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INFECTION MARKERS AS PREDICTION OF NEONATAL SEPSIS

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ABSTRACT
Neonatal sepsis is one of the most common causes of neonatal death in the first month of life. Neonatal sepsis often shows atypical clinical features include temperature instability, lethargy, skin changes, feeding problems, and many others. Isolation of bacteria from the culture is the gold standard for diagnosing sepsis, but this approach is frequently time-consuming and even in cases of negative blood cultures, sepsis cannot be conclusively ruled out, posing a major challenge in its diagnosis and management. Early diagnosis and timely intervention are essential to improve the prognosis of neonatal sepsis. Aim: The aim of this study is to discuss how infection markers can aid in the early identification of neonatal sepsis and what are the best infection markers to predict neonatal sepsis mortality. Method: This study assessed the diagnostic accuracies of infection marker used in the diagnosis of neonatal sepsis. Included studies were retrieved by searching three major databases (Google Scholar, Pubmed, and Science Direct) using MeSH words and relevant references, and reviewed based on the inclusion/exclusion criteria. The article discusses potential advancements and future prospects for biomarkers. An excellent marker can guide antibiotic administration and duration if sepsis is confirmed, reducing unnecessary use. The marker should have high sensitivity, specificity, positive predictive value, negative predictive value and accuracy.

Keywords: early diagnosis; early predictor; infection marker; neonatal sepsis

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INTRODUCTION

Neonatal sepsis is a clinical state of systemic disease characterized by bacteremia that develops in newborns during their first month of life. Sepsis is a condition in which bacteria or toxins attack the blood or body tissues, resulting in systemic signs of the infection (Mahmoud et al., 2023). Neonatal sepsis is divided into two categories: early onset sepsis (EOS) and late onset sepsis (LOS). EOS is a type of sepsis that occurs within 72 hours of delivery. It is typically caused by vertical transmission from a maternal urogenital infection, chorioamnionitis, or protracted membrane rupture. The most frequent symptom of EOS is respiratory distress, particularly in severe cases, and the early stages of EOS in preterm infants are frequently difficult to distinguish from respiratory distress syndrome (Rose et al., 2024). LOS is sepsis that occurs more than 72 hours after birth in term infants. It is primarily caused by hospital-acquired, healthcare-associated infections, invasive instrumentation, parenteral nutrition, and mechanical ventilation, or community-acquired infections acquired from the environment (Kariniotaki et al., 2025).Neonatal sepsis is the third leading cause of neonatal death after preterm birth and related complications during labor. It has a significant mortality rate with an estimated 3 million cases worldwide and a fatality rate ranging from 11

to 19% (Fleischmann-Struzek et al., 2018). Every year, 214.000 newborn babies, mostly in low- and middle-income countries, die of sepsis that has become resistant to antibiotics. The study, conducted from 2018 to 2020, found there was high mortality among infants with culture-positive sepsis (almost 1 in 5 across the hospital sites), and a significant burden of antibiotic resistance (Russell et al., 2023).

The global pooled incidence of neonatal sepsis is 22/1000 live births (1-4/1000 live births in high-income countries and 49-170 cases per 1000 births in low-income countries), with an 11–19 percent mortality rate. Neonatal sepsis rates rise as gestational age (GA) declines, with very low birth weight (VLBW) preterm newborns having a higher incidence of culture-positive episodes. EOS has been recorded in 0.5-3.1% of VLBW babies, with LOS episodes occurring in 2-32% (Stoll et al., 2020). This is confirmed by data from Riset Kesehatan Dasar (Riskesdas) in 2017, which found that sepsis was the most common cause or risk of neonate death, with 12% at the age of 0-6 days and 20.5% at the age of 7-28 days. Nosocomial infection in very low birth weight newborns is the leading cause of death after 5 days of life (Riskesdas, 2017).Several risk factors influence the incidence of neonatal sepsis. The incidence of EOS may be elevated by preterm pregnancy (less than 37 weeks gestation), maternal sepsis, such as diarrhea or urinary tract infection (UTI), within 7 days prior to delivery, chorioamnionitis or foul-smelling amniotic fluid with or without meconium, prolonged rupture of membranes (PROM) >18 hours, history of unclean bimanual examination >3 times, and prolonged labor (first and second stage >24 hours), and perinatal asphyxia (Appearance, Pulse, Grimace, Activity and Respiration (APGAR) score less than in one minute) (Moftian et al., 2023). Low birth weight (LBW), prematurity, intensive care unit admission, mechanical breathing, invasive procedures, parenteral fluid delivery, and inadequate sanitation, such as unsterilized umbilical cord care or bottle-feeding, all increase the risk of LOS (Bernardi et al., 2024).

