Original Article

Association of Raised C-Reactive Proteins with Prolonged ICU Stay in Children with Bronchopneumonia: A Cross-Sectional Study

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Abstract

Objective: To study the association of raised CRP with prolonged ICU stay in children with bronchopneumonia at Ghurki Trust Teaching Hospital, Lahore, Pakistan.

Methodology: This cross-sectional study was conducted in Paediatric Intensive Care Unit of Ghurki Trust Teaching Hospital, Lahore, Pakistan, for a duration of six months (June 2023 to December 2023). Out of 127 children admitted into ICU, 82 met the inclusion criteria, aged 2-60 months, diagnosed with bronchopneumonia. Upon admission, blood sample was taken for CRP levels and these levels were correlated with ICU stay, TLC count, O2 dependency, and antibiotics duration of the patients. Patients were divided into five groups based on CRP counts. CRP counts less than 0.3 mg/dL were taken as normal. CRP counts from 0.4-0.9 mg/dL were taken as mild, 1-10 mg/dL were considered moderate, 11-49 mg/dL were considered marked, and ≥50 mg/dL were considered severe.

Results: Out of 82 patients, 45 (54.88%) were males and 37 (45.12%) were females. This study found that raised CRP was present in 73 (89.02%) out of 82 children ($p<0.04$). Amongst 73 (89.02%), 08 (10.96%) patients had mild elevation of CRP, 36 (49.32%) had moderate elevation, 22 (30.14%) had marked, 07 (9.59%) had severe elevation. Moreover, a direct relation was observed among CRP and ICU stay (3.82±3.12), O2 requirements (3.72±3.07), TLC (13.36±5.18), antibiotic treatment duration (9.52±3.94) of broncho pneumonic patients.

Conclusion: Higher CRP levels significantly result in longer ICU stays and higher oxygen requirements in children with bronchopneumonia.

Keywords: Bronchopneumonia, Creactive proteins, Paediatric Intensive Care Unit, World Health Organization.

Introduction

In numerous developing countries, pneumonia is the most prevalent cause of mortality among children under the age of five.[1] It is a contributing factor to sepsis or mortality.[2] Approximately 30% of community-acquired pneumonia cases develop into severe pneumonia because of delayed detection and treatment.[3] Furthermore, compelling data indicates a rise in severe pneumonia cases.[4] Severe pneumonia is characterized by the need for admission to an intensive care unit and often leads to death.[5] Prompt and efficient therapy for pneumonia is essential. The World Health Organization (WHO) advises using established therapies for moderate and severe pneumonia cases.[6] Nevertheless, the unavailability of suiTable medications and equipment in developing nations still needs to be improved. Moreover, severe pneumonia contributes to the continuation of mortality rates related to nosocomial infections.[7] To decrease the death rate and enhance prognosis, diagnosing pneumonia promptly before it reaches a severe stage is crucial. Various organisms cause pneumonia; however, it is challenging to pinpoint the specific infections responsible. Determining moderate and severe pneumonia primarily relies on the clinical manifestation and physical assessment.[8] The predictability of the clinical course and prognosis of pneumonia may be enhanced through an integrated assessment of the clinical symptoms and CRP levels. The diagnostic significance of the CRP level in patients with a significant risk of pneumonia is unknown. The role of clinical signs, inflammatory markers, and symptoms in predicting the onset of severe pneumonia remains uncertain.

Therefore, it is necessary to conduct a comprehensive investigation on a large population to validate the diagnostic precision of CRP regarding clinical signs and symptoms in predicting the occurrence of severe pneumonia. Severe pneumonia can result from bacterial, viral, or combination illnesses.[9] This study aims to show the association and direct link of increasing CRP with increasing hospital stay primarily and the TLC, O_2 and antibiotics duration.

Methodology

This cross-sectional study was undertaken

Table I: Patients demographic variables with mean age and mean weight

Sr. No.	Gender	Frequency (%)	Mean Age (months) (Mean ± SD)	Mean Weight (Mean ± SD)
01	Male	45 (54.88%)	9.97±8.12	7.34±2.81
02	Female	37 (45.12%)	9.54±10.00	6.92±3.08
03	Total	82	10.06±11.52	7.45±3.47

at the Department of Paediatric Medicine, Lahore Medical and Dental College / Ghurki Trust Teaching Hospital, Lahore, following authorization from the Ethical Review Committee of LMDC/GTTH (Ref No.2023/06/R-03). Non-probability consecutive sampling technique was used to select patients admitted to the hospital. Sample size was calculated using WHO sample size calculator (version 1.1) having 95% confidence interval, anticipated population proportion of 0.79, and absolute precision of 0.09.[10] Out of 127 children admitted into PICU, we enrolled 82 patients fulfilling the inclusion criteria within the given time frame of 21st June 2023 to 21st December 2023. Diagnosis was established based on tachypnea (respiratory rate>50/min), signs of respiratory distress (intercostal and subcostal recessions) and radiological findings in form of chest X ray.[11] The respiratory rate thresholds established by WHO for the identification of children with pneumonia are as follows: Infants under 2 months of age: For children aged 2-12 months, a respiratory rate of 60 breaths per minute or higher is considered normal. For children aged 1-5 years, a respiratory rate of 50 breaths per minute or higher is considered normal.

