DOI: https://doi.org/10.54393/pjhs.v5i08.1822

PAKISTAN JOURNAL OF HEALTH SCIENCES
https://thejas.com.pk/index.php/pjhs
ISSN (P): 2790-9352, (E): 2790-9344
Volume 5, Issue 8 (August 2024)

Original Article

OPEN ACCESS

Evaluating the Diagnostic Accuracy of C-Reactive Protein in Diagnosing Pneumonia in Children Using Blood Culture as the Gold Standard

Nasir Ayaz[1*], Adeela Ilyas[1], Aneesa Iqbal[1], InamUllah[1], Iftikhar Khan[1] and Iffat Mehmood[2]

[1]Department of Pediatric Medicine, Muhammad Teaching Hospital, Peshawar, Pakistan
[2]Department of Pediatric Cardiology, Hayatabad Medical Complex, Peshawar, Pakistan

ARTICLE INFO

Keywords:
Pediatrics, Pneumonia, Diagnostic Accuracy, Antibiotic Stewardship

How to Cite:
Ayaz, N., Ilyas, A., Iqbal, A., Ullah, I., Khan, I., & Mehmood, I. (2024). Evaluating the Diagnostic Accuracy of C-Reactive Protein in Diagnosing Pneumonia in Children Using Blood Culture as the Gold Standard: C-Reactive Protein in Diagnosing Pneumonia. Pakistan Journal of Health Sciences, 5(08). https://doi.org/10.54393/pjhs.v5i08.1822

***Corresponding Author:**
Nasir Ayaz
Department of Pediatric Medicine, Muhammad Teaching Hospital, Peshawar, Pakistan
drnasirayaz@gmail.com

Received Date: 5th June, 2024
Acceptance Date: 24th August, 2024
Published Date: 31st August, 2024

ABSTRACT

C-Reactive Protein (CRP) is important in identifying and evaluating bacterial infections as a conventional biomarker. **Objective:** To determine the diagnostic accuracy of CRP in diagnosing pneumonia keeping blood culture and radiological findings as a gold standard. **Methods:** A descriptive cross-sectional study was conducted in the Department of Pediatrics at Lady Reading Hospital, Peshawar Pakistan from December 2022 to December 2023. After selecting 246 patients who satisfied the required inclusion criteria for pneumonia, an immunoturbidimetric assay was utilized to quantitatively measure CRP levels. To compare the results to those of the gold standard of blood culture, patients with both positive and negative cultures were included. Among the 246, the mean age of the children was 9±2.73 years. There were 136 males (55%) and 110 females (45%), with male to female ratio of 1.24:1. **Results:** Results were true positive in 207 (84.15%), true negative in 7 (2.85%), false positive in 9 (3.66%) and false negative in 23 (9.35%). Diagnostic accuracy was analyzed as CRP had a sensitivity of 87.77%, specificity of 52.94%, Positive predictive value of 96%, negative predictive value of 24.32%, and overall diagnostic accuracy was 85.36%. **Conclusions:** Clinicians and laboratory professionals face difficulties in making a precise and prompt diagnosis of pneumonia. However, by conducting a single, inexpensive, and rapid test using CRP as a qualitative estimator, physicians can prevent the unnecessary use of antibiotics with an accuracy of 85.36%.

INTRODUCTION

Community-acquired Pneumonia (CAP) is a significant source of illness in developed nations and a crucial cause of morbidity and mortality in underdeveloped nations [1].CAP impacts 0.3%–1.5% of children every year in Western nations [2]. The current conventional treatment approach in international guidelines for CAP involves administering 7–10 days of oral amoxicillin, irrespective of the etiology [3]. Viruses, either alone or in mixed infections with bacteria, dominate as the primary cause of CAP in children below the age of 5 years [4]. Studies have established that Mycoplasma pneumoniae contributes to over 50% of cases in children above 10 years of age, but the efficacy of antibiotics in such cases remains unclear [5]. Streptococcus pneumoniae is the most significant bacterial pathogen in all age groups [6]. Overlapping symptoms, non-specific physical exam findings, and limited access to diagnostic tests are challenges in diagnosis of pneumonia, in low-resource settings. Chest X-rays and blood cultures are still thought to be the gold standards for diagnosis [7]. However, these methods are not always feasible or affordable in such settings, which highlights the need for a rapid, accurate, and affordable diagnostic tool for pneumonia, especially in low-resource settings. Tillet and Francis discovered C-Reactive Protein (CRP) in 1930, which is a homopentameric protein that is highly conserved in plasma. CRP is an acute-phase inflammatory agent that shows increased expression in inflammatory conditions such as cardiovascular disease,

