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Can platelet and leukocyte counts guide the early prediction of neonatal sepsis?

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ABSTRACT

Aims: Early recognition of neonatal sepsis, which is an important cause of neonatal mortality and morbidity, contributes positively to clinical outcomes. Although culture methods are the gold standard for diagnosis, they take time and can delay critical treatment decisions. Therefore, there is a need for validation of easily accessible, cost-effective practical approaches in the diagnosis of neonatal sepsis. Our study aimed to evaluate the leukocyte and platelet counts as diagnostic markers in early neonatal sepsis.

Methods: In our prospective study, the contribution of platelet and leukocyte counts to the diagnostic accuracy of two groups of patients diagnosed with sepsis (group I) and without sepsis (group II) in the neonatal intensive care unit (NICU) were evaluated on days 1, 3, 5, and 7.

Results: The group diagnosed with sepsis showed a significant difference in terms of low platelet count and platelet reduction rates. The specificity and sensitivity of thrombocytopenia in the diagnosis of sepsis were 88.8% and 81.3%, respectively. In addition, thrombocytopenia in the early period was informative about the unfavorable prognosis.

Conclusion: Our findings suggest that thrombocytopenia can be used as a red flag for early sepsis diagnosis.

Keywords: Premature, sepsis, thrombocytopenia

INTRODUCTION

Mortality and morbidity due to sepsis in premature infants are still high.[1] Because of the rapid course, multiorgan involvement, and high mortality in sepsis, prompt diagnosis and initiation of treatment are extremely important to improve the prognosis. However, making the correct diagnosis is difficult work for the clinician, and diagnostic tests are needed to predict neonatal sepsis early and accurately.[2,3] One of the most important of these tests is complete blood count (CBC). It is performed on consecutive days in every infant hospitalized in the neonatal intensive care unit (NICU). Changes in leukocyte and platelet counts have also been used in the diagnosis of sepsis in many studies.[2,3]

In this study, we aimed to evaluate the role of leukocyte and platelet counts, which are cost-effective and easily accessible CBC parameters, in the early prediction of sepsis in premature infants.

METHODS

The study was carried out with the permission of the Ethics Committee of Kırıkkale University Faculty of Medicine (Date: 22.12.2005, Decision No: 2005/159). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This prospective study included a total of 207 premature infants with a gestational age between 24-37 weeks who were followed up in the NICU of Kırıkkale University Medical Faculty Hospital between September 2005-November 2005.

Demographic data and sepsis risk factors of premature and their mothers were recorded. Töllner scoring system was used to diagnose sepsis.[3] Physical examinations were performed by the same physician every day, and findings consistent with those of the sepsis clinic were evaluated. CBC and C-reactive protein (CRP) were measured in premature newborns on postnatal days 1, 3, 5 and 7. Blood and urine cultures were obtained from those with a prediagnosis of sepsis, and tracheal aspirate cultures were obtained from those who were intubated. Indications for cesarean section in both groups were placental abruption, placenta previa, fetal distress, breech presentation, eclampsia, preeclampsia, prolonged premature rupture of membranes, oligohydramnios, multiple pregnancies, repeated C/S, HELLP syndrome, non-progressive labor, cord presentation, pregnancy by invitro fertilization and chorioamnionitis.

The study group was divided into two groups. Premature with suspected sepsis (Töllner score 5-10), clinical (Töllner score >10), and definite sepsis (bacterial and fungal growth in blood culture) were included in group I. Premature without a diagnosis of sepsis (Töllner score <5 and no culture growth) were included in group II. Clinical signs of sepsis (cyanosis, skin color changes, hypotonia, respiratory problems, feeding intolerance, decreased sucking, hypo-hyperthermia, bradycardia, distension, irritability, convulsions, vomiting, petechiae) were recorded daily in the patient file.

CBCs in premature infants were performed on days 1, 3, 5, and 7 in groups I and II. Leukocyte and platelet values were also recorded.

Statistical Analysis

The data obtained as a result of the study were analyzed in the SPSS program, and p<0.005 was accepted as the significance limit. Values other than the number of pregnancies were given as mean±SD and number of pregnancies as median. Chi-Square, Mann-Whitney-U test, and Wilcoxon test were used to compare variables. ROC analysis and the Cox regression model were tested.

RESULTS

The study included 207 premature infants. Of these, 29 (14%) were in group I and 178 (86%) were in group II. **Table 1** shows the demographic characteristics of both groups and the comparison of these characteristics.

