Caspian Journal of Pediatrics
Babol University of Medical Sciences
e-ISSN: 2383-3106

Eosinopenia and Neutrophil to Lymphocyte Ratio as Diagnostic Tools in Neonatal Early Onset Sepsis: A Single Center Observational Study

Rajithasundaran Annapoorneswary [1], Krishnaswami Devi meenakshi [1*], Sridevi A Naaraayan [2]

1. Department of Pediatrics, Government Kilpauk Medical College, India.
2. Government Kilpauk Medical College, India.

*Corresponding Author: Dr. Krishnaswami Devimeenakshi;

Address: Department of Pediatrics, Government Kilpauk Medical college, Poonamalle high road, Kilpauk, Chennai-600010, Tamil nadu, India.

Tel: +91 8825853811 E-mail: drdevi_1804@yahoo.in

Article Info.

Article type:
Research Article

Received: 31 July 2022
Revised: 14 Nov 2022
Accepted: 11 Dec 2022
Published: 12 March 2023

Keywords:
Eosinophils,
Neonatal sepsis,
Neutrophils,
Lymphocytes

ABSTRACT

Background and Objective: Neonatal sepsis is associated with high mortality and has a favourable outcome when recognized and treated in a timely manner. In resource-limited settings, there is need for an affordable test with a short turnaround time for timely diagnosis of sepsis. The study was aimed to find out the role of eosinopenia and neutrophil-to-lymphocyte ratio (NLR) in screening for early-onset sepsis (EOS) and to determine the cut-off point for absolute eosinophil count (AEC) and NLR to predict early-onset neonatal sepsis.

Methods: This descriptive study was conducted on neonates with suspected EOS at Medical College Hospital, Chennai, Tamil Nadu, India. Complete blood count, C-reactive protein, blood culture, and antibacterial sensitivity were assessed, and neonates with laboratory evidence of sepsis were considered as EOS group. AEC and NLR were compared between groups. Specificity, sensitivity, positive predictive value (PPV) and negative predictive value (NPV) were calculated. Receiver operating characteristic (ROC) analysis was performed. The median value of AEC and NLR was compared with the Mann -Whitney test.

Findings: Among the 140 neonates studied, 72(51.4%) had low birth weight. The absolute neutrophil count was higher (8954 vs. 7322) and the absolute lymphocyte count (3040 vs. 5593) and platelet count were lower in sepsis (126074 vs. 239151). Eosinopenia with cut-off point of 194.5 and NLR with a cut-off point of 1.565 had higher sensitivity than specificity and a high negative predictive value (NPV).

Conclusion: It can be concluded that eosinopenia and NLR are useful tools in the diagnosis of early-onset sepsis.

Cite this Article: Annapoorneswary R, Devi meenakshi K, Naaraayan SA. Eosinopenia and Neutrophil to Lymphocyte Ratio as Diagnostic Tools in Neonatal Early Onset Sepsis: A Single Center Observational Study. *Caspian J Pediatrs* March 2023; 9: e1.

[DOI: 10.22088/CJP.BUMS.9.1.1]

Introduction

Neonatal sepsis is associated with high mortality and timely diagnosis and treatment leads to a favourable outcome. Because early warning symptoms are nonspecific, administration of antibiotics based solely on clinical suspicion may lead to overtreatment and result in multidrug resistance [1]. Although blood culture is the gold standard in confirming sepsis, its yield is highly variable [2]. The unavailability of blood cultures in resource-limited settings is an additional handicap. The majority of neonatal blood cultures are sterile, leading to unnecessary use of antibiotics [3]. Reports of blood cultures are usually not available for 48 to 72 hours, and clinical suspicion is required for timely diagnosis [4]. Though tests such as umbilical cord procalcitonin have shown to be a useful tool in diagnosing proven sepsis [5], facilities may not be available in low- and middle-income countries. Hence, a test which is affordable and has a short turnaround time is needed to diagnose neonatal sepsis in a clinical setting with limited resources.

Eosinopenia occurs during infection due to increased peripheral eosinophil sequestration, decreased eosinophil production, and eosinophil destruction [6]. Increased release of corticotropin-releasing hormone in response to inflammatory mediators such as interleukin 1 and 6 (IL1, IL6) and tumour necrosis factor alpha (TNF α) stimulates the pituitary gland to release adrenocorticotropic hormone (ACTH), which stimulates the synthesis and release of glucocorticoids that prevent the release of eosinophils from the bone marrow [7].