DOI: https://doi.org/10.54393/pjhs.v5i08.1822

and rheumatoid arthritis, infection. Inflammatory disorders cause the CRP levels in plasma to deviate by at least 25% [8]. Recent meta-analyses have highlighted the variability in diagnostic approaches and the effectiveness of CRP in distinguishing between bacterial and viral pneumonia in pediatric populations. Such analyses have provided the need for improved diagnostic algorithms for pneumonia diagnosis in resource-limited environments [9, 10]. CRP is important in identifying and evaluating bacterial infections as a conventional biomarker. Among the several tests available, CRP's role in pneumonia has been extensively studied which indicates its high sensitivity and specificity in diagnosing bacterial infections in children with pneumonia.

This study aimed to assess the diagnostic accuracy of C-Reactive Proteins (CRP) in diagnosing pneumonia by utilizing radiological findings and blood cultures as the gold standard. Although pneumonia is a prevalent disease worldwide, it can be difficult to diagnose the illness early and accurately. Studies that have already been conducted have shown conflicting results about the validity of CRP as a stand-alone marker. Some of these studies have not included a thorough comparison with gold-standard diagnostics, or they have given inconsistent information about the predictive usefulness of CRP. By carefully measuring CRP levels in addition to using recognized diagnostic techniques, this work fills up these gaps. In doing so, it hopes to provide light on whether CRP can serve as a trustworthy early indicator of pneumonia, facilitating prompt clinical decision-making. In the end, the results may contribute to a decrease in the overuse of antibiotics, and enhance patient outcomes.

METHODS

A descriptive, cross-sectional study was carried out at the Department of Pediatrics at Lady Reading Hospital, Peshawar Pakistan from December 2022 to December 2023. The study was conducted after obtaining the necessary approvals from the Department of Pediatrics at Lady Reading Hospital, Peshawar (Reference No. 422/CBW/LRH). The sample size was 246 patients, using 95% sensitivity, 45% specificity, and 52% proportion of pneumonia with a margin of error for sensitivity as 3.2% and specificity as 8% using Raosoft software for diagnostic accuracy. The sensitivity value of 95% was selected based on existing literature indicating that CRP has a high potential to correctly identify true positive cases of pneumonia [11]. Specificity was set at 45% to account for the possibility that CRP, while sensitive, may also be elevated in other conditions, reflecting a moderate ability to exclude non-pneumonia cases. The proportion of pneumonia was estimated at 52% based on local epidemiological data, providing a realistic reflection of the prevalence of pneumonia in the pediatric population studied. A non-probability purposive sampling technique was followed. All children from 2 to 14 years of age with high suspicion of pneumonia were involved in the study. Pneumonia was suspected when children had a fever of more than 100°F at the time of presentation and tachypnea upper limit according to age. Children with a history of surgical intervention, renal insufficiency (serum urea level of>50mg/dl and creatinine level of >1.1mg/dl), and trauma were excluded from the study. The exclusion criteria was set to eliminate factors that could confound CRP levels and affect the accuracy of the study. Patients with a history of surgical intervention and trauma were excluded due to the potential for surgery-induced or trauma-induced inflammation, which could falsely elevate CRP levels. Children with renal insufficiency were excluded because renal dysfunction can alter CRP metabolism, leading to inaccurate measurements. An explanation was provided to the parents of the child regarding the purpose and benefits of the study. They were reassured of the study's objectives and advantages, informed of any associated risks, and made aware that the study was solely conducted for research and data publication. Once the parents agreed to participate, written consent was obtained. A thorough clinical examination was conducted on all children, and a brief history was obtained from their parents. To detect pneumonia, 5cc of blood was collected from each child using strict aseptic techniques and sent to the hospital laboratory for CRP testing. An immunoturbidimetric assay was utilized to quantitatively measure CRP levels, with a threshold of 5mg/dL. The same blood specimen was also sent for complete blood culture analysis in the same laboratory to confirm the presence of pneumonia. Additionally, a chest X-ray was performed for the results in the meantime. The laboratory investigations were conducted under the supervision of a microbiologist who had a minimum of five years of experience. A pre-designed form was used to record all the relevant information. To ensure control of confounders and bias in the study results, strict exclusion criteria were followed. The collected data were analyzed using SPSS version 24.0, with numerical variables such as age calculated for mean and standard deviation. Categorical variables, including qualitative CRP and blood culture results were presented as frequency and percentages. Furthermore, sensitivity, specificity and negative, and positive predictive values for CRP in identifying children with blood culture and x-ray-proven pneumonia were also computed.

