Research Article / Araştırma Makalesi
doi: 10.18678/dtfd.1148936

Duzce Med J, 2023;25(1):68-72
Düzce Tıp Fak Derg, 2023;25(1):68-72

A New Parameter for Erythropoiesis: The Relationship of Immature Reticulocyte Fraction Values in Cord Blood with Clinical Factors and Reference Values for Newborns

Eritropoez için Yeni Bir Parametre: Kordon Kanında Immatür Retikülosit Fraksiyon Değerlerinin Klinik Faktörlerle İlişkisi ve Yenidoğan için Referans Değerleri

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Received / Geliş Tarihi : 08.09.2022
Accepted / Kabul Tarihi : 20.03.2023
Available Online / Çevrimiçi Yayın Tarihi : 13.04.2023

ABSTRACT

Aim: The immature reticulocyte fraction (IRF) is a new parameter for the reticulocyte maturity index, representing an independent parameter of erythropoiesis that may be useful to better assess erythropoietic activity in neonates. In this study, the relationship between IRF values and clinical features in newborns was investigated and reference values were obtained.
Material and Methods: Newborns between 28-40 weeks of gestation were included in this prospective study. At birth, maternal venous and cord blood samples were obtained for measurements of complete blood count (CBC), blood gases, and plasma concentrations of various biochemical parameters.
Results: A total of 123 newborns, 99 term and 24 preterm, were included in the study. When the laboratory characteristics of the premature and term babies were compared according to their gestational weeks, while the median IRF value of cord blood was higher in term babies than in premature babies (p=0.039), other laboratory findings did not differ significantly. The median IRF value was 0.52 (range, 0.15-1.00) in term infants and 0.34 (range, 0.16-0.76) in preterm infants. IRF reference values for the term and preterm newborns were determined in cord blood. Moderately positive correlations were observed between the IRF levels and both the RDW (r=0.423, p<0.001) and the CRP (r=0.389, p<0.001) levels.
Conclusion: The results of this study showed that newborns' IRF values were not affected by maternal variables and changed with the week of birth. The results of this study might be considered a guide for future studies using IRF value in newborns.
Keywords: Cord blood; newborn; immature reticulocyte fraction.

ÖZ

Amaç: Olgunlaşmamış retikülosit fraksiyonu (immature reticulocyte fraction, IRF), retikülosit olgunluk indeksini gösteren yeni bir parametredir ve yenidoğanlarda eritropoietik aktiviteyi daha iyi değerlendirmek için yararlı olabilecek bağımsız bir eritropoez parametresini temsil eder. Bu çalışmada yenidoğanlarda IRF değerleri ile klinik özellikler arasındaki ilişki araştırılmış ve referans değerler elde edilmiştir.
Gereç ve Yöntemler: Bu prospektif çalışmaya 28-40 gebelik haftaları arasında olan yenidoğanlar dahil edildi. Doğumda, tam kan sayımı (complete blood count, CBC), kan gazları ve çeşitli biyokimyasal parametrelerin plazma konsantrasyonlarının ölçümleri için maternal venöz ve umbilikal kord kan örnekleri alındı.
Bulgular: Çalışmaya 99 term ve 24 preterm olmak üzere toplam 123 yenidoğan dahil edildi. Prematüre ve term bebeklerin gebelik haftalarına göre laboratuvar özellikleri karşılaştırıldığında, kordon kanı ortanca IRF değeri term bebeklerde prematüre bebeklere göre daha yüksek bulunurken (p=0.039), diğer laboratuvar bulguları anlamlı farklılık göstermedi. Ortanca IRF değeri term bebeklerde 0,52 (aralık, 0,15-1,00) ve prematüre bebeklerde 0,34 (aralık, 0,16-0,76) idi. Term ve preterm yenidoğanlar için kordon kanında IRF referans değerleri belirlendi. IRF düzeyleri ile hem RDW (r=0,423, p<0,001) hem de CRP (r=0,389, p<0,001) düzeyleri arasında orta düzeyde pozitif korelasyonlar gözlendi.
Sonuç: Bu çalışmanın sonuçları, yenidoğanların IRF değerlerinin maternal değişkenlerden etkilenmediğini ve doğum haftası ile değiştiğini göstermiştir. Bu sonuçlar yenidoğanlarda IRF değerini kullanarak yapılacak olan sonraki çalışmalar için bir rehber olarak kabul edilebilir.
Anahtar kelimeler: Kordon kanı; yenidoğan; immatür retikülosit fraksiyonu.

