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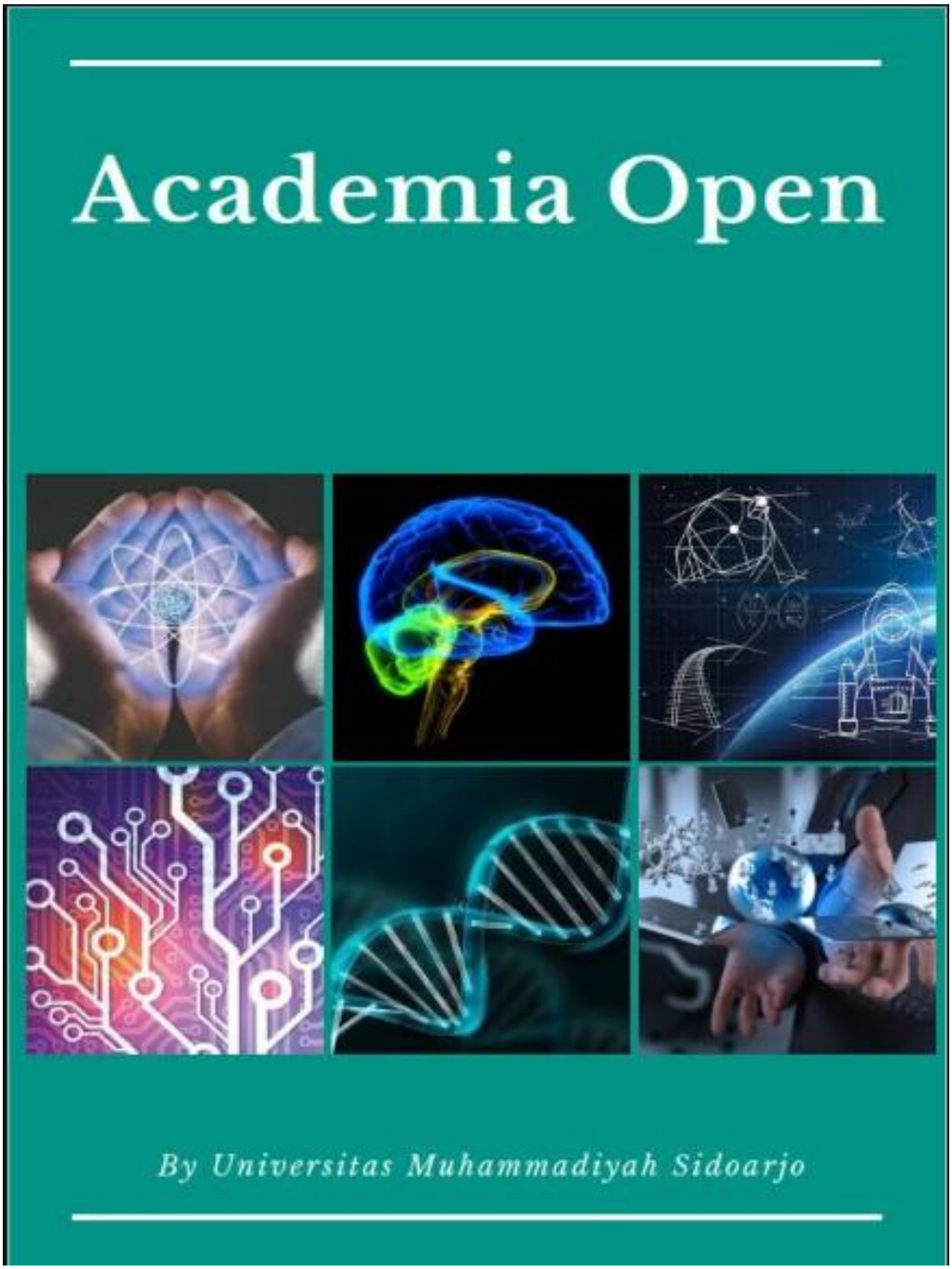

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Evaluation of Serum Ferritin and CRP Levels in Children with Bacterial Pneumonia

