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ORIGINAL ARTICLE

Clinical Value of Hematological Inflammatory Indices in the Early Diagnosis of Neonatal Pneumonia

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SUMMARY

Background: **Neonatal pneumonia is a common and serious infectious disease in the neonatal period, particularly affecting preterm, low birth weight, and immunodeficient neonates, and poses a significant threat to their life and health. Finding convenient, reliable, and minimally invasive biomarkers is a key focus of clinical research. This study investigated the clinical value of the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic inflammatory index (SII) in the early diagnosis of neonatal pneumonia.**
Methods: **In this study, we retrospectively analyzed the clinical data of 322 patients with neonatal pneumonia diagnosed at our hospital from January through December 2023 and selected 80 healthy neonates from the same period as a control group. The severity of pneumonia was assessed using the Downes score, and general data and laboratory findings of the patients were collected and compared. Spearman's correlation analysis was used to explore the relationship between disease severity and each index, while multifactorial logistic regression analysis was employed to investigate the influencing factors. The value of NLR, PLR, and SII in the early diagnosis of neonatal pneumonia was evaluated using the receiver operating characteristic curve.**
Results: **Neutrophil count (NEU), platelet count (PLT), C-reactive protein (CRP), interleukin-6 (IL-6), NLR, PLR, and SII were significantly higher in the pneumonia group compared to the control group ($p < 0.05$). Correlation analysis showed that the Downes score positively correlated with NEU, PLT, NLR, PLR, SII, CRP, and IL-6 ($p < 0.05$). Multivariable logistic regression analysis indicated that PLR, CRP, and IL-6 were independent risk factors for the development of neonatal pneumonia ($p < 0.05$). The area under the curve (AUC) for diagnosing neonatal pneumonia was 0.770 for NLR, 0.805 for PLR, and 0.807 for SII.**
Conclusions: **PLR and SII have high diagnostic efficacy in the early diagnosis of neonatal pneumonia, while PLR, CRP, and IL-6 may be independent risk factors for neonatal pneumonia.**
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KEYWORDS

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INTRODUCTION

Neonatal pneumonia is a common and serious infectious disease in the neonatal period that poses a significant threat to life and health [1]. Its global incidence varies by region and health conditions, and even in developed countries, factors such as prematurity, low birth weight, and immunodeficiency continue to contribute to its high prevalence [2,3]. Clinical manifestations in-

clude shortness of breath, feeding difficulties, cyanosis, and apnea [4]. The Downes score is a simple clinical tool used to quantify the severity of neonatal pneumonia and guide treatment [5,6]. Early diagnosis relies on identifying risk factors and using multiple diagnostic tools [7], while genetic testing and molecular diagnostic techniques offer new detection options [8]. However, there is still a need for affordable, reliable, and less invasive biomarkers.

As the immune system of neonates is not fully developed, pathogenic infections often spread rapidly and trigger systemic reactions [4]. Various blood inflammatory markers can reflect the inflammatory state of the body. Neutrophils are usually elevated in acute inflammation and infection [9]; lymphocytes play a role in chronic inflammation and immune response [10]; and platelets play an important role in acute inflammation and coagulation [11]. NLR, PLR, and SII are important biomarkers for evaluating the level of inflammation and have been shown to highly correlate with a variety of inflammation-related diseases such as neoplasms, cardiovascular diseases, and sepsis [12-16]. However, the role of NLR, PLR, and SII in neonatal pneumonia is unclear, so it is necessary to evaluate their clinical value in the early diagnosis of neonatal pneumonia.