RESULTS

In this study, 246 patients with pneumonia were included. The mean age of the children was 9 ± 2.73 years. There were 136 males (55%) and 110 females (45%), with male to female

DOI: https://doi.org/10.54393/pjhs.v5i08.1822

ratio of 1.24:1. Results were true positive in 207 (84.15%), true negative in 7 (2.85%), false positive in 9 (3.66%) and false negative in 23(9.35%)(Table 1).

Table 1: Total Accuracy of CRP in Diagnosis of Pneumonia(n=246)

Blood Culture Sensitivity and X-Ray Diagnosis					
CRP levels	**Positive**	**Negative**	**Total**	**False Positive (%)**	**False Negative (%)**
Positive	207	9	216	84.15%	2.85%
Negative	23	7	30	3.66%	9.35%
Total	230	16	246	87.81%	12.19%

Diagnostic accuracy was analyzed as CRP had a sensitivity of 87.77%, specificity of 52.94%, Positive predictive value of 96%, negative predictive value of 24.32% and overall diagnostic accuracy was 85.36% (Table 2). To align with the study objectives, the results demonstrate a high diagnostic accuracy of CRP in diagnosing pneumonia, keeping blood culture and radiological findings as the gold standard. Specifically, CRP exhibited a high sensitivity (87.77%) in identifying true cases of pneumonia, which supports its effectiveness as a diagnostic tool. However, the 9 false positives and 23 false negatives observed in the study indicate potential limitations in CRP diagnostic accuracy. Moreover, the lower specificity (52.94%) indicates that while CRP is useful in detecting pneumonia, it may not be sufficient as a standalone marker.

Table 2: Validity and Predicted Outcomes of CRP

Diagnostic Test	(%)
Sensitivity	87.77%
Specificity	52.94%
Positive Predictive Value	96%
Negative Predictive Value	24.36%
Accuracy	85.36%