Maternal infectious risk factors and gestational age have a significant impact on the pathogenic microorganisms that cause newborn sepsis. Escherichia coli and Group B Streptococcus (GBS) are primarily transmitted vertically from mothers with chorioamnionitis and GBS colonization, which results in EOS. (Vulcănescu et al., 2025). In LOS, Streptococcus pneumonia was the leading cause of invasive bacterial infection, followed by Neisseria meningitidis, Staphylococcus aureus and Group A Streptococcus, Haemophilus influenzae type B, and Bordetella pertussis(Tsang, 2021).Early stages of newborn sepsis may exhibit atypical clinical signs of infection, and blood cultures frequently show false negative results, posing a major challenge in diagnosis and management. Early diagnosis and timely intervention are critical for improving the prognosis of infants with sepsis, as delayed treatment can result in neurodevelopmental disorders such as cerebral palsy, impaired mental and psychomotor development, visual and hearing impairment, and long-term neurological deficits (Lestari & Rahmawati, 2023).Thus far, there is no single marker of infection for identifying sepsis in newborn, therefore efforts to enhance diagnostic criteria are moving forward. The current gold standard for sepsis diagnosis is microbiological testing, particularly blood culture, although this procedure is time-consuming (2-5 days) and fails to identify all bacteria. Furthermore, many healthcare facilities do not support this test (Chang et al., 2021). The low positive rate and bias caused by specimen collecting procedures and contamination with other bacteria make early identification extremely difficult. Currently, an accessible and inexpensive infection marker with high sensitivity and specificity is required to assist detect sepsis in newborns by taking into account supporting clinical signs prior to getting a positive blood culture (Sethi et al. 2023).

Infection markers are the initial examination needed to help distinguish between bacterial and non-bacterial infections. The role of infection marker examination in cases of infection is that the examination results are positive in infected patients, negative examination results in patients without infection, able to distinguish the etiology, and play a role in diagnosing the severity of the disease (Berlina et al., 2020). An excellent marker can guide antibiotic administration and duration if sepsis is confirmed, reducing unnecessary use. Some previous studies have investigated the role of infection markers as diagnostic markers in neonatal sepsis. However, their value in predicting remains unclear (Aulin et al., 2021).A good infection marker should increase rapidly after the onset of disease and decrease rapidly after the infection has resolved (Song et al., 2021) Such markers should have high sensitivity (~100%) and specificity (>85%) in the diagnosis of neonatal sepsis, with high negative predictive value (~100%) and positive predictive value (>85%) (Celik et al., 2022). In addition, such markers should provide reliable information on when to start and when to stop antibiotic therapy to reduce antibiotic overuse, arrest the development of bacterial resistance, avoid significant modification of gut microbiota whose physiological kinetics are not influenced by maternal, perinatal, or postnatal factors. Methods for infection marker detection should be easy to perform, feasible in all laboratories, require a small number of samples, and be cost-effective. Currently, no single marker of infection has sufficient diagnostic accuracy, so clinical manifestations remain important in the diagnostic and therapeutic process (Boscarino et al., 2023).