MATERIALS AND METHODS

Patients

Three hundred and sixty-two patients diagnosed with neonatal pneumonia between January and December 2023 at our hospital were retrospectively studied. The study was approved by the Ethics Committee of Dazhou Integrated Traditional Chinese Medicine. According to the diagnostic criteria for neonatal pneumonia, the diagnosis was based on respiratory symptoms (e.g., shortness of breath, dyspnea, and generalized fever), confirmed by imaging and laboratory findings [17]. Patients with congenital bronchial disease, neonatal cerebral palsy, immunodeficiency, tuberculosis, bronchial asthma, and aspiration pneumonia were excluded. Forty cases with ineligible data were also excluded. Ultimately, 322 patients were included in the pneumonia group, consisting of 173 males and 149 females, with a day age range of 3 - 26 days and a gestational age range of 32 - 41 weeks. Additionally, 80 healthy newborns were selected as the control group during the same period, including 42 males and 38 females, with a day age range of 5 - 25 days and a gestational age range of 37 - 42 weeks.

Downes score

The Downes score is based on five dimensions: respiratory rate, cyanosis, retractions, grunting, and air entry, with each dimension rated from 0 to 2 points. Higher scores, ranging from 0 to 10, indicate a more severe disease [5].

Data collection

Blood samples were collected from the subjects in the morning after fasting. Complete blood cell analysis was performed using the CAL-7000 automated hematology analyzer (Mindray, China), which recorded white blood cell count, neutrophil count, lymphocyte count, platelet count, and CRP results. NLR, PLR, and SII were calculated from these results. Specifically, NLR is the ratio of neutrophil count to lymphocyte count, PLR is the ratio of platelet count to lymphocyte count, and SII is the product of NLR and platelet count. Serum IL-6 levels were measured using the CARIS 2000 automated chemiluminescence analyzer (WANTAI Biopharm, China).

Statistical analysis

Statistical analyses and plotting were performed using GraphPad Prism 9.0. For count data, frequencies and percentages were used, and the chi-squared test was applied to compare between two groups. The Kolmogorov-Smirnov test was used to assess the normality of continuous data. Data that met the normal distribution were presented as mean ± standard deviation, and an independent samples *t*-test was used for comparing two groups; data that did not meet the normal distribution were presented as medians (interquartile ranges, IQRs), and the Mann-Whitney U test was used for comparing two groups. Spearman correlation analysis was used to explore the relationship between the severity of neonatal pneumonia and various indicators. Multivariate logistic regression analysis was performed to investigate the factors affecting the severity of neonatal pneumonia. Receiver operating characteristic (ROC) curves were used to evaluate the diagnostic value of NLR, PLR, and SII for neonatal pneumonia. A p-value of < 0.05 was considered statistically significant.

RESULTS

Characteristics and laboratory test indicators of participants

The differences between the pneumonia group and the control group in terms of gender composition, postnatal age, and white blood cell (WBC) count were not statistically significant ($p > 0.05$). However, the gestational age and lymphocyte (LYM) counts in the pneumonia group were significantly lower than those in the control group ($p < 0.05$). Meanwhile, NEU, PLT, CRP, IL-6, NLR, PLR, and SII were significantly higher in the pneumonia group compared to the control group ($p < 0.05$), as detailed in Table 1. Our results indicated that serum inflammation-related markers were significantly elevated in patients with neonatal pneumonia and that the onset of neonatal pneumonia may be associated with a shorter gestational age.

Table 1. Comparison of clinical characteristics and laboratory examination indicators between the pneumonia group and the control group.

	Control group (n = 80)	Pneumonia group (n = 322)	p
Gestational age, weeks, median (IQR)	39.5 (39 - 40)	38 (35 - 39)	< 0.001
Postnatal age, days, median (IQR)	9 (5.25 - 10)	9 (1 - 16)	0.192
Gender, male, n (%)	42 (52.5%)	173 (53%)	0.883
WBC, x 10^9/L, median (IQR)	10.96 (9.63 - 13.41)	11.51 (9.68 - 14.16)	0.384
NEU, x 10^9/L, median (IQR)	3.56 (2.67 - 4.88)	5.18 (3.52 - 7.77)	< 0.001
LYM, x 10^9/L, median (IQR)	5.89 (4.92 - 7.09)	4.47 (3.33 - 5.89)	< 0.001
PLT, x 10^9/L, median (IQR)	230 (187 - 316)	300 (259 - 358)	< 0.001
CRP, mg/L, median (IQR)	0.50 (0.21 - 1.25)	2.10 (1.40 - 2.59)	< 0.001
IL-6, pg/mL, median (IQR)	3.69 (2.10 - 5.50)	5.50 (1.50 - 30.06)	0.019
NLR, median (IQR)	0.55 (0.43 - 0.80)	1.15 (0.63 - 2.04)	< 0.001
PLR, median (IQR)	38.18 (29.29 - 48.00)	72.61 (46.76 - 98.21)	< 0.001
SII, median (IQR)	134.13 (86.98 - 215.96)	344.54 (187.93 - 745.73)	< 0.001

