



NEUTROPHIL TO LYMPHOCYTE RATIO AND MEAN PLATELET VOLUME AS NEW DIAGNOSTIC MARKERS FOR DETECTION OF EARLY-ONSET NEONATAL SEPSIS IN TERM AND PRETERM INFANTS

Pathology

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ABSTRACT

Background: The clinical state of systemic inflammation brought on by infection is known as sepsis. The second most frequent cause of death in this age group is neonatal sepsis. **1** Early-Onset Neonatal Sepsis (EONS) is a major cause of morbidity and mortality that develops in a newborn within the first three days of life. **4** Aim of current study was to find the significance of neutrophil to lymphocyte ratio (NLR) and Mean Platelet volume (MPV) as the auxiliary parameter for the diagnosis of EONS. **Methodology:** A retrospective cross-sectional study was conducted in the Department of Pathology from January 2020 to 2022. A total of 146 subjects (73 sepsis & 73 non-sepsis) were studied. Control group: Babies diagnosed with neonatal hyperbilirubinemia (age < 72 hours). Data were collected from hospital's electronic data system. Total leucocyte count, Absolute Neutrophil Count, Absolute Lymphocyte Counts, NLR, MPV, and CRP of septic neonates were compared with gestational age-matched non-septic neonates by an unpaired t-test. **Results:** As indicators of EONS, Comparison of the NLR between the two groups shows that sensitivity of NLR and MPV was 100%, specificity of NLR was 97.3% and MPV was 100% and PPV of NLR was 97.3%, MPV was 100%. **Conclusion:** NLR, a component of complete blood count, can be used as an alternative simple marker and reasonably inexpensive for detection of neonatal sepsis, particularly in developing nations. Combining NLR with CRP has also been shown to enhance the diagnosis of neonatal sepsis.

KEYWORDS

Neonatal sepsis, neutrophil-to-lymphocyte ratio, MPV

INTRODUCTION:

According to the infant's age at time of commencement of symptoms, sepsis is categorized as follows: Some experts limit the definition to infections occurring within the first 72hrs of life, early-onset sepsis is defined as the onset of symptoms before 7 days of age. Late-onset sepsis is defined as the onset of symptoms at or after 7 days of age, although there is variation in the definition ranging from onset at or after > 72hrs of life to or after 7 days of age. 60% of 1.6 million neonatal deaths/year from infection occur in underdeveloped nations.⁵ one of the main causes of illness and mortality in newborns is neonatal sepsis. Early identification and treatment of neonatal sepsis can minimize mortality by preventing life-threatening consequences. Early recognition of EONS in neonates remains difficult because of nonspecific signs and symptoms.⁷ Early detection of EONS is done by assessing total WBC count, CRP, Procalcitonin, and blood culture.

WBCs are essential component of the immune system. Increased Total WBC is a sign of infection & inflammation. Neutrophils become activated during sepsis/ tissue infection, causing a sharp increased amount in bloodstream. Elevated WBC count once thought to be a reliable sign of infection is one of the regular diagnostic tests for sepsis workup. In some instances, the WBC count may be normal or even decline. Because of its low specificity, total WBC is not a very useful biomarker of sepsis.^{6,9}

CRP, major acute phase reactant, for the early stages of neonatal sepsis starts to increase 10–12hrs & reaches peak during 24–48hrs. CRP is still the biomarker that is frequently used in conjunction with other biomarkers.⁷ Procalcitonin, a precursor of calcitonin is a marker of sepsis in critically ill patients. Blood culture, the gold standard investigation in diagnosis of neonatal sepsis, takes more than 3 days to obtain at least the initial result.

In contrast to other test parameters that are comparatively more expensive and time consuming, NLR and MPV are inexpensive and readily available.⁴

The average volume of each platelet is known as Mean platelet volume (MPV), and it has been used as a measure of platelet size, function &

reactivity. More active the platelets, the higher the MPV.¹¹

A few research studies have shown that sepsis, thrombocytopenia, and elevated (MPV) are strongly linked in newborn newborns.¹² Changes in neutrophil and lymphocyte counts are reflected in NLR. Sepsis may lead to elevated neutrophil counts & decreased lymphocyte counts as a consequence of the infection, suggesting that sepsis patients have higher NLR. Several studies have shown that higher the NLR, poorer the prognosis. There aren't many published data on neonatal sepsis, despite numerous studies linking adult sepsis with elevated NLR.

MATERIALS AND METHODS:

This was a retrospective cross-sectional study. Patient's data from January 2020 to January 2022 was collected from hospital electronic data system. A total of 146 patients (73 sepsis & 73 non sepsis) were included. Control group (non-sepsis): Babies diagnosed with neonatal hyperbilirubinemia (age < 72hrs). Complete blood count was determined using an automated hematology analyzer sysmex XN-1000 and data was collected from hospital digital data system. CRP was quantitatively determined using immune turbidometric method from serum in the vitros 5600 integrated system. NLR was obtained from dividing the absolute count of neutrophils from lymphocytes manually. Mean Platelet Volume = Total mass of the platelets (plateletcrit)/Total number of platelets. Total leucocyte count, Absolute Neutrophil Count, Absolute Lymphocyte Counts, NLR, MPV and CRP of septic neonates was compared with gestational age-matched non-septic neonates by an unpaired t-test.

