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RESEARCH ARTICLE

Diagnostic Value of Presepsin, CRP and Procalcitonin as Markers of Infection in Children with Community-Acquired Pneumonia

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Abstract

Introductıon: Community-acquired pneumonia (CAP) is a common pediatric infection desaese.Biomarkers such as C-reactive protein (CRP) and procalcitonin are frequently used for diagnosis and disease monitoring. Presepsin, has emerged as a novel marker involved in the early immune response to bacterial infections. This study aimed to evaluate the diagnostic value of CRP, procalcitonin, and presepsin in children with CAP.

Methods: A total of 61 children aged 1 month to 17 years were included in this prospective observational study conducted between December 5, 2018, and December 5, 2019. Thirty-seven patients with clinically and radiologically confirmed CAP who were admitted to the Pediatric Outpatient Clinics and Pediatric Emergency Department of Mersin University Faculty of Medicine Hospital, and 24 healthy age-matched children without chronic diseases were enrolled. Detailed demographic, clinical, laboratory, and radiological data were collected. Biomarker levels were measured at the time of diagnosis.

Results: The mean age of patients was 4.3±4.7 years, and 51% were female; the control group had a mean age of 9.6±4.1 years. The most common symptoms were cough (94.6%), fever (75.7%), and wheezing (32.4%). Chest radiography showed lobar pneumonia in 29.7% and interstitial/bronchial pneumonia in 70.3% of cases. CRP, procalcitonin, and presepsin levels were significantly higher in the CAP group than in controls ($p<0.001$, $p<0.001$, $p=0.001$).

Conclusion:CRP and procalcitonin remain valuable markers in diagnosing and managing pediatric CAP. Although presepsin demonstrated high specificity, its lower sensitivity limits its role as a primary diagnostic marker.It may, however, serve as a supportive tool in select clinical settings.

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Introduction

Community-acquired pneumonia (CAP) is one of the leading causes of childhood morbidity and mortality.[1] Early diagnosis and appropriate management are critical to improving outcomes. Biomarkers such as C-reactive protein (CRP) and procalcitonin (PCT) are widely used for diagnosing bacterial infections[2,3] However, their specificity is limited. Presepsin, a soluble CD14 subtype, has been proposed as a more specific biomarker for bacterial infections and sepsis.[4,5] This study evaluates the diagnostic value of presepsin in comparison with CRP and PCT in pediatric CAP cases.

Material and Methods

Research population

Our study is a prospective, observational and analytical case-control study. The study population consisted of a total of 61 participants (37 patients aged between 1 month and 18 years and 24 healthy controls) who were admitted to Mersin University Faculty of Medicine Hospital Pediatric Outpatient Clinics and Pediatric Emergency Department between 05.12.2018-05.12.2019 with complaints of fever, respiratory distress (tachypnea, retraction, cyanosis), and findings compatible with pneumonia in lung listening and chest radiography examinations. Out of a total of 51,711 patients admitted to Mersin University Faculty of Medicine Hospital Pediatric Outpatient Clinics and Pediatric Emergency Department, 246 patients were diagnosed with CAP. 47 of these patients were excluded from the study because they had chronic diseases and 16 patients refused to participate in the study. The remaining 183 participants were randomly selected.

Patients were selected based on clinical symptoms (fever, respiratory distress) and radiological findings, while those with chronic illnesses or recent hospitalization were excluded. Among the participants who met the inclusion criteria, 5 ml of blood was collected in two serum tubes before treatment and on the third day of treatment from patients diagnosed with CAP in the first evaluation. Sera of the patients were stored in a deep freezer at -80°C until the day of analysis. Serum presepsin level was determined by ELISA method using presepsin-ELISA kit (Thermo Multiscan Go Thermo Fisher Scientific Multiscan Go, Finland) according to the manufacturer's instructions. Serum CRP and PCT levels were determined on a Roche-Cobas

6000 device according to the manufacturer's instructions. The reference range was 0.01-0.50 mg/dl for CRP and 0-0.5 ng/ml for procalcitonin.[6] Sociodemographic and routine examination data were obtained from the hospital information management system. Chest radiographs were interpreted by the same clinician.

Statistical Analysis

Statistical analysis and interpretation were performed by Mersin University Department of Biostatistics Laboratory using IBM SPSS 21 program. Shapiro-Wilk test assessed whether data were normally distributed. Mann-Whitney U test compared non-normally distributed continuous variables between groups. Chi-square test was used for categorical variables, with post-hoc analysis for significant results. Wilcoxon Rank Sum test compared paired measurements (day 1 vs. day 3). Spearman correlation analyzed the relationship between biomarkers and clinical findings. ROC curve analysis assessed the diagnostic performance of CRP, PCT, and presepsin, calculating their AUC, sensitivity, and specificity. $p<0.05$ was considered statistically significant.ROC analysis was performed with MedCalc v.10.3.

