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# A retrospective observational study of biomarker levels and severity assessment in pediatric community-acquired pneumonia

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**Abstract**

Multiple studies have investigated the role of biomarkers in predicting pneumonia severity in adults but minimal conclusive research exists for children. This study aimed to determine if the following biomarker levels, collected within 72 hours of hospital arrival: white blood cell count (WBC), platelet count, C-reactive protein (CRP), procalcitonin (PCT), neutrophil-lymphocyte ratio, neutrophil count, or band count associated with community-associated pneumonia (CAP) severity in children.

**Methods:** A retrospective chart review was conducted on children (aged 60 days to 18 years) diagnosed with CAP, and admitted to a regional, tertiary hospital (Charleston, WV, USA) for 3 years (2015–2018). Patients were stratified into 2 severity cohorts, mild (no ICU care), and moderate/severe (required ICU care). Biomarker values were then compared between the severity cohorts and area under the curve (AUC), and cut-off values and performance characteristics were calculated.

**Results:** A total of 108 patients met inclusion criteria with 46% having moderate/severe CAP. Elevated levels of CRP (51.7 mg/L in mild vs. 104.8 mg/L in moderate/severe, $P = .003$, PCT (0.29 ng/ml in mild vs. 4.02 ng/mL in moderate/severe, $P = .001$) and band counts (8% in mild vs. 15% moderate/severe, $P = .009$) were associated with increased pneumonia severity. In predicting moderate/severe CAP, PCT had the highest AUC of 0.77 ($P = .001$) followed by bands AUC of 0.69 ($P = .009$) and CRP AUC of 0.67 ($P = .003$). Cut-off for PCT of 0.55 ng/mL had a sensitivity of 83% and a specificity of 65%. Cut-off level of 53.1 mg/L for CRP had a sensitivity of 79% and specificity of 52%. Cut off level of 12.5% bands had a sensitivity of 61% and specificity of 71%. In a multivariable model controlled for patient demographics and other biomarker levels, only PCT levels significantly predicted moderate/severe CAP (adjusted odds ratio: 1.40 [95% CI, 1.14–1.73], $P = .002$).

**Conclusion:** Biomarkers, in particular PCT, obtained early in hospitalization may perform as possible predictors for CAP severity in children and be beneficial in guiding CAP management. However, biomarkers in pneumonia should not drive severity assessment or patient management independent of clinical presentation.

**Abbreviations:** AUC = area under curve, CAP = community acquired pneumonia, CI = confidence interval, CRP = C reactive protein, ED = emergency department, NLR = neutrophil to lymphocyte ratio, NPV = negative predictive value, PCT = procalcitonin, PPV = positive predictive value, WBC = white blood cell count.

**Keywords:** C-reactive protein, procalcitonin, band count, pneumonia

## 1. Introduction

Community-acquired pneumonia (CAP) is the leading cause of mortality in children worldwide[1] and remains one of the most common causes of pediatric hospitalization in the United States.[2] The percentage of children hospitalized for CAP after presenting to the Emergency Department (ED) ranges widely, from 19% to 69%.[3] CAP severity variation in hospitalized patients suggests a lack of standardized tools for predicting prognosis. Our current study aimed to determine if laboratory values obtained early after hospital presentation are associated with pneumonia severity. Early identification of poor prognosis of children with pneumonia could help guide patient management in terms of inpatient versus ICU admission, appropriate referrals, and choice of antibiotic therapy.

CAP presenting clinical symptoms can have low specificity for diagnosis and the need for antibiotics.[4] In adults, scoring systems to estimate pneumonia severity and prognosis include CURB-65 (confusion, uremia, respiratory rate, blood pressure, age > 65), PSI (pneumonia severity index), and SOAR (systolic

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blood pressure, oxygenation, age, and respiratory rate). The PIRO (predisposition, insult, response, and organ dysfunction) score is the CAP prognosis sole scoring system developed in adults and then later examined in children, albeit in a single pediatric study.[5] Biomarkers can be used in deciding the need for antibiotic therapy, prognosis, and follow-up treatment for pneumonia.[6] Research has been performed in adults regarding CAP prognostic models and biomarkers. However, additional research is needed to define the role of biomarkers in pediatrics CAP prognosis and management as previous research is inconclusive and contradictory.

We examined if the regularly obtained biomarkers of white blood cell count (WBC), platelet count, C-reactive protein (CRP), procalcitonin (PCT), neutrophil-lymphocyte ratio (NLR), neutrophil count, and band count are associated with CAP severity in children independent of signs and symptoms.

