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Comparison Between the Serum Level of C-Reactive Protein and Severity of Community-Acquired Pneumonia in Infants

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Author`s Contribution

[1,2]Study conception and design, data collection and proof reading [3,5]Manuscript drafting, [6]data analysis and interpretation, [4]Final approval, critical review & Supervision

Funding Source: None
Conflict of Interest: None

Received: Oct 29, 2024
Accepted: Nov 26, 2024

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ABSTRACT

Objective: To compare the mean serum C-reactive protein (CRP) levels in infants diagnosed with non-severe community-acquired pneumonia (Pneumonia Severity Index I & II) versus those with severe pneumonia (Pneumonia Severity Index III–V).

Methodology: A cross-sectional study was conducted at the Department of Pediatrics, Khyber Teaching Hospital, Peshawar from Mar 2024 to Sept 2024. A total of 144 male and female infants diagnosed with pneumonia in the age range of 2 to 12 months were enrolled. The mean CRP level of the patients was determined by patient's laboratory test reports from the patients with pneumonia. The analysis of the data was done using the SPSS version 22. Independent sample t-test was applied to compare the mean CRP level among patients with severe and non-severe pneumonia, mean an median, frequencies and percentages were calculated for the quantitative variables.

Results: 144 patients, the mean age of the patients was 7.13±2.55 months, the disease duration was 6.61±3.05 the male-to-female ratio was 1.61: 1, and 42.4 % were un vaccinated. The mean CRP level was 11.12±6.33 mg/dl, among these the non-severe pneumonia was recorded in 88 (61.1%) patients (61.1%) with a mean CRP of 7.97±4.14mg/dl, and severe pneumonia was recorded in 56 patients (38.9%) with a mean CRP of 16.07±6.009 mg/dl. The p-value of independent sample t-test unveil significant level of mean difference of CPR values in severe versus non-severe groups (P = 0.000).

Conclusion: The mean CRP level in patients with severe pneumonia is significantly high than in patients with non-severe pneumonia. The CRP could be a potential tool for measuring the severity of the pneumonia.

Keywords: Pneumonia, Severity of Pneumonia, C-reactive protein, infants

Cite this article as: Shabir M, Khan N, Khan A, Muhammad Z. Ikramullah, Shahzad S. Comparison Between the Serum Level of C-Reactive Protein and Severity of Community-Acquired Pneumonia in Infants. Ann Pak Inst Med Sci. 2024; 20(4):824-828. doi. 10.48036/apims.v20i4.948.

Introduction

Pneumonia is an infectious disease classified into two main groups: hospital-acquired and community-acquired pneumonia. It is a severe condition and one of the leading causes of mortality among children under five years of age.[1] Globally, these epidemics result in an estimated 3 to 5 million cases of severe illness and 250,000 to 500,000 deaths each year.[13] Despite fluctuations in epidemiological data and deviations from guidelines, CRP remains a key diagnostic marker for pneumonia.

According to the World Health Organization (WHO), one million children suffer from pneumonia annually, making it a significant contributor to infant deaths.[2] The diagnosis of community-acquired pneumonia (CAP) is based on laboratory data and radiological findings.[3] International guidelines have established diagnostic criteria that rely on the signs and symptoms of patients.[4]

The incidence of CAP has decreased over time due to the availability of conjugated pneumococcal vaccines. However, atypical factors have begun to replace pneumococcal strains.[5] CAP remains a critical health issue for infants and children, affecting millions globally each year.[6] Streptococcus pneumoniae is recognized as the primary causative agent of CAP worldwide. In adults, pneumococcal pneumonia typically remains confined to the alveoli of the lungs and is generally treatable.[7]

Its production is stimulated by cytokines, particularly interleukins. CRP serves as both a marker and driver of inflammation caused by pathogens. CAP is one of the leading causes of morbidity and mortality among children and infants, making it a major reason for hospitalization in many countries, including the United States.[8, 10] One of the most common infectious diseases, pneumonia continues to be a significant cause of mortality and the use of medical resources. Accurate diagnosis is crucial for effectively managing CAP through appropriate prognostic approaches. C-reactive protein (CRP) is an acute-phase protein produced in the liver in response to infection and tissue inflammation.[11]

Despite extensive data from different countries, there are significant variations in children's care, diagnostic approaches, hospitalization rates, therapeutic regimens, and antibiotic use. CRP levels increase in response to inflammation triggered by infectious agents, making it an important marker for bacterial infections in children.[12-13]

The rationale behind this study is to highlight the practical use of CRP as an inflammatory marker in response to infections such as pneumonia among the children patients. Despite its potential, the use of CRP in routine diagnostics remains underutilized in some developed countries. This study focuses on the etiology of CAP and the routine use of CRP as an inflammatory marker, specifically investigating the relationship between CAP and CRP levels in infants. It aims to compare mean CRP levels in infants with non-severe pneumonia (Pneumonia Severity Index I & II) versus those with severe pneumonia (Pneumonia Severity Index III, IV and V).