Table 1 also shows the comparison of the groups in terms of maternal and neonatal risk factors. The maternal history of foul-smelling vaginal discharge and urinary tract infection were more prominent in the sepsis group, and the difference between the groups was significant (p=0.003, p=0.001, respectively). The rates of resuscitation were 72.4% in group I and 16.8% in group II, and the difference between them was significant (p<0.001).

Blood cultures grew in 31% of patients with sepsis. Of the microorganisms, 33.3% were gram-positive (*Staphylococcus aureus, Enterococcus faecium*), 55.6% were gram-negative (*Klebsiella ozanea, Enterobacter aeroginoza, Enterobacter sakazakii*) and 11.1% were fungal (*Candida sp*.). There was no significant difference in clinical and laboratory values of the microorganisms.

While there was no significant difference between the groups in terms of leukocyte counts, a statistically significant difference was found in terms of the decrease in platelet counts on days 1, 3, 5, and 7 (p=0.02, pCRP, p<0.001, p<0.001, **Tables 2, 3**, respectively). The mean platelet counts of group I showed a decrease of 5.8% on day 3, 17.69% on day 5, and 17.94% on day 7 compared to the value obtained on the first day (**Table 3**). It was observed that the early reduction started on day three and markedly decreased later. The lowest platelet values on day 1 were 15.000, 19.000 on day 3, 25.000 on day 5, and 11.000/ mm^3 on day 7.

Cyanosis (100%), changes in skin color (96.6%), hypotonia (96.6%), respiratory problems (75.9%), and non-suction (62.1%) were the most common clinical findings in infants with sepsis (group I). The onset of clinical findings in patients with sepsis was usually on days 3-4, whereas thrombocytopenia usually started on day 3. It took an average of 16 days for the patients to completely recover clinically and 13 days for thrombocytopenia to resolve.

It was observed that the sensitivity and specificity of the decrease in platelet count detected on the first day and the following days increased concerning sepsis. **Table 4** shows the specificity and sensitivity rates of thrombocytopenia for the diagnosis of sepsis on days 1, 3, 5, and 7.

To show the effect of platelet count on prognosis in patients who developed sepsis, the presence of early sepsis was included as a categorical variable, and platelet count on the first day was included as a continuous variable in the Cox regression model.

Table 1. Demographic characteristics and comparison of group I and group II

	Group I (n=29)		Group II (n= 178)		p value
Gestational age (weeks)	29.4±4.2		33.3±2.9		0.000
Birth weight (kg)	1438.79±687.8		2026.19±561.56		0.000
Gender (M/F)	19/10		111/67		0.74
Mode of delivery (NSVD-C/S)	15/14		67/111		0.15
APGAR Scores ($1^{st}/5^{th}$ min)	5±2/9±1		7±1/10		0.000
Comparison of maternal and neonatal sepsis risk factors of the groups					
Maternal factors	n	%	n	%	
Hypertension	3	10.3	19	10.6	0.90
DM	2	6.9	12	6.7	0.97
UTI	2	6.9	0	0	0.001
Foul-smelling vaginal discharge	3	10.3	2	1.12	0.003
Preeclampsia	1	3.4	6	3.3	0.97
Cigarette smoking	5	17.2	26	14.6	0.65
EMR (24 hours a day)	4	13.8	20	11.2	0.74
Factors related to the baby					
Multiple pregnancy	4	13.8	21	11.7	0.70
Resuscitation practice	21	72.4	29	16.2	0.000
Congenital malformation	3	10.3	7	3.9	0.15
Mechanical ventilation therapy	21	72.4	21	11.7	0.000
Umbilical catheter insertion	2	6.9	1	0.56	0.010
Surfactant therapy	12	41.4	12	6.7	0.000

DM: Diabetes mellitus, EMR: Early membrane rupture, UTI: Urinary tract infection

Table 2. Platelet (mean±SD) and leukocyte (median-value range) counts on days 1, 3, 5 and 7 in groups I and II

