



The Relationship of Leukocyte and Neutrophil Count, C-Reactive Protein, and Erythrocyte Sedimentation Rate With the Severity of Childhood Pneumonia Without Conjugated Pneumococcal Vaccine Use

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Abstract

Background: Pneumonia is one of the leading causes of diseases in children that remains a serious threat. This study aimed to investigate the laboratory and inflammatory markers in children with pneumonia and their relationship with the severity of the disease.

Materials and Methods: This retrospective descriptive-cross-sectional study included 400 children with pneumonia patients, aged 1 month to 12 years, who were referred to Bandar Abbas Children's Hospital. In this study, the severity of the disease was compared with variables such as age, gender, white blood cell (WBC) count, neutrophil percentage, erythrocyte sedimentation rate (ESR), and community-acquired pneumonia (CAP).

Results: Of the 400 people who participated in the survey, 57.5% and 42.5% of cases were males and females, respectively. The mean age of the studied patients was 16.53 ± 21.57 months. There was no significant relationship between the severity of pneumonia and leukocyte count, neutrophil count, and inflammatory markers ($P > 0.05$).

Conclusion: Based on the findings, the severity of the disease was mild to moderate in 90% of patients. ESR, C-reactive protein (CRP), leukocyte count, and neutrophil count were not significantly associated with the severity of pneumonia in children ($P > 0.05$).

Keywords: Pneumonia, Leukocyte, Neutrophil, Inflammatory markers, Severity

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Introduction

Pneumonia is one of the leading causes of death from an infectious cause in children. Community-acquired pneumonia (CAP) is an important causative mechanism of pneumonia in infants and young children (1, 2). Despite advances in the treatment of pneumonia in recent years, it is highly difficult to determine its severity in children because the diagnosis, especially at younger ages, is more difficult. More than one-third of CAP cases progress to severe pneumonia due to the absence of expedient diagnosis and treatment (3). Most studies also indicate an increase in the number of severe pneumonia cases (4). Severe pneumonia is defined as requiring advanced therapies in a pediatric intensive care unit (5); the condition frequently results in morbidity and mortality. Risk factors for pneumonia and severe disease are poor nutrition, including micronutrient deficiency, lack of breastfeeding, exposure to indoor air pollution or passive smoke exposure, HIV infection, premature birth, overcrowding, and poor living circumstances. (6). Determining the etiology of pneumonia is challenging in

the absence of reliable diagnostic tests. In most studies, a set of clinical findings, chest imaging, and various inflammatory markers have been used in the diagnosis, severity, and prognosis of pediatric pneumonia. Early and effective treatment of pneumonia is crucial. Before pneumonia progresses to a severe state, timely diagnosis is essential to reduce the mortality rate and improve prognosis. Although the diagnosis of severe pneumonia in children is limited, and different scores have been used to determine its severity; this issue has different results and need more studies. In addition, the diagnosis relies primarily on clinical symptoms (7). A diagnosis based on clinical suspicion and traditional clinical experience tends to delay therapy, resulting in severe consequences (3, 8).

Therefore, the use of inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) in addition to clinical examination and chest X-ray in the diagnosis, assessment of severity, and response to the treatment of children with pneumonia has been associated with different results (9).

A previous study showed that continued high levels of serum CRP in the incipient stage of acute respiratory infections increase the risk of progression to a critical disease state (10), but another study reported poor diagnostic accuracy in terms of predicting severe pneumonia (11). The diagnostic value of the CRP level is unknown in patients with a high risk of pneumonia. Before the development of severe pneumonia, the significance of clinical symptoms, signs, and inflammatory markers in patients with pneumonia is unclear. Baseline peripheral white blood cell (WBC) count was not independently associated with either outcome (12).

Objectives

The association between the elevation of CRP, leukocyte count, neutrophil count, and ESR, and diagnostic accuracy in terms of predicting severe pneumonia is also unclear. This study aimed to determine the significance of leukocyte count, neutrophil count, CRP, and ESR in the clinical diagnosis of severe pneumonia. It was designed and performed on the children of Bandar Abbas.

Materials and Methods

Participants

The present retrospective descriptive cross-sectional study included 400 children with pneumonia who were referred to Bandar Abbas Children's Hospital in 2019. All cases were primarily hospitalized and evaluated by a pediatric infectious disease subspecialist, who confirmed pneumonia diagnosis.

Study Design

In general, 400 cases with pneumonia disease based on the clinical and laboratory-confirmed diagnoses were evaluated in this research. Demographic data and disease lab information were recorded in a prepared questionnaire. Data on different variables were also extracted, including WBC, neutrophil count, CRP, and ESR. Then, the obtained data were evaluated on five components (i.e., respiratory rate, wheezing, accessory muscle use, SpO₂, and feeding difficulties) using the PRESS. Each component was given 0 or 1 point, and the PRESS total score was classified as mild (0-1 points), moderate (2-3 points), or severe (4-5 points). The respiratory rate was estimated based on the American Heart Association guidelines (13).

Data Analysis

The data were analyzed using SPSS software, version 22 (SPSS Inc., Chicago, IL, USA). To describe quantitative and qualitative data, mean and standard deviation and frequency and percentage were applied. Due to the abnormal distribution, a nonparametric Kruskal-Wallis test was applied to compare laboratory variables based on

pneumonia severity.

Results

Of the 400 people who participated in the survey, 57.5% were males and 42.5% were females. The mean age of the studied patients was 16.53 ± 21.57 months. The results of the study are presented in Tables 1, 2, and 3.