Neutrophils and lymphocytes are important components of the immune system. In sepsis, adhesion between neutrophils and endothelium prevents neutrophils from migrating to the site of infection [8]. In addition, bacterial products and cytokines delay neutrophil apoptosis. Lymphocytopenia in sepsis is due to the recruitment of lymphocytes to the site of infection. Moreover, there is significant lymphocyte apoptosis. Overall, this results in an increased neutrophil-to-lymphocyte ratio (NLR) in sepsis. NLR is a marker of the inflammatory process and can be estimated from simple laboratory data without additional expenditure [9].The aim of the present study was to determine the diagnostic value of eosinopenia and NLR in early-onset neonatal sepsis.

Methods

Design and participants

This descriptive study evaluated a screening test. Neonates admitted to the neonatal intensive care unit (NICU) of a tertiary care medical college hospital in Chennai, Tamil Nadu, India, between November 2019 and August 2020 who had risk factors for early-onset sepsis (EOS), with or without clinical features suggestive of sepsis occurring within 72 hours of life, were included in the current study.

Sample Size

The sample size was estimated to be 138, assuming a prevalence of early-onset sepsis in neonates at risk for sepsis of 75% with a confidence interval of 95% and a z value of 1.96. The confidence interval or margin of error was estimated to be +/-10%. Thus, a sample size of 140 was obtained. All neonates who had risk factors and/or clinical features of sepsis occurring within 72 hours of birth were enrolled for investigation in the present study.

Risk factors included chorioamnionitis, foul-smelling liquor, prolonged rupture of membranes (>18 hours), an unclean or repeated (>3) sterile vaginal examination(s) during labour, prolonged duration of labour (duration of first and second stage of labour longer than 24 hrs), birth weight less than 2500 grams and gestational age less than 37 weeks. The clinical manifestations considered were temperature instability, secondary apnoea (after exclusion of causes), increased oxygen demand, abdominal distension, feeding intolerance, refusal to feed, lethargy, shock (after exclusion of other causes), skin and subcutaneous changes like sclerema, mottling and so on. Neonates with hypoxic ischemic encephalopathy, meconium aspiration syndrome, haemolytic disease of the newborn, severe congenital neutropenia, neonates born to mothers with fever/pre eclampsia/allergic disorders/immunocompromized state were excluded from the study.

[DOI: 10.22088/CJP.BUMS.9.1.1]

Data collection

Basic demographic data were collected from neonates at risk for early-onset sepsis and from neonates with suspected sepsis based on symptomatology. This included information on gender, birth weight, gestational age, risk factors for sepsis, and clinical symptoms of sepsis.

Evaluation of laboratory parameters

Newborns who were eligible according to the inclusion criteria were examined. Baseline clinical data were noted, and 3 ml of venous blood was drawn and sent for complete blood count (CBC) and C-reactive protein (CRP) determination. The CBC was analyzed using a fully automated haematology analyzer (Sysmex Auto Analyser, Japan). The CRP level was analyzed by ELISA. For blood cultures, samples of 1 ml of blood were collected into bottles containing 10 ml of nutrient broth. The inoculum was placed on nutrient agar, blood agar plates, and MacConkey agar (manufactured in India) to grow both aerobic and anaerobic organisms. Absolute eosinophil count (AEC) was observed and NLR was calculated.

Diagnosis of sepsis

In newborns who had a positive blood culture and/or two of the following, total white blood cell count greater than 20000 or less than 5000, platelet count less than 100000, absolute neutrophil count less than 1000, the ratio of immature to total neutrophils (IT ratio) greater than 0.2, positive CRP (greater than 10mg/L), EOS was considered to include clinical and definite sepsis. The other neonates were categorised as non-EOS. All neonates were treated with first-line antibiotics according to the ward protocol until sepsis screening results were available.

Statistical analysis

SPSS 26 was used for statistical analysis. The Mann-Whitney U test was applied to compare the median values of AEC and NLR between the two groups. The chi-square test was used to compare the proportions within the cut-off value of eosinopenia and NLR in the confirmed-EOS and non-EOS groups to test for any significant differences. Specificity, sensitivity, negative predictive value and positive predictive value were calculated to determine the diagnostic value of AEC and NLR for different cut-off points using definitive sepsis as the gold standard. Receiver operating characteristic (ROC) analysis was used to determine the optimal cut-off points for AEC and neutrophil-to-lymphocyte ratio for predicting EOS in neonates.

