International Journal of Medical Arts

Volume 4, Issue 6, June 2022

https://ijma.journals.ekb.eg/

Print ISSN: 2636-4174

Online ISSN: 2682-3780

Available online at Journal Website
https://ijma.journals.ekb.eg/
Main Subject [Pediatrics]

Original Article

Diagnostic Values of Platelet to Lymphocyte Ratio and Neutrophil to Lymphocyte Ratio in the Early Diagnosis of Early-Onset Neonatal Sepsis in Full-term Newborns

Elham Abd-Elmagied Gebaly Soliman [1]*, Mostafa Abd-Elazeem Hassan [1], Esmail Abd- Elraziek Kassem [1], Mohamed Ahmed Bashir [2]

[1] Department of Pediatrics, Faculty of Medicine, Al-Azhar University [Assiut], Egypt

[2] Department of Clinical Pathology, Faculty of Medicine, Al-Azhar University [Assiut], Egypt

Article information

Received: 09-05-2022

Accepted: 16-07-2022

DOI: 10.21608/IJMA.2022.137452.1452

*Corresponding author

Email: elhamelgebaly88@gmail.com

Citation: Soliman EAG, Hassan MA, Kassem EA, Bashir MA. Diagnostic Values of Platelet to Lymphocyte Ratio and Neutrophil to Lymphocyte Ratio in the Early Diagnosis of Early-Onset Neonatal Sepsis in Full-term Newborns. IJMA 2022 June; 4 [6]: 2412-2419. doi: 10.21608/IJMA.2022.137452.1452

ABSTRACT

Background: Neonatal sepsis is regarded as one of the major health problems throughout the world. Neutrophil to Lymphocyte ratio [NLR] ratios as well as Platelet to Lymphocyte ratio [PLR] are simple, low cost and easily calculated biomarkers that may be employed for earlier diagnosing of neonatal sepsis.

Aim of the work: The present study aims for the assessment of the Platelet to Lymphocyte ratio [PLR] as well as the Neutrophil to Lymphocyte ratio [NLR] in full-term neonates with early-onset sepsis [EOS], and its impact on management.

Patients and Methods: The study involved 50 full-term neonates divided into two groups; patients' group included 30 full-term neonates, diagnosed with EOS [positive blood culture] compared with control group which included 20 healthy full-term neonates.

Results: The study showed no significant difference between cases and controls as regards demographic data. Patients with early-onset sepsis showed significant elevation of absolute neutrophil counts, NLR, PLR, C-reactive protein, in comparison with the control group. Positive predictive value [PPV] of NLR was 99%, PLR was 73%.

Conclusion: NLR and PLR are predictive reliable markers in diagnosing and detecting early onset neonatal sepsis. NLR and PLR showed higher specificity results compared to CRP.

Keywords: Lymphocyte; Neutrophil; Platelets; Newborn; Early-onset sepsis.

INTRODUCTION

Neonatal sepsis is regarded as a major problem in neonates all over the world that leads to significant mortality and morbidity, specifically in developing countries [1]. Sepsis is a common illness among newborns, affecting up to 1–5 per 1000 neonates in developed countries, and about 10–50 per 1000 neonates in the developing countries [2].

Clinical Sepsis and proven Sepsis in neonates is classified in accordance with the absence or the presence of the positive blood culture. As for the time of symptoms onset, they are categorized as Early-Onset Sepsis [EOS] and Late-Onset Sepsis [LOS]. In case the neonate is presented with clinical signs and inflammation with increase in the biomarker, but the blood culture is negative, then sepsis is defined as clinical Sepsis [3, 4].

On the contrary, in case of proven sepsis, the neonate is presented with positive blood cultures as well as clinical and laboratory signs of infection or inflammation [5]. The time of onset defines the type of sepsis. Those developing in the first three days of neonate's life are called EOS, while the ones developing from 4 to 28 days of neonate's life are called LOS [6].

Early onset sepsis is primarily due to maternal transmission of organism either intrauterine or early after delivery. An immune system reaction is caused by microorganism transmission to the blood circulation of neonates that leads to systemic inflammatory response syndrome [SIRS], which may lead to sepsis, multiple organ failure, and finally death [7]. Early diagnosis and therapy may inhibit the SIRS to progress and prevent sepsis-related morbidity and mortality [8].

The suspension of EOS depends largely on the presence of maternal risk factor, in addition to certain clinical and laboratory signs. Clinical signs are nonspecific and subtle in neonatal EOS. Non-specific clinical signs of the newborn and the deficiency of accurate biomarkers can result in antibiotic resistance due to delayed diagnosis and introduction of treatment, unnecessary hospitalization, and antibiotic misuse [9].

