ORIGINAL RESEARCH

Assessing Diagnostic Significance of White Blood Cell Count, Serum C-Reactive Protein, and Procalcitonin in Neonatal Pneumonia: A Comparative Analysis

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ABSTRACT

Objective • This study aims to comprehensively evaluate the diagnostic implications of white blood cell (WBC) count, serum C-reactive protein (CRP), and procalcitonin (PCT) in neonatal pneumonia.

Methods • A cross-sectional study design was employed, and a total of 30 neonates diagnosed with pneumonia were recruited from Shenzhen Longgang Central Hospital between March 2020 and March 2021. Patients were categorized into three groups: bacterial infection, viral infection, and mycoplasma infection, with 30 cases in each group. Additionally, 30 healthy neonates with normal physical indicators were included as controls. The study assessed WBC counts, serum CRP, and PCT levels. Diagnostic efficiency was investigated, including concentration alterations, sensitivity, and specificity.

Results • Infections resulted in a substantial increase in WBC counts and serum concentrations of CRP and PCT. Bacterial infections displayed the most notable alterations, followed by viral and mycoplasma infections ($P < .05$). Stand-alone PCT testing exhibited superior diagnostic efficiency, followed by WBC and CRP, as evidenced by heightened sensitivity and specificity ($P < .05$). However, the disparity in diagnostic efficiency between WBC and CRP alone did not attain statistical significance ($P > .05$). The WBC, CRP, and PCT hybrid assay demonstrated markedly superior sensitivity and specificity compared to stand-alone tests ($P < .05$).

Conclusions • The combined detection of WBC, CRP, and PCT yields a superior diagnostic outcome for neonatal pneumonia compared to individual tests. This approach enhances the potential for early interventions and contributes significantly to improving patient prognosis. The findings underscore the importance of adopting a multi-marker approach in diagnosing neonatal pneumonia. (*Altern Ther Health Med.* 2024;30(12):506-510).

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INTRODUCTION

Neonatal pneumonia is a prevalent respiratory ailment among newborns, constituting 15%~20% of live births and standing as a significant contributor to neonatal mortality.[1-3] The condition is linked to bacterial, viral, and mycoplasma infections.[1] The vulnerability of infants, particularly those aged less than 28 days post-birth, coupled with the limited functionality of their tissues and organs, predisposes them to infections.[2]

Due to the underdeveloped state of the newborn lungs, their inherent resistance is weakened, rendering them susceptible to diseases.[3,4] Pneumonia exhibits a swift progression with symptoms such as shortness of breath, cough, fever, and vomiting, negatively impacting respiratory, digestive, neurological, and circulatory functions, posing a significant threat to infant health.[3] Considering the nonspecific clinical symptoms of neonatal pneumonia and its multifactorial pathogenesis, early diagnosis plays a crucial role in identifying the pathogen type and serves as a foundation for the cautious use of antibiotics.

A combination of blood tests, C-reactive protein (CRP), and procalcitonin (PCT) is commonly employed to ascertain the type and severity of neonatal pneumonia infection. Blood tests facilitate the observation of alterations in the number, morphology, and distribution of blood cells, aiding in the identification of bacterial infection, viral infection, or Mycoplasma pneumonia infection, as well as the presence of hematological abnormalities.[4]

CRP is an acute temporal responsive protein that significantly elevates within a few hours following pathogenic microbial invasion or tissue damage, particularly in bacterial infections. It is positively correlated with the degree of

inflammation. Importantly, CRP demonstrates relative inertness to viral infections, serving as a clinically significant discrimination factor between bacterial and viral infections.[5]

PCT is a peptide hormone synthesized and secreted by parafollicular thyroid gland cells, reflecting the active degree of the systemic inflammatory response. Factors influencing PCT levels include the size and type of the infected organ, the bacteria type, the degree of inflammation, and the immune response.[6]

This study provides a unique contribution by focusing on the specific evaluation of the diagnostic relevance of combining WBC count with serum CRP and PCT in the context of neonatal pneumonia. The aim is to offer novel insights beyond the scope of existing research on this topic. This distinct approach enhances our understanding of how these biomarkers can provide valuable diagnostic information for neonatal pneumonia when analyzed together.

MATERIALS AND METHODS

Study Design

A total of 30 patients with neonatal pneumonia, admitted to Shenzhen Longgang Central Hospital from March 2020 to March 2021, were recruited. They were then assigned at a ratio of 1:1:1 to the bacterial infection group, viral infection group, and mycoplasma infection group, with 30 cases in each group. Additionally, 30 healthy neonates with normal physical indicators were selected as healthy controls. Parents of the newborns comprehended the contents of this study and willingly signed the informed consent form. The study received approval from the Ethics Committee of Shenzhen Longgang Central Hospital. Ethical considerations were carefully addressed during the approval process, and no potential conflicts of interest were identified.