Discussion

Pneumonia is considered as one of the leading causes of death from an infectious cause in children. Infants and young children are especially vulnerable. Even with appropriate early antibiotics, we still have not been able to improve the outcomes in these patients since the 1950s (14). Considering the main role of the clinical diagnosis of pneumonia in children, in addition to clinical examinations, the role of pneumonia is less important when the child is younger, thus the use of other methods such as inflammatory markers, chest X-rays, and WBC to diagnose and, more specifically, determine the severity of the disease can be helpful. One of the most challenging problems in the diagnosis of pneumonia is the lack of clinical findings in favor of pulmonary involvement. This condition occurs in children under three years of age who present with fever without focus as silent pneumonia. In these cases, high fever and leukocytes have been suggested as risk factors.

In this study, 170 (42.5%) and 230 (57.5%) patients were females and males. The mean age of patients was 16.53 ± 21.57 months, and the lowest and highest age ranges were one month old and 12 years old, respectively. The prevalence of pneumonia severity in this study was 65.8% (mild), 24.2% (moderate), and 10% (severe). Finally, the main finding showed that CRP, leukocyte, neutrophil count, and ESR, which were measured within 24 hours of hospital admission, were not associated with

Table 1. Frequency of the Severity of Pneumonia

Severity of Pneumonia	Severity of Pneumonia	Frequency	Percent
0	Mild	161	40.3
1	Mild	102	25.5
2	Moderate	59	14.8
3	Moderate	38	9.5
4	Severe	36	9
5	Severe	4	1

Table 2. Mean and SD of Patients' Laboratory Information

Variable	Mean	SD
WBC (10 ⁹ /L)	10420	4910
Neutrophil (10 ⁹ /L)	4175	1855
ESR (mm/h)	28.44	24.72
CRP (mg/L)	13.22	12.89

Note. SD, Standard deviation; WBC, White blood count; ESR, Erythrocyte sedimentation rate; CRP, C-reactive protein.

Table 3. Comparison of Laboratory Variables According to the Severity of Pneumonia

Variable	Severity						Test Statistics	P Value
	0	1	2	3	4	5		
WBC (10 ⁹ /L)	188.50	197.04	210.83	233.24	215.96	169.25	6.281	0.28
Neutrophil (10 ⁹ /L)	203.63	199.25	180.87	203.25	224.50	153.63	40.61	0.541
ESR (mm/h)	212.33	199.61	186.96	182.57	191.29	200	3.647	0.601
CRP (mg/L)	208.47	191.29	207.87	171.47	214.93	151.75	5.339	0.376

Note. WBC, White blood count; ESR, Erythrocyte sedimentation rate; CRP, C-Reactive Protein.

the severity of pneumonia in children. Biomarkers can be monitored to evaluate response to treatment, which can impact the length of antibiotic use and predict outcomes, which was not the purpose of our study (14).

In our study, there was no significant relationship between the severity of pneumonia and leukocyte count, neutrophil count, and inflammatory markers ($P > 0.05$), which is consistent with the findings of Florin et al. They evaluated the association with and predictive ability for disease severity of 4 widely available conventional host biomarkers (WBC count, absolute neutrophil count, CRP, and procalcitonin) in a prospective cohort of children with emergency department (ED) encounters for suspected or radiographic CAP. In this study, none of the biomarker levels differed based on the severity of pneumonia among patients, but in terms of age, previous antibiotic use, duration of fever, and viral disease, a moderate association was observed with CRP (15). In other studies by Williams et al, Bircan et al, and Saleh et al, a significant relationship was reported between the severity of pneumonia with the leukocyte count, neutrophil count, and inflammatory markers. Their results suggested that CRP, measured at admission, may be useful for predicting outcomes among hospitalized children with pneumonia. Thus, CRP should be considered for inclusion in the development of pediatric pneumonia severity scores (16-17). Based on our findings, none of these variables such as leukocyte count, neutrophil count, and inflammatory markers could predict the course of the disease and its prognosis. However, it is noteworthy that the relationship between CRP and pneumonia severity was quite significant in the study conducted in adult populations (18).

This contradictory information about the severity of pneumonia and its relationship with WBC count, absolute neutrophil count, CRP, and ESR is due to the use of different systems for determining the severity of pneumonia in those studies.

Of recent biomarkers, less reliance has come to be placed on the WBC count and ESR because they have lower sensitivity and specificity compared with CRP. The present evidence indicates that biomarkers can also be used to predict complications, outcomes, and mortality. They recommend that pro-adrenomedullin has better predictive power even compared to CRP and procalcitonin (14).

Some studies have reported that CRP was useful for

diagnosing CAP, but CRP is not a specific biomarker of bacterial infections because it can be increased in malignant and collagen vascular diseases (19). In addition, CRP is decreased by corticosteroid therapy. It remains difficult to accurately determine the relationship between the severity of pneumonia with the leukocyte count, neutrophil count, and inflammatory marker. These studies are limited by their retrospective nature, difficulty in specific diagnosis, relatively small sample size, and different respiratory methods for respiratory distress scoring.

Accordingly, more studies are needed to evaluate the role of leukocyte count, neutrophil count, and inflammatory markers in predicting the severity of pneumonia in Iranian children.

It is recommended that further studies use the same pneumonia scoring system and biomarkers such as procalcitonin or pro-adrenomedullin for better results.

Conclusion

Based on the results of this study, ESR, CRP, leukocyte count, and neutrophil count were not significantly associated with the severity of pneumonia in children.

A major limitation of the current study was the existence of incomplete files and the lack of access to complete patient information.

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Availability of Data and Materials

The datasets used and/or analyzed during the current study are available upon request.

Conflict of Interest Disclosures

The authors declare that they have no competing interests.

Ethical Statement

The study received ethics approval from the Ethics Committee of Hormozgan University of Medical Sciences (ethics code: IR.HUMS.REC.1399.076), and it complies with the statements of the Declaration of Helsinki. Written informed consent was obtained from all the participants.

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