1).

ROC analysis

The ROC analysis was performed to determine the most compatible cut-off point of the PIGF level and summarized in Figure 1. The best cut-off point that can distinguish between the IFC- and IFC+ cases was determined as 32 pg/mL.
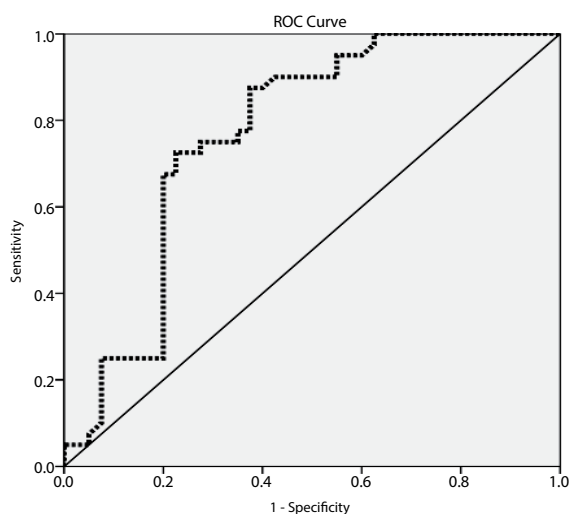

Figure 1. ROC analysis for PIGF

Table 1. Distribution of the characteristic properties of the cases			
	IFC+ N = 40	IFC- N = 40	P value
Age (years), [mean ± SD]	26.15 ± 6.35	26.22 ± 6.34	0.958$^\Omega$
Gravida , [median (IQR)]	2 (2)	2 (3)	0.808$^£$
Parity, [median (IQR)]	1 (2)	1 (3)	0.808$^£$
Blood pressure mmHg, [mean ± SD] - Systolic - Diastolic	113.25 ± 15.75 72.25 ± 10.97	109.75 ± 17.02 70.50 ± 10.85	0.343$^\Omega$ 0.475$^\Omega$
Gestational age (wk), [mean ± SD]	39.83 ± 1.58	39.92 ± 1.37	0.763$^\Omega$
Admission indication, (n) % -oligohydroamnios -post-term pregnancies -FGR -pre-eclampsia	13 (32.5%) 12 (30.0%) 9 (22.5%) 6 (15.0%)	17 (42.5%) 12 (30.0%) 6 (15.0%) 5 (12.5%)	0.747$^\psi$
Type of delivery, n % -vaginal -emergency cesarean	40 (100.0%) 0 (0.0%)	0 (0.0%) 40 (100.0%)	---
Placental weight (g), [mean ± SD]	547.13 ± 69.87	606.25 ± 66.99	0.001$^\Omega$
Birth weight (g), [mean ± SD]	2989.50 ± 530.06	3203.50 ± 388.72	0.043$^\Omega$
1-minute APGAR [median (IQR)	8 (0.75)	8 (0)	0.162$^£$
1-minute APGAR < 7, n [%]	8 (20.0%)	8 (20.0%)	1.000$^\psi$
5-minute APGAR [median (IQR)]	9 (0.75)	9 (0)	0.996$^£$
5-minute APGAR < 7, n [%]	6 (15%)	0 (0.0%)	0.013$^\xi$
Umbilical cord pH < 7.20, n [%]	6 (15.0%)	0 (0.0%)	0.013$^\xi$
NICU, n [%]	8 (20.0%)	1 (2.5%)	0.014$^\xi$
PIGF pg/mL, [mean ± SD (median)]	23.81 ± 17.12 (17.18)	40.92 ± 13.70 (43.91)	0.001$^£$

NICU — neonatal intensive care unit; FGR — fetal growth restriction; PIGF — Placenta growth factor; IFC — intrapartum fetal compromise; wk — week, g — gram; $^\Omega$ — t test for independent sample; $^£$ — Mann-Whitney U test; $^\psi$ — Chi-Square test; $^\xi$ — Fisher-Exact test; IQR — Interquartile Range

Table 2. Comparison of IFC groups according to PIGF classification

PIGF	IFC-		IFC+		Spe.	Sen.	NPV	PPV	OR	95%CI for OR	P $^{\Psi}$
	n	%	n	%							
> 32	30	73.2	11	26.8	73.2	74.4	75.0	72.5	7.91	2.91–21.43	0.001
≤ 32	10	25.6	29	74.4							

PIGF — Placenta growth factor; IFC — intrapartum fetal compromise; NPV — negative pedictive value; PPV — positive predictive value; OR — Odds Ratio 95% CI — 95% confidence interval; $^{\Psi}$ — Chi-Square test

Logistic regression analysis

The comparison of the IFC groups according to the PIGF classification is summarized in Table 2. Sensitivity of the test was determined as 74.4%, specificity as 73.2%, NPV as 75.0% and PPV as 72.5% in the prediction of IFC+ cases according to the PIGF 32 pg/mL cut-off point value, and a statistically significant difference was found between the two groups (p < 0.001). The IFC development risk increased 7.91-fold in patients with PIGF ≤ 32 pg/mL (Tab. 2).