Presented as a poster at the 24. National Neonatology Congress (April 17-20, 2016; Antalya, Türkiye)

INTRODUCTION

Erythropoiesis in newborns can differ compared to older children and adults. The commonly used forms of erythrocyte series in the clinic are reticulocytes and mature erythrocytes. The reticulocyte or non-nucleated erythrocyte counts that contain immature RNA provide useful information about erythrocyte synthesis and circulating capacity in response to the ability of bone marrow to respond to a physiological condition, such as anemia. With the latest technological advances, the newest measurement parameter is the immature reticulocyte fraction (IRF) which can be useful in the evaluation of erythropoietic activity in newborns. IRF may be an economical alternative to the measurement of plasma transferrin receptor and serum erythropoietin levels. We also investigated the place of IRF in the early diagnosis of sepsis. There are only a few studies available about IRF because it is a new parameter and there are no international standards, like for other complete blood count parameters (1-2).

The aims of this study were to assess the relationship between the cord blood IRF values and the clinical characteristics of newborns and to obtain reference values for IRF from the cord blood samples.

MATERIAL AND METHODS

In this prospective study, 123 newborns who were born with normal or cesarean section in Kırıkkale University Medical Faculty Hospital between February 2015 and June 2015 with antenatal follow-up and over 28 weeks of gestation were enrolled. Babies with a gestational age of less than 28 weeks, a major congenital anomaly, and hydrops fetalis were excluded from the study.

Umbilical cord blood samples of the infants were studied prospectively. Maternal age, chronic illnesses, obstetric complications, maternal drug abuse, the number of previous pregnancies and deliveries for the mother, maternal blood group, type of delivery, gestational age of the baby, resuscitation, Apgar scores, birthweights, and gender were recorded.

In the delivery room, umbilical cord blood samples were taken by the pediatrician immediately after umbilical cord clamping. Then, 2 ml of cord blood was taken up in tubes containing K3 EDTA for a sample of the complete blood count. The complete blood count, reticulocytes, and IRF measurements were automatically performed on the Beckman Coulter LH 780 device. Additionally, 1 ml of heparinized injectors was prepared for blood gas measurements. The Siemens RaPIDLab 348 instrument was used to determine the blood gas parameters. Blood for the CRP (2 ml) was centrifuged for five minutes at 3,500 rpm, and the serum was separated. In a Beckman Coulter AU 480-680, the CRP levels were quantitatively determined using an immuno-nephelometric method with the appropriate kit.

Local ethics committee approval was obtained before the study (Clinical Research Ethics Committee of Kırıkkale University (23.02.2015, 04/02).

Statistical Analysis

Statistical analyses were performed with the SPSS v.15.0 statistical program (SPSS, Inc., Chicago, IL, USA). For categorical variables, frequencies and percentages were used for descriptive statistics, and the chi-square and Fisher's exact tests were used for comparing groups. The distributions of the measured data were analyzed by Kolmogorov-Smirnov and Shapiro-Wilk tests and were confirmed using histograms. The mean and standard deviation were provided for normally distributed variables, and the median and minimum-maximum values were provided for not normally distributed variables. The IRF reference values were created using the 2.5 and 97.5 percentiles. The significance of the inter-group differences was tested using the Independent samples t-test and Mann-Whitney U test. Correlations between the variables were analyzed using Pearson or Spearman correlations, respectively, according to whether they were distributed normally or not. The statistical significance level for all tests was set to <0.05.