For children aged 1-5 years, a respiratory rate of 40 breaths per minute or higher is considered normal.[12] Those with malnutrition, suspected viral etiology, primary immune deficiency, congenital heart disease and chronic lung pathology were excluded from study. Informed consent was taken from parents of the patients. Demographic data (including name, age, gender, and weight) was collected. Upon admission, a blood sample was collected from each patient and sent to the Ghurki hospital laboratory for analysis; CRP levels were measured and correlated with ICU stay, TLC count, O_2 dependency and antibiotics duration of the patients. To do so, patients were divided into five groups based on CRP counts. CRP counts less than 0.3 mg/dL were taken as normal. CRP counts from 0.4-0.9 mg/dL were taken as mild, 1-10 mg/dL were considered moderate, 11-49 mg/dL were considered marked, and ≥50 mg/dL were considered severe.[13] The data analysed using the Statistical Package for the Social Sciences, version 27 (SPSS).

Results

During the study period, 127 patients, with the clinical diagnosis of bronchopneumonia, were admitted in the Paediatrics Department of Ghurki Trust Teaching Hospital, Lahore. Out of 127, 82 patients with the clinical diagnosis of bronchopneumonia, fulfilling the inclusion criteria, participated in the study. The admission mean age was 10.06±11.52 months ranging from 02 to 60 months, respectively. Out of the 82 patients, 45 (54.88%) were males and 37 (45.12%) were females with male to female ratio of 1.2:1. Their mean weight at the time of admission was 7.45±3.47 as given in Table I.

Signs of respiratory distress (intercostal and subcostal recessions) and increased respiratory rate thresholds were recorded in all children. Among clinical characteristics, cough, fever, diarrhoea and pleural effusion were taken under consideration. Patients' clinical characteristics are given in Table 2. In this study, we found that CRP was noticeably raised in 73 out of 82 neonates accounting for 89.02% of total patients ($p<0.04$). Out of 73 (89.02%), 08 (10.96%) patients had mild elevation of CRP, 36 (49.32%) had moderate elevation, 22 (30.14%) had marked, 07 (9.59%) had severe elevation. Patients who showed a noTable rise in CRP levels had longer stays in the paediatric intensive care unit, with an average duration of 5.86±1.77 days. Furthermore, these patients exhibited elevated levels of total leukocyte count (TLC), with an average of 19.47±6.28. In addition, they exhibited a higher reliance on oxygen, with an average duration of 5.57±1.90 days. These individuals also necessitated extended durations of antibiotic treatment, with an average length of 11.86±4.95 days (Table 3).When a graph was plotted between CRP levels and ICU stay, O_2 requirement, TLC, and antibiotic treatment duration of broncho pneumonic patients, a direct relation was observed as dshown in graph 1 below. It means raised CRP not only increases ICU stay, but also increased TLC, duration of antibiotic treatment, and O_2 requirement in broncho pneumonic children.

Discussion

This study examines the association between increased levels of C-reactive protein (CRP) and extended hospitalizations in the paediatric intensive care unit among children with bronchopneumonia at Ghurki Trust Teaching Hospital in Lahore. During a six-month study including 82 patients, it was discovered that elevated levels of CRP are strongly linked to longer hospitalizations in the paediatric intensive care unit, increased need for oxygen, higher total leukocyte count (TLC), and longer durations of antibiotic treatment (Table 3). The study highlights the significance of CRP as an indicator for the seriousness of bronchopneumonia and its potential function in directing clinical treatment.