DISCUSSION

This study has shown that PIGF levels are statistically significantly lower in IFC+ cases compared to IFC- cases in induced term high-risk pregnant women. The test was found to have moderate-high specificity and sensitivity for the prediction of IFC+ cases at a cut-off value of PIGF 32 pg/mL. In addition, the risk of IFC development increased 7.91-fold in those with PIGF level ≤ 32 pg/mL. Similar to the current study, Bligh et al [2] determined that the PIGF levels in cases who developed IFC in term low-risk pregnant women were significantly lower than those who did not develop IFC. In addition, consistent with the results of the study by Bligh et al [2] and those of the current study, Sherrell et al [17] stated an association between PIGF levels and IFC.

An adequate placental reserve assists in mitigating the influence of short-term reduction in oxygen supply during contractions that occur in the intrapartum process in the majority of fetuses [2]. *Osol* et al. [5] reported that PIGF assumes a vital role in ensuring the low resistance blood flow in the placental bed for supplying an adequate fetoplacental reserve. The observation of low PIGF levels in cases with decreased placental perfusion such as preeclampsia and FGR, is compatible with the results of the study by *Osol* et al. [5, 9, 18–21]. The determination of low PIGF levels in pregnant women developing IFC in the current study may be related with the inability to provide the low resistance blood flow in the placental bed, which is of vital significance because of the decrease in the PIGF levels [5]. To the best of our knowledge, this is the first prospective research on PIGF levels for the prediction of IFC in term-induced high-risk pregnancies. Although the prospective study by Bligh et al [2] was similar to the current study, they evaluated the effectiveness of PIGF levels in predicting IFC in term low-risk

pregnancies. However, the management of term high-risk pregnancies is much more challenging for obstetricians and this highlights the significance of the current research [2].

In high-risk pregnancies such as FGR, pre-eclampsia and post-term pregnancy, there is no effective and reliable test that can be used to predict which women will develop IFC when labor is induced because continuation of the pregnancy would constitute a problem for both mother and infant [1, 2]. However, PIGF levels have been examined in order to predict this high-risk patient group in several studies [2, 11, 17, 22, 23]. There also are papers where the fetal cerebroplacental ratio (CPR) has been used to identify IFC in this patient group [24–27]. The purpose of all of these studies, similar to the current study, was to predict pregnant women who will develop IFC, and thereby reduce the rates of emergency caesarean section (CS), as there is a significant increase in maternal and neonatal complications following emergency CS compared to elective CS [28, 29]. In the current study, the sensitivity of the test in identifying IFC+ cases in this patient group according to the PIGF 32 pg/ml cut-off point value was 74.4%. In these cases, the situation could be discussed with the patient before starting labor induction, and a planned CS could be performed if that decision is made, thereby reducing maternal and neonatal complications.

The results of the current study showed that patients in the IFC+ group with significantly low PIGF levels, had significantly lower infant birth weight and placental weight compared to the IFC- cases, while the 5-minute APGAR score < 7 rate, umbilical cord pH < 7.20 and NICU hospitalization rate were determined to be significantly higher. These results are consistent with the findings of many previous studies which have shown an increase in adverse pregnancy results at low PIGF levels [9, 18–21]. However, no statistically significant difference was determined between the two groups in respect of the other parameters of age, gravida, parity, systolic blood pressure, diastolic blood pressure, pregnancy week, oligohydroamnios, FGR, pre-eclampsia, post-term pregnancies, 1-minute APGAR scores, 1-minute APGAR scores < 7, and 5-minute APGAR scores.

The limitations of the current study were that it was single-centered, the number of cases was low, and the IFC+ cases were diagnosed by continuous fetal monitor-

ing during the intrapartum period according to the FIGO 2015 guidelines, without taking fetal scalp blood samples from the infants and checking the fetal blood gas values. Our hospital serves a large population in southeast Turkey and there were 25,043 births in 2017. In the delivery unit, all pregnant women are monitored by continuous fetal monitoring during the intrapartum period. Fetal compromise in the intrapartum period is also diagnosed during continuous fetal monitoring according to the FIGO 2015 guidelines, and interventions are made. Nevertheless, the strengths of this study were its prospective, cross-sectional design, inclusion of term-induced high-risk pregnant women, and that the control group was formed of similar pregnant women.