Methodology

A Cross-sectional study was conducted at the Department of Pediatrics, Khyber Teaching Hospital Peshawar from Mar 2024 to Sept 2024 using a non-probability consecutive sampling procedure. The Sample size was calculated using a WHO calculator for sample size, keeping a 95% confidence level, 80% power of the study.[14] The required sample size was 144 patients, Patients aged 2 to 12 months from both genders were included in the study. However, patients not willing to participate were excluded. A written informed consent was also obtained from parents of enrolled patients.

Demographic data including age, gender, duration of symptoms, vaccination status, and residence was noted. A complete history was taken and physical examination records were obtained from patient's records. Baseline labs including Complete Blood Count (CBC), CRP, Liver Function Test (LFT), Renal Function Test (RFT), serum electrolyte, Arterial Blood Gases (ABGs), and chest X-ray were done as part of routine diagnostic procedures and to calculate the pneumonia severity index. Patients were admitted to the pediatric ward and treated as per hospital protocols. CRP level and pneumonia severity index were determined in all patients as per the operational definition.

All the parameters were collected on a structured proforma, and mean± standard deviation was calculated for quantitative variables like age, duration of symptoms, and CRP level. Frequency and percentages were calculated for demographic variables most importantly age group, and disease profile Pneumonia severity index (PSI I&II/III-V) was calculated for classifying severity of pneumonia. Mean CRP was compared in patients with non-severe and severe pneumonia using an independent sample t-test. Data can be stratified for duration of the disease and area of living through regression analysis to estimate the risk

Operational Definition: Inflammation and fluid in the lungs brought on by a bacterial, viral, or fungal infection is known as pneumonia.

Results

The mean age of the patients was 7.13±2.55 months. The mean duration of pneumonia among enrolled patients stands at 6.611±3.052 days, in addition mean CRP of all enrolled patients stands at 11.12±6.330 mg/dl .

Furthermore, male to female ratio was 1.61: 1, and majority of the patients belonged to the age group 7 months or below (n = 79, 54.9%). In addition, 80 patients (55.6%) belonged to rural areas and 61 patients (42.4%) were unvaccinated. Majority of patients (n=84 ,58.34%) had Pneumonia symptoms for more than 5 days (Table I).

Table no I: Details of Patients and vaccination status.

Parameters		**(n)**	**(%)**
Gender	Male	89	61.8%
	Female	55	38.2%
Age in months	7 or below	79	54.9%
	More than 7	65	45.1%
Disease duration (days)	5 or below	60	41.7%
	More than 5	84	58.34%
Residence	Rural	80	55.6%
	Urban	64	44.4%
Vaccination	Vaccinated	83	57.6%
	Unvaccinated	61	42.4%

Table II: Severity, Gender and vaccination status-based variation in CRP values of enrolled patients.

Stratification of data	Group	N	Mean	SD	Std. Error Mean	P value
CRP (mg/dl)	Non-Severe	88	7.97	4.145	0.442	0.000
	Severe	56	16.07	6.009	0.803	
CRP (mg/dl)	Male	89	11.11	6.560	0.695	0.419
	Female	55	11.13	5.997	0.809	
CRP (mg/dl)	Un vaccinated	61	14.44	6.712	0.859	0.005
	Vaccinated	83	8.67	4.758	0.522	

Mean comparison of CRP level in severe versus non-severe groups of enrolled patients based on their gender, age and vaccination status is given in Table II. The mean CRP level among the severe group was 16.07±6.09 mg/dl and 7.97±4.14 mg/dl among the non-severe group. The p-value for the mean difference in severe versus non-severe groups was 0.000.

Gender based segregation of CRP values among severe and non-severe pneumonia patients show that the mean CRP level among male and female patients with non-severe pneumonia stands at 11.11±6.56 and 11.13±5.997.

