Research Article

World Journal on Immunology

Neutrophil-Lymphocyte Ratio And Neonatal Sepsis Presence Correlates

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Received Date: 01 April 2024
Accepted Date: 16 April 2024
Published Date: 22 April 2024

Citation:
Tiewei Li. Neutrophil-Lymphocyte Ratio And Neonatal Sepsis Presence Correlates. World Journal on Immunology 2024.

1. Introduction

One of the main causes of illness and mortality in newborns [1] is neonatal sepsis, which is also a significant worldwide public health concern [2]. According to Fleischmann-Struzek et al., neonatal sepsis affects about 2202 out of every 100,000 live births, and death rates range from 11% to 19% [3]. Severe and even fatal consequences from newborn sepsis can be avoided with early diagnosis and treatment.lower the death rate. newborn sepsis can manifest as feeding intolerance, tachycardia, respiratory distress, pneumonia, and temperature instability. However, it can be challenging to diagnose newborn sepsis because these symptoms frequently coexist with other noninfectious diseases [1]. Blood culture is the gold standard for diagnosing newborn sepsis [4].However, blood cultures typically need a lengthy waiting period, and the low percentage of positive cultures is caused by contaminated blood or the administration of antibiotics prior to blood culture, as well as the tiny volume of blood used for inoculation [5, 6]. It's obvious that improved predictors are required for the diagnosis of sepsis in neonates. Blood biomarkers that are circulating and could be helpful in the early diagnosis of newborn sepsis have been analyzed [7].Sepsis is a state of systemic inflammatory response brought on by infection, and inflammation is crucial to the development and course of sepsis. Subpopulations of white blood cells play a critical role in the immune system's defenses against pathogen infection. Numerous clinical investigations have demonstrated that the neutrophil to lymphocyte ratio (NLR), lymphocyte numbers, and neutrophil counts are all predictive of sepsis [8–10]. Journal of Immunology Research, Volume 2020, Article ID 7650713, 8 pages: https://doi.org/10.1155/2020/7650713, NLR is thought to be more stable thanabsolute counts of neutrophils or lymphocytes, since the computation takes both counts into account [11].Because NLR may be a novel risk factor for sepsis, it has garnered a lot of interest [12–14]. Nevertheless, the majority of research on the connection between NLR and sepsis is done on adult patients [8], and the few findings on the subject of NLR and newborn sepsis have all had rather small sample sizes [15–18]. Thus, the purpose of this research is to assess, in a relatively large neonatal cohort, the association between NLR and neonatal sepsis.

2. Materials and Methods

Population and Study Design. Henan Children's Hospital carried out a hospital-based retrospective case-control study from January 2016 to December 2019. Clinical and laboratory data were gathered, and a total of 1480 neonates were included in the study. Patients with missing total and differential leukocyte counts and other disorders such significant congenital malformations, cyanotic congenital heart disease, and hematological system diseases were excluded from the study. The study protocol was approved by the hospital ethics review board and adhered to the Declaration of Helsinki. For each individual, written informed consent was acquired. Definition and Clinical Assessment. The International Pediatric Sepsis Consensus [4] states that two independent physicians diagnosed clinical neonatal infection and sepsis. Perforated viscus, chest radiograph consistent with pneumonia, petechial or purpuric rash, purpura fulminans, cough, white blood cells in a normally sterile bodily fluid, and any other clinical sign associated with a high probability of infection were all considered indicators of infection, whether they were suspected or proven. When two or more systemic immune response syndrome (SIRS) criteria are present due to a suspected or confirmed infection—among them, an elevated body temperature orleukocyte mass. The following are the SIRS criteria: (1) body temperature higher than 38.5°C or lower than 36°C; (2) mean heart rate greater than 2 SD above age-appropriate in the absence of external stimuli, or unexplained persistent elevation for children under 1 year old; (3) mean heart rate less than the 10th percentile for age-appropriate or unexplained persistent depression over a half-hour period;

(4) abnormal leukocyte count or more than 10% immature neutrophils. The published International Pediatric Sepsis Consensus [4] has detailed information. Measurements in the lab. At the time of hospital admission, blood samples were taken. Sysmex Corporation, Kobe, Japan, provided an automated blood cell counter for measuring the counts of white blood cells, neutrophils, and lymphocytes. By dividing the total neutrophil count by the lymphocyte count, the NLR was computed. An assay for latex-enhanced immunoturbidimetric measurement of high-sensitivity C-reactive protein (hsCRP) was used (Ultrasensitive CRP kit, Upper Bio-Tech).Shanghai, China) using a UPPER analyzer manufactured by Upper Bio-Tech in Shanghai. hsCRP values were regarded as 0.7 mg/L if they were less than the measurement limits of 0.8 mg/L.

