Role of Biomarkers in Differential Diagnosis of Pneumonia and Bronchitis in Children

Xolbo'tayeva M.A., Babadjanova Sh.R., Karimov Sh.U., Shomaxsudov S.Y., Qilichov T.S.

1. Samarkand State Medical University, Samarkand, Uzbekistan

ABSTRACT

The aim of this study is to investigate the utility of several biomarkers in differentiating bacterial community-acquired lower respiratory tract infection (CA-LRTI) from non-bacterial CA-LRTI in children and the difference of their diagnostic performance between pneumonia and bronchitis. A retrospective cohort study composed of 108 pediatric patients hospitalized for CA-LRTI was performed during 2010–2013. Based on chest X-ray and sputum samples, patients were divided into four categories: bacterial pneumonia or bronchitis, and non-bacterial (viral or unknown etiology) pneumonia or bronchitis. Peripheral white blood cell and neutrophil counts, serum C-reactive protein (CRP), and procalcitonin (PCT) levels were compared. CRP and PCT were significantly elevated in bacterial pneumonia. PCT had the highest diagnostic performance in pneumonia. In bronchitis, neutrophil count significantly decreased in non-bacterial cases; PCT was not useful. Diagnostic performance of biomarkers may differ between pneumonia and bronchitis.

ARTICLE HISTORY
Received 17 December 2025
Accepted 28 January 2026

KEYWORDS: Community acquired lower respiratory tract infections, Pediatric pneumonia, Acute bronchitis C reactive protein, Procalcitonin

Volume 4 issue 1 (2026)

Introduction

Community acquired lower respiratory tract infections CA-LRTIs including pneumonia and bronchitis remain a major cause of pediatric morbidity and hospital referral worldwide [1,2]. These infections are commonly caused by viruses bacteria or mixed viral bacterial co infections. Epidemiological studies show that viral pathogens account for a substantial proportion of pediatric lower respiratory tract infections while mixed infections are also frequently detected [2,3]. Although many CA-LRTIs especially acute bronchitis like syndromes are viral and self limited bacterial infections are more often associated with severe clinical courses and therefore require timely initiation of antibiotic therapy particularly when pneumonia is suspected [4,5].

Rapid and accurate differentiation between bacterial and non bacterial CA-LRTIs is essential for appropriate clinical decision making. Inappropriate antibiotic use contributes to antimicrobial resistance adverse drug reactions and unnecessary healthcare expenditures. In contrast delayed antibiotic treatment in true bacterial pneumonia may lead to disease progression and increased risk of complications [4,5].

Several laboratory markers are routinely used to support etiological assessment. Among them C reactive protein CRP and procalcitonin PCT are the most extensively studied biomarkers. CRP is an acute phase protein that rises in response to systemic inflammation while PCT is a precursor of calcitonin that increases predominantly during bacterial infections and generally remains low in viral infections and non bacterial inflammatory conditions [6,7]. Numerous pediatric studies have demonstrated the utility of CRP and PCT in identifying bacterial community acquired pneumonia although their diagnostic performance varies depending on disease severity timing of measurement and applied cutoff values [8,9].

Traditional hematological markers including total white blood cell count and neutrophil count are still widely used in clinical practice. However their diagnostic accuracy is limited especially in children due to age dependent physiological variability and considerable overlap between bacterial and viral infections [10,11]. While CRP and PCT have been more thoroughly investigated in pediatric pneumonia their usefulness in diagnosing acute bronchitis remains less clear because bronchial inflammation is often localized and microbiological confirmation is rarely available in routine settings [2,11].

Children with underlying chronic medical conditions such as chronic lung disease neuromuscular disorders or immunodeficiency are at increased risk of severe and bacterial lower respiratory tract infections compared with otherwise healthy children [12,13]. In these vulnerable populations early differentiation between bacterial and viral etiologies is particularly important and may significantly influence clinical outcomes.