## 2. Methods

The study was a case-control study utilizing a retrospective chart review of patients (aged 60 days to 18 years old) diagnosed with CAP and admitted to Charleston Area Medical Center Women and Children's Hospital (Charleston, WV) between October 1, 2015, and October 1, 2018. CAP was defined as meeting each of the following 3 criteria: (1) Fever of more than 38° C, (2) Documented acute respiratory symptoms including cough, dyspnea, tachypnea, pleuritic chest pain, and (3) Radiographic evidence of pneumonia (lobar consolidation or pleural effusion or new pulmonary infiltrate).[2,5] Exclusion criteria included discharge from ED without inpatient admission, diagnosis of bronchiolitis, diagnosis of any other infection different from pneumonia at presentation including ear infections, and chronic conditions including immunosuppression, cystic fibrosis, cardiac diseases, renal diseases, sickle cell disease, tuberculosis, or diagnosis of hospital-acquired pneumonia. Hospital-acquired pneumonia was defined as pneumonia occurring ≥ 48 hours after admission to the hospital that was not present at the time of admission.[7] Records for inclusion were initially identified using ICD-10 discharge diagnosis codes for pneumonia with chart review confirming CAP diagnosis.

Patients were stratified into cohorts based on CAP severity similar to Williams et al.[3] The severe CAP was defined as requiring mechanical ventilation, shock requiring vasoactive medications (e.g., dopamine, norepinephrine, vasopressin), Glasgow coma scale (GCS) <11, or altered mental status, hospitalizations of ≥10 days, pleural effusion, or death. The moderate CAP was defined as requiring intensive care unit (ICU) admission for any length of time, with severe and moderate severities combined into a single cohort for analysis. The mild CAP was defined as patients requiring non-ICU hospitalization.

Biomarkers of interest included the following when obtained within 72 hours of ED/hospital arrival: WBC count (minimal and maximal levels), platelet count (minimal and maximal levels), neutrophil count (maximal level), CRP (maximal level), PCT (maximal level), NLR (maximal level), and band counts (maximal level). Thus, if labs were obtained more than once within the initial 72 hours of hospitalization, the highest value was used for WBC, platelets, neutrophils, CRP, PCT, NLR, and bands. The lowest value was also obtained for WBC and platelet counts. The median time of lab draws used in data analysis was 8 hours (interquartile range: 1–20 hours) post ED arrival. Patient demographics and hospital length of stay were also obtained via chart review. All aspects of the study were reviewed and approved by the CAMC/West Virginia University – Charleston Division Institutional Review Board. Waivers of consent and assent were requested from and approved by the Institutional Review Board for this retrospective study due to no more than minimal risk to the subjects and the research could not be feasibly conducted without the requested waivers.

Basic descriptive statistics were performed on each data element. Categorical data were summarized as numbers and percentages. Median patient age and biomarker levels are reported with interquartile ranges (IQR), that is, 25th and 75th percentiles due to age values skewing to the left (high proportion of patients being under the age of 2 years), while biomarkers skewed to the right due to large, outlying values. Length of stays are reported as median with IQR with minimal, maximal number of days due to data not being normally distributed. Data distribution was examined via histogram creation, skewness and kurtosis statistics, and Kolmogorov–Smirnov $Z$ testing. Demographic characteristics and laboratory values were compared between the 2 CAP severity cohorts (mild vs. moderate/severe). Comparisons were performed using Chi-square for the categorical variable of sex and Mann–Whitney $U$ statistical tests were employed to compare continuous variables of age and biomarker levels due to data not being normally distributed. Binomial logistical models examining biomarkers' ability to predict moderate/severe CAP were adjusted for patient age and sex. Biomarker concentrations were logbase-2 transformed for modeling due to being right-skewed, similar to analyses reported in Florin at al.[8] Odds ratios (ORs) were thus interpreted as the change in odds for a doubling of each biomarker concentration.