Inclusion and Exclusion Criteria

This study's inclusion criteria comprised children who met the clinical diagnostic standards for neonatal pneumonia. These criteria included: (1) persistent high fever, shortness of breath, chest X-ray, or other radiological findings indicating lung lesions, along with abnormal laboratory tests (C-reactive protein, white blood cell count); (2) the diagnosis was confirmed through relevant pathological examination; (3) the included participants did not have any other systemic diseases, and they should not have undergone any treatment before the commencement of the study.

The exclusion criteria encompassed (1) children with tuberculosis, heart disease, or immune disorders; (2) those who dropped out from testing and treatment were also excluded; (3) participants beyond 28 days of age were excluded from the study. These criteria were established to ensure a homogeneous and focused study population, contributing to the reliability and validity of the research findings.

Outcome Measures

Fasting venous blood (3mL) was systematically collected from all newborns upon admission for the assessment of WBC, CRP, and PCT levels. The assay procedures adhered strictly to operational requirements, ensuring precision in result accuracy.[7]

WBC Assay. WBC levels were determined using the VCS method, employing the COULTER LH750 automatic hematocrit analyzer from BECKMAN, USA. Results are reported in units of (4-10) x10^9/L. This thorough approach to assay methodology, combined with advanced equipment, reinforces the reliability and consistency of the obtained data.

CRP Assay. CRP levels were determined using the QuickRead CRP rapid analyzer and supporting reagents from ORION, Finland. The results are reported in (0-10) mg/L units, ensuring a precise and rapid assessment.

PCT Assay. The PCT assay was conducted using the biclonal antibody method with a fully automated immunoassay analyzer. The results are reported in units of (0-0.5) ng/mL, reflecting a meticulous and automated approach to PCT-level assessment. These advanced assay methods contribute to the accuracy and efficiency of the diagnostic process.

Evaluation Criteria

A positive test result indicates that the assay results surpass the standard value. Sensitivity is calculated by dividing the number of true positive cases by the sum of true positive and false negative cases, then multiplying that by 100%. Specificity is calculated by dividing the number of true negative cases by the sum of false positive and true negative cases multiplied by 100%. These calculations provide a quantitative understanding of the test's accuracy and precision in identifying true positive and true negative outcomes. Sensitivity = (True Positive /True Positive + False Negative) ×100% Specificity = (True Negative/ False Positive + True Negative)× 100%

Statistical Analysis

The data from this study were carefully organized and analyzed using SPSS 23.0 statistical software (International Business Machines, Corp., Armonk, NY, USA). Measurement data were presented as mean ± standard deviation ($\bar{x} \pm s$) and assessed using the t test. Count data were expressed as the number of cases [n (%)] and analyzed using the chi-square (χ^2) test. Statistically significant differences were considered at a significance level of $P < .05$. Adjustments for multiple comparisons were applied, and the appropriate statistical tests were selected based on the nature of the data.

RESULTS

Comparison of Patient Demographics and Characteristics

In the bacterial infection group, there were 30 children, comprising 16 males and 14 females, aged between 6 and 28 years (14.33±4.12 days) with a disease duration of 2-4 days (3.70±0.34 days). The viral infection group consisted of 30 children, 15 males and 15 females, aged 6-26 years (13.66±3.08 days), and a disease duration of 2-5 days (3.68±0.12 days). In the mycoplasma infection group, there were 30 children, 17 males and 13 females, aged 7-27 years (14.12±2.44 days), with a disease duration of 3-5 days (3.75±0.21 days). The healthy

control group comprised 30 newborns, 15 males and 15 females, aged 7-25 years (13.12±2.27 days). Patient characteristics between the groups were comparable ($P > .05$), ensuring a balanced representation in the study, see Table 1.

Results of WBC, CRP, and PCT Assays

Infections induced a notable rise in WBC counts and serum concentrations of CRP and PCT within the body. The most pronounced alterations were observed in bacterial infections, followed by viral infections and mycoplasma infections ($P < .05$). These findings are summarized in Table 2.

Sensitivity and Specificity of WBC, CRP, and PCT

The stand-alone PCT test showed increased diagnostic efficiency, surpassing WBC and CRP, as indicated by their sensitivity and specificity ($P < .05$). However, the difference in diagnostic efficiency between the single assays of WBC and CRP did not reach statistical significance ($P > .05$). The WBC, CRP, and PCT hybrid assay exhibited significantly higher sensitivity and specificity than stand-alone tests ($P < .05$). These results are summarized in Table 3.