RESULTS

The study group consisted of 99 term and 24 preterm infants. The demographic characteristics of the infants were shown in Table 1. In comparing the laboratory characteristics of the infants according to gestational week, the umbilical cord blood median IRF value in term infants was higher than for preterm infants (p=0.039). The other laboratory findings were not significantly different between preterm and term infants (Table 2).

When the IRF value of umbilical cord blood was analyzed according to the individual variables for both the term and preterm infants, there was no significant relationship between gender, birth percentiles, mode of delivery, the need for resuscitation, hospitalization, gestational complication, antenatal steroid, and multiple pregnancies (Table 3).

The IRF reference values for the term infants have a lower limit (2.5 percentile) of 0.17, an upper limit (97.5 percentile) of 0.89, and a median of 0.52. For the preterm infants, the lower limit (2.5 percentile) was found to be 0.16, the upper limit (97.5 percentile) to be 0.73, and the median to be 0.34 (Figure 1).

Table 1. Distribution of infant and mother characteristics in the study group by gestational week

	Term (n=99)	**Preterm (n=24)**
Gender, n (%)		
Female	48 (48.5)	11 (45.8)
Male	51 (51.5)	13 (54.2)
Birth percentile, n (%)		
SGA	15 (15.2)	4 (16.7)
AGA	78 (78.8)	20 (83.3)
LGA	6 (6.1)	0 (0.0)
Type of delivery, n (%)		
Vaginal delivery	27 (27.3)	5 (20.8)
Cesarean section	72 (72.7)	19 (79.2)
Resuscitation, n (%)	5 (5.1)	3 (12.5)
Hospitalization, n (%)	45 (45.5)	11 (45.8)
Maternal preeclampsia, n (%)	7 (7.1)	3 (12.5)
Maternal diabetes, n (%)	6 (6.1)	1 (4.2)
Multiple pregnancies, n (%)	1 (1.0)	3 (12.5)
Antenatal steroid, n (%)	0 (0.0)	2 (8.3)
Mother's smoke, n (%)	13 (13.1)	1 (4.2)

SGA: small for gestational age, AGA: appropriate for gestational age, LGA: large for gestational age

Table 2. Laboratory findings from cord blood samples for both term and preterm infants

	Term (n=99)	Preterm (n=24)	p
RBC ($x10^6$ uL)	4.48±0.65	4.59±0.73	0.459
HGB (g/dl)	15.7±2.1	15.9±2.5	0.647
HCT (%)	47.0 (9.0) [34-67]	48.5 (12.0) [33-69]	0.638
MCV (fl)	107.3±4.9	108.9±4.4	0.511
MCHC (g/dl)	32.0 (3.0) [30-36]	31.0 (3.0) [28-35]	0.315
RDW (%)	17.0 (2.0) [13-22]	17.0 (2.8) [13-20]	0.805
WBC ($x10^3$ uL)	12100 (4600) [6000-27500]	12600 (5250) [5900-25100]	0.898
PLT ($x10^3$ uL)	230.86±58.84	216.67±51.73	0.281
RTC (%)	3.71 (0.73) [2.32-6.68]	3.50 (1.02) [2.23-5.98]	0.098
IRF	0.52 (0.30) [0.15-1.00]	0.34 (0.28) [0.16-0.76]	**0.039**
pH	7.26 (0.11) [6.83-7.49]	7.26 (0.13) [7.10-7.41]	0.783
BE (mmol/L)	-4.7 (2.7) [-20-1.4]	-4.8 (4.1) [-8.9- -1.1]	0.568
HCO_3 (mmol/L)	21.2±3.0	21.3±2.0	0.814
PCO_2 (mmHg)	46.8±10.3	45.8±11.5	0.667
PO_2 (mmHg)	23.0 (9.0) [16-62]	24.5 (9.3) [16-55]	1.246
CRP (mg/L)	0.65 (1.15) [0-4]	1.07 (1.21) [0.01-3.8]	0.213