	Day 1		Day 3		Day 5		Day 7	
	Platelets (/mm^3)	Leukocytes (/mm^3)	Platelets (/mm^3)	Leukocytes (/mm^3)	Platelets (/mm^3)	Leukocytes (/mm^3)	Platelets (/mm^3)	Leukocytes (/mm^3)
Group I	185000±60	14200 (6480-86000)	174107±75	11750 (2890-43190)	152269±84	9930 (2160-42200)	151800±104	8210 (2010-51900)
Group II	207309±66	14100 (5670-87350)	249928±65	11690 (5240-39580)	292263±68	9860 (6300-20100)	319117±74	9443 (4610-16400)
p value	0.02	0.61	0.000	0.71	0.000	0.67	0.000	0.66

SD: Standart deviation

Table 3. Comparison of both groups according to changes in platelet counts

	Group I		Group II	
	Mean±SD	Reduction rates (%)	Mean±SD	Increase rates (%)
Day 1	185000±60	-	207309±66	-
Day 3	174107±75	5.8	249928±65	20.5
Day 5	152269±84	17.6	292263±68	40.9
Day 7	151800±104	17.9	319117±74	53.9

SD: Standart deviation

Table 4. Sensitivity and specificity rates of thrombocytopenia in the diagnosis of sepsis according to days in group I

	Day 1	Day 3	Day 5	Day 7
Sensitivity (Sensitivity) (%)	23.8	66.7	81.3	81.3
Specificity (%)	88.5	88.8	88.2	85.2

The odds ratio for platelet count on the first day was 0.990, 95% confidence interval (0.983-0.997) (p=0.008).

DISCUSSION

Despite advances in neonatal intensive care management, difficulties in the diagnosis and treatment of neonatal sepsis still pose a severe problem for neonatologists. Despite increasing precautions against infections, the incidence of neonatal sepsis is reported to be 1-20% in different studies,[4-9] with mortality rates between 19.4% and 26.7%.[1,4,6,7,10-12] Mortality is more than 30% in early-onset, late-diagnosed and fulminant sepsis.[10-12] In our study, the incidence of sepsis in our NICU unit was 14%, and the mortality rate was 6.2%, consistent with the literature.

Clinical findings constitute the first step in the diagnosis of sepsis, and laboratory investigations support the diagnosis. Clinical findings are not specific and vary in a wide spectrum. Sepsis is a diagnosis that should be considered in almost every newborn with a sick appearance. Clinical findings may be subtle, and it is an important problem that the picture may be aggravated when sepsis clinic occurs.[2,4,7,13-22]

The definitive diagnosis of neonatal sepsis is made by bacterial growth in blood cultures. However, the time lost until the results of blood cultures are obtained will negatively affect morbidity and mortality.[18]

Easy, inexpensive tests with high specificity and sensitivity are needed for early recognition of sepsis in the NICU. CBC is an accessible and cost-effective test. Leukocyte and platelet counts have been previously used in different studies to diagnose and follow up on infection.[14,16,19,23]

In our study, we investigated the efficacy of the changes in leukocyte and platelet counts in CBCs on days 1, 3, 5, and 7 in the early recognition of sepsis in the follow-up of premature infants in our NICUs. When platelet and leukocyte counts were compared between group I, which was followed up with a diagnosis of sepsis, and group II, which was not diagnosed with sepsis, it was found that platelet counts decreased in group I on days 1, 3, 5 and 7 (p=0.02, p<0.001, p<0.001, p<0.001, p<0.001, respectively), whereas leukocyte count variability was not significantly different (p>0.05).

We found that platelet count decreased during the early sepsis period in the groups at risk for sepsis. No significant change was seen in platelet values in group II, which included non-sepsis individuals. In the sepsis prediction score developed by Sofouli et al.[13] in 2023, it was stated that thrombocytopenia as a laboratory marker was as strong in predicting sepsis as other findings. In a study conducted in patients with proven sepsis, it was reported that platelet indices (platelet count, MPV, PCT, and immature platelet fraction) act as acute phase reactants and change with inflammation and may be both predictive and prognostic biomarkers in neonatal sepsis.[14,23,24] Many studies in the literature have reported that thrombocytopenia is frequently observed in neonates with sepsis. It has been suggested that bacteria and their endotoxins cause thrombocytopenia in sepsis by increasing platelet adhesion to the vascular endothelium, suppressing megakaryocytes, decreasing platelet production, and accelerating their consumption.[19,21,25] In the study by Worku et al.[19] the role of CBC parameters in the diagnosis of neonatal sepsis was evaluated, and total leukocyte count and platelet count showed a significant association with neonatal sepsis. It was also reported that these parameters had high sensitivity and specificity in the diagnosis of neonatal sepsis.[19] In our study, the specificity of thrombocytopenia in the diagnosis of sepsis reached its highest value on day 3 (88.8%), and the sensitivity (81.3%) reached its highest value on day 5. This suggests that thrombocytopenia can be used to rule out the diagnosis of sepsis in the early period and may help confirm the diagnosis in late sepsis.