DISCUSSION

Pneumonia remains a significant cause of morbidity and mortality, particularly in the developing world where its incidence was significantly higher. The delay in diagnosis and initiating therapy were the main reasons for high mortality. Diagnostic tests for pneumonia may include chest X-rays, blood tests, sputum analysis, and sometimes a CT scan. Starting from the early 1990s, the World Health Organization (WHO) has suggested using quantitative tachypnea to identify children who may need antibiotic treatment for potential Pneumonia [12]. However, this technique relies on subjective assessment. Blood culture and chest x-ray were still considered as a gold standard for diagnosis. Among the different tests used to diagnose pneumonia, the role of CRP in the diagnosis of pneumonia has been vastly considered. Based on the results, there were 246 total children, of which 84.15% (207 children) were classified as true positive for pneumonia based on CRP results, and 9.35% (23 children) were classified as false negative. This means that the CRP test correctly identified the majority of cases of pneumonia, but missed a small number of cases. The efficacy of CRP in identifying pneumonia in children was also reported by previous studies [9, 13, 14]. Studies should also explore its effectiveness in diverse clinical settings, especially where advanced diagnostics were limited. Additionally, examining CRP role in monitoring treatment response and disease progression could be beneficial for clinical practice. A similar study was conducted by Barek-Corren Y *et al* in 2021 [15]. In that study, 835 children with CSP were examined, out of which 87 had viral pneumonia and 89 had invasive bacterial pneumonia. According to the study, the viral pneumonia group exhibited lower levels of PCT and CRP in the absence of malaria parasites compared to the invasive bacterial pneumonia group. PCT and CRP cut-offs were determined at 0.72 ng/ml (with a sensitivity of 94.6% and specificity of 74.2%) and 20.9 mg/l (with a sensitivity of 95% and specificity of 54.2%), respectively. Wrotek A *et al.*, also compared prolactin and CRP and showed similar results [16]. Another study by Dudognon D *et al.*, which included 586 children under 5 years of age with severe clinical pneumonia, also yielded similar results [17]. The positive bacterial culture (BC+) group comprised all children with bacteremia, while a random selection of other children was placed in the negative bacterial culture (BC-) group. The results indicated that at a sensitivity of 95%, the specificity of CRP was 45%, similarly, at a sensitivity of 85%, the specificity of CRP was 57%. The Area under the curve for evaluating BC+ was 0.79 for CRP, slightly lower than the AUC of 0.80 for Procalcitonin. However, the difference between the two markers was not statistically significant (P = 0.617). The meta-analysis by Gunaratnam LC *et al.*, Tsou PY *et al.*, and Gentilotti E *et al.*, also comply with these results [10, 18, 19]. Gunaratnam LC *et al.*, aimed to evaluate the effectiveness of various biomarkers in diagnosing bacterial pneumonia in children, particularly in resource-poor settings. The study analyzed 31 observational studies and found that CRP and procalcitonin were the most effective in distinguishing bacterial from viral pneumonia. Their results demonstrated moderate accuracy with the though their accuracy was moderate, with sensivities from 60% to 85% and specificities from 76% to 83%. CRP slightly outperformed procalcitonin. The study concluded that while CRP and PCT were useful diagnostic tools [10]. Another study by Tarhani F *et al.*, evaluated the diagnostic accuracy of CRP level for pneumonia in children presenting at an emergency department [20]. Of the 687 children, 286 went through CRP measurement and chest radiography and 148 had pneumonia. The study found that higher CRP levels were related to a higher proportion of pneumonia and that CRP level was independently associated with pneumonia, even after adjusting baseline characteristics. However, low CRP levels did not exclude pneumonia. The study suggests that CRP could have a diagnostic significance for pneumonia in children and prompts further evaluation in primary care settings.

DOI: https://doi.org/10.54393/pjhs.v5i08.1822

CONCLUSIONS

The study's radiological findings suggested that CRP can be a useful tool for clinicians to accurately diagnose pneumonia and avoid unnecessary antibiotic use with an accuracy of 85.36%, as they have difficulty in making an accurate and timely diagnosis of pneumonia. However, CRP alone cannot be relied upon to definitively diagnose pneumonia, as it has limitations. It should be used in conjunction with other diagnostic tests and clinical assessments to make an accurate diagnosis.

Authors Contribution

Conceptualization: NA
Methodology: AI[1], IU, IK, IM
Formal analysis: IU
Writing, review and editing: NA, AI[1], AI[2], IK, IM

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Eshwara VK, Mukhopadhyay C, Rello J. Community-acquired bacterial pneumonia in adults: An update. Indian Journal of Medical Research. 2020 Apr; 151(4): 287-302. doi: 10.4103/ijmr.IJMR_1678_19.

[2] Nascimento-Carvalho CM. Community-acquired pneumonia among children: the latest evidence for an updated management. Jornal de Pediatria. 2020 Apr; 96: 29-38. doi: 10.1016/j.jped.2019.08.003.

[3] Bielicki JA, Stöhr W, Barratt S, Dunn D, Naufal N, Roland D *et al.* Effect of amoxicillin dose and treatment duration on the need for antibiotic re-treatment in children with community-acquired pneumonia: the CAP-IT randomized clinical trial. Journal of the American Medical Association. 2021 Nov; 326(17): 1713-24. doi: 10.1001/jama.2021.17843.

[4] McLaren SH, Mistry RD, Neuman MI, Florin TA, Dayan PS. Guideline adherence in diagnostic testing and treatment of community-acquired pneumonia in children. Pediatric Emergency Care. 2021 Oct; 37(10): 485-93. doi: 10.1097/PEC.0000000000001745.

[5] Tong L, Huang S, Zheng C, Zhang Y, Chen Z. Refractory Mycoplasma pneumoniae pneumonia in children: early recognition and management. Journal of Clinical Medicine. 2022 May; 11(10): 2824. doi: 10.3390/jcm11102824.

[6] Feldman C and Anderson R. Recent advances in the epidemiology and prevention of Streptococcus pneumoniae infections. F1000Research. 2020 May; 9: F1000. doi: 10.12688/f1000research.22341.1.