Complete blood count (CBC) and type count have been studied extensively for the diagnosis of sepsis in neonates. Although the CBC has low predictive value, its component series can increase the likelihood of a bacterial sepsis diagnosis. CBC is used in various ways, including obtaining a one-time CBC or serially, evaluating the total white blood cell count, ANC, NLR and PLR counts and analyzing the size and morphology of red blood cells and platelets (Boscarino et al., 2023).

METHOD

The search strategy was conducted through three databases (Google Scholar, Pubmed, Science Direct) for potentially eligible studies using an algorithm based on combined words. Additional inclusion criteria of the reviewed references were those published during the last ten years, from 2105 to 2025 or in the past 10 years, medical subject headings (MeSH) mainly included “neonatal sepsis”, “infection marker”, “leukocyte”, “ANC”, “absolute neutrophil count”, “NLR”, “neutrophil to lymphocyte ratio”, “PLR”, “platelet to lymphocyte ratio”, “MPV”, “mean platelet volume”, “CRP”, “C reactive protein”, “procalcitonin”, “IT ratio”, “Immature to total lymphocyte ratio”. Reference lists of included studies were also searched for potentially eligible studies. Inclusion and exclusion criteria studies meeting the following criteria were included: (a) Evaluating the diagnostic performance of infection markers for neonatal sepsis; (b) Retrospective study, prospective study, or cross-sectional study. Articles will be excluded for the following reasons: (a) Case-report, literature review, conference summary, abstract unavailable, meta-analysis, letter, and comments; (b) Data unextractable; (c) Study reported and published in non-English. The article focuses on the advantages and disadvantages of each infectious marker that can be used to early recognize neonatal sepsis, as well as the diagnostic value such as sensitivity, specificity and accuracy of each infectious marker so that it can be compared and found the simplest, economical, efficient, easy-to-use yet accurate marker, when compared to blood culture as the gold standard.