Diagnostic performances of each biomarker for prediction of moderate/severe CAP were evaluated via receiver operating characteristic (ROC) curves and areas under the curve (AUC) with 95% confidence intervals (CIs). For the minimal WBC and platelet variables, smaller values were tested for predicting severe/moderate CAP while for the other biomarkers increasing values were examined. AUC values were interpreted as AUC values of 0.5–0.6 having no discrimination (unable to distinguish moderate/severe CAP from mild CAP), 0.6–0.7 poor discrimination, 0.7–0.8 as acceptable, 0.8–0.9 as excellent, and more than 0.9 as having outstanding discrimination.[9]

For "optimal" cut-point selection, we identified the biomarker value corresponding to the maximal Youden index, maximizing the difference between true positive rates and false positive rates among all the possible cut-point values. Sensitivity, specificity, positive predictive value (PPV), negative-predictive value (NPV) and accuracy ([True Positive + True Negative]/ [True Positive + True Negative + False Positive + False Negative]) was calculated for the optimal cut-point for each biomarker. Statistical significance was defined as $P < .05$. Data analysis was performed using IBM SPSS 19 (IBM, Chicago, IL, USA).

## 3. Results

A total of 108 patients were included in the study and of these 53 were male (49%). The median age at admission was 4 years, IQR 1-11 years, range: 62 days to 17 years, with 39 (36%) children less than 2 years of age. The median hospital length of stay was 3.5 days, IQR 2–8 days, range: 1–55 days, and for patients requiring intensive care the median ICU length of stay was 8 days, IQR: 5–14 days, range: 2–55 days. There were no deaths during CAP admissions. The patients were stratified by CAP severity with 58 patients (54%) in the mild CAP cohort versus 50 patients (46%) in the moderate/severe CAP cohort (10 patients with moderate CAP plus 40 patients with severe CAP).

Table 1 shows patient demographics and biomarker levels stratified by CAP severity. The age of patients and the sex distribution did not differ between the 2 severity levels. Overall CRP, PCT, and band count median values were found to be significantly higher in the moderate/severe cases of pneumonia compared to mild cases (Table 1). The median CRP value was elevated in patients with moderate/severe CAP (104.75 mg/L) as compared to 51.65 mg/L in mild CAP ($P = .003$). PCT showed a similar trend with higher levels associated with moderate/severe CAP, with a median value of 0.29 ng/mL in mild versus 4.02 ng/mL in the moderate/severe CAP cohort ($P \leq .001$).

Median percentage of band count were 8.0% in mild CAP compared to 15% in moderate/severe cohort ($P$ = .009). Maximal WBC values were significantly higher in patients with moderate/severe CAP compared to levels in patients with mild CAP ($P$ = .04), however, minimal WBC levels did not differ between mild and moderate/severe CAP ($P$ = .48). Minimal platelet values were lower in patients with moderate/severe CAP compared to mild CAP ($P$ = .01) but maximal platelet counts did not differ between CAP severities ($P$ = .32). The nadir values for neutrophil and NLR levels did not significantly differ between mild and moderate/severe CAP.

In analyses examining biomarkers' ability to predict moderate/severe CAP, each biomarker was examined independently while adjusted for age and sex. Minimal WBC count, maximal WBC count, maximal platelet count, neutrophil count, NLR, and band percentage failed to be associated with CAP severity (Table 2). However, increasing PCT levels significantly associated with moderate/severe CAP severity (adjusted odds ratio (aOR) 1.45: [95% CI: 1.22–1.72], $P$ < .01) as did CRP (1.35 [1.06–1.72], $P$ = .01) while increasing minimal platelets counts had an aOR of 0.42 [0.22–0.80], $P$ = .01 in the prediction of moderate/severe CAP. When the 3 significant biomarkers were entered into the same model and adjusted for age and sex, only PCT levels significantly predicted moderate/severe CAP (aOR 1.40 [95% CI, 1.14–1.73], $P$ = .002).

Overall, PCT had the highest AUC of 0.77 (95% CI: 0.68–0.86) for predicting moderate/severe CAP (Table 3). The biomarkers of band counts (AUC = 0.690), CRP (AUC = 0.672), and minimal platelets (AUC = 0.644) exhibited statistically significant but poor discrimination for moderate/severe CAP. The optimal cutoff value of 0.55 ng/mL for PCT had a sensitivity of 83% and specificity of 65% with PPV 69% and NPV 81% (Table 4). For band count, the optimal cut-off value of 12.5% was determined to have a sensitivity of 61% and specificity of 71% while the optimal cut-off value of 53.1 mg/L for CRP had a sensitivity of 79% and specificity of 52%. The other biomarkers were unable to discriminate moderate/severe CAP from mild pneumonia.

