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Original article

# Value of Blood Heparin-Binding Protein in the Diagnosis and Severity Assessment of Community-acquired Pneumonia

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## Abstract

**Background:** In children, community-acquired pneumonia (CAP) is a leading cause of hospitalization and mortality. It incurs significant healthcare costs. **This study aimed to** detect the serum levels of heparin binding protein (HBP) in healthy children and in those with severe and non-severe CAP. **Methods**: The study included two main groups: Patients' group of sixty patients with pneumonia. Control group: 30 healthy children. All children were subjected to full history taking, complete clinical examination, investigations and assessment of Human Azurocidin/Heparin Binding Protein (AZU/HBP), using ELISA Kit. **Results**: The median HBP level was significantly higher in patients compared to controls, $P < 0.001$. The median HBP level was significantly higher in the severe pneumonia group compared to the non-severe pneumonia group, $P < 0.001$. Heparin-binding protein levels showed a significant negative correlation with oxygen saturation (SPO2) ($r = -0.276$, $P = 0.033$). and positive correlations with C-reactive protein (CRP) ($r = 0.362$, $P = 0.004$), CO2 ($r = 0.343$, $P = 0.007$), duration of hospital stay ($r = 0.297$, $P = 0.021$) and severity of illness ($r = 0.457$, $P < 0.001$). **Conclusion:** HBP is a circulating marker of CAP in children. The level of HBP indicates the severity of CAP, and the constructed nomogram based on HBP can help predict the probability of severe or complicated pneumonia in children. Rapidly identifying children at high risk for severe or complicated pneumonia could signal the need for closer monitoring or prolonged hospital stay for therapy.

**Keywords:** Heparin-Binding Protein; HBP; Severity; CAP; pneumonia

## Introduction

Community-acquired pneumonia (CAP) is a leading cause of hospitalization and mortality. It incurs significant healthcare costs. As the disease presentation varies from a mild illness that can be managed at home to a severe illness requiring treatment in the intensive care unit. Early diagnosing and determining the appropriate level of care is important for improving the outcomes (1)**.** The majority of deaths attributed to pneumonia in children are mostly in the developing world (2)**.**

Pneumonia incidence among under-five children is estimated to be 0.05 and 0.29 episodes per child-year in developed and developing countries, respectively. Every year, nearly 156 million new episodes occur worldwide; 151 million episodes are in developing countries, and 7–13% of these episodes are severe enough to be life-threatening and require hospitalization (3)**.**

Heparin-binding protein (HBP), also known as azurocidin or cationic antimicrobial protein of 37 kDa (CAP 37), is a member of the serine proteinases derived from the polymorphonuclear neutrophils (PMN) family (4)**.** It was originally discovered in 1984 because of its potent antibacterial activity against Gram-negative pathogens. Later, it was reported that several Gram-positive organisms, such as *Streptococcus pyogenes* and *Listeria monocytogenes*, are also sensitive to HBP. A number of studies have demonstrated that the peptide 20-44 portion of HBP plays an essential role in its antimicrobial activity by binding to lipopolysaccharide (LPS) directly (4)**.**

Heparin-binding protein proved to be a valuable diagnostic marker for suspected sepsis. It demonstrated excellent prognostic and discriminatory properties in detecting the most severely ill patients suffering from sepsis. Experimental and clinical evidence supports a prominent role for this protein in the pathophysiology of sepsis-induced organ dysfunction (5)**.**

Heparin-binding protein was reported to be associated with pneumonia in adults (6)**,** and recent studies showed that the level of HBP in patients with severe or complicated pneumonia was nearly twice that in patients with mild pneumonia. The levels of HBP were independently associated with the radiographic severity of CAP in children, which were mainly related to the immune response after the tissue damage associated with pulmonary infection (7)**.**

Our study aimed to detect the serum levels of heparin binding protein in healthy children and those with severe and non-severe CAP.

### Subjects and methods

This single-center, case-control observational study included children with community-acquired pneumonia admitted to the Pediatric Department and Intensive Care Unit of Benha University Hospital, during the period from October 2023 to March 2024, and

30 apparently healthy children as a control group.

We included all children having CAP, aged from 2 years up to 5 years, of both gender. Children with any disease other than pneumonia including cardiovascular diseases, perinatal abnormality, other pulmonary disease or immunodeficiency and children on immunosuppressant were excluded from the study.