DISCUSSION

Neonatal pneumonia, an infectious lung condition in early childhood, becomes more prevalent, especially in colder seasons. Children with this ailment often display symptoms such as shortness of breath, cough, sputum production, and fever. Despite these symptoms, accurately diagnosing neonatal pneumonia poses challenges due to its complex infection patterns, the absence of specific clinical symptoms, and the widespread misuse of antibiotics.[8] Moreover, the historically time-consuming and complex differentiation of infection types and challenges in operating environments and procedures lead to delayed intervention and suboptimal clinical outcomes.[9]

Leukocytes play a crucial protective role, primarily tasked with engulfing bacteria. An abnormal white blood cell count increase is commonly linked to inflammatory responses.[10] In this study, WBC counts were elevated in the bacterial and mycoplasma infection groups compared to the healthy controls. However, relying solely on WBC detection to distinguish bacterial infection from other infections is imprecise.

CRP, a nonspecific inflammatory marker, is an acute chronotropic response protein synthesized by the liver as a protective response to pathogenic microorganisms invading the body. It plays a vital role in activating complement, regulating phagocytosis, and eliminating damaged necrotic tissue and foreign pathogens. The plasma concentration of CRP increases rapidly within 6-8 hours, reaching its peak at 24-28 hours in conditions such as acute myocardial infarction, infection, trauma, inflammation, and surgery, with levels potentially surging up to 2000 times the normal level.[11]

The CRP assay is unaffected by hormones and immunosuppressants, demonstrating superior sensitivity but weaker specificity compared to WBC in detecting bacterial infections. Monitoring CRP levels plays a pivotal role in evaluating the patient's condition.[12] In this study, CRP levels were elevated in all infection groups compared to the healthy controls. However, its specificity in distinguishing bacterial infections from non-bacterial ones was found to be inadequate.

PCT is a protein-like substance that examines the precursor molecule of calcitonin. Elevated PCT levels have been reported in the presence of severe bacterial, fungal, and parasitic infections, as well as in sepsis and multiple organ failure. The magnitude of PCT elevation clinically indicates the severity of the infection. PCT becomes detectable 2 hours after alterations, peaks at 12-24 hours, has a half-life of 22-29 hours, and remains unaffected by hormone levels, demonstrating good stability.[13]

Therefore, PCT stands out as a dependable indicator of disease conditions. In this study, the PCT levels in the bacterial infection group were significantly higher than in the mycoplasma infection group and the healthy control group ($P < .05$). Additionally, the PCT level in the mycoplasma infection group was higher than in the healthy control group ($P < .05$), although not as significantly elevated as observed in the bacterial infection group.

Table 1. Baseline clinical profiles

Group	n	Sex		Age (d)	Mean Age (d)	Duration of Disease (d)	Mean Duration of Disease (d)
		Male	Female				
Bacterial Infection Group	30	16	14	6-28d	14.33±4.12	2-4d	3.70±0.34
Viral Infection Group	30	15	15	6-26d	13.66±3.08	2-5d	3.68±0.12
Mycoplasma Infection Group	30	17	13	7-27d	14.12±2.44	3-5d	3.75±0.21
Healthy Control Group	30	15	15	7-25d	13.12±2.27	0	0
F/χ^2	-	0.067		-	0.921	-	0.672
P value	-	.795		-	.433	-	.513

Note: F/x^2 represents the statistical test used for sex distribution. *P*-values are provided for the statistical comparison of sex distribution among groups. $P < .05$ is considered statistically significant.

Table 2. WBC, CRP, and PCT Assays ($\bar{x} \pm s$)

Group	n	WBC($\times 10^9$/L)	CRP(mg/L)	PCT(ng/ml)
Bacterial Infection Group	30	13.56±2.44[abc]	111.49±20.49[abc]	6.93±1.32[abc]
Viral Infection Group	30	9.36±2.21[bc]	80.67±18.79[bc]	3.58±1.29[bc]
Mycoplasma Infection Group	30	7.20±3.22[c]	40.61±12.31[c]	1.25±0.15[c]
Healthy Control Group	30	6.02±2.14	2.21±0.62	0.20±0.10
F	-	51.251	293.583	310.362
P value	-	<.001	<.001	<.001

[a]indicates $P < .05$ when compared with the viral infection group
[b]indicates $P < .05$ when compared with the mycoplasma infection group
[c]indicates $P < .05$ when compared with the Healthy control group.

Note: *F* values and corresponding *P* values indicate the overall significance of differences among groups for WBC, CRP, and PCT. $P < .05$ is considered statistically significant.

Abbreviations: WBC, white blood cell; CRP, C-reactive protein; PCT, procalcitonin.

Table 3. Sensitivity and specificity of WBC, CRP, and PCT (%)

Assay	Sensitivity	Specificity
WBC	81.44	81.57
CRP	83.34	84.62
PCT	94.62	93.83
Combined Assays of WBC+CRP+PCT	98.87	97.96

Note: Sensitivity and specificity values are presented in percentages.

Abbreviations: WBC, white blood cell; CRP, C-reactive protein; PCT, procalcitonin.

