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NLR AND PLR IN NEONATAL SEPSIS- MAKING WAY FOR NEW DIAGNOSTIC MARKERS

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ABSTRACT **Objective:** The purpose of this study was to investigate the clinical significance of the platelet to lymphocyte ratio (PLR) and the neutrophil to lymphocyte ratio (NLR) in term neonates and its impact on management of neonatal sepsis **Materials and Methods:** This retrospective observational study was conducted with 40 term neonates diagnosed with neonatal sepsis. Exclusion criteria were prematurity, post- maturity, small or large for gestational age according to week of pregnancy, babies born to mothers with GDM or pre-eclampsia and congenital defects. **Results:** NLR and PLR as predictors of neonatal sepsis, The sensitivity of NLR was 94.44 % while specificity was 86.36%. We noted that the sensitivity of PLR was 84.21%, while specificity of PLR was 80.95%. There was a positive correlation between TC and NLR, weak positive correlation with PLR and a weak negative correlation with lymphocyte levels. **Conclusions:** NLRs and PLRs were positively correlated with sepsis in term neonates, and these ratios can be used to aid diagnoses in term neonates suspected with sepsis.

KEYWORDS : NLR, PLR, neonatal sepsis, neonatal care

Introduction

Neonatal sepsis is a major contributor to both morbidity and mortality in newborn infants. Despite the fact that the incidence of sepsis in term and late preterm infants is low, the risk of serious adverse outcomes is of such great consequence that carers should set a low tolerance for assessment and treatment for possible sepsis in neonates (1).

Neonatal sepsis is a systemic condition of bacterial, viral, or fungal (yeast) origin that is attributed with hypoperfusion in an infant that is 28 days of life or younger. The definition of sepsis has included the isolation of a microorganism from a normally sterile body fluid such as blood or cerebrospinal fluid and can be fatal if left untreated.

In spite of this, the term systemic inflammatory response syndrome (SIRS) has also been employed when describing neonatal sepsis. This is due to the fact that the clinical manifestations of sepsis can be brought on by highly potent pro-inflammatory cytokines (2). The presence of sequential organ dysfunction, as objectively ascertained by the sequential organ failure assessment (SOFA score), is a reliable indicator of mortality (for example, a SOFA score of 4 or higher is a reliable indicator of mortality) and admission to the intensive care unit, with death serving as the ultimate outcome measure.

Based on age of the infant when the first symptoms appear, sepsis can be broken down into the following categories: Early-onset sepsis is defined by Wynn et al (2) as the symptoms that appear before 7 days of age, although some experts limit it to infections occurring within the first 72 hours of life while Late-onset sepsis is when symptoms occur after 7 days of age. (2)

In utero transmission of bacteria can cause early-onset neonatal sepsis; this can occur either transplacentally or, more commonly, as a result of ascending bacteria entering the uterus from the vaginal environment following membrane rupture. (5). A premature rupture of membranes, also known as PROM, is a common occurrence in obstetrics that can have a significant effect on the outcome of a pregnancy. (6).

There can be anywhere from one to five cases of neonatal sepsis for every thousand live births.

Also, it is observed that neonatal sepsis and other severe infections were responsible for approximately 15% of all neonatal deaths in the world in 2013, causing over 4 lakh deaths (7). The risk is significantly higher with a preterm delivery. (8). In term neonates, the incidence of sepsis (both early-onset and late-onset) is estimated to be between one and two cases for every 1000 live births (9).

Both early- and late-onset sepsis are most commonly caused by Group B Streptococcus (GBS) and Escherichia coli, seen in 2/3rd of cases (10).

In unusual sporadic cases of neonatal sepsis, which are typically acquired transplacentally, Listeria monocytogenes is often isolated (11). In neonatal sepsis, Staphylococcus aureus is a potential pathogen. This includes methicillin-resistant Staphylococcus aureus that was acquired in the community (12). Bacteremic staphylococcal infections in term infants typically manifest themselves in conjunction with sites of involvement in the skin, bones, or joints. Herpes simplex virus is one of the most common viral causes of sepsis, being associated with significant morbidity and mortality. The onset of these manifestations for viral sepsis typically occurs between days 5 and 9 of a newborn's life (13).