## 4. Discussion

Major decisions regarding CAP management depend on disease severity. Our study examined frequently collected biomarkers' association with increased CAP severity. PCT, followed by CRP and band count had the highest accuracy in for identify moderate/severe CAP severity. Only PCT predicted moderate/severe CAP severity in a multivariable model.

The use of standardized scales predicting CAP severity would be ideal to guide disease management and assist decision-making. The lack of pediatric standardized scales leads to wide severity variation in patients admitted for CAP

**Table 1**

**Comparisons of patient demographics and biomarkers in mild versus moderate/severe community-acquired pneumonia.**

| | Mild n = 58 | Moderate/severe n = 50 | *P* value |
|---|---|---|---|
| Patient demographics | | | |
| Age, y, median (IQR) | 4.0 (1.0–9.5) | 4.0 (1.0–13) | .98 |
| Male Gender, n (%) | 29 (50%) | 24 (48%) | .84 |
| Biomarkers, median (IQR) | | | |
| WBC min, × $10^9$/L | 11.30 (9.20–14.25) | 11.20 (7.38–14.35) | .48 |
| WBC max, × $10^9$/L | 13.10 (10.10–21.20) | 17.35 (13.78–23.20) | .04 |
| Platelet Min,/mcL | 315,000 (242,000–423,000) | 236,000 (145,250–345,250) | .01 |
| Platelet Max,/mcL | 340,000 (260,500–459,500) | 339,000 (217,250–438,000) | .32 |
| CRP, mg/L | 51.7 (16.4–107.5) | 104.8 (55.9–213.3) | .003 |
| PCT, ng/mL | 0.29 (0.06–2.41) | 4.02 (0.73–9.42) | <.001 |
| Neutrophil Count,/$mm^3$ | 8352 (6062–13258) | 11686 (6361–16775) | .15 |
| NLR | 3.68 (2.03–7.40) | 4.82 (2.47–9.96) | .27 |
| Bands, % | 8.0 (1.5–15.3) | 15.0 (6.0–26.0) | .01 |

**Table 2**

**Multivariable logistic regression analysis of biomarkers and moderate/severe pediatric community-acquired pneumonia adjusted for age and sex.**

| Biomarkers was examined separately for association with moderate/severe CAP, adjusted for age and sex | | |
|---|---|---|
| **Biomarker** | **OR (95% CI)** | ***P* value** |
| WBC min, × $10^9$/L | 0.67 (0.37–1.19) | .17 |
| WBC max, × $10^9$/L | 1.47 (0.83–2.62) | .19 |
| Platelet min,/mcL | 0.42 (0.22–0.80) | .01 |
| Platelet max,/mcL | 0.69 (0.37–1.30) | .26 |
| CRP, mg/L | 1.35 (1.06–1.72) | .01 |
| PCT, ng/mL | 1.45 (1.22–1.72) | <.001 |
| Neutrophil count,/$mm^3$ | 1.23 (0.82–1.85) | .32 |
| NLR | 1.08 (0.84–1.37) | .55 |
| Bands, % | 1.30 (0.86–1.96) | .21 |
| **Significant biomarkers entered into a multivariate model to predict moderate/severe CAP, adjusted for age and sex** | | |
| **Biomarker** | **OR (95% CI)** | ***P* value** |
| Age (y) | 1.01 (0.90–1.12) | .92 |
| Gender (female vs. male) | 1.27 (0.47–3.47) | .64 |
| Platelet min,/mcL | 0.56 (0.26–1.23) | .15 |
| CRP, mg/L | 0.94 (0.69–1.29) | .70 |
| PCT, ng/mL | 1.40 (1.14–1.73) | .002 |

**Table 3**

**Biomarkers' areas under the curves for predicting moderate/severe community-acquired pneumonia (CAP).**

| Biomarker | AUC | 95% confidence interval | Std. error | *P* value |
|---|---|---|---|---|
| WBC min | 0.540 | 0.426–0.654 | 0.058 | .477 |
| WBC max | 0.616 | 0.506–0.726 | 0.056 | .039 |
| Platelet min | 0.644 | 0.537–0.752 | 0.055 | .010 |
| Platelet max | 0.556 | 0.445–0.667 | 0.057 | .316 |
| CRP | 0.672 | 0.565–0.779 | 0.055 | .003 |
| PCT | 0.769 | 0.675–0.862 | 0.048 | <.001 |
| Neutrophil | 0.583 | 0.470–0.695 | 0.057 | .146 |
| NLR | 0.562 | 0.452–0.673 | 0.056 | .271 |
| Bands | 0.690 | 0.560–0.819 | 0.066 | .009 |