RBC: red blood cell, HGB: hemoglobin, HCT: hematocrit, MCV: mean corpuscular volume, MCHC: mean corpuscular hemoglobin concentration, RDW: red cell distribution width, WBC: white blood cell, PLT: platelet, RTC: reticulocyte count, IRF: immature reticulocyte fraction, pH: potential hydrogen, HCO_3: bicarbonate, PCO_2: partial pressure of carbon dioxide, PO_2: partial pressure of oxygen, CRP: C-reactive protein, descriptive statistics were presented as mean±standard deviation or median (interquartile range) [minimum-maximum]

Table 3. Cord blood immature reticulocyte fraction values according to the other variables in term and preterm infants

	Term	p	Preterm	p
Gender				
Female	0.56 (0.29) [0.17-0.78]	0.760	0.31 (0.33) [0.16-0.59]	0.353
Male	0.51 (0.29) [0.15-1.00]		0.36 (0.27) [0.16-0.76]	
Birth percentile				
SGA	0.42 (0.32) [0.21-0.86]		0.45 (0.40) [0.31-0.76]	
AGA	0.53 (0.31) [0.15-1.00]	0.859	0.33 (0.28) [0.16-0.62]	0.176
LGA	0.52 (0.24) [0.30-0.67]		-	
Cesarean section	0.52 (0.29) [0.17-0.92]	0.753	0.36 (0.10) [0.16-0.76]	0.114
Resuscitation	0.43 (0.29) [0.26-0.58]	0.492	0.30 (-) [0.25-0.31]	0.558
Hospitalization	0.46 (0.30) [0.17-0.92]	0.947	0.35 (0.26) [0.25-0.76]	0.090
Maternal preeclampsia	0.43 (0.25) [0.31-0.86]	0.929	0.31 (-) [0.25-0.62]	0.972
Maternal diabetes	0.41 (0.28) [0.30-0.59]	0.628	0.30 (-) [0.30-0.30]	0.595
Multiple pregnancies	0.71 (-) [0.71-0.71]	0.121	0.33 (-) [0.30-0.58]	0.887
Antenatal steroid	0.50 (0.33) [0.26-0.86]	0.780	0.53 (-) [0.31-0.76]	0.209
Mother's smoker	0.58 (0.35) [0.17-0.92]	0.265	0.42 (-) [0.42-0.42]	0.860

SGA: small for gestational age, AGA: appropriate for gestational age, LGA: large for gestational age, descriptive statistics were presented as median (interquartile range) [minimum-maximum]