Ethics

This study was conducted following the amended Helsinki Declaration and approved by our center's clinical research ethics committee (Mersin University Clinical Research Ethics Committee on 20.12.2018 with the number 923913). Informed consent was obtained from the patients and their relatives who participated in the study.

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The authors have no financial relationships relevant to this article to disclose.

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Results

The study population consisted of two groups, 37 patients diagnosed with CAP and 24 healthy controls, totaly 61 patients. The mean age of the CAP group was 4.3±4.7 years, while the control group had a mean age of 9.6±4.1 years. (Table-1). Fever (76%), cough (95%), and wheezing (32%) were the most common symptoms. Chest radiography showed lobar pneumonia in 29.7% and interstitial/bronchial pneumonia in 70.3%. The chest radiographs of the patient group are mentioned in Table-2.

Table-1. Demographic data of patient and control groups

	Patient	Control	p
Age (n (mean±sd))	37 (4.29±4.74)	24 (9.6±4.07)	<0.001
Gender			
Girl	19 (51.4%)	8 (33.3%)	0.166
Male	18 (48.6%)	16 (66.7%)	

Table-2. Findings of the patients according to chest radiography findings

Infiltration	Number	Percentage
Infiltration	31	83,8
Infiltration + ARDS	1	2,7
Infiltration + atelectasis	4	10,8
Infiltration + effusion	1	2,7
Total	37	100,0

*ARDS: Acute respiratory distress syndrome

CRP, PCT, and presepsin levels were significantly higher in CAP patients than in controls ($p<0.001$, $p<0.001$, $p=0.001$, respectively). CRP levels correlated with fever ($p=0.003$) and lobar pneumonia ($p=0.001$). CRP, procalcitonin and presepsin values were significantly higher in the patient group compared to the control group (Table-3).

Diagnostic accuracy for CAP differentiation :
-CRP: AUC=0.979, sensitivity=97.3%, specificity =91.67%
-PCT: AUC=0.834, sensitivity=97.3%, specificity =70.83%
-Presepsin: AUC=0.759, sensitivity=59.46%, specificity =91.67%

Table-3: The relationship between infection marker levels of the patient group and control groups

Token	Patient Group (n=37) Median[25P.-75P.]	Control Group (n=24) Median [25P.-75P.]	p
CRP (mg/dL)	3,54 [1,11-11,07]	0,03 [0,01-0,15]	<0,001
Procalcitonin (ng/mL)	0,31 [0,08-2,03]	0,05 [0,03-0,09]	<0,001
Presepsin (ng/mL)	1,43 [0,56-6,12]	0,69 [0,28-0,88]	0,001

Discussion and Conclusion

Pneumonia is an important cause of morbidity in children. In the follow-up process of cases, infection markers can be used for early diagnosis, evaluation of infection severity, and evaluation of response to treatment. The sensitivity of the markers varies according to the severity of the infection and whether it is systemic, local or invasive.[7-9] In our study, the variables affecting CRP, procalcitonin and presepsin levels, which are used as infection markers in children diagnosed with pneumonia, in the diagnosis and treatment follow-up of community-acquired pneumonia were examined and the relationship between each other was evaluated.

In our study, CRP, which is used in many infections; procalcitonin, which is elevated in serious infections and sepsis as well as noninfectious conditions such as infarction and aspiration pneumonia; and presepsin, which is prominent in septic shock and community-acquired pneumonia, were examined.[10-12] The mean CRP, procalcitonin and presepsin levels of the patient group were higher than those of the control group. Lee et al. found that elevated procalcitonin and CRP levels were significant in lobar pneumonia. However, they reported that elevated procalcitonin levels were more reliable in diagnosing lobar pneumonia than elevated CRP levels.[13] In our study, CRP was found to be similarly elevated in lobar pneumonia.

Noh et al. reported that procalcitonin and CRP were correlated with body temperature and an increase in body temperature may be associated with the severity of sepsis.[14] It is thought that the increase in presepsin level is also associated with an increase in body temperature.[15] In our study, it was observed that the presence/absence of fever significantly affected the difference in CRP level only on the first day.

Agnello et al. reported that CRP was more predictive than procalcitonin in children with lobar consolidation and pleural effusion and may be useful in predicting the severity of the disease and in the management of pneumonia in a study of 119 children aged 1-14 years with community-acquired pneumonia.[16] This finding is consistent with the difference in day 3 CRP levels in our study. After statistical analysis, it was observed that only the presence/absence of lobar involvement significantly affected the difference in the third day CRP level. From these findings, it was thought that CRP level among the markers of infection in patients with fever on the first day would be more useful for the follow-up of patients with a definitive diagnosis. However, presepsin and procalcitonin levels did not change according to the presen-

ce or absence of fever on the first day and remained high in all patients. Interpretation based only on CRP level on the first day of admission may result in the omission of patients who do not show symptoms. Therefore, according to the results of our study, taking presepsin and procalcitonin levels into consideration during the evaluation of patients for the diagnosis of community-acquired pneumonia may help to prevent subclinical diseases. For further clarification of this situation, it may be recommended to evaluate these markers together with other diagnostic criteria for pneumonia.