In group I, the effectiveness of the number of platelets obtained from the babies on the first day of diagnosis and prognosis was studied in the Cox regression model, and the odds ratio was

0.990, 95% confidence interval (0.983-0.997) (p=0.008). It was also found that premature infants with thrombocytopenia on the first day had high mortality rates due to sepsis.

In our study, no significant difference was found when leukocyte counts were compared between the groups. Although leukocyte count is one of the most commonly used biomarkers for the diagnosis of infection, it may be affected by many factors, such as stress, trauma, drugs, hemolysis, and hypoxia, its use in newborns is limited, and its sensitivity and specificity are low.[26] However, contrary to our data, there are studies in the literature reporting that an increase in leukocyte count is significant in sepsis.[19,27,28]

Limitations

Intrauterine growth retardation and hypoxic delivery affect platelet counts in newborns. The fact that patients with growth retardation and low APGAR scores were not excluded and that subgroup evaluation for gestational age could not be performed due to the small number of patients in the groups may be limitations of our study. Large-scale multicenter studies are needed to confirm our findings.

CONCLUSION

In conclusion, consecutive CBC assessments performed within the first week of life can be used as a screening test for the early diagnosis of sepsis in premature infants. Monitoring platelet count variability starting from the first day of life will save time in the diagnosis of sepsis and help the neonatologist in sepsis follow-up as a simple, easily accessible, and cost-effective test. However, validation with different prospective studies on CBC parameters and sepsis is needed.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Ethics Committee of Kırıkkale University Faculty of Medicine (Date: 22.12.2005, Decision No: 2005/159).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Fleischmann C, Reichert F, Cassini A, et al. Global incidence and mortality of neonatal sepsis: a systematic review and meta-analysis. *Arch Dis Child.* 2021;106(8):745-752. doi:10.1136/archdischild-2020-320217
2. Satar M, Arısoy AE, Çelik İH. Türk Neonatoloji Derneği yenidoğan enfeksiyonları tanı ve tedavi rehberi 2023 güncellemesi. Available at: http://neonatology.org.tr/uploads/content/tanı-tedavi/1_min.pdf
3. Tekinalp G, Yurdakök M, Yiğit Ş, Korkmaz A. Yenidoğan bakımında Hacettepe uygulamaları. Güneş Tıp Kitabevleri, 2nd ed. Ankara; 2009.
4. Jiang JH, Chiu NC, Huang FY, et al. Neonatal sepsis in the neonatal intensive care unit: characteristics of early versus late onset. *J Microbiol Immunol Infect* 2004:37;301-306
5. Ghosh S, Mittal M, Jaganathan G. Early diagnosis of neonatal sepsis using a hematological scoring system. *Indian J Med Sci.* 2001;55(9):495-500.
6. Chacko B, Sohi I. Early onset neonatal sepsis. *Indian J Pediatr.* 2005;72(1):23-26. doi:10.1007/BF02760574
7. Bizzarro MJ, Raskind C, Baltimore RS, Gallagher PG. Seventy-five years of neonatal sepsis at Yale:1928-2003. *Pediatrics.* 2005;116(3):595-602. doi:10.1542/peds.2005-0552
8. Baltimore RS, Huine SM, Meek JI, Schuchat A, O'Brien KL. Early-onset neonatal sepsis in the era of group B streptococcal prevention. *Pediatrics.* 2001;108:1094-1098. doi:10.1542/peds.108.5.1094
9. Kusuda S, Fujimura M, Sakuma I, et al. Morbidity and mortality of infants with very low bird weight in Japan: center variation. *Pediatrics.* 2006;118(4):1130-1138. doi:10.1542/peds.2005-2724
10. Ojukwu JU, Abonyi LE, Ugwu J, Orji IK. Neonatal septicemia in high risk babies in South-Eastern Nigeria. *J Perinat Med.* 2006;34(2):166-172. doi:10.1515/JPM.2006.030