Bronchopneumonia is prevalent in children, particularly newborns and young children due to developing respiratory

Table 2: Clinical characteristics of broncho pneumonic children

Sr, No.	Groups	Patients with raised CRP (n=73)	Cough (n=60)	Fever (n=63)	Diarrhoea (n=31)	Pleural Effusion (n=51)
01	Normal	09	00	00	00	00
02	Mild	08	05 (62.50%)	07 (87.5%)	02 (25%)	03 (37.5%)
03	Moderate	36	31 (86.11%)	31 (86.11%)	11 (30.56%)	27 (75%)
04	Marked	22	18 (81.82%)	18 (81.82%)	14 (63.64%)	15 (68.18%)
05	Severe	07	06 (85.71%)	07 (100%)	04 (57.14%)	06 (85.71%)
06	Total	82	60	63	31	51

system, variation in pathogens and underdeveloped immune system lower levels of antibodies, and impaired function of respiratory epithelial cell cilia. Consequently, this can lead to a swift progression of diseases.[14] Hence, timely detection plays a crucial role in the medical administration of bronchopneumonia. The conventional approach to diagnosing pneumonia involves identifying a fresh infiltration on chest radiographs and recently developed respiratory signs and symptoms.[15] Primary care physicians depend exclusively on the patient's health record and physical examination for diagnosis. Empirical evidence has shown that assessing clinical symptoms and signs is inadequate for diagnosing pneumonia. Several variables need to be considered to forecast the progression of severe pneumonia. Prior research has examined the diagnostic importance of pneumonia. At the same time, further studies have suggested that pneumonia is linked to the severity of the disease and the likelihood of death in patients who are hospitalized with pneumonia.[16] Nevertheless, there has been no reported correlation between CRP and severe pneumonia, as far as we know. However, this study investigated that mild, moderate, marked and severely increased levels of CRP can enlengthen number of ICU admission days. The study findings revealed that individuals with severe pneumonia had greater CRP levels than those with mild pneumonia. This suggests that the continuous increase in serum CRP levels may be linked to the patient's health and the progression of severe pneumonia. One of the studies demonstrated that measuring CRP levels could provide more insight into distinguishing pneumonia from other lower respiratory tract infections.[17] Elevated CRP levels demonstrate positive predictive values (PPVs) of up to 97%. The high positive predictive values suggest that it may be reasonable to initiate therapy for pneumonia in children with elevated levels without waiting for the results of chest radiography.[18] This study had a total of 82 individuals diagnosed with bronchopneumonia, with 45 being male (54.88%) and 37 being female (45.12%). The average

Table 3: Mean values of dependant variables based on independent CRP variable

Sr. No.	CRP Category	Patients	ICU Stay (Mean ±SD)	TLC	O_2 dependency (days)	Days of Antibiotic Treatment (Mean±SD)	p value
1	Normal	09	2.00±2.35	9.08±3.79	1.56±1.81	7.78±1.79	0.12
2	Mild	08	1.88±3.48	11.05±2.75	2.14±3.67	7.50±3.12	0.37
3	Moderate	36	3.19±2.47	12.04±4.10	2.97±2.40	9.36±3.56	0.31
4	Marked	22	4.91±3.69	14.43±5.61	4.86±3.63	9.77±4.29	0.41
5	Severe	07	5.86±1.77	19.47±6.28	5.57±1.90	11.86±4.95	0.11
	Total (excluding normal)	73 (89.02%)	3.82±3.12	13.36±5.18	3.72±3.07	9.52±3.94	0.04

age of patients was 10.06±11.52 months, and the average weight was 7.45±3.47 kg (Table 1). The male-to-female ratio was 1.2:1, suggesting a somewhat greater occurrence in men. The considerable variation in average age (10.06±11.52 months) indicates that bronchopneumonia can affect a wide range of ages among children. The average weight of 7.45 kg accounts for the presence of newborns and young children. Nair et al., 2013 also reports a greater prevalence of respiratory illnesses in male children. The study conducted by Nair et al. also emphasizes the susceptibility of newborns and young children to respiratory infections as a result of their growing immune systems and respiratory anatomy.[19] Amongst 73