WBC - leucocyte (white blood cell), NEU - neutrophil, LYM - lymphocyte, PLT - platelet, CRP - C-reactive protein, IL-6 - interleukin-6, NLR - neutrophil-to-lymphocyte ratio, PLR - platelet-to-lymphocyte ratio, SII - systemic inflammatory index. Underlining indicates a statistically significant difference.

Table 2. Correlation analysis of Downes score with various laboratory tests.

	r	p
Gestational age	0.080	0.151
Postnatal age	-0.2667	< 0.001
WBC	0.340	< 0.001
NEU	0.347	< 0.001
LYM	-0.051	0.359
PLT	0.613	< 0.001
NLR	0.284	< 0.001
PLR	0.347	< 0.001
SII	0.420	< 0.001
CRP	0.171	0.002
IL-6	0.475	< 0.001

Correlation between the severity of neonatal pneumonia, as assessed by Spearman's correlation analysis, and various laboratory indices. WBC - leucocyte (white blood cell), NEU - neutrophil, LYM - lymphocyte, PLT - platelet, NLR - neutrophil-to-lymphocyte ratio, PLR - platelet-to-lymphocyte ratio, SII - systemic inflammatory index, CRP - C-reactive protein, IL-6 - interleukin-6. Underlining indicates a statistically significant difference.

Correlation analysis between the Downes score of newborns and laboratory test indicators

The results of the correlation analysis showed that Downes score in patients with neonatal pneumonia positively correlated with WBC, NEU, PLT, NLR, PLR, SII, CRP, and IL-6, but negatively correlated with postnatal age ($p < 0.05$), as shown in Table 2.

Independent predictors of the development of neonatal pneumonia

Multivariate logistic regression analysis was performed with the presence of neonatal pneumonia as the dependent variable (coded as 1 for yes and 0 for no) and postnatal age, NLR, PLR, SII, CRP, and IL-6 as independent variables (all measured values). The results showed that PLR, CRP, and IL-6 were independent risk factors for neonatal pneumonia ($p < 0.05$), as shown in Table 3.

Table 3. Independent predictors of neonatal pneumonia identified by multivariate logistic regression analysis.

	β	Standard error	Odds ratio	95% CI	p
Postnatal age	**-0.008**	**0.018**	**0.992**	**0.957 - 1.028**	**0.661**
NLR	**0.433**	**0.805**	**1.541**	**0.315 - 7.490**	**0.591**
PLR	**0.032**	**0.011**	**1.033**	**1.011 - 1.057**	**0.004**
SII	**0.002**	**0.003**	**1.002**	**0.996 - 1.008**	**0.620**
CRP	**-0.041**	**0.014**	**0.960**	**0.932 - 1.002**	**0.004**
IL-6	**0.081**	**0.027**	**1.084**	**1.038 - 1.154**	**0.003**

NLR - neutrophil-to-lymphocyte ratio, PLR - platelet-to-lymphocyte ratio, SII - systemic inflammatory index, CRP - C-reactive protein, IL-6 - interleukin-6. Underlining indicates a statistically significant difference.

Table 4. Diagnostic value of NLR, PLR, and SII in neonatal pneumonia.