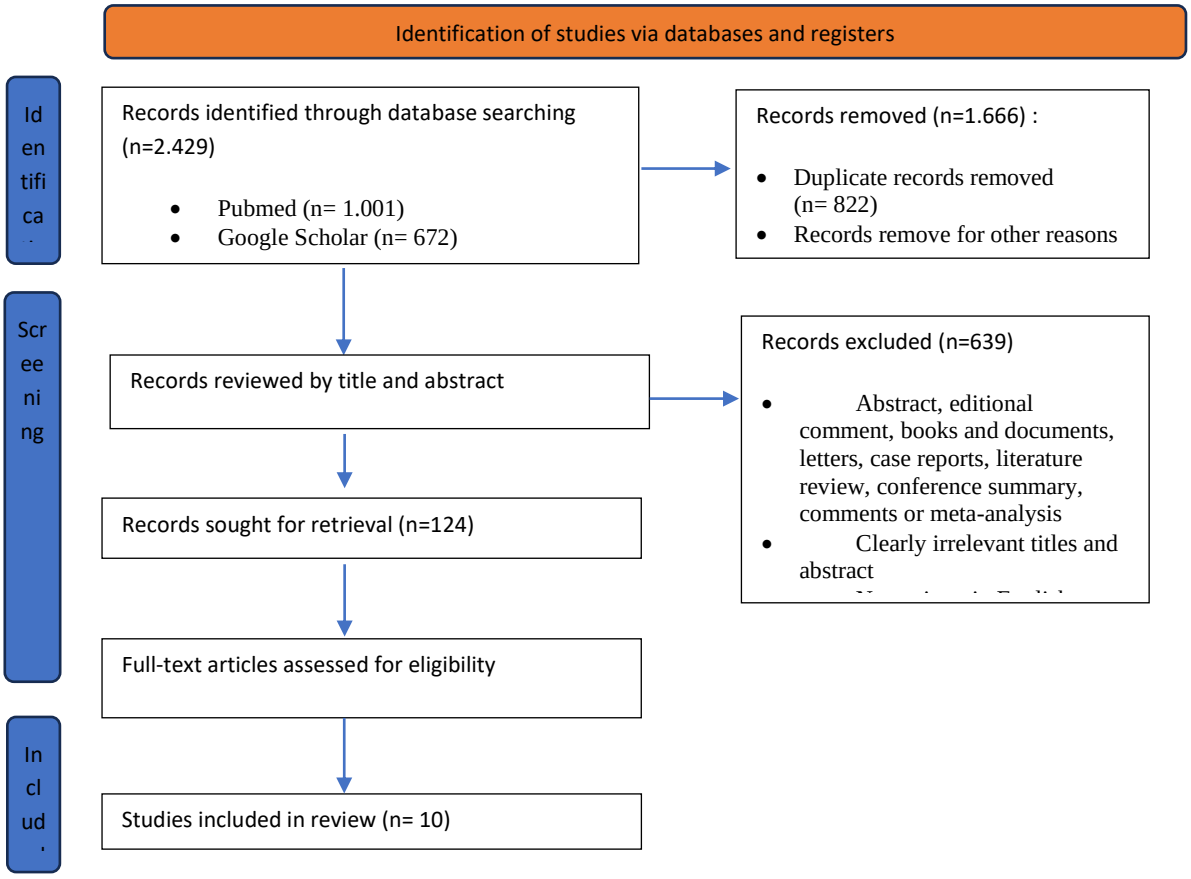

Diagram 1. Flowchart Prisma

RESULT

Table 1. Literature Review Results

Authors	Year	Title	Location	Study design	Sample	Results
Harmansyah et al.	2015	Absolute Neutrophil Count as Predictor of Early Onset	Makassar, Indonesia	Prospective cohort observational study	120 patients	- Newborn from mother with risk factor of infection with ANC >5400/mm^3 and ANC 1800-5399/mm3 shows a significant difference with p = 0.000 (p<0.001); OR 8.143; IK 95% 2.440-27.173. - Cut off point of 10.710-10890/mm^3 was found from ROC analyses in ANC >5400/mm^3 group with sensitivity and specificity 89.47% and 80.95% respectively; PPV (Positive predictive value) 80.95%; NPV (Negative predictive value) 89.47%; p=0.000; OR 36.125; IC 95% 5.820 – 224.224. - Absolute neutrophil count >10.710/mm^3 in a term newborn from mother with infection risk factors can be used as predictor for early onset sepsis 36 fold higher than the ANC <10.710/mm3.
Wirawati et al.	2018	Role of Immature/Total Neutrophil Rasio, Leukocytes Count, and	Surabaya, Indonesia	Cross-sectional study	59 patients	- Along with blood culture as the gold standard in determining diagnosis of sepsis and with I/T ratio cut off of 0.2, the sensitivity of manual I/T ratio was 69.2%, specificity 83.9%,