Results

The current study included 140 newborns with risk factors for EOS and/or clinical features of sepsis that developed within 72 hours of birth. Seventy-two (51.4%) were low birth weight babies. Only 1 (0.7%) neonate was born with foul-smelling liquor and 4 (2.9%) had maternal risk factors for prolonged labour. Seventy (50%) neonates had the risk factor of prolonged rupture of membranes of more than 18 hours, 19 (27.1%) of whom had sepsis.

Of the study participants, 79 (56.4%) were male, and 54 (38.6%) newborns had EOS. Of those with EOS, 34(62.9%) were male. There were 81 (57.9%) term infants. The remaining 59 (42.1 %) were preterm with a variable distribution of gestational age, and the majority (45 (32.1%)) of them were between 32 and 37 weeks. Comparing the gestational age of the newborns studied, of the 13 neonates between 28 and 32 weeks, 8 (61.5%) had sepsis. Of the 81 term neonates, only 26 (32.1%) had sepsis, indicating that the incidence of sepsis is higher in preterm than term neonates and increases with decreasing gestational age (Table 1).

In this study, common clinical features of sepsis were lethargy in 47 (33.6%) neonates, temperature instability in 37 (26.4%) neonates, shock in 37 (26.4%) neonates, feeding intolerance in 23 (16.4%) neonates, and refusal to feed in 16 (11.4%) neonates, whereas abdominal distension in 9 (6.4%) neonates, secondary apnoea in 2 (1.4%) neonates , increased oxygen demand in 9 (6.4%) neonates, and skin lesions of sepsis in 4 (2.9%) neonates were observed less frequently.

In the current study, among 54 neonates with EOS, there were 40 positive blood cultures in the EOS group. The blood cultures in 4 patients returned Gram-positive and in 36 of them returned

[DOI: 10.22088/CJP.BUMS.9.1.1]

Gram-negative bacteria. The most common organisms isolated were Klebsiella pneumoniae 21 (52.5%) and Acinetobacter 9 (22.5 %). The other organisms isolated in blood culture were Pseudomonas aeruginosa (10%), Escherichia coli (5%), coagulase negative staphylococci (2.5%), and enterococci (7.5%).

Mean values of total leukocyte counts between the EOS and non-EOS groups were not significantly different. The mean (SD) total leukocyte counts in the EOS group was 12453.7 (7070.9), whereas it was 14386.05 (5729.042) in the non-EOS group. The mean platelet count was lower in the EOS group. The mean (SD) platelet count in neonates with EOS was 126074.1 (92541.65), while it was 239151.2 (60880.31) in the non-EOS group. The mean absolute neutrophil count was increased in the EOS group. The mean (SD) absolute neutrophil count in the EOS group was 8954.63 (5413.873), while it was 7322.093 (3929.914) in the non-EOS group. The mean absolute lymphocyte count was lower in the EOS group than in the non-EOS group. The mean (SD) absolute lymphocyte count in the EOS group was 3040.593 (3051.489), whereas it was 5593.488 (2417.817) in the non-EOS group (Table 2).

The mean total AEC was 241.55+/-186.79, and it was low in the EOS group. The mean AEC was lower in the EOS group (105.963 (75.62244)) than in the non-EOS group (326.686 (185.6888)).Mean NLR in the EOS group was high. The mean NLR in the EOS group was 3.811685 (1.948509) compared with 1.560256 (1.237021) in neonates in non-EOS group (Table 3).The median AEC and NLR values of the two groups were significantly different (P<0.001) (Table 4).

In the present study, the optimal cutoff value of AEC of 194.5 had a high area under the curve (AUC) of 0.939 (confidence interval 0.891-0.987) (p<0.001) and yielded a sensitivity of 98.1%, a specificity of 86.2%, a positive predictive value of 81.7%, and a negative predictive value of 98.6% (Table 5) (Figure 1). The cut-off value of 1.565 for NLR had a sensitivity of 96.2%, a specificity of 69%, a positive predictive value of 66.1%, and a negative predictive value of 96.6%, and the AUC was 0.876, which was significant ((p <0.001) ;(Table 6) (Figure 1)). As no facilities were available to perform a quantitative CRP test, values between the two groups were not compared.