Studies have reported that presepsin levels are significantly elevated in the presence of infection. However, the elevation in presepsin levels is mostly in the first 24 hours of infection.[17] It was observed that the median presepsin level of the participants on the first day was higher than the median presepsin level of the patients on the third day. However, in some patients, day three presepsin levels were higher than day one. This may be due to increased severity of infection. The same was true for CRP and procalcitonin levels. Infection markers of all participants were evaluated on the first day and only the patient group was evaluated on the third day. In this way, it was aimed to ensure that all participants sampled on the first day were representative of the population and the second group was representative of the patient group followed up. It was thought that CRP and procalcitonin levels would give more meaningful results in the long term during pneumonia follow-up. However, considering that presepsin measurement may increase the accuracy of other infection markers and may be valuable in bacterial infections, it is thought that these markers should be evaluated together.12 In a study of 144 adult intensive care unit patients, high presepsin levels predicted progression to severe CAP and increased the diagnostic accuracy of other markers. Similarly, in our study, very high presepsin levels were found in a case of pneumonia progressing to ARDS.[18]

Using symptoms, examination and radiological imaging methods, the markers of patients diagnosed with pneumonia were examined and then the reliability of infection markers in differentiating patients from healthy patients was tested. Povoa et al. reported that CRP had 93.4% sensitivity and 86.1% specificity at the cut-off point of 8.7mg/dL in pneumonia patients.[19] Vugt et al. found that a CRP level of 3 mg/dL was the optimal cut-off point for differentiating patients and healthy individuals in community-acquired pneumonia.[20] Holm et al. found that procalcitonin was 70% sensitive at a cut-off point of 0.06 ng/ml and CRP was 73% sensitive at a cut-off point of 2 mg/dL in pneumonia.[21] Morgenthaler et al. reported the optimal cut-off point of procalcitonin as 0.05 ng/ml with 77.8% sensitivity and 98.5% specificity.[22] In a study of 300 febrile patients, 46 of whom had LRTI, Liaudat et al. found the sensitivity and specificity of procalcitonin to be 56% and 92%, respectively, and 83% and 43%, respectively, at the cut-off points of 0.5 and 0.2 ng/ml for the diagnosis of bacteremia.[23] In our study, the sensitivity, and specificity of CRP were found to be high in differentiating sick and healthy individuals. Procalcitonin had relatively lower sensitivity, and specificity at the optimal cut-off point. Presepsin, on the other hand, has a low sensitivity at the optimal cut-off point, and is insufficient to differentiate sick individuals, while its specificity is the same as CRP with 91.67%.

Liu et al. reported that the elevated presepsin levels of patients with severe community-acquired pneumonia and the presepsin levels of patients with mild and moderate community-acquired pneumonia were statistically significant. They also found that presepsin was an independent predictor of 28-day mortality in community-acquired pneumonia.[24] In our study, presepsin failed to differentiate community-acquired pneumonia compared to CRP and procalcitonin. This may be attributed to the low number of patients diagnosed with severe pneumonia. Again, in correlation with our study, Halıcı et al. reported that presepsin was useful in detecting pneumonia in adult patients presenting with COPD exacerbation, but its diagnostic accuracy was not higher than CRP and procalcitonin.[25]

This study has certain limitations. The control group consisted of generally healthy pediatric outpatients, and despite the absence of clinical symptoms, subclinical infections could not be completely ruled out, which may have influenced biomarker levels. A more thorough assessment of infection presence in controls could improve the accuracy of comparisons. Additionally, some patients presented after 3-4 days of symptoms, leading to variability in biomarker levels. Since presepsin is known to peak early in infection, delayed sampling may have influenced its diagnostic performance.

Standardizing the timing of sample collection in future studies could yield more precise results. The sample size was limited due to the high cost of presepsin testing, restricting broader applicability. Larger multicenter studies are needed to validate presepsin's role in pediatric CAP diagnosis and follow-up.

CRP is the most reliable marker for early CAP detection and disease monitoring. PCT provides additional value but is not superior to CRP. Presepsin may help identify subclinical infections, but its low sensitivity limits its standalone diagnostic use. Further large-scale studies are needed to explore the clinical utility of presepsin in pediatric infections. Combining presepsin with CRP and PCT may improve diagnostic accuracy, especially in differentiating bacterial and viral pneumonia.

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