The data showed that mean CRP level among unvaccinated was 14.44 ±6.712 and among vaccinated it was calculated to be 8.67±4.758

Discussion

Community-acquired pneumonia (CAP) is a leading cause of mortality and morbidity worldwide. While significant advancements in diagnosis and treatment regimens have contributed to a substantial reduction in CAP cases, developing countries continue to struggle with inadequate treatment. Therefore, accurate diagnosis remains a critical component in the effective management of severe diseases like pneumonia.[16]

This study was conducted in infants of age between 2 to 12 months. Infants below 7 months and rural areas were more prone to pneumonia, with a high proportion of male infants. In addition, most infants had pneumonia symptoms for more than 5 days. Low age is linked to high vulnerability to different diseases as infants of this age lack the required immunity to resist pathogens and diseases.[17] Community acquired pneumonia assessment studies also reported that males are more prone to pneumonia as revealed in research.[17]

Assessing severity of pneumonia geographically remains a challenging factor in the pediatrics field. Various diagnosis strategies and possibilities remain unsolved, as reported by various studies.[18-19] The CRP marker is one of the main factors in diagnosis; thus, our study assessed CRP levels among severe and non-severe patients. Vaccination plays a crucial role in altering the course of disease in infants.[11]

The problem of un vaccination was high among the sampled infants (42.4%) and was likely a contributing factor to pneumonia severity in this group. Non-severe pneumonia was reported in the majority of patients (61.1%), who had relatively low mean CRP levels. In contrast, the mean CRP value of patients with severe pneumonia was significantly higher than that of non-severe pneumonia patients, making it an important diagnostic factor in determining pneumonia severity.]. Serum CRP levels that remain elevated over time may be linked to the patient's health and the onset of severe pneumonia. This finding is consistent with other studies that have established a direct correlation between patients' mean CRP levels and the severity of their pneumonia.[20-21]. Furthermore, in the Philippines, viruses were frequently found in children who had severe pneumonia.[22] Clinically, the important predictors of severe pneumonia were age, dyspnea, body temperature, and sputum output[23]

The ROC curve using the new variables generated by multivariate regression analysis and the diagnostic gold standard for severe pneumonia demonstrated the reliability of these factors in diagnosing severe pneumonia.[24-25]

Certain limitations of study may be considered important while addressing the findings of the study. We probably underestimated the wrong diagnosis of CAP since the evaluation of diagnostic mistake was based on a review of medical records, which has constraints related to the reporting of alternative reasons for signs, symptoms, or radiographic findings. The risk factor analysis may be skewed toward the null if patients with incorrect diagnoses are included in the CAP group. Additionally, patients with a proper diagnosis of CAP may have been incorrectly classified as inappropriate if patient-reported symptoms had been omitted from the record. Future research directions and recommendations include replicating this study on a larger scale across multiple regions and hospitals to compare the severity of pneumonia with CRP levels, ensuring broader

applicability. Furthermore, this should also be conducted in children of age more than 1 year. Additionally, launching public awareness campaigns can educate parents and the general public about recognizing early symptoms of pneumonia, promoting timely diagnosis, and advocating for prompt treatment in hospitals. A multichannel awareness strategy leveraging mass media, social media, and influential community leaders, including religious figures and role models, can emphasize the importance of timely infant vaccination, ultimately improving vaccination rates and reducing pneumonia-related morbidity and mortality.

Conclusion

In the current study, the mean CRP value in patients with severepneumonia was significantly higher than in patients with non-severe pneumonia (p-value <0.05). Measuring the CRP levels may assist in the diagnosis and treatment of CAP by physicians in clinical practice. In addition, vaccinated infants were less likely to develop severe pneumonia and exhibited significantly low mean CRP values. The high morbidity and mortality rates of severe pneumonia attracts worldwide attention. It is crucial to raise awareness about the importance of early pneumonia detection, coupled with preventive measures to reduce mortality and hinder disease progression.

Acknowledgement: The authors would like to acknowledge the Medical Affairs Department of Getz Pharma for their technical support and assistance in the publication process.