The parameters routinely used for neonatal sepsis have variable diagnostic values such as absolute neutrophil count [ANC], total leukocyte count, C-reactive protein [CRP], and immature/total neutrophil [I/T] ratio. Procalcitonin, which is a marker of specific bacterial infection, is expensive and not always available in all health service facilities such as rural areas [10]. Blood culture is the gold standard for the diagnosis of neonatal sepsis, but it is time consuming and often with negative results [1].

In recent studies, it has been reported that platelet and lymphocytes have a major role in the inflammatory process. PLR is an indicator of the balance between inflammation and thrombosis. Therefore, the inflammatory status leads to accelerated megakaryocyte proliferation and associated thrombocytosis [11-13].

The neutrophil-lymphocyte ratio [NLR] and platelet-lymphocyte ratio [PLR] are inexpensive, simple marker in our community and easily calculated as a part of complete blood counts and due to lack of studies in Egypt.

THE AIM OF THE WORK

This study aims for assessment of the Neutrophil to Lymphocyte ratio [NLR] and the Platelet to Lymphocyte ratio [PLR] in full-term neonates with early-onset sepsis [EOS].

PATIENTS AND METHODS

A cross-sectional study of 50 full-term neonates admitted to the neonatal intensive care unit of Sohag General Hospital, from December 2020 to August 2021. The study included two groups; **1] Cases Group**: 30 full term neonates with postnatal age of 1 to 3 days and gestational age ≥ 37 weeks and < 42weeks, selected based on standard risk factors, symptoms as well as signs of neonatal sepsis. Cases with proven sepsis in neonates [positive blood culture] were included, and **2] Control Group**: Included 20 apparently normal healthy newborns [admitted due to conditions other than sepsis, e.g. neonatal jaundice and transient tachypnea of newborn].

Exclusion criteria: Small for gestational age [SGA], intrauterine growth restriction [IUGR], perinatal asphyxia, congenital abnormality, maternal Pre-eclampsia and gestational diabetes mellitus [GDM], chorioamnionitis, as well as cases where the mother uses tobacco during pregnancy are all excluded.

Methods and Sampling: At admission, samples are obtained from a peripheral vein. Automated hematology analyzer [CELLTAC G; NIHON KOHDEN CORPORATION] determined the complete blood count while Differential leucocytic count was confirmed by microscopic examination of Leishman stained blood film and the immature/total

neutrophil ratio was used to calculate I/T ratio. The NLR was calculated by the neutrophil /lymphocyte ratio, and PLR by the platelets / lymphocyte ratio. Immune-turbidimetric method has been used to measure CRP levels. All previous venous blood samples were collected under complete aseptic conditions.

Ethical considerations: Every parent of infants was informed about the nature and steps of the study. Written consent form has been attained from parents. The patients have the right to withdraw from the study at any time. Approval of local ethical committee was obtained.

Statistical analysis: Data were organized, charted, and statistically analyzed by IBM personal computer and statistical package SPSS version 23. Descriptive statistics was presented as percentage [%], means and standard deviation [SD]. Student [t] test or Mann-Whitney test were applied to study statistical significance between two quantitative variables. Chi-square test [x^2] has been also applied to study statistical significance between two qualitative variables. The ROC [receiver operating characteristic] curve was used for the evaluation of the performance of classification schemes where there is one variable of two categories by which subjects are classified. They were constructed by calculating the sensitivities and specificities of the variable. The cutoff value with the highest accuracy was selected as the diagnostic cutoff points. The ROC curve is a graphic representation of the relationship between sensitivity and specificity at different cut-off points for a diagnostic test. Pearson correlation was used to correlate variables. P-value of < 0.05 was considered statistically significant.

RESULTS

There were no statistically significant differences between patients and controls as regard general characteristics. PROM was more frequent among the case group [P = 0.003]. Regarding vital data, patients group had higher RR and lower SPO2 [Table 1].

Table [2] shows a statistically significant decrease in platelet count among cases than controls, while there was statistically significant increase in WBCs, immature neutrophils, IT ratio, lymphocytes count, CRP, PLR and NLR between cases and controls.

Table [3] shows that Klebsiella was the most common organism in blood culture [20%] followed by E. coli and group B streptococci [13.3%].

Regarding the relation between clinical findings with NLR and PLR values, it was found that cases with GIT disturbances and temperature instability were significantly associated with positive NLR and PLR among the case group [table 4].

Table [5] and figure [1] show that NLR had a sensitivity of 74%, specificity 96% and positive predictive value [PPV] 99%, negative predictive value [NPV] of 77%, while PLR had a sensitivity of 84%, specificity 75%, PPV 73%, NPV 74% in comparison to CRP which had sensitivity 70%, specificity 73%, PPV 72%, NPV 69%.

Table [6] shows a significant positive correlation between PLR and with WBCs and Total neutrophils, but no significant correlation with the other parameters.