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Abstract

General Background: Bacterial pneumonia remains a major cause of pediatric morbidity and hospitalization, characterized by systemic inflammatory responses involving acute-phase reactants and iron metabolism. **Specific Background:** C-reactive protein (CRP) and serum ferritin are recognized inflammatory biomarkers; however, their combined evaluation in pediatric bacterial pneumonia and their association with disease severity and clinical indicators require further clarification. **Knowledge Gap:** Limited data are available regarding the diagnostic and prognostic relevance of ferritin alongside CRP in children with clinically and radiologically confirmed bacterial pneumonia. **Aims:** This case–control study aimed to evaluate serum ferritin and CRP levels in 60 children with bacterial pneumonia compared with 40 healthy controls and to determine their relationship with severity classification and clinical parameters. **Results:** Serum ferritin and CRP levels were significantly higher in pneumonia patients than controls ($p < 0.001$) and demonstrated a progressive increase from mild to severe cases ($p < 0.001$). Both biomarkers showed significant positive correlations with body temperature, white blood cell count, and length of hospital stay. **Novelty:** The study demonstrates a graded rise of ferritin and CRP corresponding to clinical severity categories within a well-defined pediatric cohort. **Implications:** Combined assessment of ferritin and CRP may support severity stratification, clinical monitoring, and prognostic evaluation in pediatric bacterial pneumonia.

Highlights:

- Inflammatory Biomarker Concentrations Were Significantly Higher in Affected Children Compared With Matched Healthy Controls.
- Progressive Increases Were Observed From Mild to Severe Clinical Classification.
- Positive Correlations Were Identified With Fever Intensity, Leukocyte Count, and Hospitalization Duration.

Keywords: Bacterial Pneumonia, Serum Ferritin, CReactive Protein, Pediatric Inflammation, Disease Severity

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Introduction:

Bacterial pneumonia is still among the major causes of morbidity and death among children globally, especially in the developing countries, where medical facilities are poor and timely diagnosis might be not easy [1]. Regardless of the development of vaccination programs, antimicrobial therapy, and other supportive care, pneumonia remains one of the primary causes of hospitalization and mortality among children, particularly of children below the age of five years. The early diagnosis of the severity of the disease and the introduction of the relevant treatment is essential to enhance the clinical outcomes and minimise the complications [2],[3].

The signs and symptoms of bacterial pneumonia in children are frequently heterogeneous and may vary between mild respiratory symptoms and severe systemic condition to disabling hospitalization. Conventional methods of diagnosis base on the clinical examination, radiological results, and the simplest lab parameters like white blood cell count and erythrocyte sedimentation rate [4]. Nevertheless, these indicators are not sensitive and specific enough to effectively differentiate between bacterial pneumonia and other respiratory diseases or accurately determine the severity of the disease. Therefore, there is increased concern to find effective inflammatory biomarkers which can assist in the diagnosis process, determining the severity of the disease and making clinical decisions [5].

C-reactive protein (CRP) is a protein secreted by the liver in an acute-phase in response to pro-inflammatory cytokines, especially interleukin-6. It has received wide clinical application as an indicator of systemic inflammation and infection. High levels of CRP have been commonly associated with bacterial infections such as pneumonia and usually characterize the severity of the disease and the response to treatment [6]. However, CRP can be different at various levels of infection, due to previous use of antibiotics, and based on the immune response of the patients and boys so, to any one, it does not have its independent diagnostic value [7].

The traditionally recognized inflammatory biomarkers, serum ferritin as an indicator of iron storage, has become a key inflammatory biomarker. Ferritin is an acute-phase reactant and rises dramatically in the case of infections and inflammation [8]. High levels of ferritin in bacterial infections are also indicative of not only amplified iron sequestration as part of host defense mechanism, but also an increase in the levels of inflammatory processes like the presence of tumor necrosis factor-alpha and interleukin-1beta [9]. Current research has proposed that hyperferritinemia could be a prognostic factor that is linked to serious infections, long hospital stay, and bad outcome, thus its possible application as a prognostic marker [10].

The use of serum ferritin as an inflammatory and severity-associated biomarker in pediatric pneumonia is not well researched relative to CRP. Although various studies have depicted a high level of ferritin in severe bacterial infection and sepsis, there is little data on the diagnostic and prognostic status of ferritin with reference to children with bacterial pneumonia [11]. Furthermore, the joint analysis of ferritin and CRP can help to get complementary results, since these biomarkers signify the variation of the inflammatory reaction and immune stimulation [12],[13].

The estimate of the connection between serum ferritin and CRP levels and clinical variables including the intensity of the fever, the number of leukocytes, and the hospital stay time can be viewed as beneficial in terms of disease evolution and the ability to categorize the progression. The discovery of viable biomarkers which are correlated with clinical outcomes may aid in the initial risk assessment to optimize treatment and curb unnecessary exposure to antibiotics or extended hospitalization [14],[15].