Statistical Analysis:

The values were recorded and documented in MS excel 2019, SPSS (Statistical Package for Social Sciences) VERSION 23 was used for statistical analysis. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated. Chi-square test and unpaired t test were used to analyze the sepsis and non-sepsis groups. The p-values < 0.005 was considered as statistically significant.

RESULTS:

The mean Total Leucocyte Count of septic neonates (18.1±8.47) was

significantly higher as compared to non-septic (11.03 ± 4.19) neonates. The mean NLR of septic neonates (6.06 ± 3.62) was significantly higher as compared to non-septic (0.71 ± 0.39) neonates. In sepsis neonates, NLR had a sensitivity and specificity of 100% and 97.3% respectively. MPV had a sensitivity and specificity of 100%. CRP had sensitivity and specificity of 80.80% and 79.50% respectively. In the ROC analysis, the area under the curve for CRP and NLR for the diagnosis of neonatal sepsis was 0.882 and 0.998 respectively. Comparison of the NLR & MPV between the two groups shows that NLR and MPV was higher in Sepsis group & was statistically significant with a p-value < 0.001. Positive Predictive Value of NLR was 97.3% and MPV was 100%. Negative Predictive Value of NLR and MPV was 100%.

Table 1: The Sensitivity, Specificity, PPV, NPV Of CRP And NLR

PARAMETER	SENSITIVITY (%)	SPECIFICITY (%)	PPV (%)	NPV (%)
NLR (Cutoff 1.5)	100.00	97.30	97.30	100.00
MPV (Cutoff 10)	100.00	100.00	100.00	100.00
CRP (Cutoff 5.15)	80.80	79.50	79.70	80.60

Table 2: Comparison Of Hematological Parameters Of CBC And CRP Between Sepsis And Non-septic Neonates Using Chi Square Test

	Normal (N (%)) 9 (12.3)	Sepsis (N (%)) 0 (0)	Chi square	P value
TLC	29 (48.3)	12 (16.4)	15.711	<0.001
	31 (51.7)	61 (83.6)		
NLR	20 (27.4)	0 (0)	85.696	<0.001
	34 (46.6)	0 (0)		
	19 (26)	73 (100)		
MPV	42 (57.5)	0 (0)	71.922	<0.001
	31 (42.5)	46 (63)		
	0 (0)	27 (37)		
CRP	40 (54.8)	5 (6.8)	55.279	<0.001
	15 (20.5)	6 (8.2)		
	18 (24.7)	62 (84.9)		

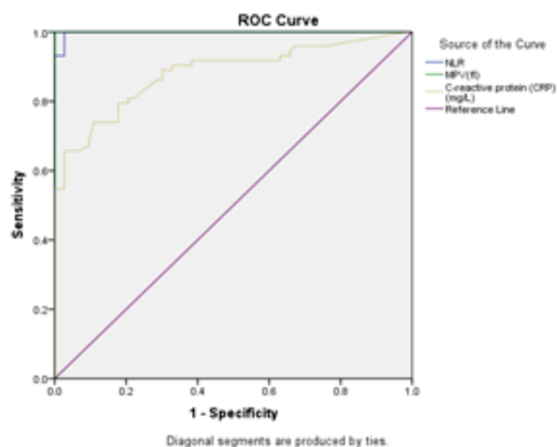


Figure 1: ROC Curve Showing Sensitivity And Specificity Of NLR, MPV & CRP

DISCUSSION:

Neonatal sepsis is a serious worldwide health issue that is linked to high mortality and poor long term outcomes for survivors, especially in places with insufficient resources. Early recognition of EOS in neonates remains difficult because of nonspecific signs and symptoms³. CRP and procalcitonin are the most used laboratory biomarkers for detection of EOS but expensive. Blood culture despite being regarded as the gold standard diagnostic test for sepsis, it has its own drawbacks, such as being unavailable in majority of developing nations, taking >3 days to obtain at least the primary result. Therefore, the diagnosis of neonatal sepsis is based on clinical evaluation & management, relies on empirical treatment protocols, leading to unnecessary hospital stays, a rise in the irrational use of antibiotics & more expenses for the family⁸. Our study's objectives were to evaluate the NLR, MPV & their efficacy as diagnostic indicators for EOS detection in term and pre neonates. Comparison of the total

leucocyte count between the two groups shows that WBC is higher in sepsis group and is statistically significant, indicating role of leukocytosis in diagnosis of neonatal sepsis this was similar to study conducted by Mahmoud.NMS et al (2022)⁸. In our study it was found that neonates in sepsis group had significantly higher CRP levels compared with tcontrol group similar to other studies conducted by Can.E et al (2018)³.

In our study, Comparison of NLR, MPV and CRP between cases and controls was performed, and cases had significant higher values of these ratios rather than controls indicating their valuable role in detection of early-onset neonatal sepsis; which was concordance to other studies done by Can.E et al (2018)³, Sumitro.KR et al (2021)⁵, Li.T (2020)⁷, Mahmoud.NMS et al (2022)⁸ and Omran.A et al (2017)¹⁰.

CONCLUSIONS:

With a PPV of 97.3% for NLR and 100% for MPV, NLR and MPV are useful prognostic indicator in identifying EONS. NLR, a component of complete blood count, can be used as an alternative simple marker and reasonably inexpensive for detection of neonatal sepsis, particularly in developing nations. Combining NLR with CRP has also been shown to enhance the diagnosis of neonatal sepsis.

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