All the included subjects were divided into three groups: Group (1) including 60 patients with pneumonia (according to WHO, 2013); Group (1A) including 30 patients with non-severe pneumonia. Group (1B) including 30 patients with severe pneumonia. Group (2) (Control group): including 30 apparently healthy children matching the patients' groups for age & sex.

**Ethical considerations**

The whole study design was approved by the local ethics committee, Faculty of Medicine, Benha University, **Approval code: MS 31-11-2023.** After explaining the value of the study and the procedures that would be commenced, an informed written consent was obtained from the guardian of every participant before being included in the study.

All the children were subjected to full history taking, complete clinical examination, laboratory investigations as complete blood count, C-reactive protein, arterial blood gases and radiological investigations as plain chest X ray and CT chest when needed. Assessment Human Azurocidin/Heparin Binding Protein (AZU/HBP) was done for all the children, using Human AZU/HBP ELISA Kit, Catalogue No. 201-12-071. The outcome included follow up until discharge or death. The duration of the hospital stay, the complications and the need for assisted ventilation were recorded.

**Statistical Analysis**

Data management and statistical analysis were done using SPSS version 28 (IBM, Armonk, New York, United States). Quantitative data were assessed for normality using the Shapiro-Wilk test and direct data visualization methods. According to normality, quantitative data were summarized as means and standard deviations or medians and ranges. Categorical data were summarized as numbers and percentages. Quantitative data were compared between the studied groups using the independent t-test or Mann-Whitney U test for normally and non-normally distributed quantitative variables, respectively. Categorical data were compared using the Chi-square or Fisher's exact test. Receiver operating characteristic (ROC) analysis was done for HBP to predict pneumonia, its severity, and mortality. The area under the curve with its 95% confidence intervals, best cutoff point, and diagnostic indices were calculated. Correlations were done using Spearman's correlation. The levels of HBP were compared according to severity and mortality using the Mann-Whitney U test. Multivariate logistic regression analyses were done to predict pneumonia, severity, and

mortality. The odds ratios with 95% confidence intervals were calculated. All the statistical tests were two-sided. P values less than 0.05 were considered significant.

**Results**

The study included two main groups. Patients' group of sixty patients with pneumonia (35 males and 25 females), their mean age was 3.3 ±1 years and a control group of thirty apparently healthy children, (14 males and 16 females), their mean age was 3.3 ±1 years. The studied groups were comparable regarding age (P = 0.935) and gender (P = 0.295).

Hemoglobin levels were lower in the patients compared to the controls (10.2 ± 1 vs. 11.7 ± 0.8 g/dL, P < 0.001). The median white blood cell count (WBC) was significantly higher in the patients than in the controls (12.4, range 5.2-29 vs. 8.4, range 3.2-11.5 x10^3/μL, P < 0.001). The platelet counts were significantly lower in the patients than for the controls (140, range 25-302 vs. 332, range 184-543 x10^3/μL, P < 0.001). C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were also elevated in the patients, with CRP showing a median of 48 (range 3-192) compared to 5 (range 2-6) mg/L in the controls (P < 0.001) and ESR being 29 ± 5 vs. 7 ± 2 mm/hr. (P < 0.001). Additionally, patients had lower pH (7.29 ± 0.08 vs. 7.37 ± 0.02, P < 0.001), higher $CO_2$ (42 ± 10 vs. 36 ± 3 mmHg, P < 0.001), and lower bicarbonate ($HCO_3$) levels (18.1 ± 3.6 vs. 23.6 ± 1.4 mmol/L, P < 0.001). The median HBP levels were significantly higher in patients compared to controls [26.8 (range 7-56.6) vs. 6.4 (range 2.7-34.3), P < 0.001], **Table 1**.

HBP, CRP levels were significantly higher in severe pneumonia compared to non-severe pneumonia and controls. Also required oxygen support, inotropic support, median duration of hospital stay, and mortality were significantly higher in severe pneumonia compared to non-severe pneumonia, Table 2.