This study aimed to evaluate serum ferritin and C-reactive protein (CRP) levels in children with bacterial pneumonia, compare them with healthy controls, and determine their relationship with disease severity and clinical indicators in order to assess their potential value as inflammatory and prognostic biomarkers in pediatric bacterial pneumonia.

Methodology :

It was a case control study that was carried out in the period between October 5 and 10, 2026, and categorized 100 children in total, 60 children with bacterial pneumonia and 40 apparently healthy children as the control group. Children in pneumonia group were recruited through the pediatric hospital admissions using clinical and radiological data of bacterial pneumonia and controls were children of age and sex-matched children with regular health visits. The inclusion criteria included children aged between 1-12 years of age with fever, cough, respiratory distress, radiological evidence of pneumonia and laboratory evidence that was suggestive of bacterial infection. The exclusion criteria were viral or fungal pneumonia, chronic inflammatory or autoimmune disease, hematological disease, iron deficiency anemia or iron supplementation, chronic hepatic or renal disease, malignancy, recent blood transfusion or iron supplementation, previous antibiotic use before admission. All the participants had their venous blood samples (5 mL) aseptically taken, left to clot, and centrifuged at 3000 rpm and 10 minutes to obtain serum, which was aliquoted and kept at freezer conditions (−20 ◦ C) until analysis. Enzyme-linked immunosorbent assay (ELISA) was used to measure serum ferritin levels, and C-reactive protein (CRP) levels were measured by immunoturbidimetric procedures as per the instructions given by the manufacturers. Combined clinical examination, chest radiography, and laboratory data were used to determine the diagnosis of bacterial pneumonia and the level of its severity was divided into mild, moderate, and severe types according to clinical characteristics.

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Statistical analysis :

The analysis of data was done using the SPSS version 26. Continuous variables are represented in the mean of SD and categorical variables in the form of frequencies and percentages. The independent t-test or Mann Whitney U test, as relevant, was used to compare the groups of persons on different aspects whereas Pearson correlation test was used to establish the correlation between the variables. The p-value of less than 0.05 was deemed to be statistically significant.

Ethical approval:

The study was approved by the human ethics committee of Middle Technical University, Everyone who took part in the study was told about it and asked to sign a consent form. The patient was also guaranteed that his information would be kept private.

Results

Baseline comparison of age, sex, residence, and presenting clinical features between study groups

The sociodemographic analysis revealed no statistically significant differences between the pneumonia and control groups regarding age (5.6 ± 2.1 vs. 5.3 ± 2.0 years; p = 0.48), gender distribution (p = 0.68), or residence (p = 0.73), indicating appropriate baseline comparability between the groups. In the pneumonia group, the mean duration of fever was 4.2 ± 1.3 days, and cough was the predominant clinical manifestation, observed in 91.7% of patients. These results indicate that there were few chances that demographic variables would have confounded the detected differences in inflammatory biomarkers in the study groups.

Table 1: Sociodemographic and Clinical Characteristics of Children with Bacterial Pneumonia and Healthy Controls

Variable	Pneumonia Group (n = 60)	Control Group (n = 40)	p-value
Age (years), Mean ± SD	5.6 ± 2.1	5.3 ± 2.0	0.48
Gender (Male), n (%)	34 (56.7%)	21 (52.5%)	0.68
Gender (Female), n (%)	26 (43.3%)	19 (47.5%)	—
Residence (Urban), n (%)	37 (61.7%)	26 (65.0%)	0.73
Residence (Rural), n (%)	23 (38.3%)	14 (35.0%)	—
Fever duration (days), Mean ± SD	4.2 ± 1.3	—	—
Cough present, n (%)	55 (91.7%)	—	—

Differences in inflammatory biomarker concentrations between study groups

Children who had bacterial pneumonia had much higher serum ferritin and C-reactive protein (CRP) than healthy controls. The average in serum ferritin concentration was significantly higher in the group of pneumonia (186.4 ± 52.8 ng/mL) compared to controls (64.7 ± 21.3 ng/mL), and the difference was highly significant ($p < 0.001$). In the same way, the level of CRP was also significantly elevated in pneumonia patients (42.6 ± 15.9 mg/L) in the group of controls (3.8 ± 1.9 mg/L; $p < 0.001$). The results suggest that there is a high level of inflammatory reaction with a bacterial pneumonia in children and therefore the use of ferritin and CRP as diagnostic biomarkers of inflammatory reactions is a possibility.