**Table 4**

**Cut-off values and performance characteristics for examined biomarkers.**

| Biomarker | Cut off | Sensitivity | Specificity | PPV | NPV | Accuracy |
|---|---|---|---|---|---|---|
| WBC min | 12.25 $10^9$/L | 44% | 68% | 55% | 58% | 57% |
| WBC max | 15.05 $10^9$/L | 68% | 65% | 63% | 70% | 66% |
| Platelet min | 496,500/mcL | 18% | 86% | 53% | 54% | 54% |
| Platelet max | 564,500/mcL | 18% | 88% | 56% | 55% | 55% |
| CRP | 53.10 mg/L | 79% | 52 % | 60% | 73% | 65% |
| PCT | 0.555 ng/mL | 83% | 65% | 69% | 81% | 74% |
| Neutrophil | 10446/$mm^3$ | 61% | 66% | 61% | 66% | 64% |
| NLR | 5.43 | 48% | 67% | 57% | 59% | 58% |
| Bands | 12.5% | 61% | 71% | 81% | 47% | 64% |

management. The PIRO scale developed in adults was examined in children with the modified scale including the factors of age less than 6 months, hypoxia <90%, hypotension, bacteremia, responses like multilobar or complicated pneumonia, and organ dysfunctions like kidney failure, liver failure, and acute respiratory distress syndrome as predictors of increased CAP severity. Araya et al found that PIRO scores positively correlated with mortality rates in children with CAP and suggested the PIRO scale could be used to identify patients needing ICU management.[5] However, the authors did not examine outcomes besides mortality. Pediatric mortality from pneumonia is less than 1% in the United States[2] so future research should test the PIRO scale's ability in predicting CAP outcomes besides mortality. William et al proposed 3 models to predict the severity of pneumonia in children (with 9 to 20 predictors), with models not including laboratory values besides WBC count. Resultant concordance indices across the models were in the modest-to-good range of 0.78–0.81.[3] Thus, the inclusion of biomarkers may increase the scales' ability to identify severe pediatric CAP. Additional studies are needed to create and validate pediatric CAP prognostic scales similar to those employed in the adult population.

One of the challenges in CAP management is that presenting clinical signs and symptoms can have low specificity for diagnosis and need for antibiotics.[4] Clinical parameters can be subjective and are dependent on clinicians' ability to perform assessments.[10] Biomarkers can provide reliable information regarding the host's response to an infection and have the benefit of being measured accurately and reproducibly from serum. Stratification and identification of patients at risk for severe CAP are important for prompt and optimal treatment. Biomarkers in pediatric CAP could objectively diagnose the infection type (bacterial or viral), identify patients at risk for a severe disease course, and to monitor clinical response to antibiotic administration. Thus, we aimed to examine biomarkers' ability and accuracy in identifying moderate/severe pediatric CAP independent of clinical presentation.

Results from studies investigating biomarkers' ability to predict pediatric CAP prognosis have been contradictory depending upon the population and outcome examined. Studies are increasingly showing a role for biomarkers, especially PCT for CAP management and prognosis,[11] supporting our finding of PCT being able to assist in identifying children at risk for moderate/severe CAP. However, published findings are inconclusive on how to best incorporate biomarkers into CAP clinical management, and remain poorly defined.

PCT which is undetectable in healthy people is a precursor of the hormone calcitonin produced by the thyroid gland and by the neuroendocrine cells in the lung and intestine. Infections stimulate the production of PCT, particularly during bacterial infections with PCT mRNA being upregulated.[12] PCT appears to serve as a diagnostic marker for bacterial (versus viral) pneumonia.[11–13] The relationship between PCT and CAP prognosis has been comprehensively examined in geriatric adults,[14] and Boussekey et al demonstrated PCT to have prognostic value in CAP in adults and was associated with septic shock, multiple organ failure, and mortality.[15] However, in pediatric studies, the association between PCT levels and CAP severity is less consistent. In children elevated PCT levels were associated with poorer CAP outcomes in some studies[12,13,16] while in others PCT levels failed to associate with CAP severity.[8,17]

In a recent study examining biomarkers' ability to predict CAP severity in children, Florin et al found no statistical difference in PCT or CRP levels across 4 levels of CAP severity ranging from mild (discharged from ED) to severe (intensive care, vasoactive infusions, chest drainage, severe sepsis).[8] Furthermore, none of the examined biomarkers adequately discriminated between severe and nonsevere CAP. CRP and PCT levels were significantly elevated in patients having specific indicators of severe CAP including empyema requiring chest drainage and sepsis-related vasoactive infusions. However, the occurrence of these outcomes was rare (~2% of patients) and findings should be replicated.