Most patients (68.3%) required nasal oxygen support, while 15% were managed with Continuous Positive Airway Pressure (CPAP), and 16.7% required mechanical ventilation (MV). Inotropic support was administered to 10% of the patients. The median duration of hospital stay was 9 days, ranging from 3 to 16 days. Death occurred in 8.3% of the patients. The median HBP level was significantly higher in the severe pneumonia group [32.4 (range 7.2 - 56.6)] compared to the mild and moderate group [19.4 (range 7 - 55.6)] (P < 0.001). **Figure 1**

Heparin-binding protein levels showed a significant negative correlation with oxygen saturation ($SPO_2$) (r = -0.276, P = 0.033). It showed positive correlations with C-reactive protein (CRP) (r = 0.362, P = 0.004), $CO_2$ (r = 0.343, P = 0.007), duration of hospital stays (r = 0.297, P = 0.021) and severity of illness (r = 0.457, P < 0.001). No significant correlations were observed with other variables, including age (P = 0.172), respiratory rate (P = 0.5), heart rate (P = 0.195), and hemoglobin (P = 0.406). **Table 3.**

A ROC analysis was done for HBP to predict pneumonia. It revealed a significant excellent AUC of 0.920, with a 95% confidence interval of 0.855 – 0.984. The best cutoff point was >8.1 ng/mL, at which sensitivity, specificity, PPV, and NPV were 95%, 80%, 90.5%, and 88.9%, respectively, **Figure 2.** Also, ROC analysis was done for HBP to predict severe pneumonia. It revealed a significant good AUC of 0.764, with a 95% confidence interval of 0.640 – 0.888. The best cutoff point was >21.1 ng/mL, at which sensitivity, specificity, PPV, and NPV were 83.3%, 63.3%, 69.4%, and 79.2%, respectively. **Figure 3**

Multivariate logistic regression analysis was used for predicting severe pneumonia. Sex emerged as a significant predictor, with an odds ratio (OR) of 4.056 (95% CI: 1.135 - 14.498, P = 0.031), indicating that being female is associated with a higher likelihood of developing severe pneumonia. Also, HBP proved to be a significant predictor, with an OR of 1.095 (95% CI: 1.034 - 1.16, P = 0.002), suggesting that higher HBP levels predict increased risk of severe pneumonia, **Table 4.**

Multivariate logistic regression analysis was done for predicting mortality. Heparin Binding Protein approached statistical significance, with an OR of 1.086 (95% CI: 0.998 - 1.181, P = 0.056), suggesting a trend indicating that higher HBP levels may be associated with increased mortality risk, **Table 5**.

**Table 1:** Demographic and laboratory characteristics of the studied groups

| Demographic & laboratory characteristics | | Patients (n = 60) | Controls (n = 30) | P-value |
|---|---|---|---|---|
| **Age (years)** | Mean ±SD | 3.3 ±1 | 3.3 ±1 | 0.935 |
| **Sex** | | | | |
| **Males** | n (%) | 35 (58.3) | 14 (46.7) | 0.295 |
| **Females** | n (%) | 25 (41.7) | 16 (53.3) | |
| **Hemoglobin (g/dl)** | Mean ±SD | 10.2 ±1 | 11.7 ±0.8 | **<0.001*** |
| **WBC ($x10^3$/L)** | Median (range) | 12.4 (5.2 - 29) | 8.4 (3.2 - 11.5) | **<0.001*** |
| **Platelets ($x10^3$/L)** | Median (range) | 140 (25 - 302) | 332 (184 - 543) | **<0.001*** |
| **CRP (mg/dl)** | Median (range) | 48 (3 - 192) | 5 (2 - 6) | **<0.001*** |
| **ESR (mm/hr)** | Mean ±SD | 29 ±5 | 7 ±2 | **<0.001*** |
| **pH** | Mean ±SD | 7.29 ±0.08 | 7.37 ±0.02 | **<0.001*** |
| **$CO_2$ (mmol/L)** | Mean ±SD | 42 ±10 | 36 ±3 | **<0.001*** |
| **$HCO_3$ (mEq/L)** | Mean ±SD | 18.1 ±3.6 | 23.6 ±1.4 | **<0.001*** |
| **HBP (µg/L)** | Median (range) | 26.8 (7 - 56.6) | 6.4 (2.7 - 34.3) | **<0.001*** |

*Significant P-value; WBC: White blood cells; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; PH: Potential of hydrogen; CO2: Carbon dioxide; HCO3: Bicarbonate; SD: Standard deviation.