References

1. Liu L, Oza S, Hogan D. Global, regional, and national causes of child mortality in 2000–13, with projections to inform post-2015 priorities: an updated systematic analysis. *Lancet*. 2015;385:430–40. https://doi.org/10.1016/S0140-6736(14)61698-6
2. Pfunter A, Wier LM, Steiner C. Costs for hospital stays in the United States, 2011. Rockville (MD): Agency for Healthcare Research and Quality, Healthcare Cost and Utilization Project; 2013.
3. Jain S, Self WH, Wunderink R. Community-acquired pneumonia requiring hospitalization among U.S. adults. *N Engl J Med*. 2015;373:415–27. https://doi.org/10.1056/NEJMoa1500245
4. Jennings LC, Anderson TP, Beynon KA. Incidence and characteristics of viral community-acquired pneumonia in adults. *Thorax*. 2008;63:42–8. https://doi.org/10.1136/thx.2006.075077
5. Johnstone J, Majumdar SR, Fox JD. Viral infection in adults hospitalized with community-acquired pneumonia: prevalence, pathogens, and presentation. *Chest*. 2008;134:1141–8. https://doi.org/10.1378/chest.08-0888
6. Charles PGP, Whitby M, Fuller AJ. The etiology of community-acquired pneumonia in Australia: why penicillin plus doxycycline or a macrolide is the most appropriate therapy. *Clin Infect Dis*. 2008;46:1513–21. https://doi.org/10.1086/586749
7. Jain S, Williams DJ, Arnold SR. Community-acquired pneumonia requiring hospitalization among U.S. children. *N Engl J Med*. 2015;372:835–45. https://doi.org/10.1056/NEJMoa1405870
8. Self WH, Williams DJ, Zhu Y. Respiratory viral detection in children and adults: comparing asymptomatic controls and patients with community-acquired pneumonia. *J Infect Dis*. 2016;213:584–91. https://doi.org/10.1093/infdis/jiv323
9. Lee GE, Lorch SA, Sheffler-Collins S. National hospitalization trends for pediatric pneumonia and associated complications. *Pediatrics*. 2010;126:204–13. https://doi.org/10.1542/peds.2009-3109
10. Marston BJ, Plouffe JF, File TM. Incidence of community-acquired pneumonia requiring hospitalization. *Arch Intern Med*. 1997;157:1709–18. https://doi.org/10.1001/archinte.1997.00440360129015
11. Griffin MR, Zhu Y, Moore MR. U.S. hospitalization for pneumonia after a decade of pneumococcal vaccination. *N Engl J Med*. 2013;369:155–63. https://doi.org/10.1056/NEJMoa1209165
12. Liu Q, Sun G, Huan L. Association of the NLR, BNP, PCT, CRP, and DD with the severity of community-acquired pneumonia in older adults. *Clin Lab*. 2023;69(12). https://doi.org/10.7754/Clin.Lab.2023.220330
13. Yadav RK, Kumar D, Gupta A, Sharma P. C-reactive protein and procalcitonin: as predictor biomarkers of severity and outcome in children with community-acquired pneumonia. *Trop Doct*. 2024;54(3):262–7. https://doi.org/10.1177/00494755241250371
14. OpenEpi. Sample size for cohort or cross-sectional study. https://www.openepi.com/SampleSize/SSCohort.htm
15. Berkley JA, Munywoki P, Ngama M. Viral etiology of severe pneumonia among Kenyan infants and children. *JAMA*. 2010;303:2051–7. https://doi.org/10.1001/jama.2010.675
16. O'Callaghan-Gordo C, Bassat Q, Morais L. Etiology and epidemiology of viral pneumonia among hospitalized children in rural Mozambique: a malaria endemic area with high prevalence of human immunodeficiency virus. *Pediatr Infect Dis J*. 2011;30:39–44.
17. García-García ML, Calvo C, Pozo F. Spectrum of respiratory viruses in children with community-acquired pneumonia.

Pediatr Infect Dis J. 2012;31:808–13. https://doi.org/10.1097/INF.0b013e3182568c67

18. Pavia AT. Viral infections of the lower respiratory tract: old viruses, new viruses, and the role of diagnosis. *Clin Infect Dis*. 2011;52(Suppl 4):S284–9. https://doi.org/10.1093/cid/cir043
19. Michelow IC, Olsen K, Lozano J. Epidemiology and clinical characteristics of community-acquired pneumonia in hospitalized children. *Pediatrics*. 2004;113:701–7. https://doi.org/10.1542/peds.113.4.701
20. Falsey AR, Hennessey PA, Formica MA. Respiratory syncytial virus infection in elderly and high-risk adults. *N Engl J Med*. 2005;352:1749–59. https://doi.org/10.1056/NEJMoa043951
21. Walsh EE, Peterson DR, Falsey AR. Human metapneumovirus infections in adults: another piece of the puzzle. *Arch Intern Med*. 2008;168:2489–96. https://doi.org/10.1001/archinte.168.22.2489
22. Fry AM, Lu X, Olsen SJ. Human rhinovirus infections in rural Thailand: epidemiological evidence for rhinovirus as both pathogen and bystander. *PLoS One*. 2011;6(3):e17780. https://doi.org/10.1371/journal.pone.0017780
23. Karhu J, Ala-Kokko TI, Vuorinen T. Lower respiratory tract virus findings in mechanically ventilated patients with severe community-acquired pneumonia. *Clin Infect Dis*. 2014;59:62–70. https://doi.org/10.1093/cid/ciu237
24. Ruuskanen O, Järvinen A. What is the real role of respiratory viruses in severe community-acquired pneumonia? *Clin Infect Dis*. 2014;59:71–3. https://doi.org/10.1093/cid/ciu242
25. Brundage JF. Interactions between influenza and bacterial respiratory pathogens: implications for pandemic preparedness. *Lancet Infect Dis*. 2006;6:303–12. https://doi.org/10.1016/S1473-3099(06)70466-2