Table [1]: General characteristics, anthropometric measures and vital data among the studied groups

		Cases [n=30]	Controls [n=20]	P Value
Age [Hours]	Mean ± SD	35.9±20.03	43.2±21.37	0.2
Weeks of gestation	Mean ± SD	38.07±0.98	38.55±1.73	0.7
Sex	Male Female	18 [60%] 12 [40%]	26 [65%] 14 [35%]	0.1
Mode of delivery	Cesarean Normal	20 [66.7%] 10 [33.3%]	11 [55%] 9 [45%]	0.29
Birth weight [KG]	Mean ± SD	2.99±0.35	2.89±0.36	0.23
Birth Height [cm]	Mean ± SD	49.6±1.07	46.65±1.04	0.45
Head circumference [cm]	Mean ± SD	33.7±1.23	34±1.17	0.45
Temperature	Mean ± SD	37.6±1.08	37.38±0.96	0.46
Respiratory rate [cycle/min]	Mean ± SD	55.67±9.7	48.7±2.9	0.003 *
Heart rate [beat/min]	Mean ± SD	138.8±26.8	130.15±23.24	0.24
Oxygen saturation [SPO_2%]	Mean ± SD	84.5±9.1	93.5±4.32	<0.001*
Maternal age	Mean ± SD	25.8±4	25.7±4.1	0.9
Premature rupture of membranes	Yes No	20 [70%] 10 [30%]	7 [35%] 13 [65%]	0.003*

Table [2]: Comparison between cases and control groups regarding laboratory data

		Cases [n=30]	Controls [n=20]	P Value
Red blood cells [×10^6/mm^3]	Mean ± SD	4.164±0.9897	4.800±0.9537	<0.05 *
Hemoglobin [gm/dl]	Mean ± SD	13.507±3.6994	16.445±3.4018	<0.05*
Hematocrit	Mean ± SD	39.387±10.2473	47.005±7.8605	<0.05*
White blood cells [x10^3/µl]	Mean ± SD	20.1±10.648	11.23±4.21	0.041*
Platelets [×10^9/mcl]	Mean ± SD	128.7±70.886	208.45±88.647	0.001*
Immature neutrophils [µl]	Mean ± SD	10067.53±6074.88	6651.8±3799.25	0.03*
Lymphocytes [µl]	Mean ± SD	5887.4±3164.5	7334±4902.60	<0.001*
I/T Ratio	Mean ± SD	0.861±3.9	0.05±0.038	<0.001*
C-reactive protein	Mean ± SD	57.93±37.03	8.35±12.67	<0.001*
Neutrophil to lymphocyte ratio	Mean ± SD	2.82±1.25	1.6±0.85	<0.001*
Platelet to lymphocyte ratio	Mean ± SD	0.084±0.032	0.043±0.02	<0.001*

Table [3]: Blood culture among septic group, Total N=30

Blood culture result	N=30	[%]
Klebsiella	6	20.0
Escherichia coli	4	13.3
Group B streptococci	4	13.3
Coagulase-negative Staphylococci	2	6.7
Enterococcus Fecalis	2	6.7
Candida albicans	1	3.3
Staphylococcus epidermis	1	3.3
Staphylococcus heamolyticus	1	3.3
Streptococcus pneumonia	1	3.3

Table [4]: Relation between clinical data and the two studied ratios among studied cases

Parameters	Number of cases	NLR			PLR		
		Mean	±SD	P-Value	Mean	±SD	P-Value
Skin changes	11	2.1	1.01	> 0.05 NS	0.0542	00.081	> 0.05 NS
Petechiae	12	2.03	1.11	> 0.05 NS	0.0478	0.079	> 0.05 NS
Hypotonia	19	2.98	2.2	> 0.05 NS	0.101	0.11	> 0.05 NS
Tachycardia	14	1.85	1.364	> 0.05 NS	0.0193	0.014	> 0.05 NS
Bradycardia	16	2.38	0.99	> 0.05 NS	0.09	0.112	> 0.05 NS
GIT disturbances	21	2.29	1.47	**< 0.05 S**	0.101	0.12	**< 0.05 S**
Poor perfusion	16	1.87	1.366	> 0.05 NS	0.0163	0.011	> 0.05 NS
Poor reflexes	18	2.9	1.003	> 0.05 NS	0.0354	0.066	> 0.05 NS
Apnea	10	1.63	1.003	> 0.05 NS	0.0354	0.066	> 0.05 NS
Grunting	6	1.84	1.849	> 0.05 NS	0.0375	0.039	> 0.05 NS
Tachypnea	13	1.9	1.828	> 0.05 NS	0.0406	0.051	> 0.05 NS
Cyanosis	2	1.27	0.084	> 0.05 NS	0.0204	0.011	> 0.05 NS
Seizures	3	2.5	2.575	> 0.05 NS	0.0268	0.023	> 0.05 NS
Temp instability	15	2.9	1.92	**< 0.05 S**	0.062	0.076	**< 0.05 S**

Table [5]: NLR and PLR as predictors of sepsis

	P Value	95% CI	Cutoff value	Sensitivity	Specificity	PPV	NPV	LR+	LR-
NLR	0.02*	0.54-0.81	≤1.21	74%	96%	99%	77%	6.1	0.32
PLR	0.015*	0.47-0.75	≤0.02	84%	75%	73%	74%	2.6	0.38
CRP	<.042*	62.1 -96.8	≤8	70%	73%	72%	69%	8.5	0.17

NLR: neutrophil to lymphocyte ratio; PLR: platelet to lymphocyte ratio; PPV: positive predictive value; NPV: negative predictive value, LR+: positive likelihood ratio, LR-: negative likelihood ratio.]