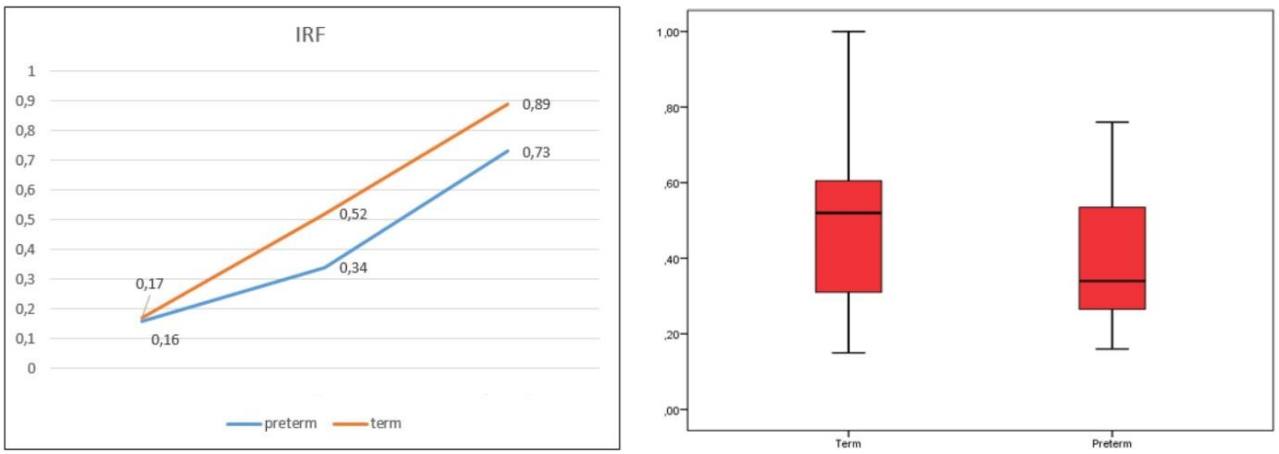

Figure 1. Immature reticulocyte fraction values in term and preterm groups

There were strong positive correlations between the IRF levels and MCHC values in the preterm and also in the term infants (r=0.775, p<0.001, and r=0.674, p<0.001, respectively). In addition, moderately strong positive correlations were observed between the IRF levels and both the RDW (r=0.423, p<0.001) and the CRP (r=0.389, p<0.001) levels (Table 4).

DISCUSSION

In our study, the median IRF value was 0.52 for term infants and 0.34 for preterm infants, as taken from a cord blood sample. The IRF values for the preterm infants were lower than for the term infants, however, there was no difference in the reticulocyte count between preterm and term babies.

There are a few studies in which different study protocols were applied and different results were obtained in newborns with IRF. However, peripheral venous blood samples were used in the majority of these studies.

Maconi et al. (3) found that the median IRF value for a sample of 98 newborns was 27.45, and the 2.5 and 97.5 percentiles were 7.64 and 41.21, respectively. There was no difference between term and preterm infants in terms of IRF values in that study. However, a different device was used for the analysis of the IRF. Ianni et al. (4) reported the reticulocyte index for a normal healthy term newborn at 24 hours of life. They found that the median IRF value for a sample of 120 was 44.7, and the 2.5 and 97.5 percentiles were 35.9 and 52.8, respectively. In a different study by Makela et al. (5), preterm infants were followed up to their 16th week with consecutive measurements from birth. In the study, the median IRF value was 0.36, and the reference values were 0.13 and 0.59 in the first measurements after birth. The reference range found in that study is similar to the reference range of our study, which could be due to the similar gestational age. In the study by Schiza et al. (6), the reticulocyte indices of late preterm infants were examined, and the role of the IRF value in erythropoiesis was investigated. They found that the IRF values were inversely proportional to the postnatal age while directly proportional to the gestational age. Additionally, Ringoringo et al. (7) demonstrated the reference range of IRF for born-term babies aged 1-4 months. Although IRF 5-95 percentile level was 5.95-22.35 in the first month; it diminished to 2.94-12.87 in the fourth month.

Christensen et al. (8) examined the reticulocyte parameters in a large population and showed that the IRF value may be an early and sensitive marker for bone marrow erythropoietic activity. In that study, the IRF values were lower in preterm infants than in term infants, like our results, though in that study, peripheral blood specimens were used, and the IRF values had been studied during the postnatal period.

The results of that study showed that the cord blood IRF levels were not affected by maternal variables, though changed with gestational age. In our study, the IRF values were higher in the term infants than in the preterm infants when only the resuscitation rates were different. Predictably, the preterm group had a higher rate of resuscitation. Nucleated erythrocytes were measured as an indicator of both acute and chronic hypoxia, and the increase in the immature erythrocyte count is reported to be an indirect indicator of hypoxemia (9-11).

However, we found that the IRF values were lower in preterm infants in our study, which is contrary to the hypothesis that these changes result from hypoxia. In addition, the fact that there were no significant differences between the groups in terms of Apgar scores and blood gases also supports the theory that the difference observed between the groups was not related to hypoxia.

Sepsis is one of the causes of morbidity and mortality in newborns. Türkmen et al. (12) compare the critical patients of pediatric age with the healthy control group, IRF level was reported higher in the critical and septic patient groups. In our study, we studied CRP in order to investigate whether the IRF of cord blood has a place in the early diagnosis of sepsis. In addition, moderately strong positive correlations were observed between the IRF levels and the CRP values.