Table 1. Comparison of gender and gestational age distribution among EOS and Non EOS groups

Factor		EOS	Non EOS	Total
Gender	Male	34(62.9)	45 (57)	79
	Female	20(37.1)	41(67.2)	61
Gestational age	<28 weeks	1(100.0%)	0(0%)	1
	28 to 32weeks	8(61.5%)	5(38.5%)	13
	32 to 37 weeks	19(42.2%)	26(57.8%)	45
	> 37 weeks	26(32.1%)	55(67.9%)	81
Intrapartum Risk factors	Foul smelling liquor	1(100%)	0(0%)	1
	PROM	19(27.1%)	51(72.9%)	70
	Prolonged labour	1(100%)	0(0%)	1

Table 2. Comparison of haematological parameters among EOS and Non EOS groups

Parameter	Group	Number	Mean	Standard deviation	P value
Total leucocyte count	EOS	54	12453.7	7070.9	0.108
	Non EOS	86	14386.05	5729.042	
Platelet count	EOS	54	126074.1	92541.65	<0.001
	Non EOS	86	239151.2	60880.31	
Absolute neutrophil count	EOS	54	8954.63	5413.873	0.035
	Non EOS	86	7322.093	3929.914	
Absolute lymphocyte count	EOS	54	3040.593	3051.489	<0.001
	Non EOS	86	5593.488	2417.817	

[DOI: 10.22088/CJP.BUMS.9.1.1]

Table 3. Comparison of mean values of Absolute Eosinophil count (AEC) and Neutrophil lymphocyte ratio (NLR) in EOS and non EOS groups

Test	Group	Number	Mean	Standard deviation	P value
Absolute Eosinophil Count	EOS	54	105.963	75.62244	<0.001
	Non EOS	86	326.686	185.6888	
Neutrophil lymphocyte ratio	EOS	54	3.811685	1.948509	<0.001
	Non EOS	86	1.560256	1.237021	

Table 4. Comparison of the median values of Absolute eosinophil count (AEC) and Neutrophil lymphocyte ratio (NLR) in EOS and non EOS groups

Test	Group	Median	Mann-Whitney U test	Standardised test statistic	P value
Absolute Eosinophil count	EOS(n-54)	0 97	4399.5	8.895	<0.001
	Non-EOS(n=86)	304.5			
Neutrophil Lymphocyte ratio	EOS(n-54)	3.475	525.5	-7.691	<0.001
	Non-EOS(n=86)	1.11			

Table 5. Receiver operating characteristic analysis for Absolute eosinophil count

Area under curve	Cut off point	P value	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.939	194.5 (sensitivity 98.1 Specificity 86.2)	<0.001	0.891	0.987

Table 6. Receiver operating characteristic analysis for Neutrophil lymphocyte ratio

Area under curve	Cut off point	P value	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.876	1.565 (sensitivity 96.2 Specificity 69.0)	<.001	0.820	0.932

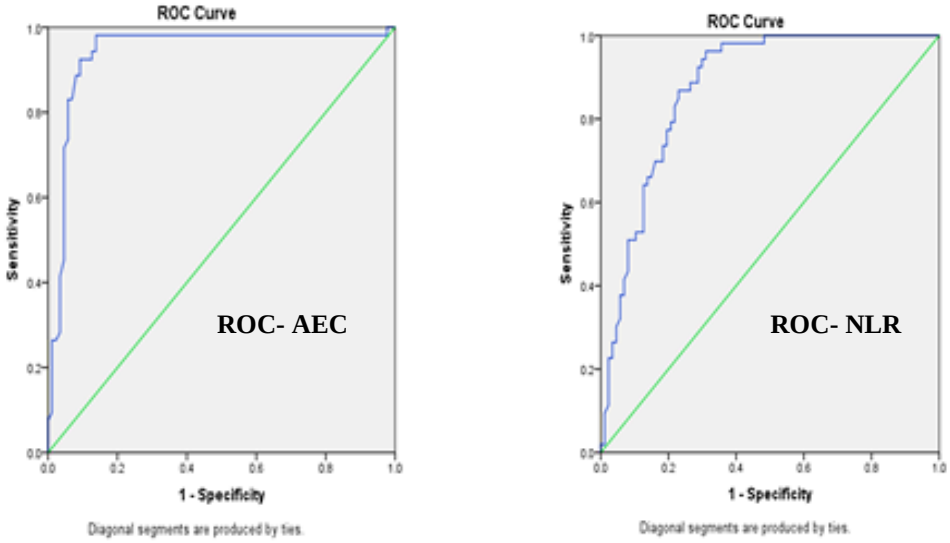

Figure 1. ROC curve for Absolute Eosinophil count (AEC) and Neutrophil to lymphocyte ratio (NLR)