Using a Cobas® 8000 modular analyzer and an electrochemiluminescence test (Elecsys® BRAHMS PCT kit, Roche Diagnostic, Rotkreuz, Switzerland), procalcitonin (PCT) levels were determined. PCT levels were defined as 101 ng/mL and 0.01 ng/mL, respectively, if they were above 100 ng/mL or below 0.02 ng/mL (measurement limits). Serum levels of aspartate aminotransferase (AST) and total bilirubin (TBIL)Ase (AST), alanine aminotransferase (ALT), total protein (TP), albumin (ALB), urea nitrogen (UREA), creatinine (CREA), and uric acid (UA) were measured using a conventional clinical analytical method and an automated biochemistry analyzer (AU5800 Clinical Chemistry Analyzers, Beckman Coulter, California). Statistical Analysis, Section 2.4. SPSS 21.0 was used to conduct the statistical analysis (SPSS Inc., Chicago, Illinois). Before conducting any statistical analysis, the normality of the variable data was checked.Variables with normal distribution were represented as mean + standard deviation (SD) and subjected to appropriate one-way ANOVA or independent t-test analyses. Variables with nonnormal distributions were examined using the Mann-Whitney U test and displayed as medians (interquartile range). Cate-gorical variables were expressed as number and percentages(n, %) and assessed by chi-squared or Fisher exact tests.A Pearson correlation test was used to analyze relationships between two continuous variables. Multivariatelogistic regression analysis was performed to identify theseparate risk factors for the occurrence of sepsis in newborns.Based on previously published research and univariate Pvalues less than 0.05, the risk factors were prespecified.The predictive value of NLR for the presence of newborn sepsis was assessed using receiver operating characteristic (ROC) curves. To find the best cut-off point, Youden's index (sensitivity + specificity − 1) was computed. A statistically significant value was defined as a two-sided P value less than 0.05.

3. Results

The study population's baseline clinical characteristics.The study included 1480 newborns in total; their average age was 8.0 (5.0, 14.7) days, and 60.0% of them were male. The neonates were then split into three groups according to whether they had been diagnosed with sepsis or an infection. Of the newborns, 555 were thought to be infected, and 737 were diagnosed with sepsis. As controls, 188 newborns with hyperbilirubinemia were used. The three groups' baseline clinical and laboratory data are compiled in Neonatals suffering from sepsis had an older age (P < 0:001) compared to both those without infection and those with infection (10.0 (5.0, 17.0) versus 7.0 (5.0, 12.0) and 7.0 (4.0, 12.0) days). Clinical results indicated that compared to controls and newborns with infection, neonates with sepsis had higher body temperatures, respiration rates, and heart rates (P < 0:001). According to serum biochemical tests, PCT, ALT, UREA, and 2 Journal of Immunology Research levelsNeonatals with sepsis had significantly greater UA (P <0:05), while their serum levels of TBIL, TP, and ALB were decreased (P < 0:001). The three groups' levels of AST and CREA did not differ from one another. Furthermore, only PCT, neutrophil count, and NLR shown a steady increase over time, despite the fact that inflammatory biomarkers like hsCRP, neutrophil count, lymphocyte count, and NLR were significantly different across the three groups (P < 0:001). NLR and Neonatal Sepsis Presence Association.We divided the research participants into three groups based on their NLR tertiles in order to examine the relationship between the NLR levels and the presence of newborn sepsis. Table 2 demonstrates that newborns in tertile 3 were younger (P < 0:001) and had higher respiratory rates and body temperatures (P = 0.001). Furthermore, there were significantly higher levels of PCT, hsCRP, UREA, CREA, and UA in tertile 3.P <0.001), whereas ter-tile 3 had lower levels of TBIL, TP, and ALB. Subsequent investigation revealed that newborns with infection were more likely to be in tertiles 1 and 2, and that the prevalence of neonatal sepsis increased considerably from 41.6% in the tertile 1 group to 66.2% in the tertile 3 group (P < 0:001).NLR Levels Are Independent in Predicting Neonatal Sepsis.An analysis of the utility of NLR in predicting the occurrence of newborn sepsis was conducted using univariate and multivariable binary logistic regression analysis. A model for multivariate analysis included variables from univariate analysis with P < 0:05, such as age, heart rate, respiration rate, weight, TP, ALB, CREA, TBIL, PCT, and hsCRP. NLR was an independent predictor of the presence of newborn sepsis, according to multivariate analysis (odds ratio ðOR\ = 1:445, 95%P < 0:001, CI 1.301-1.604) (Table 4). Subsequent investigation revealed that NLR remained unaffected by PCT and hsCRP (OR = 1:331, 95% CI 1.190-1.604, P < 0:001). Furthermore, our multivariate logistic regression models verified that there was an independent correlation between NLR tertiles and a higher incidence of newborn sepsis. Analysis of the Receiver Operating Characteristic Curve. NLR's predictive value for newborn sepsis was assessed using a Receiveroperating Characteristic (ROC) curve study. The NLR's well-defined discriminatory capacity was demonstrated by the area under the ROC curve (AUC) (AUC = 0:63, 95% CI0.60–0.66, P < 0:001). With a sensitivity of 51% and specificity of 75%, the ideal cut-off value of NLR for predicting the existence of newborn sepsis was 1.62 (Figure 2). We separated the participants into two groups (high NLR group ≥ 1:62 and low NLR group < 1:62) based on the cut-off value.In comparison to the low NLR group, the high NLR group tended to have a lower proportion of no stenosis and a higher prevalence of newborn sepsis, as seen.