**Table 2**: Comparison between the three groups regarding HBP, CRP levels, required oxygen support, Inotropic support, median duration of hospital stay and mortality

| | | Non-severe pneumonia (n=31) | Severe pneumonia (n=29) | Controls (n = 30) | P-value |
|---|---|---|---|---|---|
| **HBP** | **Median (range)** | 19.4 (7 - 55.6) | 32.4 (7.2 - 56.6) | 6.4 (2.7 - 34.3) | **<0.001*** |
| **CRP** | **Median (range)** | 24 (3 - 192) | 48 (24 - 192) | 5 (2 - 6) | **<0.001*** |
| **Oxygen support** | | | | | |
| **CPAP** | **n (%)** | 0 (0) | 9 (31) | | **<0.001*** |
| **MV** | **n (%)** | 0 (0) | 10 (34.5) | | **<0.001*** |
| **Nasal O2** | **n (%)** | 31 (100) | 10 (34.5) | | **<0.001*** |
| **Inotropes** | **n (%)** | 0 (0) | 6 (10) | | **<0.001*** |
| **Duration of hospital stay (days)** | **Median (range)** | 4 (3 - 8) | 9 (6 - 16) | | **<0.001*** |
| **Mortality** | **n (%)** | 0 (0) | 5 (17.2) | | **<0.001*** |

*Significant P-value; CRP: C-reactive protein; SD: Standard deviation, CPAP: Continuous positive airway pressure; MV: Mechanical ventilation; O2: Oxygen.

**Table 3:** Correlation between HBP and other parameters in the patients' group

| **Parameters** | **HBP (µg/L)** | |
|---|---|---|
| | **r** | **P** |
| **Age (years)** | 0.179 | 0.172 |
| **Respiratory rate/min** | 0.089 | 0.5 |
| **Heart rate/min** | 0.17 | 0.195 |
| **Temperature $^{o}$C** | 0.001 | 0.994 |
| **$SPO_2$ (%)** | -.276 | **0.033*** |
| **Weight (P)** | 0.062 | 0.639 |
| **Height (P)** | -0.011 | 0.934 |
| **BMI (P)** | 0.108 | 0.41 |
| **Hemoglobin (g/dl)** | -0.109 | 0.406 |
| **WBC ($x10^3$/L)** | 0.208 | 0.111 |
| **Platelets ($x10^3$/L)** | -0.027 | 0.839 |
| **CRP (mg/dl)** | .362 | **0.004*** |
| **ESR (mm/hr)** | -0.194 | 0.137 |

| | | |
|---|---|---|
| **PH** | -0.133 | 0.311 |
| **$CO_2$ (mmol/L)** | .343 | **0.007*** |
| **$HCO_3$ (mEq/L)** | -0.122 | 0.352 |
| **Duration of hospital stay (days)** | .297 | **0.021*** |
| **Severity** | .457 | **<0.001*** |
| **Dyspnea grade** | 0.199 | 0.128 |

*Significant P-value; HBP: Heparin binding protein; SPO2: Oxygen saturation; BMI: Body mass index; WBC: White blood cell count; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; PH: Potential of hydrogen; CO2: Carbon dioxide; HCO3: Bicarbonate.

**Table 4:** Multivariate logistic regression analysis to predict severe pneumonia

| Variables | OR (95% CI) | P-value |
|---|---|---|
| **Age (years)** | 1.209 (0.618 - 2.365) | 0.578 |
| **Sex** | 4.056 (1.135 - 14.498) | **0.031*** |
| **BMI (P)** | 0.998 (0.971 - 1.026) | 0.888 |
| **HBP (µg/L)** | 1.095 (1.034 - 1.16) | **0.002*** |

*Significant P-value; OR: Odds ratio; 95% CI: 95% Confidence interval; BMI: Body mass index; HBP: Heparin binding protein

**Table 5:** Multivariate logistic regression analysis to predict mortality

| Variables | OR (95% CI) | P-value |
|---|---|---|
| **Age (years)** | 0.548 (0.174 - 1.724) | 0.303 |
| **Sex** | 0.309 (0.028 - 3.452) | 0.34 |
| **BMI (P)** | 0.966 (0.917 - 1.019) | 0.204 |
| **HBP (µg/L)** | 1.086 (0.998 - 1.181) | 0.056 |

OR: Odds ratio; 95% CI: 95% Confidence interval; BMI: Body mass index; HBP: Heparin-binding protein