[DOI: 10.22088/CJP.BUMS.9.1.1]

Discussion

The current study evaluated the utility of eosinopenia and neutrophil-to-lymphocyte ratio in predicting EOS in neonates with cut-off values used for neonates. Both are readily available markers for predicting early-onset neonatal sepsis, particularly in resource-poor settings. When the diagnostic accuracy of eosinopenia was evaluated with a cut-off point of 194.5, it was found that the sensitivity (98.1%) was higher than specificity (86.2%), and NLR with a cut-off point of 1.565 showed higher sensitivity (96.2%) than specificity (69%) in the ongoing study.

In the present study, male neonates were more commonly affected, which is consistent with reports from previous studies that early-onset neonatal sepsis is more common in males (63.3%) [10, 11]. The increased incidence of sepsis in male neonates is thought to be due to the location of gene on the X chromosome involved in thymic gland function or immunoglobulin synthesis [10].

In the current study, sepsis was more common in preterm than term infants, and the risk increased with decreasing gestational age. The incidence of sepsis was 100% in preterm infants with gestational age less than 28 weeks, whereas it was only 42.2% in preterm infants with gestational age between 32 and 37 weeks. Term infants had a lower risk of developing neonatal sepsis than preterm neonates [12]. In a previous study, it was observed that confirmed sepsis (69%) than probable sepsis (57%) was more common in preterm infants [1]. The higher incidence of sepsis in preterm infants was likely due to the impaired defence mechanisms and low immunoglobulin G levels in preterm neonates [1].

The most common manifestations of sepsis were lethargy and temperature instability, whereas respiratory symptoms were not common. However, observations in a previous study revealed that respiratory symptoms were most common and poor nutrition was least common [10]. In a previous study of early-onset neonatal sepsis, it was found that tachycardia (83%), feeding intolerance (77%) and lethargy (70%) were the most common symptoms observed in neonates with sepsis [11].

In the present study, a high rate of positive blood cultures (74%) was observed in the EOS cases. Other studies reported lower rates of culture positivity (one study reporting 20% [7] and another 23.3%) [10].The low yield of blood cultures in some other studies could be due to insufficient amount of blood collected, incorrect timing of blood collection, and administration of antibiotics to the mother. In the ongoing study, among culture-positive cases of EOS, Gram-negative sepsis 36 (90%) was more common than Gram-positive sepsis. Similar observations have been made in previous studies, with 72% of cases being Gram-negative sepsis in one study [7] and 75% caused by Gram-negative organisms in another study [13]. These findings suggested that Gram-negative organisms were more common than Gram-positive organisms as etiologic agents in neonatal sepsis. In the present study, the most commonly identified organism was Klebsiella pneumonia.

This result was consistent with observations made in other studies [4, 7, 10, 13]. However, in another study, Staphylococcus Haemolyticus was identified as the most common organism causing EOS [6]. These differences could be due to different bacterial pattern in different regions. Total leukocytecount did not vary in the two groups. Similar observations were also made in a previous study [10]. In a previous study performed in neonates with sepsis, the total leukocyte count was normal in approximately 90% of culture-positive sepsis. Therefore, relying on total leukocyte count alone to diagnose sepsis may be misleading.

When the mean platelet counts in the EOS and non EOS groups were compared, the values in the sepsis group were found to be lower. Similar results were provided by an earlier study in which the mean platelet count was significantly lower in neonates with sepsis than in control subjects [10].

In the current study, it was found that the mean absolute neutrophil count was higher in the sepsis group. In a previous study, it was observed that the neutrophil count was significantly higher in neonates with sepsis [14]. Similar results to ours were obtained in a previous study, in which the absolute neutrophil count was significantly higher in the sepsis group than in the control group [10]. However, in a previous multicenter study of neonatal sepsis, it was observed

[DOI: 10.22088/CJP.BUMS.9.1.1]

that a low absolute neutrophil count was associated with an increased likelihood of EOS [15].