11. Stoll BJ, Gordon T, Korones SB, et al. Early-onset sepsis in very low birth weight neonates: a report from the National Institute of Child Health and Human Development Neonatal Research Network. *J Pediatr.* 1996;129(1):72-80. doi:10.1016/s0022-3476(96)70192-0
12. Stoll BJ, Hansen NI, Higgins RD, et al. Very low birth weight preterm infants with early onset neonatal sepsis: the predominance of gram-negative infections continues in the National Institute of Child Health and Human Development Neonatal Research Network. 2002-2003. *Pediatr Infect Dis J.* 2005;24(7):635-639. doi:10.1097/01.inf.0000168749.82105.64
13. Sofouli GA, Tsintoni A, Fouzas S, Vervenioti A, Gkentzi D, Dimitriou G. Early diagnosis of late-onset neonatal sepsis using a sepsis prediction score. *Microorganisms.* 2023;11(2):235. doi:10.3390/microorganisms11020235
14. Khadka P, Maharjan G, Chapagain G, Thapaliya J, Paudyal P. Economic and diagnostic biomarker tests of neonatal sepsis: a prospective study from a tertiary care hospital in a low-income country. *Biomed Res Int.* 2022;2022:5166380. doi:10.1155/2022/5166380
15. Edwards MS, Baker CJ. Sepsis in the newborn. Katz SL, Gershon AA, Hotez PJ, eds. Krugman's infection diseases of children, 10th ed. St. Louis, Missouri:Mosby. 1998.
16. Celik IH, Hanna M, Canpolat FE, Pammi M. Diagnosis of neonatal sepsis: the past, present and future. *Pediatr Res.* 2022;91(2):337-350. doi:10.1038/s41390-021-01696-z
17. Gonzalez BE, Mercado CK, Johnson L, Brodsky NL, Bhandari V. Early markers of late-onset sepsis in prematüre neonates: clinical, hematological and cytokine profile. *J Perinat Med.* 2003;31(1);60-68. doi:10.1515/JPM.2003.009
18. Roberts I, Murray NA. Neonatal thrombocytopenia: causes and management. *Arch Dis Child Fetal Neonatal Ed.* 2003;88(5):F359-F364. doi:10.1136/fn.88.5.f359
19. Worku M, Aynalem M, Biset S, Wondu B, Adane T, Tigabu A. Role of complete blood cell count parameters in the diagnosis of neonatal sepsis. *BMC Pediatr.* 2022;22(1):411. doi:10.1186/s12887-022-03471-3
20. Dağoğlu T, Ovalı F. Neonatoloji. Bakteriyel infeksiyonlar. Nobel Tıp Kitabevi. 2000.
21. McPherson RJ, Juul S. Patterns of of thrombocytosis and thrombocytopenia in hospitalized neonates. *J Perinatol.* 2005;25(3):166-172. doi:10.1038/sj.jp.7211230
22. Ramasethu J. Thrombocytopenia in the newborn. *Curr Hematol Rep.* 2004;3(2):134-142.
23. Parmar D, Desai H, Goswami H. Study of thrombocytopenia and platelet indices in neonatal sepsis. *Int J Clin Diagnostic Pathol.* 2020;3(4):39-42. doi:10.33545/pathol.2020.v3.i4a.312
24. Panda SK, Nayak MK, Thangaraj J, Das P, Pugalia R. Platelet parameters as a diagnostic marker in early diagnosis of neonatal sepsis- seeking newer answers for older problems. *J Family Med Prim Care.* 2022;11(5):1748-1754. doi:10.4103/jfmpc.jfmpc_1271_21
25. Ghost TK, Khan N, Malik A. Platelet auto-antibadies in septicaemic patients. *Indian J Pathol Microbiol.* 1999;(42(1):31-35.
26. Gude SS, Peddi NC, Vuppalapati S, Gopal SV, Ramesh HM, Gude SS. Biomarkers of neonatal sepsis: from being mere numbers to becoming guiding diagnostics. *Cureus.* 2022;14(3):e23215. doi:10.7759/cureus.23215

27. Gomathi V, Chitrasivasankari G, Uma T, Saravanan MP, Gurumoorthy K. Serial quantification of CRP and total leukocyte count as a complementary tool in neonatal sepsis. *Bioinformation.* 2022;18(10):920-924. doi:10.6026/97320630018920

28. Goswami S, Gupta R, Ramji S. Sepsis screen: a useful parameter in early diagnosis of neonatal sepsis in preterm neonates. *Int J Lab Hematol.* 2020;42(6):e283-e286. doi:10.1111/ijlh.13321