After symptoms such as poor feeding, lethargy, fever, irritability, hypoperfusion, and jaundice associated with an enterovirus infection, a patient may go on to develop meningoencephalitis, myocarditis, and hepatitis (14).

In many developing countries such as hours, with limited modalities to diagnose neonatal sepsis for reasons such as high patient volume and high cost of test, which most patients cannot afford, assessment of simple and cost-effective tests will help improve outcomes in neonatal sepsis, especially in tier 2 and 3 cities.

Hence, with this study, we evaluate the role of NLR and PLR in identification of neonatal sepsis in a tertiary care centre.

Methods and methodology

This is a retrospective observational study that was performed in the Department of paediatrics in a tertiary care centre. All term neonates born after 37 completed weeks of gestation via an uncomplicated and uneventful vaginal delivery were included in the study. The neonates that were diagnosed with fever within 48 hours of delivery, and positive blood cultures were taken in the sepsis wing of the study, while neonates without fever and cultures negative were taken in the control wing.

Those neonates born before 37 or after 40 weeks gestation, with congenital anomalies to mothers with co-morbidities were excluded from the study.

Neonates were subjected to routine blood investigations such as CBC, ESR, CRP, peripheral smears and cultures.

NLR and PLR was calculated for each of the neonates and correlated with the presence of sepsis.

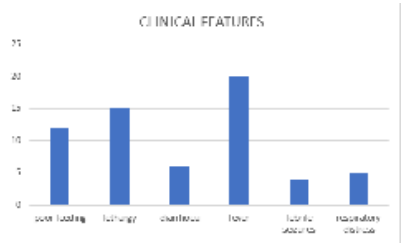
Statistical analysis- data was collected and recorded in an MS excel spreadsheet. Continuous variables were represented as mean and median, while categorical variables were represented as percentages and frequency. Correlation was calculated using student's t test, ANOVA test for independent means and Fisher's exact test. Sensitivity, specificity, positive and negative predictive value was calculated for NLR and PLR. P value less than 0.05 was considered to be statistically significant.

Results

The study included 40 neonates born via full term vaginal delivery. The mean gestational age of the neonates was 38.9 +/- 4.3 weeks. The mean birth weight of the neonates was found to be 2802 +/- 342 gm.

Maternal factors can also be a contributory factor for the onset of neonatal sepsis. In our study we found that the most common maternal factor was fever > 102 degree F within 48 hours of delivery (56.4%), followed by PROM (32.56%).

The most common clinical features in the neonates was fever followed by lethargy.



In all neonates, blood, urine and CSF cultures were drawn. Any temperature spikes were documented.

Mean NLR was found to be 2.34 +/- 0.43, while mean PLR was 62.4± 14.9 in the sepsis group vs 0.72+/- 0.23 and 15.3 ± 2.1 respectively in the control group.

NLR	SEPSIS	NO SEPSIS
NORMAL	1	19
RAISED	18	2

Statistic	Value	95% CI
Sensitivity	94.44%	72.71% to 99.86%
Specificity	86.36%	65.09% to 97.09%
Positive Likelihood Ratio	6.93	2.41 to 19.94
Negative Likelihood Ratio	0.06	0.01 to 0.44
Disease prevalence (*)	45.00%	29.26% to 61.51%
Positive Predictive Value (*)	85.00%	66.31% to 94.23%
Negative Predictive Value (*)	95.00%	73.74% to 99.23%
Accuracy (*)	90.00%	76.34% to 97.21%

The sensitivity of NLR was 94.44 % while specificity was 86.36%. there was a positive correlation between NLR and TC in neonates.