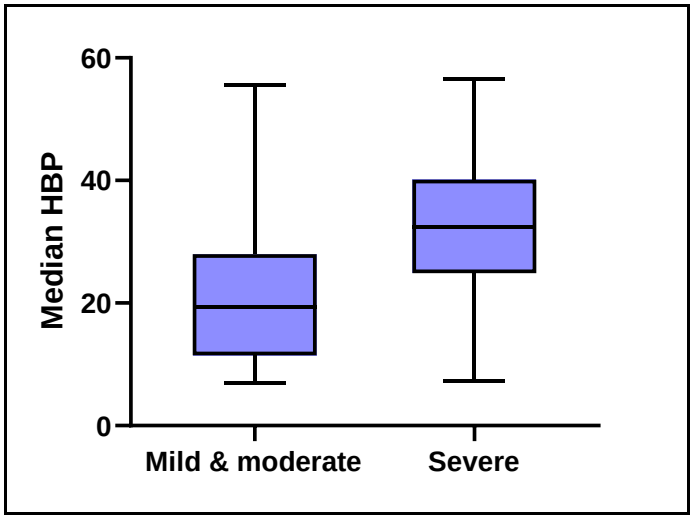


**Figure 1:** HBP according to severity in the patients' group

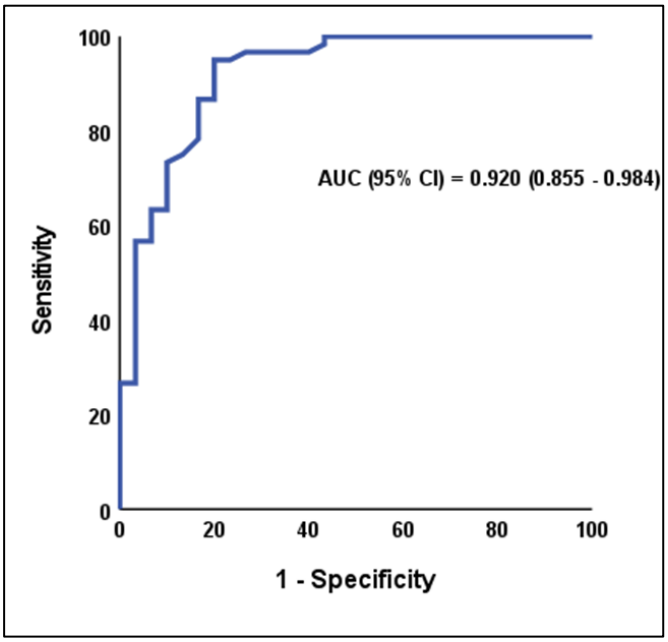


**Figure 2:** ROC analysis of HBP to predict pneumonia

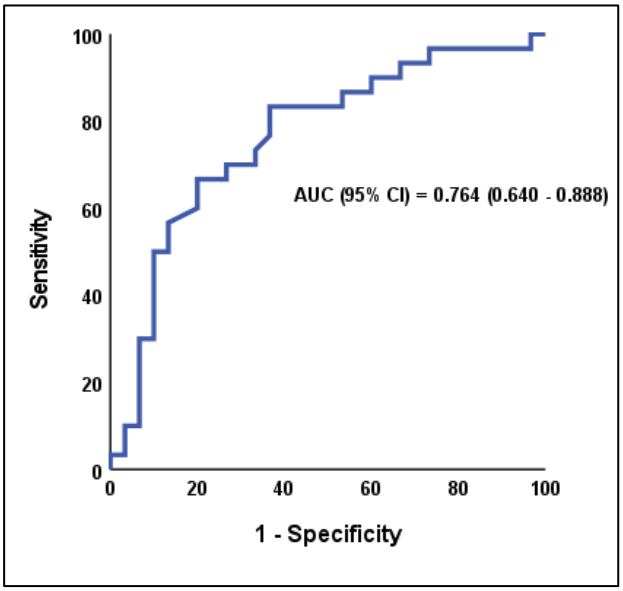


**Figure 3:** ROC analysis HBP to predict severe pneumonia

## Discussion

HBP has been reported as a promising biomarker in predicting infectious diseases worsening or progression (8).

Heparin-binding protein can exert significant effects on the immune system. It is a potent chemoattractant for many types of cells, particularly monocytes, and it is a powerful inducer of vascular leakage and edema formation. It is also secreted following the extravasation of PMNs, where it interacts with other cell types such as

corneal epithelial cells and smooth muscle cells to facilitate similar biological functions. These characteristics make HBP a promising candidate for use in the detection of early infection (9).