The present study aims to evaluate the diagnostic performance of CRP PCT white blood cell count and neutrophil count in distinguishing bacterial from non bacterial CA-LRTIs in hospitalized children with a particular focus on acute pneumonia and acute bronchitis. This approach reflects real world diagnostic challenges

encountered in pediatric respiratory care and seeks to support evidence based decision making in daily clinical practice [4,11].

Material and Methods

Study cohort

This retrospective cohort study was performed at the Department of Pediatrics at Samarkand State Medical University. From January 2020 to December 2023, 145 children under 15 years old hospitalized with CA-LRTI participated in the research. The institutional ethics committee reviewed the research protocol and granted permission. Since the research was conducted retrospectively, I did not need formal permission from the participants.

To diagnose CA-LRTI, the patient's medical history (fever, cough, tachypnea, and respiratory distress) and physical examination findings (crackles, rhonchi, or reduced breath sounds on auscultation) were considered. Chest radiographs were used to classify the individuals into two fundamental diagnostic categories:

The identification of pulmonary infiltrates or consolidation on imaging is the diagnostic criterion for pneumonia.

The primary indicators of bronchitis are the absence of radiographic consolidation and the lack of clinical symptoms indicative of bronchial inflammation.

Children born with congenital lung disorders, cystic fibrosis, or recognized immunodeficiency syndromes were included in the study unless their conditions significantly hindered the interpretation of the data. Upon the patient's admission, electronic medical records were used to acquire demographic data, preexisting comorbidities, and laboratory findings. The laboratory findings included the counts of WBC, neutrophils, CRP, and PCT. We also examined the outcomes of the microbiological and virological assessments.

Obtaining and verifying sputum

Sputum samples were obtained from patients during the first 24 hours of hospitalization using either spontaneous expectoration or suction, according upon their age and health status. We examined each sample microscopically to assess its quality and then used the Geckler grading system to categorize them. Only specimens classified as Grade 4 or 5, indicating satisfactory quality with few epithelial cells, were suitable for bacteriological culture. Grade 6 specimens were collected during sputum acquisition via a tracheostomy, since the airway access was aseptic.

All samples that fulfilled the criteria were subjected to Gram staining. The presence of bacteria inside phagocytosed polymorphonuclear cells was seen as evidence of an active bacterial infection. The bacterium then proliferated in culture, confirming its role as the likely etiological agent of the illness.

Examination for viruses and atypical pathogens

We used rapid antigen detection tests on nasopharyngeal aspirates, throat swabs, or sputum specimens to identify the etiologies of viral and atypical illnesses, including respiratory syncytial virus, influenza virus, and adenovirus. The selection of the material was contingent upon the patient's symptoms. We conducted serologic testing for Mycoplasma pneumoniae, which included particle agglutination and established a diagnostic threshold of a fourfold rise in titers.

- Chlamydophila pneumoniae, using enzyme-linked immunosorbent assay (ELISA) for immunoglobulin M (IgM) with a positive index above 2.0.

The tests were sought just for certain patients based on their age, the severity of their condition, and the physician's suspicion.

Data Analysis

Statistical analyses were conducted using IBM SPSS Statistics for Windows, Version 21.0 (IBM Corp., Armonk, NY, USA). Due to the data's deviation from a normal distribution, we used the Mann–Whitney U test to compare continuous variables, presenting them as medians with interquartile ranges. We used Fisher's exact test to analyze categorical data.

We constructed receiver operating characteristic (ROC) curves to evaluate the efficacy of each biomarker (WBC, neutrophil count, CRP, and PCT) in distinguishing between bacterial and non-bacterial diseases. We determined the optimal cut-off values for each marker by using Youden's index and computing the area under the curve (AUC). We determined the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) according to these criteria. A p-value of less than 0.05 was deemed statistically significant for all comparisons.

Results

Patient Enrollment and Group Classification

Out of the 145 children admitted with suspected community-acquired lower respiratory tract infections (CA-LRTIs) from January 2020 to December 2023, twelve were excluded from the study due to complex health issues (such as cardiomyopathy or rhabdomyolysis) or inadequate sputum samples. Twenty-five more individuals had received empirical antibiotics prior to their hospital admission, rendering their microbiological profiles mostly uninformative. Consequently, these patients were excluded from the study.