Authors	Year	Title	Location	Study design	Sample	Results
		Procalcitonin in Diagnosing Neonatal Sepsis				PPV 63.9%, NPV 87% and likelihood ratio was 3.06. - The sensitivity of automatic I/T ratio was 47.6%, specificity 85.8%, PPV 55.1%, NPV 81.4% and likelihood ratio was 2.25. - Based on the normal range of leukocyte count (9.1 - 34 x 103/µl), sensitivity of leukocyte count was 59%, specificity 71.5%, PPV 46.7%, NPV 80.9% and likelihood ratio was 1.59. - With PCT cut -off 0.5 ng/mL, the obtained sensitivity of PCT was 64.3%, specificity 85.8%, PPV 64.3%, NPV 85.8% and likelihood ratio was 3.13.
Gomathi et al.	2022	Serial quantification of CRP and total leukocyte count as a complementary tool in neonatal sepsis	Chennai, India	Cross-sectional study	148 patients	- CRP1 and WBC1 were measured within 6 hours of clinical symptoms. - CRP2 and WBC2 were measured after 48 hours of clinical symptoms. - Sensitivity, specificity, PPV, NPV of CRP1 and CRP2,WBC 1and WBC 2 were compared with culture positive and negative sepsis. - CRP 2 showed high sensitivity 96% and high NPV95% with significant p value < 0.001.WBC1 has lowest sensitivity (62.2%) and NPV (71.4%) compared to all other parameters. - Serial CRP and WBC measurements are useful in the diagnosis of neonatal sepsis. - Measurement of CRP and Total Leukocyte Count (WBC) after 48 hours of clinical symptoms were considered promptly for diagnose neonatal sepsis
Sorsa .	2018	Epidemiology of Neonatal Sepsis and Associated Factors Implicated: Observational Study at Neonatal Intensive Care Unit of Arsi University Teaching and Referral Hospital, South East Ethiopia	South East Ethiopia	Prospective cross-sectional study	303 patients	- Positive CRP and abnormal WBC were reported in 136(45%) and 99(32.7%) of study subjects respectively. - Blood culture turned to be positive in 88(29.4%) of study subjects. - The sensitivity, specificity, PPV and NPV of WBC count were 59.5 %, 79.6%, 52%, 64.5% respectively while the sensitivity, specificity, PPV and NPV of CRP were 65.6%, 78%, 42% and 91% respectively. - By combining both WBC and CRP, the sensitivity, specificity, PPV and NPV improve to 78.5%, 83%, 60% and 93% respectively. - CRP positivity rate was comparable across gram positive and gram negative bacteria while high WBC

Authors	Year	Title	Location	Study design	Sample	Results
						count were more reported among gram positive sepsis than gram negative (OR 4.8, (95% CI 1.45-15.87, P 0.01)
Rompis et al.	2022	Platelet-to-lymphocyte ratio in early onset neonatus	Manado, Indonesia	Cross sectional observational study	176 patients	- Blood cultures confirmed sepsis in 84 neonates (47.7%), with Klebsiella pneumoniae being the most common causative organism. - There is a significant positive correlation between PLR and EONS (p<0.001), and a PLR cut-off point of 61.806 was identified to predict EONS with high sensitivity (90.2%) and specificity (85.7%) - PLR can be used as a valuable marker for predicting EONS in neonates with suspected sepsis. These findings could aid in the early identification and treatment of neonates with sepsis, ultimately improving patient outcomes.
Sumitro et al.	2021	Neutrophil-to-Lymphocyte Ratio as an Alternative Marker of Neonatal Sepsis in Developing Countries	Surabaya, Indonesia	Cross sectional study	104 patients	- Neonatal sepsis in this study had an incidence of 10.6% with 52 (50.0%) neonates categorized as proven neonatal sepsis. - Gram-negative bacteria dominated as the cause of neonatal sepsis (75.0%), with extended-spectrum β-lactamase producing *Klebsiella pneumoniae* (+) isolates making up 61.5%. - The median NLR value of the 104 neonates who met the inclusion and exclusion criteria was 3.63 (2.39–6.12). - Neonates with NLR of 2.12 have the area under the curve of 0.630 (95% confidence interval (CI): 0.528–0.741) and 0.725 (95% CI: 0.636–0.814) when combined with CRP = 2.70 mg/dL. - Neonates with NLR ≥ 2.12 in clinical neotnatal sepsis had almost double the risk of providing positive blood culture results (relative risk = 1.867, 95% CI: 1.077–3.235; p = 0.011).
Takassi et al.	2022	Neutrophil-to-Lymphocyte Ratio as an Alternative Marker of Neonatal Sepsis in Developing Countries	Paris, France	Case control study	50 patients	- The results showed a statistically significant relationship between the birth of a child with EOS and between a premature rupture of membranes of > 18 h (68% of cases vs. 36% of controls; p = 0.042); a positive culture of the placenta (p = 0.0002) - There are significant relationship between C-reactive protein levels of