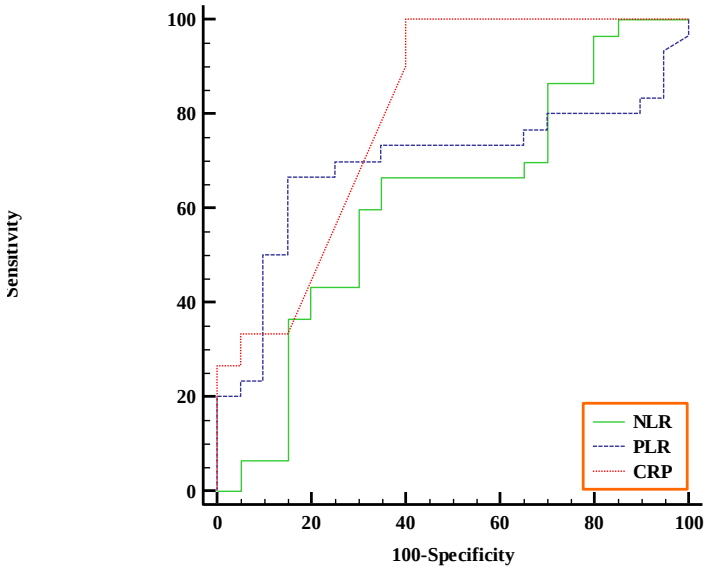

Figure [1]: NLR and PLR as predictors of sepsis

Table [6]: Correlation between CBC parameters and two studied ratios among studied cases

	NLR		PLR	
	r	P	r	P
C-reactive protein	0.26	0.16	0.025	0.89
Red blood cells [×10^6/mm^3]	-0.119	0.53	-0.18	0.32
Hemoglobin [gm/dl]	0.001	0.9	0.14	0.46
Hematocrit	0.024	0.89	-0.07	0.71
MCV/fl	0.32	0.086	0.27	0.15
MCH/pg	0.33	0.072	0.037	0.85
White blood cells [x10^3/µl]	0.118	0.5	0.64	**<0.001**
Total Neutrophils [x10^3/µl]	0.22	0.24	0.53	**<0.001**

DISCUSSION

Neonatal sepsis is a worldwide major health problem leading to high mortality resulting in some long-term health problems, especially in environments with poor services [14]. In Egypt, the rate of total mortality for the proven neonatal sepsis was 51% and 42.9% for EOS and LOS, respectively [15].

In the present study, 60% of the newborns in the patients' group were males, which agree with many previous studies [16-19]. This could be due to defects in X-linked immunoregulatory genes which are involved with the function of the thymus or with synthesis of immunoglobulin [20]. However, Trotman and Bell [21] found that female gender was associated with poor outcome in with bacterial sepsis. So, the effect of gender on sepsis was inconsistent.

In this study, 66.7% of neonatal septic group were delivered by cesarean section. In agreement with our findings, Naher *et al.* [19] had reported that out of 50 cases of suspected sepsis, 56% of them born by caesarean section. Also, in the study by Signore [22], cesarean delivery is related to a greater risk of neonatal sepsis. On the other hand, Stoll *et al.* [23] observed that infants born by normal delivery were more likely to have EOS. The reason behind this may be the good sterilization and intrapartum chemoprophylaxis which dramatically decrease the risk of sepsis in neonates delivered by caesarean section.

In this study, there was no significant difference between cases and controls as regard of birth weight [p=0.23], disagree with many studies [17, 24, 25] whose found that low birth weight [<2500 grams] was associated with higher risk for sepsis. Odabasi and Bulbul [26] also stated that the neonatal sepsis risk increases with decreasing birth weight and gestational age.

In our study, 70% of septic group had history of PROM>18 h, which agrees with Glaser *et al.* [27] who reported that PROM more than 18 hours is a strong risk factor for neonatal sepsis. This also agrees with Procianoy and Silveira [28] who stated that PROM >18 h is considered as a risk factor for early onset neonatal sepsis.

The clinical signs of sepsis in neonates are very broad and nonspecific and are associated with the characteristics of the causative organism and the body's response to the invasion [29].