In our study, we think that lower IRF values in preterm infants compared to term infants may be related to low EPO levels in preterm infants. This speculation was based on the strong correlation observed between IRF and MCHC values in term and preterm infants. In the preterm infants, besides the lower IRF levels, the association between the IRF levels and the MCHC values was assumed to be the result of lower IRF levels associated with lower EPO concentrations. However, the lack of similarity between the groups in terms of reticulocyte counts suggests that the IRF values are much more sensitive markers compared with reticulocyte counts. A study to support this assumption was conducted in Japan by Butthep et al. (13). In this study, patients with α and β thalassemia were compared with carriers and healthy subjects, and it was found that EPO levels were positively correlated with the immature reticulocyte fraction. In the USA, in the study by Warwood et al. (14), the IRF was examined in infants with anemia who were born younger

Table 4. The correlations between the cord blood immature reticulocyte fraction levels and hematological indices

	Term		Preterm	
	r	**p**	**r**	**p**
RBC	0.077	0.448	-0.218	0.306
HGB	0.192	0.057	0.004	0.983
HCT	-0.025	0.856	-0.249	0.240
MCV	-0.246	**0.014**	-0.177	0.407
MCHC	0.674	**<0.001**	0.775	**<0.001**
RDW	0.423	**<0.001**	0.309	0.142
WBC	0.067	0.511	-0.164	0.444
PLT	-0.107	0.292	0.353	0.091
RTC	0.280	**0.005**	0.318	0.130
pH	0.251	**0.012**	0.278	0.188
BE	0.279	**0.005**	0.174	0.417
HCO_3	0.016	0.879	0.051	0.814
PCO_2	-0.096	0.347	-0.267	0.207
PO_2	-0.198	0.050	-0.306	0.146
CRP	0.389	**<0.001**	0.235	0.269

RBC: red blood cell, HGB: hemoglobin, HCT: hematocrit, MCV: mean corpuscular volume, MCHC: mean corpuscular hemoglobin concentration, RDW: red cell distribution width, WBC: white blood cell, PLT: platelet, RTC: reticulocyte count, pH: potential hydrogen, HCO_3: bicarbonate, PCO_2: partial pressure of carbon dioxide, PO_2: partial pressure of oxygen, CRP: C-reactive protein

than 32 weeks and weighing less than 1500 grams and were followed up in the neonatal intensive care unit, and it was observed that the IRF value increased after darbepoetin administration, and a greater increase was observed at higher doses. In a study from Finland, a correlation between the IRF levels and the MCHC and MCV values in cord blood was reported, which is similar to the results found in our study (15). In our study, it can be speculated that the higher IRF values in term babies may be related to EPO. The absence of this difference between reticulocyte values suggests that IRF value is a much more sensitive marker than reticulocyte. However, the fact that EPO levels were not studied in our study is one of the limiting factors. Evaluation of EPO levels in future studies will be useful in demonstrating this relationship.

The study has several limitations. The first limitation of our study is that the EPO levels of the newborns were not studied. The other limitation is the small sample size and the relationship between IRF value and anemia in neonatal follow-up and the lack of follow-up on whether there is a need for transfusion or not. Therefore, there is a need for new studies by increasing the sample size, studying EPO levels, and examining the relationship between IRF value and neonatal anemia and transfusion need.

CONCLUSION

IRF values are significantly higher in term infants than in preterm infants, and the reference IRF values in the cord blood have been established for term and preterm newborns. We suggest that the results of this study can be a guide for the next new research into using IRF values in newborns.

Ethics Committee Approval: The study was approved by the Clinical Research Ethics Committee of Kırıkkale University (23.02.2015, 04/02).

Conflict of Interest: None declared by the authors.

Financial Disclosure: None declared by the authors.

Acknowledgments: None declared by the authors.