Neutrophil counts increase in sepsis because neutrophils are released from the bone marrow into the bloodstream in response to infection. In severe sepsis, granulocyte depletion occurs in the bone marrow, resulting in neutropenia. The present study revealed a significantly lower mean absolute lymphocyte count in the sepsis group. Similar results have been reported in other studies of neonatal sepsis [10]. This may be explained by the physiological response of circulating leucocytes to sepsis.

The current study suggested that AEC was low in neonates with sepsis, and this proved to be statistically significant. Similar observations were made in a previous study, indicating that the mean value of eosinophil count was 169.8±197.1 and 405.7±288.9 cells/ mm3 in EOS and non-EOS groups, respectively, which was significant [7].

In evaluating the diagnostic accuracy of eosinopenia using a cut-off value of 194.5, the sensitivity (98.1%) was higher than specificity (86.2%) in the ongoing study, making it a very useful screening test for EOS in neonates. In a previous study, eosinopenia was found to be a marker for EOS with a specificity of 100%, sensitivity of 28.6%, PPV of 100% and NPV of 48.3% [6]. In another study, the AUC was 83.5% with a cut-off value of 140 cells/mm^3 and a specificity of 90%, sensitivity of 60%, PPV of 94.7%. and NPV of 42.9% [7]. In contrast to our study, the other two studies mentioned above claim that eosinopenia is a specific rather than sensitive marker for EOS.

In the present study, the mean values of NLR were higher in the EOS group than in the non-EOS group. Similar observations have been made in other studies of neonatal sepsis [7, 10, 13, 14]. In a previous study, the mean value of NLR was 2.82±2.29 and 0.82±0.32 in EOS and non-EOS groups, respectively, and this difference was statistically significant ($p< 0.001$) [7]. The current study indicated that the NLR with a cut-off point of 1.565 had a higher sensitivity (96.2%) than specificity (69%), making it a very useful screening test for early-onset neonatal sepsis. Other studies have used lower cut-off values with varying sensitivity and specificity. One study determined a sensitivity of 83.3% and a specificity of 93.3% with a cut-off point of 1.24, [7] while another study found a sensitivity of 63% and a specificity of 58.5% with an NLR value of 1.39 [16].With a cut-off value of 1.42 for NLR, the likelihood ratio (LR) was 5.5, and the sensitivity, specificity, PPV, and NPV values were 88%, 84%, 84.6%, and 87.5%, respectively [17].

Other studies using a higher cut-off value than ours have observed a sensitivity of 96.7% and a specificity of 100 % with a cut-off value of 2.52 [10] and a sensitivity of 97.4% and a specificity of 100% with a cut-off value of 6.76 [14]. These two studies concluded higher specificity and sensitivity using a higher cut-off value than our study. However, another study done on term neonates with a higher cut-off value (2.7) than our study found lower sensitivity (80%) and specificity (57.1%) [9]. Another study in preterm neonates with late-onset sepsis using a cut-off value close to the one we used (1.57) estimated a sensitivity of 68% and a specificity of 82%, both lower than our values [18].

Limitations of the study

The limitations of the ongoing study were that we included only neonates admitted to the NICU of a single center. In addition, our study was performed with a small sample size of 140 with a margin of error of 10%.

Conclusion

Mean platelet count, mean lymphocyte count and mean and median AEC were lower in EOS neonates, whereas mean absolute neutrophil count, and mean and median NLR were higher in EOS neonates. In the present study, it was found that both eosinopenia and NLR had very high sensitivity and could be used as screening tools in the diagnosis of EOS neonates.

Acknowledgments:

The authors would like to thank the Department of Pathology and the Department of Microbiology, Govt Kilpauk medical college, Chennai for their valuable support in the conduct of the study.

[DOI: 10.22088/CJP.BUMS.9.1.1]

Ethical approval

Approval was obtained from the Institutional Ethics Committee meeting (ID No. 257/2019) on Nov. 7, 2019. The newborns who met the inclusion criteria were recruited after obtaining informed consent from the parents.

Funding

There was no financial support for this research.