In our study, clinical evaluation of studied neonates showed that the most frequent clinical findings in the case group were GIT symptoms [gastric residue, vomiting, abdominal distention and diarrhea] in 70%, hypotonia [65%], respiratory distress [65%], poor perfusion [60%], poor reflex [55%] and temperature instability [50%]. This comes in agreement with two studies [30, 31] who described feeding intolerance, respiratory distress, lethargy and poor perfusion as the major clinical presentation of sepsis. Clinical signs and symptoms of sepsis are nonspecific. As a result, the differential diagnosis is broad including most if not all body systems as neonatal infection may be limited to a single organ or may include multiple organs [32].

In the present study, it has been found that hemoglobin and the platelet Counts in the septic group were statistically significantly decreased compared with the corresponding values in the control groups of infants. These results correlated with those of two recent studies [33, 34]. In such cases, the low Hb level could be explained as a result of increased hemolysis of red blood cells caused by bacterial infection in blood [34].

From the variable results obtained from different studies, it is evident that the causative organisms causing neonatal septicemia vary from nursery to nursery, between different geographical areas and in the same catchment area with time. This variation may be due to environmental differences, microbial etiology of sepsis, and practice of supportive care between centers [35]. In this study, we include cases with only positive blood culture, which is a strength point of this study as blood culture is the main standard laboratory test for diagnosis [36, 37], and blood cultures laboratory processing has been static over the past 30 years, in spite of the increase in antibiotic resistance and advances in analyzer design [38].

Conversely; although blood culture is believed to be the main standard diagnostic test for sepsis, there is a number of limitations including; unavailability of the test in the majority of developing countries, associated technical problem and that it is a time-consuming test [takes more than three days to see at least the first preliminary result] [39]. As a result, diagnosis of neonatal sepsis is established based on the clinical evaluation and the treatment also relies on practical treatment protocol which usually leads to unnecessary hospitalization, increased unreasonable use of antibiotics and excessive family cost [40].

Thus, there is a continuous need for presenting new available, easy to perform and accurate biomarkers helping physician to early diagnose and manage early onset neonatal sepsis, especially in developing countries with low resources.

In this study, were significantly associated with early onset neonatal sepsis, with much better diagnostic performance than routinely used parameters such as CRP level. Can *et al.* [41] reported a significantly higher NLR among Full term neonates with sepsis compared to control group [$p = 0.02$], which consisted also with Omran *et al.* [42] [$p < 0.001$]. In general, researches conducted among neonates with sepsis have elevated NLR values in comparison with NLR values formerly reported by Hamiel *et al.* [43] in healthy neonates or in the pediatric population. High NLR levels in the septic patients are owing to a disparity between neutrophil and lymphocyte levels. Increased neutrophil count is a front-line defense mechanism in the major role of neutrophils in response to the innate immune system to combat bacterial infections and stimulates the emergency granulopoiesis process. An increase in neutrophil count is accompanied by a decrease in lymphocyte and monocyte synthesis, as well as a decrease in neutrophil apoptosis, but with an increase in lymphocyte apoptosis, resulting in neutrophilia and lymphopenia [1, 44].

During systemic or localized infections, neutrophils are stimulated, leading to a rapid increase of the numbers in circulation [45]. Neutrophils are the most abundant leukocyte circulating in the bloodstream, comprising over 50% of leukocytes, and these cells are particularly adept at phagocytosing and killing microbes [46].

Platelet–neutrophil interactions take place in various groups of inflammatory conditions and infections. Stimulated platelets attach to neutrophils in the circulation and facilitate the recruitment of neutrophils to the site of injury and infection [47].

In addition, the present study found that cases had significant higher leucocyte count in comparison with controls indicating role of leukocytosis in diagnosis of neonatal sepsis [$p = 0.04$]. In addition, cases had significant lower platelet count and lymphocytes in comparison with controls. This observation correlates relation of thrombocytopenia and neonatal morbidity as major consequences of neonatal sepsis.

Although white blood cell [WBC] count, immature/total leukocyte ratio [IT ratio], absolute leukocyte count and acute phase reactants such as C-reactive protein [CRP], procalcitonin [PC] and interleukin-6 [IL-6] are the most commonly used parameters in the diagnosis of newborn sepsis. However, those inflammatory markers, may be

affected by maternal and fetal non-infectious conditions, and their different half-lives may decrease their ability to provide a definitive diagnosis of sepsis [48].

The main limitation of the study is the small sample size, and being single center study. In addition, included cases had proven neonatal sepsis diagnosed by positive blood culture, which is not sensitive enough, and many cases with sepsis may have normal blood culture. Thus, cases with sepsis and normal blood culture were excluded from the study.

Conclusion: NLR, PLR are reliable predictive markers in the early detection of neonatal sepsis onset as PPV of NLR was 99%, PLR was 73%. NLR and PLR shows higher specificity results compared to CRP.

Conflict of interest: The authors declare that there is no any financial conflict regarding the research and publication.