Heparin-binding protein level in plasma can be used as a new diagnostic marker for bacterial skin infection, acute bacterial meningitis, leptospirosis, protozoan parasites, and even some noninfectious diseases. Especially for sepsis, a systemic inflammatory response syndrome caused by infection, HBP is an effective early and predictive biomarker. In fact, it has been found that HBP levels in plasma are elevated in septic patients a few hours before the onset of hypotension or organ dysfunction (10).

In the present study, the median HBP levels were significantly higher in the patients compared to the controls [26.8 (range 7-56.6) vs. 6.4 (range 2.7-34.3) ng/ml, P < 0.001]. A ROC analysis was done for HBP in predicting CAP. It revealed a significantly excellent AUC of 0.920, with a 95% confidence interval of 0.855 – 0.984. The best cutoff point was >8.1 ng/ml, at which sensitivity, specificity, PPV, and NPV were 95%, 80%, 90.5%, and 88.9%, respectively .

Our results run in accordance with a previous study (11), which declared that HBP was significantly higher in CAP group 68.28 (41.62-146.92) ng/ml, compared to controls 16.18 (11.46-27.81) ng/ml, p<0.001. The AUCs of HBP in identifying patients with CAP and non-infected controls were 0.931. The best cut-off value was 35.40 ng/mL, at which sensitivity was 87.38%, specificity was 90.38, positive predictive value (PPV) was 94.74% and the negative predictive value (NPV) was 78.33%. Similarly, another study enrolled 157 children with severe CAP. Severe sepsis occurred in 21.7% of them. Serum HBP could predict disease progression to severe sepsis with an area under the ROC curve of 0.80. (١٢)

In the current study, HBP showed a significant negative correlation with oxygen saturation ($SPO_2$) (r = -0.276, P = 0.033). Additionally, HBP was positively correlated with C-reactive protein (CRP) (r = 0.362, P = 0.004) and $CO_2$ levels (r = 0.343, P = 0.007), duration of hospital stay (r = 0.297, P = 0.021), and severity of illness (r = 0.457, P < 0.001). No significant correlations were observed with other variables, including age (P = 0.172), respiratory rate (P = 0.5), heart rate (P = 0.195), and hemoglobin level (P = 0.406) .

Our results agreed with other researchers (7), who observed that inflammatory biomarkers, including neutrophil counts, CRP, ESR, and serum amyloid A (SAA), were significantly correlated with the level of HBP (estimated correlations were 0.31, 0.26, 0.36, and 0.26, respectively; p<0.05). This also agreed with another study (13), who reported that in children with pneumonia, there was a significant positive correlation between HBP and CRP and serum lactate.

Other researchers (12) reported that plasma levels of HBP were positively correlated with levels of CRP, D-dimer, PCT, and WBC (r = 0.411, 0.336,

0.327, 0.283, respectively, P < 0.001). Similarly, another study (14), reported that HBP was positively correlated with inflammatory markers like WBC (r=0.38, P<0.05), N (r=0.26, P<0.05), CRP (r=0.47, P<0.05), IL-6 (r=0.76, P<0.05), and ESR (r=0.35, P<0.05). This finding suggests that serum HBP might aid in the clinical judgment of the degree of systemic inflammation. Linear relationships were evaluated between HBP and these candidate biomarkers.

In the same way Kaukonen et al. (15) found that HBP concentrations correlated with the lowest ratio of the partial pressure of oxygen in arterial blood to a fraction of inspired oxygen (PF ratio) during the ICU stay, indicating that HBP levels were associated with more pronounced respiratory dysfunction.

In the present study, the median HBP level was significantly higher in severe pneumonia [32.4 (range 7.2 - 56.6)] than in mild and moderate disease [19.4 (range 7 - 55.6)] (P < 0.001) .

Our results run in accordance with another study (7), which revealed that the median level of HBP in patients with severe pneumonia was nearly twice that in patients with mild pneumonia (43.0 ng/mL vs 24.3 ng/mL, p<0.05). Our results also agreed with other researchers (14), who studied the application of heparin-binding protein in children with adenovirus pneumonia. The HBP level was significantly higher in the severe group than in the non-severe group [(82.88±44.02) μg/L vs. (35.15±13.08) μg/L, t=15.349, P<0.05].