[7] Yan C, Hui R, Lijuan Z, Zhou Y. Lung ultrasound vs. chest X-ray in children with suspected pneumonia confirmed by chest computed tomography: A retrospective cohort study. Experimental and Therapeutic Medicine. 2020 Feb; 19(2): 1363-9. doi: 10.3892/etm.2019.8333.

[8] Florin TA, Ambroggio L, Brokamp C, Zhang Y, Rattan M, Crotty E *et al.* Biomarkers and disease severity in children with community-acquired pneumonia. Pediatrics. 2020 Jun; 145(6). doi: 10.1542/peds.2019-3728.

[9] Ebell MH, Bentivegna M, Cai X, Hulme C, Kearney M. Accuracy of biomarkers for the diagnosis of adult community-acquired pneumonia: a meta-analysis. Academic Emergency Medicine. 2020 Mar; 27(3): 195-206. doi: 10.1111/acem.13889.

[10] Gunaratnam LC, Robinson JL, Hawkes MT. Systematic review and meta-analysis of diagnostic biomarkers for pediatric pneumonia. Journal of the Pediatric Infectious Diseases Society. 2021 Sep; 10(9): 891-900. doi: 10.1093/jpids/piab043.

[11] Weisz OA and Rodriguez-Boulan E. Apical trafficking in epithelial cells: signals, clusters and motors. Journal of Cell Science. 2009 Dec; 122(23): 4253-66. doi: 10.1242/jcs.032615.

[12] Marangu D and Zar HJ. Childhood pneumonia in low-and-middle-income countries: An update. Paediatric Respiratory Reviews. 2019 Nov; 32: 3-9. doi: 10.1016/j.prrv.2019.06.001.

[13] Zheng HH, Xiang Y, Wang Y, Zhao QS, Fang R, Dai R. Clinical value of blood related indexes in the diagnosis of bacterial infectious pneumonia in children. Translational Pediatrics. 2022 Jan; 11(1): 114. doi: 10.21037/tp-21-568.

[14] Rashad M, Ismail Y, Sobeih AA, Abdel Aziz O. Procalcitonin, C-reactive Protein and White Blood Cells Count in Children with Community Acquired Pneumonia. Benha Medical Journal. 2021 Apr; 38(1): 125-36. doi: 10.21608/bmfj.2021.142187.

[15] Barak-Corren Y, Horovits Y, Erlichman M, Picard E. The prognostic value of C-reactive protein for children with pneumonia. Acta Paediatrica. 2021 Mar; 110(3): 970-6. doi: 10.1111/apa.15580.

[16] Wrotek A, Robakiewicz J, Pawlik K, Rudzinski P, Pilarska I, Jaroń A *et al.* The etiology of community-acquired pneumonia correlates with serum inflammatory markers in children. Journal of Clinical Medicine. 2022 Sep 20; 11(19): 5506. doi: 10.3390/jcm11195506.

DOI: https://doi.org/10.54393/pjhs.v5i08.1822

[17] Dudognon D, Levy C, Chalumeau M, Biscardi S, Dommergues MA, Dubos F *et al.* Diagnostic accuracy of routinely available biomarkers to predict bacteremia in children with community-acquired pneumonia: A Secondary analysis of the GPIP/ACTIV pneumonia study in France, 2009-2018. Frontiers in Pediatrics. 2021 Oct; 9: 684628. doi: 10.3389/fped.2021.684628.

[18] Tsou PY, Rafael J, Ma YK, Wang YH, Raj S, Encalada S *et al.* Diagnostic accuracy of procalcitonin for bacterial pneumonia in children-a systematic review and meta-analysis. Infectious Diseases. 2020 Oct; 52(10): 683-97. doi: 10.1080/23744235.2020.1788719.

[19] Gentilotti E, De Nardo P, Cremonini E, Górska A, Mazzaferri F, Canziani LM *et al.* Diagnostic accuracy of point-of-care tests in acute community-acquired lower respiratory tract infections. A systematic review and meta-analysis. Clinical Microbiology and Infection. 2022 Jan; 28(1): 13-22. doi: 10.1016/j.cmi.2021.09.025.

[20] Tarhani F, Nezami A, Heidari G. Evaluating the usefulness of lab-based test for the diagnosis of pneumonia in children. International Journal of General Medicine. 2020 May: 243-7. doi: 10.2147/IJGM.S249221.