REFERENCES

1. Alkan Ozdemir S, Arun Ozer E, Ilhan O, Sutcuoglu S. Can neutrophil to lymphocyte ratio predict late-onset sepsis in preterm infants? J Clin Lab Anal. 2018 May;32[4]:e22338. doi: 10.1002/jcla.22338.
2. Hasibuan BS**.** Comparison of microbial pattern in early and late onset neonatal sepsis in referral center Haji Adam Malik hospital Medan Indonesia. IOP Conf Ser Earth Enviromental Sci 2018;125[1]:012053
3. Sumitro KR, Utomo MT, Widodo ADW. Neutrophil-to-Lymphocyte Ratio as an Alternative Marker of Neonatal Sepsis in Developing Countries. Oman Med J. 2021 Jan 6;36[1]:e214. doi: 10.5001/omj.2021.05.
4. Fattah MA, Omer AF, Asaif S, Manlulu R, Karar T, Ahmed A, *et al*. Utility of cytokine, adhesion molecule and acute phase proteins in early diagnosis of neonatal sepsis. J Nat Sci Biol Med. 2017 Jan-Jun;8(1):32-39. doi: 10.4103/0976-9668.198362.
5. Puopolo KM, Benitz WE, Zaoutis TE; COMMITTEE ON FETUS AND NEWBORN; COMMITTEE ON INFECTIOUS DISEASES. Management of Neonates Born at ≥35 0/7 Weeks' Gestation With Suspected or Proven Early-Onset Bacterial Sepsis. Pediatrics. 2018 Dec;142[6]: e20182894. doi: 10.1542/peds.2018-2894.
6. Cohen J, Vincent JL, Adhikari NK, Machado FR, Angus DC, Calandra T, *et al.* Sepsis: a roadmap for future research. Lancet Infect Dis. 2015 May;15[5]:581-614. doi: 10.1016/S1473-3099[15]70112-X.
7. Scheel M, Perkins S. Hit or Miss? A Review of Early-Onset Sepsis in the Neonate. Crit Care Nurs Clin North Am. 2018 Sep;30[3]:353-362. doi: 10.1016/j.cnc.2018.05.003.
8. Mukhopadhyay S, Taylor JA, Von Kohorn I, Flaherman V, Burgos AE, Phillipi CA, *et al*. Variation in Sepsis Evaluation Across a National Network of Nurseries. Pediatrics. 2017 Mar;139[3]:e20162845. doi: 10.1542/peds.2016-2845.
9. Jyothi P, Basavaraj MC, Basavaraj PV. Bacteriological profile of neonatal septicemia and antibiotic susceptibility pattern of the isolates. J Nat Sci Biol Med. 2013 Jul;4[2]:306-9. doi: 10.4103/0976-9668.116981.
10. Holub M, Beran O, Kaspříková N, Chalupa P. Neutrophil to lymphocyte count ratio as a biomarker of bacterial infections. Open Med. 2012 Apr 1;7[2]:258-261. doi: 10.2478/s11536-012-0002-3.
11. Wang Z, Peng S, Wang A, Xie H, Guo L, Jiang N, Niu Y. Platelet-lymphocyte ratio acts as an independent predictor of prognosis in patients with renal cell carcinoma. Clin Chim Acta. 2018 May;480:166-172. doi: 10.1016/j.cca.2018.02.014.
12. Chen H, Xue H, Liu W, Wu F, Wang Y, Gao H. [Meta-analysis of Platelet Lymphocyte Ratio as A Prognostic Factor for Non-small Cell Lung Cancer]. Zhongguo Fei Ai Za Zhi. 2019 May 20;22[5]:289-298. Chinese. doi: 10.3779/j.issn.1009-3419.2019.05.05.
13. Shen Y, Huang X, Zhang W. Platelet-to-lymphocyte ratio as a prognostic predictor of mortality for sepsis: interaction effect with disease severity-a retrospective study. BMJ Open. 2019 Jan 25;9[1]:e022896. doi: 10.1136/bmjopen-2018-022896.
14. Wynn JL, Polin RA. Progress in the management of neonatal sepsis: the importance of a consensus definition. Pediatr Res. 2018 Jan;83[1-1]:13-15. doi: 10.1038/pr.2017.224.
15. Shehab El-Din EM, El-Sokkary MM, Bassiouny MR, Hassan R. Epidemiology of Neonatal Sepsis and Implicated Pathogens: A Study from Egypt. Biomed Res Int. 2015;2015:509484. doi: 10.1155/2015/509484.
16. Sonawane VB, Mehkarkar N, Gaikwad S, Kadam N. Comparison between sepsis markers and blood culture in diagnosis of neonatal sepsis: a prospective study. Int J Res Med Sci. 2017 Mar 28;5(4):1662-6. doi: 10.18203/2320-6012.ijrms20171283
17. Shrestha RK, Rai SK, Khanal LK, Manda PK. Bacteriological study of neonatal sepsis and antibiotic susceptibility pattern of isolates in Kathmandu, Nepal. Nepal Med Coll J. 2013 Mar;15[1]:71-3. PMID: 24592800.
18. Dong Y, Basmaci R, Titomanlio L, Sun B, Mercier JC. Neonatal sepsis: within and beyond China. Chin Med J [Engl]. 2020 Sep 20;133[18]:2219-2228. doi: 10.1097/CM9.0000000000000935.
19. Naher BS, Mannan MA, Noor K, Shahiddullah M. Role of serum procalcitonin and C-reactive protein in the diagnosis of neonatal sepsis. Bangladesh Med Res Counc Bull. 2011 Aug;37[2]:40-6. doi: 10.3329/bmrcb.v37i2.8432.
20. Satar M, Ozlü F. Neonatal sepsis: a continuing disease burden. Turk J Pediatr. 2012 Sep-Oct;54[5]:449-57. PMID: 23427506.
21. Trotman H, Bell Y. Neonatal sepsis in very low birthweight infants at the University Hospital of the West indies. West Indian Med J. 2006 Jun;55[3]:165-9. doi: 10.1590/s0043-31442006000300007.
22. Signore C. VBAC: what does the evidence show? Clin Obstet Gynecol. 2012 Dec;55[4]:961-8. doi: 10.1097/GRF.0b013e318263c55d.