In conclusion, the PIGF levels were determined to be significantly lower in IFC+ cases compared to IFC- cases. With a cutoff value of 32 pg/mL, PlGF was determined to have moderate-high specificity and sensitivity for the prediction of IFC+ cases. However, further, large-scale randomized controlled research is necessary to demonstrate this relationship better.

REFERENCES

1. Pashte SV, Choudhari SS. Diagnosis and management of fetal dıstress: a review based on modern concept and ancient ayurvedic granthas. European Journal of Biomedical and Pharmaceutical Sciences. 2016; 3(12): 560–562.
2. Bligh LN, Greer RM, Kumar S. The relationship between maternal placental growth factor levels and intrapartum fetal compromise. Placenta. 2016; 48: 63–67, doi: 10.1016/j.placenta.2016.10.007, indexed in Pubmed: 27871474.
3. Rasmussen LG, Lykke JA, Staff AC. Angiogenic biomarkers in pregnancy: defining maternal and fetal health. Acta Obstet Gynecol Scand. 2015; 94(8): 820–832, doi: 10.1111/aogs.12629, indexed in Pubmed: 25753566.
4. Prior T, Kumar S. Expert review--identification of intra-partum fetal compromise. Eur J Obstet Gynecol Reprod Biol. 2015; 190: 1–6, doi: 10.1016/j.ejogrb.2015.04.002, indexed in Pubmed: 25917435.
5. Vrachnis N, Kalampokas E, Sifakis S, et al. Placental growth factor (PIGF): a key to optimizing fetal growth. J Matern Fetal Neonatal Med. 2013; 26(10): 995–1002, doi: 10.3109/14767058.2013.766694, indexed in Pubmed: 23330778.
6. Osol G, Celia G, Gokina N, et al. Placental growth factor is a potent vasodilator of rat and human resistance arteries. Am J Physiol Heart Circ Physiol. 2008; 294(3): H1381–H1387, doi: 10.1152/ajpheart.00922.2007, indexed in Pubmed: 18192215.
7. Poon LCY, Akolekar R, Lachmann R, et al. Hypertensive disorders in pregnancy: screening by biophysical and biochemical markers at 11-13 weeks. Ultrasound Obstet Gynecol. 2010; 35(6): 662–670, doi: 10.1002/uog.7628, indexed in Pubmed: 20232288.
8. Audibert F, Boucoiran I, An Na, et al. Screening for preeclampsia using first-trimester serum markers and uterine artery Doppler in nulliparous women. Am J Obstet Gynecol. 2010; 203(4): 383.e1–383.e8, doi: 10.1016/j.ajog.2010.06.014, indexed in Pubmed: 20691410.
9. Chappell LC, Duckworth S, Seed PT, et al. Diagnostic accuracy of placental growth factor in women with suspected preeclampsia: a prospective multicenter study. Circulation. 2013; 128(19): 2121–2131, doi: 10.1161/CIRCULATIONAHA.113.003215, indexed in Pubmed: 24190934.
10. Molvarec A, Szarka A, Walentin S, et al. Circulating angiogenic factors determined by electrochemiluminescence immunoassay in relation to the clinical features and laboratory parameters in women with pre-eclampsia. Hypertens Res. 2010; 33(9): 892–898, doi: 10.1038/hr.2010.92, indexed in Pubmed: 20535121.
11. Benton SJ, McCowan LM, Heazell AEP, et al. Placental growth factor as a marker of fetal growth restriction caused by placental dysfunction. Placenta. 2016; 42: 1–8.
12. Åsvold BO, Vatten LJ, Romundstad PR, et al. Angiogenic factors in maternal circulation and the risk of severe fetal growth restriction. Am J Epidemiol. 2011; 173(6): 630–639, doi: 10.1093/aje/kwq373, indexed in Pubmed: 21317220.
13. von El, Altman DG, Egger M, et al. STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. 2008; 61(4): 344–9.
14. Declaration of Helsinki. Ethical Principles for Medical Research Involving Human Subjects. Jahrbuch für Wissenschaft und Ethik. 2009; 14(1), doi: 10.1515/9783110208856.233.
15. Hedriana HL. Ultrasound measurement of fetal urine flow. Clin Obstet Gynecol. 1997; 40(2): 337–351, indexed in Pubmed: 9199845.