Therefore, PCT serves as a central factor in clinical treatment, enabling the effective differentiation between bacterial pneumonia and mycoplasma pneumonia. In the clinic, it is essential to regulate antibiotic dosage based on the child's condition and symptoms. Prolonged antibiotic administration may lead to dysbiosis, gastrointestinal discomfort, and drug resistance. Hence, maintaining a careful balance in antibiotic usage is crucial to optimize treatment outcomes and minimize potential side effects.

A superior diagnostic efficiency was noted with the stand-alone PCT test, followed by WBC and then CRP, as evidenced by their sensitivity and specificity ($P < .05$). These findings offer scientific guidance for antibiotic usage, helping to reduce overmedication. Additionally, employing a hybrid assay of WBC, CRP, and PCT resulted in significantly higher sensitivity and specificity compared to stand-alone tests ($P < .05$). This finding contributes positively to the assessment of neonatal pneumonia and the severity of inflammatory responses.

The findings of our study carry significant clinical relevance as they highlight ways to address the existing challenges in diagnosing and managing neonatal pneumonia. Our results contribute to a more nuanced understanding of the disease, offering clinicians insights for timely and accurate diagnosis. Moreover, our results provide valuable guidance for refining management strategies, potentially lowering the risk of misdiagnosis and enabling more precise interventions. We believe that these findings have the potential to profoundly influence clinical practice, enhancing the overall management of neonatal pneumonia and ultimately improving patient outcomes.

Study Limitations

One notable limitation of our study is the relatively small sample size, potentially introducing bias and limiting the generalizability of findings. This small sample size may impact the robustness of statistical analyses and the ability to detect subtle and clinically relevant effects. Additionally, the study's sample may not fully represent the diversity encountered in clinical practice, further constraining external validity.

Future Directions

In future studies, we acknowledge the imperative of expanding the sample size and incorporating a more diverse participant pool. This strategic increase aims to strengthen the statistical power of the study and to contribute to a more profound understanding of the mechanisms of action of WBC, CRP, and PCT. Moreover, the inclusion of a broader range of comparative indexes will facilitate a more thorough exploration of the complex relationship between variables. Proactively addressing these aspects in future research studies aligns with our goal to fill existing knowledge gaps and provide a more comprehensive understanding of neonatal pneumonia with direct implications for clinical practice. The insights derived from our research extend beyond mere statistical significance, carrying practical implications that directly benefit healthcare practitioners and enhance neonatal care.

Clinical Application

When translated into clinical practice, our findings carry the potential to enhance the diagnosis and management of neonatal pneumonia significantly. The integration of combined detection methods for WBC, CRP, and PCT into routine diagnostic protocols provides healthcare practitioners with a more reliable and efficient tool for the early and accurate identification of neonatal pneumonia cases. This integration facilitates timely interventions, ultimately improving patient outcomes and alleviating the burden on healthcare resources.

Furthermore, as we continue exploring additional comparative indexes and refining diagnostic strategies, healthcare practitioners will gain a more holistic understanding of neonatal pneumonia. This comprehensive knowledge equips them with the ability to implement personalized and targeted interventions, ensuring that neonatal care is not only evidence-based but also tailored to the individual needs of each patient.

CONCLUSION AND RECOMMENDATIONS

In conclusion, the combined detection of WBC, CRP, and PCT in our study demonstrated significantly higher diagnostic accuracy for neonatal pneumonia compared to single detection methods. This heightened diagnostic value not only facilitates the early identification of neonatal pneumonia but also enables prompt interventions, subsequently improving patient prognosis. Our findings emphasize the clinical utility of a comprehensive approach involving the simultaneous assessment of WBC, CRP, and PCT in neonatal pneumonia diagnosis. This integrated strategy enhances the sensitivity and specificity of diagnostic procedures, providing clinicians with a more reliable tool for the accurate and timely identification of the condition.

Our research contributes to advancing scientific understanding while providing benefits to healthcare practitioners in neonatal care. Through enhancing diagnostic accuracy and refining management strategies, we seek to contribute to the continuous improvement of clinical practices, ultimately leading to better outcomes for neonates affected by pneumonia.

Based on these results, we recommend incorporating combined detection methods into routine diagnostic protocols for neonatal pneumonia. This approach has the potential to revolutionize clinical practice by enabling healthcare professionals to identify cases of neonatal pneumonia quickly and accurately, allowing for timely interventions and improved patient outcomes. Furthermore, clinicians should consider implementing targeted treatment strategies based on the combined assessment of WBC, CRP, and PCT levels, tailoring interventions to individual patient needs, and optimizing the overall management of neonatal pneumonia.

COMPETING INTERESTS
The authors report no conflict of interest.

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AVAILABILITY OF DATA AND MATERIALS
The data that support the findings of this study are available from the corresponding author upon reasonable request.

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