23. Stoll BJ, Hansen NI, Sánchez PJ, Faix RG, Poindexter BB, Van Meurs KP, *et al.* Early onset neonatal sepsis: the burden of group B Streptococcal and E. coli disease continues. Pediatrics. 2011 May;127[5]:817-26. doi: 10.1542/peds.2010-2217.

24. Schrag SJ, Cutland CL, Zell ER, Kuwanda L, Buchmann EJ, Velaphi SC, Groome MJ, Madhi SA; PoPS Trial Team. Risk factors for neonatal sepsis and perinatal death among infants enrolled in the prevention of perinatal sepsis trial, Soweto, South Africa. Pediatr Infect Dis J. 2012 Aug;31[8]:821-6. doi: 10.1097/INF.0b013e31825c4b5a.

25. Wynn JL, Polin RA. A neonatal sequential organ failure assessment score predicts mortality to late-onset sepsis in preterm very low birth weight infants. Pediatr Res. 2020 Jul;88[1]:85-90. doi: 10.1038/s41390-019-0517-2.

26. Odabasi IO, Bulbul A. Neonatal Sepsis. Sisli Etfal Hastan Tip Bul. 2020 Jun 12;54[2]:142-158. doi: 10.14744/SEMB.2020.00236.

27. Glaser MA, Hughes LM, Jnah A, Newberry D. Neonatal Sepsis: A Review of Pathophysiology and Current Management Strategies. Adv Neonatal Care. 2021 Feb 1;21[1]:49-60. doi: 10.1097/ANC.0000000000000769.

28. Procianoy RS, Silveira RC. The challenges of neonatal sepsis management. J Pediatr [Rio J]. 2020 Mar-Apr;96 Suppl 1:80-86. doi: 10.1016/j.jped.2019.10.004.

29. Rashwan NI, Hassan MH, Mohey El-Deen ZM, Ahmed AE. Validity of biomarkers in screening for neonatal sepsis - A single center -hospital based study. Pediatr Neonatol. 2019;60[2]:149-155. doi: 10.1016/j.pedneo.2018.05.001.

30. Ogundare E, Akintayo A, Aladekomo T, Adeyemi L, Ogunlesi T, Oyelami O. Presentation and outcomes of early and late onset neonatal sepsis in a Nigerian Hospital. Afr Health Sci. 2019 Sep;19[3]:2390-2399. doi: 10.4314/ahs.v19i3.12.

31. Bekhof J, Reitsma JB, Kok JH, Van Straaten IH. Clinical signs to identify late-onset sepsis in preterm infants. Eur J Pediatr. 2013 Apr;172[4]:501-8. doi: 10.1007/s00431-012-1910-6.

32. Stoll BJ, Puopolo KM, Hansen NI, Sánchez PJ, Bell EF, Carlo WA, *et al.* Early-Onset Neonatal Sepsis 2015 to 2017, the Rise of Escherichia coli, and the Need for Novel Prevention Strategies. JAMA Pediatr. 2020 Jul 1;174[7]: e200593. doi: 10.1001/jamapediatrics.2020.0593.

33. Utomo MT, Sumitro KR, Etika R, Widodo ADW. Current-proven neonatal sepsis in Indonesian tertiary neonatal intensive care unit: a hematological and microbiological profile. Iran J Microbiol. 2021 Jun;13[3]:266-273. doi: 10.18502/ijm.v13i3.6386.