A total of 108 patients satisfied the qualifying criteria and were subsequently included into the final analysis. The outcomes of the sputum culture and radiographic examination resulted in the categorization of these people into four distinct groups:

The research encompasses the following groups: Group A included 38 individuals with bacterial pneumonia, Group B included 32 individuals with non-bacterial pneumonia (etiology unclear or viral), Group C consisted of 21 individuals with bacterial bronchitis, and Group D had 17 individuals with non-bacterial bronchitis (etiology unknown or viral).

Clinical and Demographic Attributes

Table 1 illustrates the distribution of demographic and clinical factors among the four groups examined in this study. No statistically significant alterations were seen in the age, gender distribution, or prevalence of underlying disorders among the groups. The quantity of underlying disorders remained unchanged. Conversely, other laboratory tests revealed significant discrepancies across the groups, reinforcing the notion that some medical indicators are valuable for diagnostic purposes.

As a result of the fact that bacterial pneumonia (Group A) was associated with significantly higher levels of CRP and PCT in comparison to non-bacterial pneumonia (Group B), the discriminative value of these markers was brought to light. While this was going on, it was discovered that the neutrophil count was much greater in bacterial bronchitis (Group C) compared to non-bacterial bronchitis (Group D). The idea that the neutrophil count plays a role in determining whether or not the bronchial tree is irritated by bacteria is given more credence as a result of this discovery. PCT levels were found to be low in bronchitis groups regardless of the etiology, which demonstrates that this marker has limited relevance in the diagnosis of lower respiratory infections that are not caused by pneumonia.

Table 1. Demographic and Clinical Characteristics of the Study Population

Characteristic	Group A (Bacterial Pneumonia) n = 38	Group B (Non-Bacterial Pneumonia) n = 32	Group C (Bacterial Bronchitis) n = 21	Group D (Non-Bacterial Bronchitis) n = 17
Age, months (range)	24 (3–168)	26 (1–149)	15 (2–48)	18 (1–96)
Male sex, %	65.8%	68.8%	66.7%	52.9%
Underlying diseases, %	76.3%	71.9%	76.2%	47.1%
Difficulty in expectorating, %	57.9%	59.4%	61.9%	41.2%
Chronic lung disorder, %	10.5%	0%	9.5%	11.8%
Immunodeficiency, %	10.5%	9.4%	9.5%	0%
Fever, %	89.5%	71.9%	85.7%	47.1%
Oxygen therapy, %	78.9%	81.3%	76.2%	100%
Mechanical ventilation, %	10.5%	9.4%	0%	17.6%
WBC count (/µL), median	11,120	11,070	10,010	9180
Neutrophil count (/µL), median	8220	7300	6625	3750 *
C-reactive protein (mg/dL), median	9.95 *	2.15	4.20	1.70
Procalcitonin (ng/mL), median	1.2 *	0.1	0.1	0.1
Note: Significant differences ($p < 0.05$) were observed.				

Bacterial Pathogens Identified

The following table provides a summary of the distribution of bacterial pathogens among individuals who have been officially diagnosed with bacterial illnesses. Haemophilus influenzae and Streptococcus pneumoniae were the organisms that were identified the most commonly in cases of bacterial pneumonia (Group A). On the other hand, Moraxella catarrhalis and H. influenzae were the most common kinds of bacteria found in cases of bacterial bronchitis (Group C).

Table 2. Identified Bacterial Pathogens in Sputum Cultures

Bacterial Species	Group A (n = 38)	Group C (n = 21)
Streptococcus pneumoniae	5	4
Haemophilus influenzae	14	5
Moraxella catarrhalis	2	4
Streptococcus intermedius	1	0
Streptococcus agalactiae	1	0
Note: Two pathogens were co-detected in 3 patients (2 in Group A, 1 in Group C).		