4. Discussion

A dangerous, perhaps fatal condition that affects newborns is neonatal sepsis. Neonatal sepsis was responsible for 15.2% of the 2.76 million

infant fatalities that occurred globally in 2015, according to a paper by Li et al. [19]. Early treatment interventions are crucial for the early detection of newborn sepsis, which can subsequently reduce the risk of major, life-threatening complications and mortality. At the moment, the primary criteria used to diagnose neonatal sepsis areon clinical indicators, yet these indicators lack specificity [20].The gold standard is blood culture, however it can take up to 48 hours to get results. Furthermore, a variety of circumstances, including inadequate blood volume, contamination, and maternal antimicrobial treatment, might impact blood culture, making it insensitive [21]. It is consequently essential to find novel biomarkers that are sensitive, quick, and specific.A systemic inflammatory response syndrome known as neonatal sepsis is brought on by the entry of particular or suspected pathogens into the bloodstream and the ongoing proliferation ofpoisons. Organ system failure and pathological inflammation coexist with it [1]. During sepsis, neutrophils are a crucial component of the innate immune response, releasing regulatory, chemokine, and inflammatory cytokines. A variety of antimicrobial peptides, proteases, and oxidants are among the ways that neutrophils can engulf and eliminate invasive pathogens [22]. A new tool in the immune system's arsenal for combating pathogen invasion has been revealed in recent years with the discovery of neutrophil extracellular traps (NETs)[23–25]. However, excessive NET formation and inflammatory cytokine expression are factors in excessivetissue injury and inflammation [26–28].

The immune response to viral and bacterial illnesses also involves lymphocytes. Antigen-presenting cells identified microbial antigens during pathogen infection and presented them to T lymphocytes. Following this, cytokines are secreted by CD4 + T cells, which aid phagocytotic cells in eliminating intracellular bacteria [29].But because of apoptosis, the number of lymphocytes drastically decreases during sepsis. This decrease is thought to be a significant role in the immunosuppressive condition that leaves patients more susceptible to infections.Leukocyte counts, both total and differential, were accessible, affordable markers of the inflammatory response. Variations in neutrophil and lymphocyte numbers are reflected by NLR. Numerous investigations have shown that NLR is a trustworthy inflammatory marker and prognostic index in a range of medical conditions, such as solid tumors [40, 41], significant adverse cardiac events [36–39], cerebral hemorrhage [34, 35], and ischemic stroke [32, 33]. Lately, the NLR has garnered significant interest as a novel risk factor associatedpotential application in sepsis diagnostics. Due to the infection of pathogenic microorganisms, sepsis can result in increased neutrophil counts and decreased lymphocyte counts, suggesting that sepsis patients may have a higher NLR level [10, 42–44]. NLR may be a useful predictor of sepsis, as several epidemiological investigations and meta-analyses have shown, and patients with increased NLR may be at higher risk of an adverse prognosis [12, 45]. But the majority of research on the connection betweenStudies on sepsis and NLR have been done on adults. Only a small number of published research (n<150) have demonstrated a positive correlation between NLR and neonatal sepsis [15–18].With 1,480 newborns involved in the current study, we found that the group of patients with neonatal sepsis had the highest level of NLR. Subjects were split into three groups based on their NLR tertiles in order to investigate the relationship between NLR levels and the occurrence of neonatal sepsis. Additional investigation revealed that there had been a steady rise in the occurrence of newborn sepsis.Even after PCT and CRP were included in the multivariate regression model, NLR remained a separate risk factor for newborn sepsis.This study has a number of drawbacks. First off, there may be some inherent biases in this study because it is cross-sectional and single-center, neither of which can forecast future events. Second, a positive blood culture was not used to confirm the diagnosis of newborn sepsis, which was made based only on clinical symptoms. Third, the NLR was only recorded once. Sequential measurementobservations of NLR and the shift in newborn sepsis would be helpful in gaining additional insight into their relationship and in investigating the dynamic link between them.

5. Conclusion

The results of the current investigation showed a connection between neonatal sepsis and NLR. Patients with newborn sepsis had greater NLR levels, which gradually increased across three groups. In the meantime, NLR was found to be independently correlated with the existence of newborn sepsis using multivariate analysis. The results demonstrate how useful NLR may be in predicting the likelihood of newborn sepsis.

Data Availability

The data used to support the findings of this study are avail-able from the corresponding author upon request Conflicts of Interest The authors declare that they have no conflicts of interest.

Acknowledgments

The Medical Science and Technology Project of Henan Province (2018020698) and the Key Research, Development, and Promotion Projects of Henan Province (202102310132) provided funding for this work.

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