34. Nabi SN, Basak AK, Kamruzzaman M, Pervez AF, Musharraf M, Sultana N, *et al.* Performance of Haematological Parameters in Early Diagnosis of Clinically Suspected Neonatal Sepsis. Mymensingh Med J. 2019 Jan;28[1]:193-199. PMID: 30755569.

35. Dzwonek AB, Neth OW, Thiébaut R, Gulczynska E, Chilton M, Hellwig T, *et al.* The role of mannose-binding lectin in susceptibility to infection in preterm neonates. Pediatr Res. 2008 Jun;63[6]:680-5. doi: 10.1203/PDR.0b013e31816fdbff.

36. Walker O, Kenny CB, Goel N. Neonatal sepsis. Paediatr Child Health. 2019 Jun 1;29[6]:263-268. doi: 10.1016/j.paed.2019.03.003.

37. Arayici S, Şimşek GK, Canpolat FE, Oncel MY, Uras N, Oguz SS. Can Base Excess be Used for Prediction to Early Diagnosis of Neonatal Sepsis in Preterm Newborns? Mediterr J Hematol Infect Dis. 2019 Mar 1;11[1]: e2019014. doi: 10.4084/MJHID.2019.014.

38. Weinbren MJ, Collins M, Heathcote R, Umar M, Nisar M, Ainger C, Masters P. Optimization of the blood culture pathway: a template for improved sepsis management and diagnostic antimicrobial stewardship. J Hosp Infect. 2018 Mar;98[3]:232-235. doi: 10.1016/j.jhin.2017.12.023.

39. Sorsa A. Diagnostic Significance of White Blood Cell Count and C-Reactive Protein in Neonatal Sepsis; Asella Referral Hospital, South East Ethiopia. Open Microbiol J. 2018;12:209-217. doi: 10.2174/1874285801812010209.

40. Hotoura E, Giapros V, Kostoula A, Spyrou P, Andronikou S. Pre-inflammatory mediators and lymphocyte sub-populations in preterm neonates with sepsis. Inflammation. 2012;35[3]:1094-101. doi: 10.1007/s10753-011-9416-3.

41. Can E, Hamilcikan Ş, 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 May;40[4]:e229-e232. doi: 10.1097/MPH.0000000000001059.

42. 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 Jan-Feb;94[1]:82-87. doi: 10.1016/j.jped.2017.03.006.

43. Hamiel U, Bahat H, Kozer E, Hamiel Y, Ziv-Baran T, Goldman M. Diagnostic markers of acute infections in infants aged 1 week to 3 months: a retrospective cohort study. BMJ Open. 2018 Jan 24;8[1]:e018092. doi: 10.1136/bmjopen-2017-018092.

44. Hwang SY, Shin TG, Jo IJ, Jeon K, Suh GY, Lee TR, *et al.* Neutrophil-to-lymphocyte ratio as a prognostic marker in critically-ill septic patients. Am J Emerg Med. 2017 Feb;35[2]:234-239. doi: 10.1016/j.ajem.2016.10.055.

45. Lawrence SM, Corriden R, Nizet V. The Ontogeny of a Neutrophil: Mechanisms of Granulopoiesis and Homeostasis. Microbiol Mol Biol Rev. 2018 Feb 7;82[1]:e00057-17. doi: 10.1128/MMBR.00057-17.

46. Mahmoud NM, Abdelhakeem M, Mohamed HH, Baheeg G. Validity of Platelet to Lymphocyte Ratio and Neutrophil to Lymphocyte Ratio in Diagnosing Early-onset Neonatal Sepsis in Full-term Newborns. J Comprehen Pediatr. 2022 Feb 28;13[1]: e115378. doi: 10.5812/compreped.115378.

47. Page C, Pitchford S. Neutrophil and platelet complexes and their relevance to neutrophil recruitment and activation. Int Immunopharmacol. 2013 Dec;17[4]:1176-84. doi: 10.1016/j.intimp.2013.06.004.

48. Çelik HT, Portakal O, Yiğit Ş, Hasçelik G, Korkmaz A, Yurdakök M. Efficacy of new leukocyte parameters versus serum C-reactive protein, procalcitonin, and interleukin-6 in the diagnosis of neonatal sepsis. Pediatr Int. 2016 Feb;58[2]:119-25. doi: 10.1111/ped.12754.

IJMA
International Journal Of Medical Arts

International Journal of Medical Arts

https://ijma.journals.ekb.eg/
Print ISSN: 2636-4174
Online ISSN: 2682-3780

IJMA is indexed in	The Egyptian Knowledge Bank supports IJMA	IJMA is listed in
SCU Supreme Council of Universities DOAJ Directory of Open Access Journals J-Gate Indexed Index Copernicus International	Egyptian Knowledge Bank بنك المعرفة المصرى	publons ISMTE Academic Resource Index ResearchBib ICMJE International Committee of Medical Journal Editors