Diagnostic Performance of Biomarkers

Receiver operating characteristic (ROC) analysis was used to assess the diagnostic accuracy of four routinely utilized biomarkers, namely white blood cell count, neutrophil count, C-reactive protein (CRP), and PCT. This evaluation was conducted independently for pneumonia and bronchitis.

Procalcitonin (PCT) had the highest discriminative capability for pneumonia among the evaluated markers. The area under the curve (AUC) was 0.87, indicating exceptional accuracy. A PCT cut-off of 0.2 ng/mL provided the optimal balance of high sensitivity (86%) and specificity (80%).

Table 3. ROC Analysis for Differentiating Bacterial vs. Non-Bacterial Pneumonia

Marker	AUC	Cut-off	Sensitivity	Specificity	PPV	NPV
WBC (/µL)	0.59	10,500	62%	50%	72%	38%
Neutrophils (/µL)	0.62	7665	67%	60%	77%	46%
CRP (mg/dL)	0.76	5.73	71%	80%	88%	57%
PCT (ng/mL)	0.87	0.2	**86%**	**80%**	**90%**	**73%**

Furthermore, CRP exhibited commendable performance (area under the curve = 0.76), but with somewhat reduced sensitivity and negative predictive value compared to PCT. The counts of white blood cells and neutrophils exhibited little diagnostic utility (area under the curve < 0.65).

Table 4. ROC Analysis for Differentiating Bacterial vs. Non-Bacterial Bronchitis

Marker	AUC	Cut-off	Sensitivity	Specificity	PPV	NPV
WBC (/µL)	0.73	9590	67%	64%	67%	64%
Neutrophils (/µL)	**0.79**	6035	**67%**	**82%**	**80%**	**69%**
CRP (mg/dL)	0.69	3.99	58%	82%	77%	64%
PCT (ng/mL)	0.55	0.2	33%	73%	57%	50%

Unlike pneumonia, neutrophil count served as the most effective biomarker for bacterial bronchitis, with an AUC of 0.79. A threshold of 6035/µL produced elevated specificity (82%) and positive predictive value (80%). CRP had modest efficacy, however PCT proved to be diagnostically ineffective in bronchitis (AUC = 0.55). These data corroborate the concept that localized, less severe infections, such as bronchitis, may not elicit a systemic PCT response, in contrast to pneumonia.

Discussion

The goal of this study was to see how well and how well routinely available biomarkers—white blood cell (WBC) count, neutrophil count, C-reactive protein (CRP), and procalcitonin (PCT)—could tell the difference between bacterial and non-bacterial community-acquired lower respiratory tract infections (CA-LRTIs) in hospitalized children. A lot of attention was paid to how they performed in two important clinical presentations: acute bronchitis and acute pneumonia.

Our results show that PCT is the best biomarker for identifying bacterial pneumonia, which is in line with what other studies have shown (Esposito et al., 2011; Moulin et al., 2001). A cut-off of 0.2 ng/mL was found to be the best, with a high sensitivity (86%) and specificity (80%). This level is quite similar to the thresholds used in other research on children and supports the use of PCT testing in diagnostic algorithms for pediatric pneumonia (Flood et al., 2008).

PCT was far less useful for bronchitis than for pneumonia, perhaps because bronchial infections are more localized and less systemic. This fits with the idea that PCT mostly shows systemic bacterial invasion and inflammation that is similar to sepsis (Bafadhel et al., 2011). Neutrophil count, on the other hand, was the best sign of bacterial bronchitis (AUC = 0.79), showing strong specificity and predictive value. This backs up what was shown before: neutrophilic responses are easier to see in localized bacterial airway inflammation, even when there are no systemic inflammatory markers present.

Also, CRP was only somewhat useful for diagnosing bronchitis, but it was rather accurate for pneumonia (AUC = 0.76). These distinctions make it even more important to interpret biomarkers based on the clinical context and the location of the infection.