CRP is an acute phase reactant produced by the liver following stimulation by interleukin 6 and tumor necrosis factor-α due to injury or inflammation.[18] In adults with CAP, Chalmers et al found CRP of less than 100 mg/L associated with a low 30-day

mortality rate, decreased mechanical ventilation, and low rates of complications, describing CRP as an indicator of CAP prognosis.[19] In children, higher CRP levels correlate with bacterial etiology and severe CAP.[17,18] CRP's predictive ability for severe CAP was greatly enhanced with the incorporation of the factors of neutrophil proportion, temperature, sputum production, age, and dyspnea,[18] highlighting the beneficial effect of combining biomarkers with clinical features for prognosis prediction.

Our study found significantly higher WBC counts and lower platelet levels in patients with moderate/severe CAP; however, the biomarkers failed to adequately discriminate moderate/severe CAP from mild. WBC counts are expected to rise in infections and inflammatory conditions. In adult patients with pneumococcal pneumonia, WBC count of less than 6000 had a 5-fold higher chance of mortality while WBC counts of more than 25,000 had a 3-fold increase in mortality risk compared to patients with WBC levels between 10,000 and 25,000.[20] Arava et al in their study on children with pneumonia found that a WBC count <4000 is associated with an increased incidence of death.[5] Conversely, Williams et al's pediatric study showed poor utility of WBC count to predict CAP outcomes. However, this study did not have enough patients with leukopenia to produce meaningful analysis.[21] Platelets are being increasingly described to be involved in the immunological response to bacterial infections.[22] Ashraf et al found a significant correlation between thrombocytosis, thrombocytopenia, and mortality in adult CAP.[23] A study conducted on pediatric patients with pneumonia showed thrombocytosis in patients with lower respiratory tract infections associated with a longer duration of stay.[24] The bio-marker, NLR has been described as a predictor of bacteremia in patients with infections.[25] NLR predicted 30-day mortality in adults with CAP.[26] Literature is scarce in children looking at the utility of NLR in predicting CAP. However, NLR has been demonstrated to predict sepsis in children with pneumonia, an indirect measure of severity.[27] We did not find an association between NLR and CAP severity.

We did not examine biomarkers' ability to differentiate bacterial versus viral pneumonia as this has been examined in children previously and recently reviewed by Gunaratnam et al.[28] However, the differentiation of bacterial versus viral pneumonia could assist in decision-making for antibiotic use. An additional study limitation is that we included the highest value of biomarkers obtained in the initial 72 hours of hospital arrival in the analyses rather than initial values. At the time of patient ED/hospital presentation, clinical decisions must be made regarding patient management and required level of care, decisions that biomarkers levels could assist in guiding. However, biomarkers levels are dynamic, changing over the disease course with a single observation not providing a comprehensive picture of disease severity.[29] Ideally, we would compare results obtained using the highest values versus initial values; however, that is a future research area. Other biomarkers such as IL-6, cytokines 7, 10 11, and tumor necrosis factor Alpha (TNF-α) which may hold promise in predicting CAP severity of pneumonia[30–32] were not evaluated in the study due to not being routinely tested in the ED. Furthermore, we only included patients who were hospitalized and did not examine patients discharged directly from the ED. These limitations highlight the complexities regarding the selection of tested biomarkers, collection times, patient inclusion criteria, and the resultant heterogeneity of CAP biomarker published findings.

We found that the biomarker, PCT, is associated with disease severity in children admitted with CAP. However, while basing prognostic scoring on biomarker levels is tempting due to their objectivity and ease of collection, biomarkers independent of clinical symptoms and presentation do not appear capable of serving as prognostic tools for pediatric CAP severity. The inclusion of biomarkers in tools containing measures of clinical presentation predicting CAP prognosis in children should potentially increase the tools' sensitivity and specificity for CAP severity and is an area of future research. Biomarkers in pneumonia should be interpreted in conjunction with a clinical presentation with patient management not solely dependent on biomarkers levels.

## Author contributions

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