Table 2: Comparison of Serum Ferritin and C-Reactive Protein Levels Between Children with Bacterial Pneumonia and Healthy Controls

Biomarker	Pneumonia Group (Mean ± SD)	Control Group (Mean ± SD)	p-value
Serum Ferritin (ng/mL)	186.4 ± 52.8	64.7 ± 21.3	<0.001
CRP (mg/L)	42.6 ± 15.9	3.8 ± 1.9	<0.001

Association between inflammatory biomarker levels and disease severity in pediatric bacterial pneumonia

The level of serum ferritin and C-reactive protein (CRP) increased gradually and significantly with the severity of pneumonia. The concentration of ferritin in mean increased to 191.6 + 39.7 ng/mL in moderate cases and to 254.8 ± 44.2 ng/mL in severe pneumonia ($p < 0.001$). Likewise, CRP levels showed an upward progression as per severity levels with 26.4 ± 8.7 mg/L in mild pneumonia cases and 41.9 ± 11.2mg/L in moderate pneumonia cases and was highest at 63.5 ± 14.6mg/L in severe pneumonia cases ($p < 0.001$). These results demonstrate a close correlation between the increase of inflammatory biomarkers and the severity of the clinical findings indicating the possible use of ferritin and CRP as helping markers in the stratification and prognosis in a bacterial pneumonia in children.

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Table 3: Distribution of Serum Ferritin and C-Reactive Protein Levels According to Pneumonia Severity

Biomarker	Mild Pneumonia (n = 22)	Moderate Pneumonia (n = 23)	Severe Pneumonia (n = 15)	p-value
Ferritin (ng/mL)	138.2 ± 31.5	191.6 ± 39.7	254.8 ± 44.2	<0.001
CRP (mg/L)	26.4 ± 8.7	41.9 ± 11.2	63.5 ± 14.6	<0.001

Relationship of serum ferritin and C-reactive protein levels with clinical and laboratory indicators of disease severity

Correlations analysis revealed that there were significant positive correlations between inflammatory biomarkers and significant clinical parameters among the children with bacterial pneumonia. The levels of serum ferritin were moderately positively related to body temperature ($r = 0.46$, $p < 0.001$), white blood cell count ($r = 0.39$, $p = 0.002$), and length of hospital stay ($r = 0.51$, $p < 0.001$). On the same note, CRP was positively related to the level of body temperature ($r = 0.52$, $p < 0.001$), WBC count ($r = 0.44$, $p < 0.001$) and the duration of hospitalization ($r = 0.58$, $p < 0.001$). These findings suggest that elevated ferritin concentrations and CRP are linked to inflammatory load and worsen clinical prognosis and may be used as prognostics in pediatric bacterial pneumonia.

Table 4: Correlation Between Inflammatory Biomarkers and Clinical Parameters in Children with Bacterial Pneumonia

Variable	Ferritin (r)	p-value	CRP (r)	p-value
Body temperature (°C)	0.46	<0.001	0.52	<0.001
WBC count (×10⁹/L)	0.39	0.002	0.44	<0.001
Length of hospital stay (days)	0.51	<0.001	0.58	<0.001

Discussion:

The baseline characteristics (Table 1) were quite comparable to the pneumonia and the control group as it showed no significant differences between the age, sex distribution, and residence. This correspondence helps to minimize the potential influence of demographic variables on the biomarker results and to conclude that the high levels of ferritin and CRP can be mostly explained by the inflammatory load of bacterial pneumonia and not by population differences. The cough preponderance and quantifiable fever duration of the pneumonia group are typical of the patterns of infecting the lower respiratory tract by bacteria in typical forms in children, supporting the suitability of selection of cases.

The most important observation of the present study is that serum ferritin and CRP levels significantly rose in children with bacterial pneumonia than in healthy children (Table 2). CRP is an established positive acute-phase reactant that is mostly stimulated by hepatic production in response to IL-6 during bacterial infection [16]. Although Ferritin is commonly regarded as a marker of iron deposits, it is a positive acute-phase reactant that increases in the cases of infection and systemic inflammation [17]. The idea of nutritional immunity has a great biologic basis in explaining ferritin rise in bacterial pneumonia, since the host restrains extracellular iron reserves to limit proliferation of microbes. The cytokine response to the presence of pro-inflammatory cytokines, especially IL-6, upregulates hepcidin which downregulates the iron exporter ferroportin, retaining iron in macrophages and enterocytes and depleting the available iron, and ferritin rises as iron is retained intracellularly and during the acute-phase response [18]. Hence, high levels of ferritin in pneumonia will be more of an immune response and redistribution of iron, which is accompanied by bacterial infection [19].