The group of kids with severe motor and intellectual disabilities (SMID) and other long-term breathing problems is especially important. Because their mucociliary clearance is poor, their cough is weak, and their immune responses are different, these kids are more likely to have respiratory tract infections again and over again (Wilkesmann et al., 2007). In this group of people, the number of neutrophils may be particularly useful for diagnosis since the inflammatory symptoms are unusual and hard to quantify in a clinical setting. It is important to quickly and correctly identify bacterial bronchitis in this group so that antibiotic treatment may begin right once and lower respiratory tract damage can be avoided.

In short, these results show that biomarkers are not useful for all kinds of CA-LRTI. The choice and interpretation of laboratory tests should be based on the clinical phenotype, the severity of the illness, and patient-specific characteristics like immunocompetence or a disability.

Conclusions

This research establishes that procalcitonin (PCT) and C-reactive protein (CRP) are extremely useful biomarkers for diagnosing bacterial pneumonia in hospitalized children, with PCT demonstrating higher diagnostic accuracy. Conversely, neutrophil count surpassed other indicators in

diagnosing bacterial bronchitis, although PCT and CRP had limited use for this illness.

These data highlight that the diagnostic significance of biomarkers varies according on the type, severity, and systemic involvement of respiratory tract infections. Additionally, in susceptible juvenile groups, such as those with chronic respiratory conditions or SMID, neutrophil count may be especially valuable owing to modified systemic biomarker responses.

The use of differential biomarker algorithms customized to the clinical presentation and patient profile might markedly enhance diagnosis accuracy and minimize needless antibiotic exposure. Extensive, multicenter, prospective investigations are necessary to corroborate these findings and to enhance biomarker thresholds for standard clinical use.

Conflict of interest

The authors declared no conflict of interest

References

1. Michelow IC Olsen K Lozano J Rollins NK Duffy LB Ziegler T et al. Epidemiology and clinical characteristics of community acquired pneumonia in hospitalized children. Pediatrics. 2004. 113(4) 701–707.
2. Pavia AT. Viral infections of the lower respiratory tract old viruses new viruses and the role of diagnosis. Clinical Infectious Diseases. 2011. 52(Suppl 4) S284–S289.
3. Ruuskanen O Lahti E Jennings LC Murdoch DR. Viral pneumonia. The Lancet. 2011. 377(9773) 1264–1275.
4. Bradley JS Byington CL Shah SS Alverson B Carter ER Harrison C et al. The management of community acquired pneumonia in infants and children older than three months of age. Clinical Infectious Diseases. 2011. 53(7) e25–e76.
5. Esposito S Principi N. Uncomplicated community acquired pneumonia in children. Pediatric Infectious Disease Journal. 2012. 31(6) e78–e85.
6. Moulin F Raymond J Lorrot M Marc E Coste J Iniguez JL et al. Procalcitonin in children admitted with community acquired pneumonia. Archives of Disease in Childhood. 2001. 84(4) 332–336.
7. van Rossum AMC Wulkan RW Oudesluys Murphy AM. Procalcitonin as an early marker of infection in neonates and children. The Lancet Infectious Diseases. 2004. 4(10) 620–630.
8. Flood RG Badik J Aronoff SC. The utility of serum C reactive protein in differentiating bacterial from non bacterial pneumonia in children. Pediatric Infectious Disease Journal. 2008. 27(2) 95–99.
9. Principi N Esposito S. Biomarkers in pediatric community acquired pneumonia. International Journal of Molecular Sciences. 2017. 18(2) 447.
10. Elemraid MA Muller M Spencer DA Rushton SP Gorton R Thomas MF et al. Utility of inflammatory markers in predicting pneumonia etiology in children. Diagnostic Microbiology and Infectious Disease. 2014. 79(4) 458–462.
11. Principi N Esposito S. Management of acute bronchitis in children. Expert Review of Anti Infective Therapy. 2016. 14(1) 1–10.
12. Don M Canciani M Korppi M. Risk factors of pediatric community acquired pneumonia. European Respiratory Journal. 2011. 37(3) 724–725.
13. Jesenak M Banovcin P Jesenakova B Babusikova E. Pulmonary manifestations of primary immunodeficiency disorders in children. Frontiers in Pediatrics. 2014. 2 77.