PLR	SEPSIS	NO SEPSIS
NORMAL	3	17
RAISED	18	2

Statistic	Value	95% CI
Sensitivity	84.21%	60.42% to 96.62%
Specificity	80.95%	58.09% to 94.55%
Positive Likelihood Ratio	4.42	1.79 to 10.91
Negative Likelihood Ratio	0.2	0.07 to 0.56
Disease prevalence (*)	47.50%	31.51% to 63.87%
Positive Predictive Value (*)	80.00%	61.85% to 90.80%
Negative Predictive Value (*)	85.00%	66.28% to 94.23%
Accuracy (*)	82.50%	67.22% to 92.66%

We noted that the sensitivity of PLR was 84.21%, while specificity of PLR was 80.95%. this is not as sensitive a marker as NLR for sepsis, but it still has a weak positive correlation with TC.

Discussion

Neonatal sepsis, also known as NS, is a common form of systemic illness that affects newborns and can lead to morbidity and mortality. However, the ideal biomarker that could be used for the early diagnosis of NS does not currently exist. (15) Recent research has shown that the platelet width to lymphocyte ratio, also known as PLR, plays an important part in the inflammatory process. Our goal in conducting this study was to make a contribution to the ongoing investigation into whether or not NLR and PLR can be utilised in the early diagnosis of NS.

Platelet–neutrophil complexes can be found in the blood of patients suffering from a wide variety of inflammatory disorders as well as sepsis. Platelets that have been activated form bonds with neutrophils in the blood and are responsible for recruiting neutrophils to the sites of injury and infection (16).

White blood cell count (WBC), which is one of the diagnostic tests that is routinely performed for sepsis work up, was once thought to be reliable indicators of infection; however, it is now known that these tests are insensitive and nonspecific.

In addition, a single leukocyte count taken not long after birth is not sensitive enough to diagnose neonatal sepsis on its own (17).

According to the findings of our research, NLR and PLR can both be utilised in the process of identifying sepsis in term neonates. Comparing NLR and PLR between cases and controls in a study by Mahmoud et al. found that cases had significantly higher values of these ratios than controls, indicating that these ratios play an important role in the detection of early-onset neonatal sepsis. (18) This finding is comparable to the one that we found in our study.

In a study by Birol et al (15), PLR was found to have sensitivity of 88.9% to 91.3% and specificity of 94.7% to 97.6%, positive predictive value of 94.3% to 97.4%, and negative predictive value of 88.6% to 91.8% in suspected and proven sepsis diagnosis, which is slightly higher than that observed in our study.

A neutrophil to lymphocyte ratio (NLR) of 6.76 was determined to be the predictive cut-off value of EOS by Can et al. (sensitivity 97.4%; specificity 100%; AUROC curve 0.99; P=0.001), and a PLR of 94.05 was determined to be the predictive cut-off value of EOS by the same researchers (sensitivity 97.4%; specificity 100%; AUROC curve 0.93). Both of these values were found to have a (19).

A study was conducted by Zhang et al. (20) to investigate the usefulness of red cell distribution width (RDW), platelet distribution width (PDW), neutrophil-lymphocyte count ratio (NLCR), procalcitonin (PCT), and C-reactive protein (CRP) in the diagnosis of neonatal sepsis NS. They discovered that PCT has the highest level of sensitivity (91.7%), while PDW has the highest level of specificity (84.7%). 40 According to this research, the sensitivity of RDW, PDW, and NLCR are respectively 73.3%, 38.3%, and 81.1%; the specificity of these tests is respectively 49.2%, 84.7%, and 62.7%; their positive predictive values (PPV) are respectively 59.1%, 71.5%, and 68.5%; and their negative predictive values (NPV) are respectively 64.8%, 57.9%, and 76.8%.

Conclusion

NLR and PLR can be used as diagnostic and prognostic markers in term neonates with sepsis.