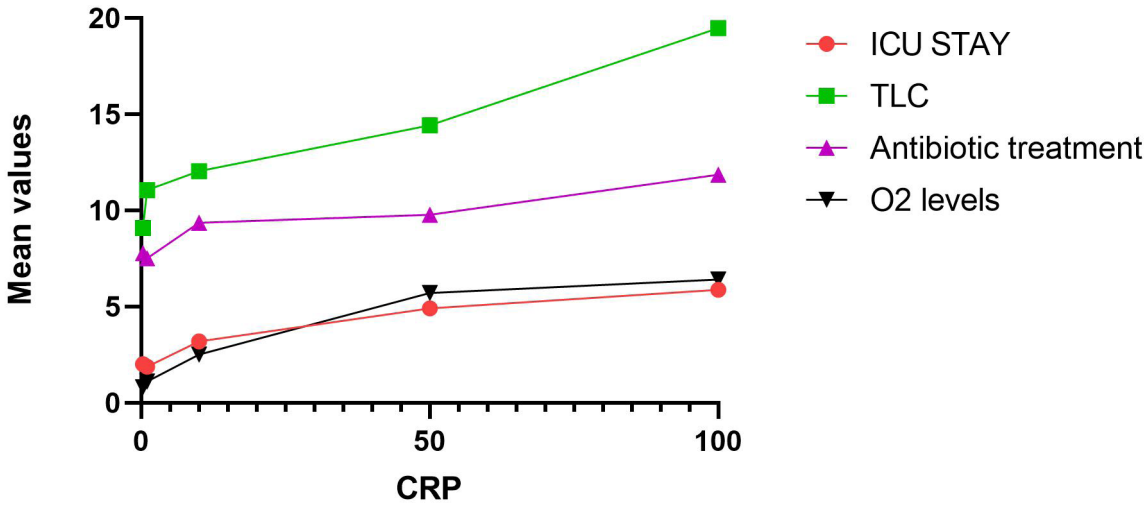

Figure 1: A direct relation observed between CRP levels and ICU stay, TLC, Antibiotic treatment, O_2 levels of mild, moderate, and severe patients

patients, 82.19% (60 patients) experienced cough, 86.30% (63 patients) had fever, 42.47% (31 patients) had diarrhoea, and 69.86% (51 patients) had pleural effusion (Table 2). The prevalence of these symptoms differed throughout the CRP categories (mild, moderate, pronounced, severe). The elevated occurrence of cough and fever aligns with the characteristic manifestation of bronchopneumonia. Diarrhoea was infrequent but noTable, and a considerable percentage of individuals exhibited pleural effusion, suggesting serious respiratory impairment. The association between symptoms and elevated CRP levels underscores the function of CRP as an indicator of the seriousness of the disease. Comparable findings observed by Holter et al. in 2015 demonstrated that severe pneumonia cases commonly exhibit symptoms such as cough, fever, and other clinical indications.[20] Holter et al. also discovered a positive correlation between these symptoms and elevated levels of inflammatory markers, such as CRP, which suggests the presence of a more severe form of the disease.[20] The study identified a noTable increase in CRP levels in 73 out of 82 patients, which accounts for 89.02% of the total. Patients exhibiting a significant increase in CRP levels experienced extended stays in the paediatric intensive care unit lasting an average of 5.86±1.77 days. These patients also had higher TLC levels, averaging at 19.47±6.28. Additionally, they displayed a greater dependency on oxygen, with an average duration of 5.57±1.90 days. Furthermore, these patients required longer courses of antibiotic therapy, lasting an average of 11.86±4.95 days (Table 3). An important connection ($p<0.04$) was found between CRP levels and the dependent variables mentioned.

The data indicates a correlation between elevated CRP levels and the severity of the disease, as seen by longer stays in the intensive care unit, greater total leukocyte count, increased need for oxygen, and prolonged use of antibiotics. This suggests that CRP can function as a dependable indicator for forecasting the seriousness of an illness and determining the appropriate level of treatment. Comparable findings may be seen in the studies conducted by Koster et al. in 2013,[21] as well as in the research conducted by Pepys and Hirschfield in 2003.[22] Koster et al. established that CRP serves as a good indicator for the diagnosis and evaluation of the seriousness of lower respiratory tract infections. Pepys and Hirschfield highlighted the significance of CRP in detecting severe infection and its ability to forecast clinical outcomes.[22]

Moreover, the graph illustrates a positive correlation between elevated CRP levels and the duration of ICU stay, TLC, oxygen need, and duration of antibiotic treatment (Figure 1). The visual data presented corroborates the statistical findings, highlighting a direct correlation between elevated CRP levels and the escalating severity of bronchopneumonia, hence requiring more aggressive medical measures. The significance of CRP as a predictive tool in the management of paediatric bronchopneumonia is emphasized by this relationship. A study conducted by Schuetz et al. in 2013 found similar findings, showing a correlation between CRP levels and the severity and prognosis of systemic infections, such as respiratory infections. Schuetz et al. emphasized that CRP could serve as a valuable tool for informing treatment choices and forecasting clinical outcomes in patients with severe illnesses.[23]

Limitations of the study

The study involved a limited sample of 82 patients from a single institution, and this limits the generalizability of the results. The small sample size used in this study may not accurately reflect the larger population, which limits the capacity to apply the findings to a wider context. The study utilized CRP levels as the main biomarker for evaluating the extent of bronchopneumonia. Nevertheless, CRP levels can be altered by diverse causes that are not connected to pneumonia, hence potentially compromising the reliability of CRP as the single indicator of illness severity.The diagnosis process of bronchopneumonia may have been affected by a certain level of uncertainty, particularly when distinguishing between bacterial and viral causes, due to the dependence on clinical signs, symptoms, and radiological findings.

Conclusion

Higher CRP levels significantly result in longer ICU stays, higher O_2 requirement, raised TLC, and increased duration of antibiotic treatment in children with broncho pneumonia.

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