Authors	Year	Title	Location	Study design	Sample	Results
						> 6 mg/L (88% of cases vs. 20% of controls; $p = 0.001$); a procalcitonin level of > 0.6 ng/mL (72% of cases vs. 16% of controls; $p = 0.001$) with EOS. - Gram-negative bacteria including *Escherichia coli* (44.5%) and Haemophilus influenzae (14.8%) were the most common pathogens found.
Sagheb et al.	2022	The Role of Mean Platelet Volume in the Diagnosis of Neonatal Sepsis	Teheran, Iran	Cross sectional study	72 patients	- There were statistically significant differences between WBC (p=0.019), CRP (Mean Difference: 9.38, 95% CI: 4.19 to 14.58, p=0.001) and MPV (Mean Difference: 0.56, 95% CI: 0.25 to 0.86, p 9.2 fL. - The ROC curve area was 68.71 for MPV [95% Confidence Interval (CI), 59.83 to 76.92]. - Diagnostic cut-off levels with the optimum sensitivity (80.56%) and specificity (52%) derived from the ROC curve were found to be MPV > 9.2 fL. - There was no significant association between MPV and disease status (case group: 9.80 ±0.88 vs. control group: 9.24 ±0.75).
Ali et al.	2024	The Relationship Between Blood Culture, C-reactive Protein, and Neonatal Sepsis: A Cross-Sectional Study	Sudan, North Africa	Prospective cross-sectional study	71 patients	- High CRP level >10 mg/L was seen in patients having positive blood culture (55.3%), mainly in preterm babies (CRP >10 mg/dL (61.1%), positive culture (55.6%)) and very low birth weight babies (CRP >10 mg/dL (83.3%) and positive culture (67%)). - With a statistical significance, the CRP was higher (more than 10 mg/dL) among patients who died (8, 21.1%). - Klebsiella was the most commonly detected organism affecting patients and led to the death of five (25%) neonates with no statistical significance.

Authors	Year	Title	Location	Study design	Sample	Results
Bharti et al.	2020	Role of procalcitonin in diagnosis of neonatal sepsis and procalcitonin guided duration of antibiotic therapy	Delhi, India	Prospective observational study	100 patients	- Elevated PCT level >0.5 ng/dl was detected in 75 and >2 ng/dl was detected in 51 whereas CRP was positive only in 61 cases. - Among the 39 culture positive cases, elevated serum PCT level was noticed in 39 (100%) cases whereas CRP level was noticed in 30 (76.9%) cases. - Mean PCT levels were significantly high according to infection severity (P<0.01). - Procalcitonin (sensitivity 87.2%, specificity 72.13%, positive predictive value 66.7% and negative predictive value 89.8% and with p value of <0.001) is more superior than CRP to predict sepsis in neonate. PCT measurement. - Serum PCT levels >2 ng/dl has got a better sensitivity and NPV, which help us not only in the early diagnosis but also in the prognosis and duration of antibiotic therapy.

Based on Table 1, 10 journals with study characteristics and research results were obtained. All of these literatures are in the range of 2015 - 2025 with inclusion and exclusion criteria met. From the 10 journals that were fully reviewed, the diagnosis of sepsis is challenging due to the non-specific clinical presentation and the lack of sensitivity and specificity of available diagnostic procedures, and the delay in blood culture results in addition to the high negative results reported. A presumptive diagnosis of sepsis should be based on clinical symptoms along with laboratory parameters. The complex pathogenesis and pathophysiology of sepsis means that many compounds can serve as sepsis markers. This 10 journals addresses eight infection markers: leukocytes, ANC, NLR, PLR, CRP, MPV, procalcitonin, and IT ratio, and explains how each measure can help with the diagnosis of newborn sepsis. The use of a single infection marker is difficult to provide enough information for the clinician, so the selection of a combination of sepsis markers is an ideal step, while still considering the availability of these types of examinations in existing health facilities. Markers of infection with high diagnostic sensitivity and specificity could be instrumental in reducing the burden of neonatal sepsis.