16. Lewis D, Downe S. FIGO Intrapartum Fetal Monitoring Expert Consensus Panel. FIGO consensus guidelines on intrapartum fetal monitoring: Intermittent auscultation. Int J Gynaecol Obstet. 2015; 131(1): 9–12, doi: 10.1016/j.ijgo.2015.06.019, indexed in Pubmed: 26433400.
17. Sherrell H, Dunn L, Clifton V, et al. Systematic review of maternal Placental Growth Factor levels in late pregnancy as a predictor of adverse intrapartum and perinatal outcomes. Eur J Obstet Gynecol Reprod Biol. 2018; 225: 26–34, doi: 10.1016/j.ejogrb.2018.03.059, indexed in Pubmed: 29631209.
18. Triunfo S, Lobmaier S, Parra-Saavedra M, et al. Angiogenic factors at diagnosis of late-onset small-for-gestational age and histological placental underperfusion. Placenta. 2014; 35(6): 398–403, doi: 10.1016/j.placenta.2014.03.021, indexed in Pubmed: 24746262.
19. Benton S, Yockell-Lelièvre J, Grynspan D, et al. Low maternal placental growth factor is associated with abnormal placental morphology in fetuses with suspected intrauterine growth restriction. Placenta. 2014; 35(9): A44, doi: 10.1016/j.placenta.2014.06.143.
20. Llurba E, Crispi F, Verlohren S. Update on the pathophysiological implications and clinical role of angiogenic factors in pregnancy. Fetal Diagn Ther. 2015; 37(2): 81–92, doi: 10.1159/000368605, indexed in Pubmed: 25659427.
21. Lobmaier SM, Figueras F, Mercade I, et al. Angiogenic factors vs Doppler surveillance in the prediction of adverse outcome among late-pregnancy small-for- gestational-age fetuses. Ultrasound Obstet Gynecol. 2014; 43(5): 533–540, doi: 10.1002/uog.13246, indexed in Pubmed: 24203115.
22. Valiño N, Giunta G, Gallo DM, et al. Biophysical and biochemical markers at 30-34 weeks' gestation in the prediction of adverse perinatal outcome. Ultrasound Obstet Gynecol. 2016; 47(2): 194–202, doi: 10.1002/uog.14928, indexed in Pubmed: 26094952.
23. Valiño N, Giunta G, Gallo DM, et al. Biophysical and biochemical markers at 35-37 weeks' gestation in the prediction of adverse perinatal outcome. Ultrasound Obstet Gynecol. 2016; 47(2): 203–209, doi: 10.1002/uog.15663, indexed in Pubmed: 26224608.
24. Prior T, Mullins E, Bennett P, et al. Prediction of intrapartum fetal compromise using the cerebroumbilical ratio: a prospective observational study. Am J Obstet Gynecol. 2013; 208(2): 124.e1–124.e6, doi: 10.1016/j.ajog.2012.11.016, indexed in Pubmed: 23159689.
25. Prior T, Mullins E, Bennett P, et al. Prediction of fetal compromise in labor. Obstet Gynecol. 2014; 123(6): 1263–1271, doi: 10.1097/AOG.0000000000000292, indexed in Pubmed: 24807326.
26. Sabdia S, Greer RM, Prior T, et al. Predicting intrapartum fetal compromise using the fetal cerebro-umbilical ratio. Placenta. 2015; 36(5): 594–598, doi: 10.1016/j.placenta.2015.01.200, indexed in Pubmed: 25771404.
27. Khalil AA, Morales-Rosello J, Morlando M, et al. Is fetal cerebroplacental ratio an independent predictor of intrapartum fetal compromise and neonatal unit admission? Am J Obstet Gynecol. 2015; 213(1): 54.e1–54.e10, doi: 10.1016/j.ajog.2014.10.024, indexed in Pubmed: 25446667.
28. Benzouina S, Boubkraoui MEM, Mrabet M, et al. Fetal outcome in emergency versus elective cesarean sections at Souissi Maternity Hospital, Rabat, Morocco. Pan Afr Med J. 2016; 23: 197, doi: 10.11604/pamj.2016.23.197.7401, indexed in Pubmed: 27347286.
29. Gurunule A, Warke H. Maternal and foetal outcome in elective versus emergency caesarean sections. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 2017; 6(4): 1222, doi: 10.18203/2320-1770.ijrcog20170927.