	AUC (95% CI)	Youden index	Sensitivity (%)	Specificity (%)	Cutoff point	p
NLR	**0.770 (0.719 - 0.821)**	**0.402**	**71.43**	**68.75**	**0.695**	**< 0.001**
PLR	**0.805 (0.757 - 0.853)**	**0.473**	**74.84**	**72.50**	**46.91**	**< 0.001**
SII	**0.807 (0.758 - 0.855)**	**0.452**	**71.43**	**73.75**	**205.2**	**< 0.001**

AUC - area under the curve, NLR - neutrophil-to-lymphocyte ratio, PLR - platelet-to-lymphocyte ratio, SII - systemic inflammatory index. Underlining indicates a statistically significant difference.

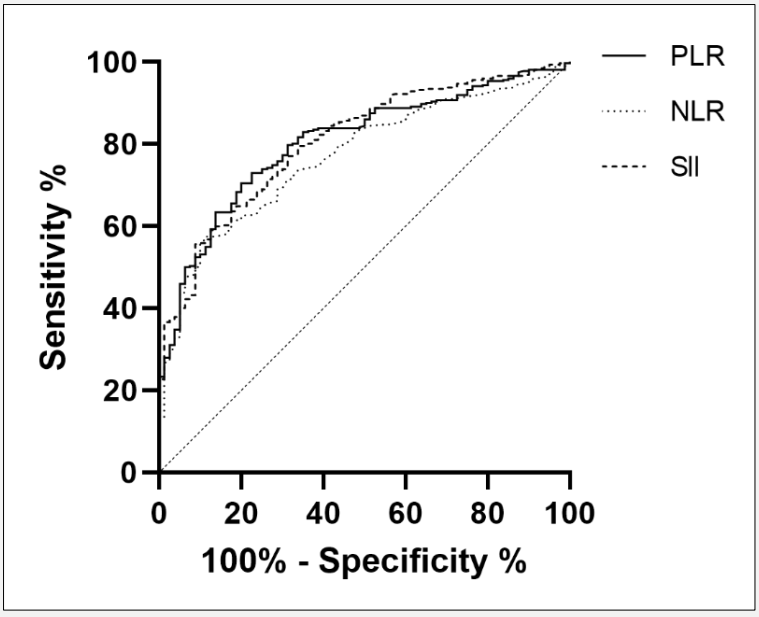

Figure 1. ROC curves of NLR, PLR, and SII for prediction of neonatal pneumonia.

Diagnostic value of NLR, PLR, and SII in neonatal pneumonia

We further assessed the diagnostic value of NLR, PLR, and SII in neonatal pneumonia. The AUC of NLR in diagnosing neonatal pneumonia was 0.770, with an optimal cutoff value of 0.695. The AUC of PLR in diagnosing neonatal pneumonia was 0.805, with an optimal cutoff value of 46.91. The AUC of SII in diagnosing neonatal pneumonia was 0.807, with an optimal cutoff value of 205.2. The results indicated that the diagnostic performance of SII and PLR for neonatal pneumonia was better than that of NLR, as shown in Table 4 and Figure 1.

DISCUSSION

Neonatal pneumonia is one of the most common and serious diseases in the neonatal period. Infection impairs gas exchange in the lungs and decreases blood oxygen levels, which can lead to hypoxemia and, in severe cases, result in organ dysfunction [18]. As the neonatal immune system is not fully mature, the inflammatory response may be more intense or uncoordinated, leading to more severe pneumonia symptoms and a higher risk of complications [19]. Given the high incidence of neonatal pneumonia, there is a need for inexpensive, reliable, and minimally invasive biomarkers. This study focused on the early diagnosis and clinical value of NLR, PLR, and SII in neonatal pneumonia. By retrospectively analyzing clinical data from 322 patients with neonatal pneumonia and 80 healthy newborns, we found that these inflammatory markers are crucial for diagnosing and assessing the severity of neonatal pneumonia.