DISCUSSION

Leukocytes have been widely used around the world in diagnosing sepsis in children. An increase in leukocyte count can be an indication of an inflammatory process in the body which is a normal response to an infection or inflammation. Neonates with early-onset sepsis had significantly higher leukocyte counts than neonates without sepsis. This remained significant even after 12-24 hours of hospital admission (Adane et al., 2022) At initial diagnosis, the leukocyte count 3 > 15.49 X 10 /µL can predict the death of sepsis patients at 144-hour evaluation (Sotianingsih et al. 2023).A large number of neutrophils are utilized at the site of infection, and are continuously supplied to the focus of infection from the bone marrow through the bloodstream. In neonatal sepsis, neutrophils have a role in the body's defense system in fighting infection (Sumitro et al., 2021). So in response to an infection, the body releases neutrophils from their reserves in the bone marrow into the circulation which will then migrate to the site or source of infection. This leads to an increase in neutrophils in the circulation to phagocytose the causative agent of infection (Rosales, 2018). Absolute neutrophil count (ANC) is the total number of neutrophils in the white blood cell count,

calculated using the formula : ANC (cells/µL) = neutrophil count (%) x leukocyte count (/µL). ANC has a high number in infants with neonatorum sepsis so that ANC can be used as a predictor to determine the occurrence of sepsis in neonates. The incidence of neonatal sepsis in the group of neonates with ANC >5,400/mm3 was 8.1 times greater than the ANC group of 1,800- 5,399/mm3 with a value of P=0.000 (P<0.01) (Harmansyah et al., 2015) ANC of 10,000/mm3 was a predictor of neonatal sepsis in the condition of white blood cell count > 15,000/mm3, with 69% sensitivity and 70% specificity in infants. ANC was a better predictor of neonatal sepsis than leukocyte count (Kuppermann et al., 2019).

Neutrophil to lymphocyte count ratio (NLR) is calculated as a simple ratio between neutrophil and lymphocyte counts measured from a complete blood test. NLR is a simple, cheap and easily obtainable marker of infection and reflects the balance between two aspects of the immune process: acute and chronic inflammation and adaptive immunity (Song et al., 2021). An increase in the number of neutrophils accompanied by a decrease in lymphocytes leads to an increase in NLR values. NLR is significantly associated with disease severity, higher mortality and with specific causes of death (Li et al., 2109) An early increase in NLR (<6 hours) after acute physiological stress is a marker of acute stress earlier than other laboratory parameters (e.g., leukocyte count, bacteremia and CRP). A lower NLR is usually associated with favorable prognostic factors and reflects preserved immune balance (Mortaz et al, 2018). A study showed that higher NLR was associated with poor prognosis in patients with sepsis especially when the value was above 10. The median NLR of 3.63 (95% CI 2.39-6.12) vs 2.67 (95% CI 1.39-4.55; p=0.018) was significantly higher in the proven neonatal sepsis group compared to the suspected neonatal sepsis group (Sumitro et al. 2021). Thus, NLR can be used as an alternative marker of neonatal sepsis that is relatively inexpensive and easy to perform even in areas with limited health facilities (Buanocera et al., 2022).Compared with CRP and white blood cell count, NLR showed moderate sensitivity (57.8%) and high specificity (84%). NLR was significantly higher in patients with septic shock (10.31 ± 2.32), indicating the potential value of NLR in assessing the severity of sepsis, especially when the value is above 10 (Gurol et al., 2015). A recent observational study showed that NLR appeared to be independent predictors of 28-day mortality in sepsis patients (Liu et al., 2021). A clustering analysis showed that age and NLR were strong predictors of sepsis (Jang et al., 2022).