Conflict of interest

There is no conflict of interest.

References

1. Shirazi H, Riaz S, TahirR. Role of the Hematological Profile in Early Diagnosis of Neonatal Sepsis. Ann Pak Inst Med Sci 2010; 6(3): 152-6.
2. Ognean ML, Boicean A, Sular FL, Cucerea M. Complete Blood Count and Differential in Diagnosis of Early Onset Neonatal Sepsis. RevRomana Med Lab 2017; 25(1): 101-8.
3. GuertiKh, Devos H, Ieven MM, Mahieu L. Time to Positivity of Neonatal Blood Cultures: Fast and Furious? J Med Microbiol 2011; 60 (no. Pt 4): 446-53.
4. Aggarwal R, Sarkar N, Deorari AK, Paul VK. Sepsis in the newborn. Indian J Pediatr 2001; 68 (12): 1143-7.
5. Akbarian-rad Z, Ehsani Sh, Hajiahmadi M, Haghshenas-Mojaveri M. Umbilical Cord serum Procalcitonin, an early diagnostic marker of early neonatal sepsis. Caspian J Pediatrs 2021; 7(1): 502-8.
6. Bagus E, Kahar H, Wardhani P. Diagnostic values of immature granulocytes, eosinopenia and I/T ratio in detection of early onset neonatal sepsis in neonates with bacterial infection risk. Folia MedicaIndonesiana 2014; 50(1): 43-7.
7. Wilar R. Diagnostic value of eosinopenia and neutrophil to lymphocyte ratio on early onset neonatal sepsis. Korean J Pediatr 2019; 62(6): 217-23.
8. Zhang F, Liu AL, Gao S, et al. Neutrophil dysfunction in sepsis. Chin Med J 2016; 129(22): 2741-4.
9. Omran A, Maaroof A, Mohammad MHS, Abdelwahab A. Salivary C-reactive protein, mean platelet volume and neutrophil lymphocyte ratio as diagnostic markers for neonatal sepsis. J Pediatr (Rio J) 2018; 94(1): 82-7.
10. Nasser MM, Afia AA, EL-Khatib GZ, Ibrahim MI. The Value of Neutrophil to Lymphocyte Ratio and Platelet to Lymphocyte Ratio and Procalcitonin Level for Detecting Early-Onset Neonatal Sepsis. Al-Azhar J Ped 2020; 23(2): 852-74.
11. Mira SM, Alkhalegy HA, Abd-Elraheem SI, Elbakry EM. Neutrophil and Platelet to Lymphocyte Ratio for Detecting Early-onset Neonatal Sepsis. Inter J Med Arts 2021; 3(2): 1274-81.
12. Jamie AH. Prevalence and determinants of neonatal sepsis among admitted neonates in Hiowt-Fana Specialized Referral Hospital, Harar, Ethiopia, 2019. Caspian J Pediatrs 2021; 7(2): 538-44.
13. Sumitro KR, Utomo MT, Widodo AD. Neutrophil-to-Lymphocyte Ratio as an Alternative Marker of Neonatal Sepsis in Developing Countries. Oman Med J 2021; 36(1): e214.
14. Can E, Hamilcikan S, Can C. The Value of Neutrophil to Lymphocyte Ratio and Platelet to Lymphocyte Ratio for Detecting Early –onset Neonatal Sepsis. J Pediatr Hematol Oncol 2018; 40(4): e229-32.
15. Hornik CP, Benjamin DK, Becker KC, et al. Use of the complete blood cell count in early-onset neonatal sepsis. Pediatr Infect Dis J 2012; 31(8): 799-802.
16. Israr S, Hayat A, Ahmad TM, et al. Comparison of procalcitonin and hematological ratios in cord blood as early predictive marker of neonatal sepsis. Pak Armed Forces Med J 2020; 70(3): 824-9.
17. Karabulut B, Alatas SO. Diagnostic Value of Neutrophil to Lymphocyte Ratio and Mean Platelet Volume on Early Onset Neonatal Sepsis on Term Neonate. J Pediatr Intensive Care 2021; 10(2): 143-7.
18. Varal IG, Dogan P. Can neutrophil-lymphocyte ratio be a predictor of late onset sepsis in preterm infants? Ann Med Res 2020; 27(1): 23-8.

[DOI: 10.22088/CJP.BUMS.9.1.1]