Author Contributions: Idea/Concept: DA; Design: ZED, NG, DA; Data Collection/Processing: ZED, ÜK, SD; Analysis/Interpretation: ZED, ÜK, SD; Literature Review: ZED, NG; Drafting/Writing: ZED, ÜK, SD; Critical Review: ZED, NG, DA.

REFERENCES

1. Qaiser DH, Sandila MP, Ahmed ST, Kazmi T. Haematological reference values for full-term, healthy, newborns of Karachi, Pakistan. J Pak Med Assoc. 2009;59(9):618-22.
2. Abdurrahman MB, Adekoje MA. Haematological values in Northern Nigerian neonates. Trans R Soc Trop Med Hyg. 1983;77(6):786-8.
3. Maconi M, Formisano D, Cavalca L, Rolfo A, Cardaropoli S, Danise P. Reticulocyte count and reticulocyte maturation profile in human umbilical cord blood from healthy newborns. Lab Hematol. 2010;16(1):3-7.
4. Ianni B, McDaniel H, Savilo E, Wade C, Micetic B, Johnson S, et al. Defining normal healthy term newborn automated hematologic reference intervals at 24 hours of life. Arch Pathol Lab Med. 2021;145(1):66-74.
5. Makela E, Takala TI, Suominen P, Matomaki J, Salmi TT, Rajamaki A, et al. Hematological parameters in preterm infants from birth to 16 weeks of age with reference to iron balance. Clin Chem Lab Med. 2008;46(4):551-7.
6. Schiza V, Giapros V, Pantou K, Theocharis P, Challa A, Andronikou S. Serum transferrin receptor, ferritin, and reticulocyte maturity indices during the first year of life in 'large' preterm infants. Eur J Haematol. 2007;79(5):439-46.
7. Ringoringo HP, Purnamasari L, Yunanto A, Syahadatina M, Hidayah N. Reference range of complete blood count, Ret-He, immature reticulocyte fraction, reticulocyte production index in healthy babies aged 1-4 months. Sci Rep. 2023;13(1):423.
8. Christensen RD, Henry E, Bennett ST, Yaish HM. Reference intervals for reticulocyte parameters of infants during their first 90 days after birth. J Perinatol. 2016;36(1):61-6.
9. James DK, Steer PJ, Weiner CP, Gonik B. Prolonged pregnancy. In: James DK, Steer PJ, Weiner CP, editors. High risk pregnancy: management options. 3rd ed. Elsevier Saunders; 2005. p.1376-82.
10. Ferber A, Fridel Z, Weissmann-Brenner A, Minior VK, Divon MY. Are elevated fetal nucleated red blood cell counts an indirect reflection of enhanced erythropoietin activity? Am J Obstet Gynecol. 2004;190(5):1473-5.
11. Ferber A, Grassi A, Akyol D, O'Reilly-Green C, Divon MY. The association of fetal heart rate patterns with nucleated red blood cell counts at birth. Am J Obstet Gynecol. 2003;188(5):1228-30.
12. Türkmen D, Özsoylu S, Akyıldız BN. Comparison of the value of immature retyculocyte and immature platelet in the diagnosis of sepsis. Pediatr Int. 2022;64(1):e14882.
13. Butthep P, Wisedpanichkij R, Jindadamrongwech S, Fucharoen S. Elevated erythropoietin and cytokines levels are related to impaired reticulocyte maturation in thalassemic patients. Blood Cells Mol Dis. 2015;54(2):170-6.
14. Warwood TL, Ohls RK, Wiedmeier SE, Lambert DK, Jones C, Scoffield SH, et al. Single-dose darbepoetin administration to anemic preterm neonates. J Perinatol. 2005;25(11):725-30.
15. Ervasti M, Kotisaari S, Sankilampi U, Heinonen S, Punnonen K. The relationship between red blood cell and reticulocyte indices and serum markers of iron status in the cord blood of newborns. Clin Chem Lab Med. 2007;45(8):1000-3.