Platelet and lymphocyte disorders are also associated with systemic inflammation. Platelet to lymphocyte count ratio (PLR) is a new infectious marker that describes acute inflammatory, neoplastic, thrombosis and metabolic disease (Jang et al., 2022). A study found a significant positive correlation between PLR and EOS (p<0.001), and a PLR cut-off value of 61.806 which was able to diagnose EOS with high sensitivity (90.2%) and specificity (85.7%) (Rompis et al. 2023). A study found that subjects with EOS had significantly higher PLR (Can et al., 2018) Neonates with confirmed and suspected EOS had higher PLR compared to the control group (Arcagok & Karabulut, 2019).Immature to Total Neutrophil (I/T) Ratio or I/T ratio is calculated based on the ratio of immature neutrophils to total neutrophils. An IT ratio >0.16 indicates bacterial infection, and a value >0.2 may indicate that sepsis is ongoing (Celik et al., 2022). A study in India reported that 70% of 100 infants with clinical manifestations of sepsis had an I/T ratio >0.2 and another study in Indonesia found a sensitivity and specificity with an I/T ratio >0.2 of 88.46% and 81.48%, respectively (Darnifayanti et al., 2015). One study found that, leukocyte values >15,000 mm3 or <5,000 mm3 and I/T ratio >0.2 combined with other tests such as positive CRP (>5 mg/L), ESR >15 mm/h, and positive hepatoglobin latex can be used as sepsis screening criteria. If 2 or more of these 5 criteria are present, the patient is positive for sepsis (Gomathi et al., 2022).

C-Reactive protein and procalcitonin are acute phase inflammatory proteins produced by monocytes and hepatocytes and shows a significant increase during infection. CRP levels begin to rise between 10 to 12 hours after infection begins and peak at 48 hours. CRP has a relatively long serum half-life of 24-48 hours making it less effective for early diagnosis of neonatal sepsis (Eichberger et al., 2022). The short half-life of PCT, which is about 20-24 hours, allows not only rapid detection but also monitoring of response to treatment. A second increase in PCT levels may be interpreted as a sign of a new a new sepsis episode. CRP concentration is associated with severity of illness, but are less effective than PCT in differentiating sepsis sepsis from other causes of disease. While PCT concentrations increase 5-20 times in sepsis, CRP levels only increase 3-8 times (Eschborn & Weitkamp, 2019).Procalcitonin shows a higher correlation with bacterial infection compared to CRP. In the study of sepsis neonatal, PCT has a higher sensitivity (82%) and specificity (95%) than CRP, which has a sensitivity of 73% and specificity of 83%. PCT tends to be higher in gram-negative infections compared to gram-positive infections. Procalcitonin increases 5-20 fold from baseline values in sepsis, compared to a 3-8 fold increase in CRP. High PCT levels have prognostic implications, as they can predict the risk of death in critically ill patients with infections (Eschborn & Weitkamp, 2019). PCT was found to be a strong predictor of mortality, as 75% of neonates who died had PCT levels higher than 10 ng/dl (Bharti et al., 2020).

There are a growing number of studies showing that leukocytes, ANC, NLR, PLR, CRP, MPV, procalcitonin and IT ratio have clinical significance for neonatal diagnosis and are associated with disease severity and prognosis. These eight indicators show good and similar diagnostic accuracy, which suggests that NLR and PLR have high accuracy in diagnosing neonatal sepsis and can be used as reliable markers of infection in the early stage.

CONCLUSION

Neonatal sepsis is an urgent global health concern and recognized as a leading cause of mortality and morbidity in newborns. The diagnosis of neonatal sepsis remains a challenge due to the non-specific clinical presentation. Leukocytes are the easiest and simplest marker but have lower diagnostic value. ANC was a better predictor of neonatal sepsis than leukocyte count. Both NLR and PLR indicators show excellent diagnostic accuracy in diagnosing neonatal sepsis, and have high accuracy values as screening tools and definitive diagnosis associated with disease severity and disease prognosis. There is no single reliable test for the early definite diagnosis of neonatal sepsis. A combination of two or more infection markers are helpful to improve a better diagnostic accuracy considering the clinical aspect of the neonate

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