The gradual increase in the levels of ferritin and CRP between mild, moderate, and severe pneumonia (Table 3) offers clinically significant data showing that the two biomarkers are disease severity indicators. It is consistent with prior literature that has found a positive association between the presence of higher levels of inflammatory biomarkers and the more severe infectious phenotypes and the degree of worse outcomes. CRP has been documented to rise as severity indices in pneumonia, showing that it is a more potent systemic inflammatory reaction in more severe disease [20],[21]. Likewise, hyperferritinemia is becoming a widely known indicator of serious infection and dysregulation of host response; pediatric critical illness research indicates that higher levels of ferritin are predictors of risk of adverse outcome, which is consistent with its prognostic utility in serious infections [22]. In a mechanistic sense, severe pneumonia is predicted to elicit exaggerated cytokine signaling (e.g., IL-6, TNF-a, IL-1b), amplified neutrophil recruitment, increased macrophage activation, and tissue damage, mechanisms which compound the production of reactants of acute phase and iron sequestrition leading to the observed gradient in biomarkers [23].

The results of the correlation (Table 4) also reinforce the clinical utility of ferritin and CRP. These two biomarkers correlate with body temperature, WBC count, and length of hospital stay, showing that the greater the level of inflammatory biomarkers, the greater the systemic inflammatory process and the further course of the clinical process. This is in line with findings that CRP dynamics may be associated with the course and severity measures of pneumonia and other severe infections in hospitals [24],[25]. Hospital stay associations with ferritin are biologically conceivable since ferritin tends to be indicative of the strength and inactive nature of cytokine communication; continued adrenergisation of hepcidin and iron sequestration can be a part of a protracted illness and healing process [26]. It is also interesting to note that CRP was somewhat more correlated with temperature and hospital stay than ferritin, which can be attributed either to the rapid action of CRP in response to acute inflammation or its close connection with IL-6 kinetics [27].

Although these results are supportive, other studies find that CRP is not a discriminatory etiologic marker nor does this test

predict unique causative pathogens in community-acquired pneumonia in children, and CRP can be increased in any of a variety of inflammatory respiratory diseases and may not be specific to a given pathogen [28],[29]. Similarly, ferritin may increase significantly in non-bacterial conditions, e.g. severe viral infections, hyperinflammatory syndromes, or cytokine storm states which might lead to overlapping values and therefore decreased specificity when it is not ensured that strict bacterial confirmation is done [30]. The disparities between researches can also be caused by differences in the definition of disease (clinical vs. culture-confirmed pneumonia), sampling period (early vs. late presentation), pre-hospital antibiotic exposure, nutritional status, and prevalence of iron deficiency. Notably, iron deficiency anemia and iron supplementation has the potential to affect the interpretation of ferritin; by ruling out these possibilities, as is done in the current design, can help reduce a significant confounder, but restrict external validity in populations with frequent iron deficiency [31].

In general, the current results confirm the hypothesis that ferritin and CRP are notably high in bacterial pneumonia in children of pediatric age, rise in proportion to the severity, and is related to clinical signs of inflammatory load and length of hospital stay. These findings are biologically consistent with IL-6–hepcidin–ferroportin signaling of acute-phase reactions and iron homeostasis coupled with iron uptake by macrophages [32],[33]. Clinically, ferritin with CRP has the potential to provide complementary information on severity stratification, risk assessment and monitoring especially when used with clinical and radiological assessment [33].

Conclusion:

This study demonstrates that serum ferritin and C-reactive protein levels are markedly elevated in children with bacterial pneumonia as a direct consequence of the acute-phase inflammatory response. Pro-inflammatory cytokines, particularly IL-6, stimulate hepatic CRP synthesis and upregulate hepcidin, leading to iron sequestration within macrophages and increased ferritin release. The progressive rise of both biomarkers with disease severity reflects escalating immune activation and tissue inflammation, supporting their usefulness in severity stratification, monitoring disease progression, and predicting clinical outcomes in pediatric bacterial pneumonia.

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