NLR, PLR, and SII are inflammatory markers derived from routine blood tests, which are simple to perform, cost-effective, and minimally invasive, making them suitable for the neonatal population [20]. In this study, NLR, PLR, and SII levels were significantly higher in the pneumonia group compared to the control group, indicating that these markers are closely related to the inflammatory response in neonatal pneumonia. NLR reflects the ratio between neutrophils and lymphocytes, with neutrophils typically increasing during acute inflammation and infections, while lymphocytes play a major role in chronic inflammation and immune responses [9,10]. PLR incorporates platelet changes, which are particularly important for assessing inflammation and coagulation processes, while SII combines changes in neutrophils, lymphocytes, and platelets to provide a more comprehensive assessment of the body's inflammatory state. In the context of neonatal pneumonia, where the immune system is still developing, the inflammatory response to infection may be more intense and rapid [21]. Our study found that increased levels of NLR, PLR, and SII may reflect the body's acute response to infection. This finding is consistent with studies of NLR, PLR, and SII in other inflammatory diseases such as sepsis, cardiovascular diseases, and cancers [10-14]. Correlation analysis further revealed that the Downes score positively correlated with NLR, PLR, SII, CRP, and IL-6, with PLR and SII showing a higher correlation with the severity of neonatal pneumonia, suggesting that these markers may be important in clinical practice. Multivariate logistic regression analysis identified PLR, CRP, and IL-6 as independent risk factors for neonatal pneumonia. ROC curve analysis showed that NLR, PLR, and SII had high sensitivity and specificity for diagnosing neonatal pneumonia. Specifically, PLR and SII demonstrated higher AUC values, indicating that they might be more effective than NLR in diagnosing neonatal pneumonia. This is consistent with our previous correlation analysis, further supporting the potential of PLR and SII as early diagnostic tools for neonatal pneumonia. While NLR had an AUC of 0.770, indicating some diagnostic efficacy, it was slightly less effective compared to PLR and SII. This may be due to the more complex changes in neutrophil-to-lymphocyte ratios in neonatal pneumonia [12,13] or the influence of other uncontrolled inflammatory or immune factors. The AUCs for PLR and SII were 0.805 and 0.807, respectively, indicating superior diagnostic performance. PLR, as a ratio of platelets to lymphocytes, may better reflect the neonatal body's response to inflammation, especially in acute inflammatory diseases. SII, which integrates platelet, neutrophil, and lymphocyte changes, provides a more comprehensive assessment of inflammatory response, as evidenced by its high AUC value.

PLR and SII, as early diagnostic indicators for neonatal pneumonia, can assist clinicians in identifying high-risk patients at an early stage and implementing timely and effective treatment measures. Additionally, because early symptoms of neonatal pneumonia are often non-specific and can be confused with other conditions, the use of markers such as PLR and SII can help improve diagnostic accuracy and reduce the likelihood of misdiagnosis and missed diagnosis. These indicators can also be used to monitor disease progression and evaluate treatment efficacy, helping clinicians adjust therapeutic strategies and further improve neonatal outcomes. Despite the promising results of this study in the early diagnosis of neonatal pneumonia, it has some limitations. Firstly, as a single-center, retrospective study, the sample size is relatively limited, which may affect the generalizability of the results. Secondly, the study did not account for other potential factors influencing NLR, PLR, and SII, such as maternal infections and delivery methods, which may affect the neonatal inflammatory response. Furthermore, while the DS score used in the study is a common tool for assessing the severity of neonatal pneumonia, it still has a degree of subjectivity.

CONCLUSION

The present study demonstrates that NLR, PLR, and SII are clinically significant for the early diagnosis of neo-

natal pneumonia, with PLR and SII showing particularly high diagnostic efficacy. PLR, CRP, and IL-6 were identified as independent risk factors for neonatal pneumonia, highlighting their potential applications in the screening and monitoring of this condition.

Declaration of Interest:

None of the authors have any commercial or other association that might pose a conflict of interest.

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