REFERENCES

1. Shane A L, P J Sánchez and B J Stoll, 2017. Neonatal sepsis. The Lancet 390, 1770-1780.
2. Wynn J L, H R Wong, T P Shanley, et al., 2014. Time for a Neonatal-Specific Consensus Definition for Sepsis. Pediatr. Crit. Care Med. 15, 523-528.
3. Edwards MS, Baker CJ, et al., 2004.Sepsis in the Newborn. In: Krugman's Infectious Diseases of Children, 11th ed, , Mosby, Philadelphia. p545.
4. Rampersaud R, T M Randis and A J Ratner, 2012. Microbiota of the upper and lower genital tract.Semin. Fetal Neonatal Med. 17, 51-57
5. Ibishi V A, R Isjanovska and A E Malin, 2018. Early-onset neonatal infection in pregnancies with prelabor rupture of membranes in Kosovo: A major challenge. Turk. J. Obstet. Gynecol. 15, 171-176.
6. Polin RA, 2012. Committee on Fetus and Newborn. Management of neonates with suspected or proven early-onset bacterial sepsis. Pediatrics ; 129:1006.
7. Nizet V and Klein JO 2016. Bacterial sepsis and meningitis. In: Infectious diseases of the Fetus and Newborn Infant, 8th ed, Elsevier Saunders, Philadelphia. p217.
8. Van den Hoogen A, Gerards LJ, Verboon-Maciolek MA, et al., 2010. Longterm trends in the epidemiology of neonatal sepsis and antibiotic susceptibility of causative agents. Neonatology;97:22.
9. Toll BJ a S A, Kliegman R, Stanton B, St Geme J, and Schor N 2015. Nelson Textbook of Pediatrics,20th edn., 909-925 pp.
10. Kaufman D A, S A Coggins, S A Zanelli, et al., 2017. Congenital Cutaneous Candidiasis: Prompt Systemic Treatment Is Associated With Improved Outcomes in Neonates. Clinical Infectious Diseases 64, 1387-1395.
11. Gnann J W and R J Whitley, 2016. Genital Herpes REPLY. New England Journal of

Medicine 375, 1906-1906.
12. Modlin J F, 2016. Treatment of Neonatal Enterovirus Infections. Journal of the Pediatric Infectious Diseases Society 5, 63-+.
13. Cetinkaya M, F Cekmez, G Buyukkale, et al., 2015. Lower vitamin D levels are associated with increased risk of early-onset neonatal sepsis in term infants. Journal of Perinatology 35, 39-45
14. Lapillonne A, Basson E, Monneret G, Bienvenu J, Salle BL. Lack of specificity of procalcitonin for sepsis diagnosis in premature infants. Lancet. 1998;351: 1211-2. https://doi.org/10.1016/S0140-6736(05)79165-0
15. Karabulut, Birol & Arcagok, Baran. (2019). Platelet to Lymphocyte Ratio in Neonates: A Predictor of Early onset Neonatal Sepsis. Mediterranean Journal of Hematology and Infectious Diseases. 11. e2019055. 10.4084/mjhid.2019.055.
16. Bassetti M, Garnacho-Montero J, Calandra T, Kullberg B, Dimopoulos G, Azoulay E, Chakrabarti A, Kett D, Leon C, Ostrosky-Zeichner L, Sanguinetti M, Timsit JF, Richardson MD, Shorr A, Cornely OA. Intensive care medicine research agenda on invasive fungal infection in critically ill patients. Intensive Care Med. 2017. https://doi.org/10.1007/s00134-017-4731-2 PMid:28255613
17. Elawady S, Botros SK, Sorour AE, et al. Neutrophil CD64 as a Diagnostic Marker of Sepsis in Neonates. J Investig Med 2014;62:644-9. https://doi.org/10.2310/JIM.0000000000000060 PMid:24463977
18. Mahmoud N M S, Abdelhakeem M , Mohamed H H A, Baheeg G . Validity of Platelet to Lymphocyte Ratio and Neutrophil to Lymphocyte Ratio in Diagnosing Early-onset Neonatal Sepsis in Full-term Newborns. J Compr Ped. 2022;13(1):e115378. doi: 10.5812/compreped.115378.
19. 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
20. Zang HB, Chen J, Lan FQ, Ma XJ, Zhang SY. Diagnostic values of red cell distribution width, platelet distribution width and neutrophil-lymphocyte count ratio for sepsis. Experimental and Therapeutic Medicine. 2016;12:2215-2219. https://doi.org/10.3892/etm.2016.3583 PMid:27698714 PMCid:PMC5038364