Similarly, a previous study (12) demonstrated that the level of plasma HBP was significantly high in children with severe CAP on admission and that HBP may be a better predictor of disease progression in children with severe CAP than routine biomarkers. The levels of HBP were independently associated with the radiographic severity of CAP in children, which were mainly related to the immune response after the tissue damage associated with pulmonary infection .

As described in previous studies, HBP is expressed in neutrophils and stored in their secretory vesicles and azurophilic granules. Neutrophil-derived HBP is involved in vascular permeability and edema formation during the host defense and the inflammatory processes since the endothelial cells were the initial targets of HBP (4). These properties offer a potential explanation for the association between HBP levels and the severity of radiographic findings, especially for the formation of consolidation of lung tissue due to the probable endothelial damage during the intense inflammatory responses in the respiratory tract.

Other investigators (7) analyzed the association between HBP levels and disease severity by logistic regression models. After adjusting for age, sex and probable pathogen, the group with higher HBP had a 3-fold risk of developing severe radiographic finding compared with the lower group (adjusted OR: 3.08, p<0.05). When HBP was included in the multivariate regression model as a continuous variable, the risk of developing severe

radiographic findings was increased by 10% with every 10 ng/mL increase in HBP ($p<0.05$). Patients with higher HBP levels had an almost 3-fold risk of severe or complicated pneumonia than the lower group (adjusted OR: 3.11, $p<0.05$). The risk of severe or complicated CAP was increased by 12% with every 10 ng/mL increase in HBP ($p<0.05$). The higher HBP group had a 3.8-fold increased risk of staying in hospital for more than 10 days compared with the lower group (adjusted OR: 3.81, $p<0.05$). However, they disagreed with us as they observed no significant differences between the severe pneumonia and mild pneumonia groups with regard to gender.

Our results also agreed with other researchers (14). Children in the severe group were significantly younger, and they had a significantly longer length of stay, lower Pediatric Critical Illness Scores (PCIS), and higher inflammatory markers like HBP, WBC, N, CRP, IL-6, and ESR compared with those of the non-severe group (all $P<0.05$) .

Our study had several limitations that should be taken into consideration. First, the exact role of HBP was unclear among CAP patients since HBP levels in lower airway samples (sputum or bronchoalveolar lavage fluid) were not detected. However, it is still reasonable to speculate that HBP in peripheral circulation may be involved in the development of CAP according to the known mechanisms. Besides, lower airway samples are not feasible for routine disease monitoring. Second, HBP circulates in the blood with a short elimination half-life between 1 and 2 h (16), suggesting a degree of variability at each point of the disease development. Therefore, dynamic detection may compensate for this limitation.

## Conclusion

High serum HBP, a circulating marker of host immune response to infection, was associated with increased mortality. The constructed nomogram based on serum HBP can help in predicting the probability of severe or complicated pneumonia in children. Rapidly identifying children at high risk for severe or complicated pneumonia could signal the need for closer monitoring or prolonged hospital stay for therapy.

## References

1. Martin-Loeches I, Torres A, Nagavci B, Aliberti S, Antonelli M, Bassetti M, et al. ERS/ESICM/ESCMID/ALAT guidelines for the management of severe community-acquired pneumonia. Intensive Care Med. 2023;49(6):615–32.

2. Rudan I, Nair H, Marušić A, Campbell H. Reducing mortality from childhood pneumonia and diarrhoea: The leading priority is also the greatest opportunity. J Glob Health. 2013 Jun;3(1):010101.

3. Fadl N, Ashour A, Yousry Muhammad Y. Pneumonia among under-five children in Alexandria, Egypt: a case-control study. J Egypt Public Health Assoc. 2020;95:1–7.

4. Yang Y, Liu G, He Q, Shen J, Xu L, Zhu P, et al. A promising candidate: heparin-binding protein steps onto the stage of sepsis prediction. J Immunol Res. 2019;2019.

5. Kahn F, Tverring J, Mellhammar L, Wetterberg N, Bläckberg A, Studahl E, et al. Heparin-binding protein as a prognostic biomarker of sepsis and disease severity at the emergency department. Shock. 2019;52(6):e135–45.

6. Paulsson M, Thelaus L, Riesbeck K, Qvarfordt I, Smith ME, Lindén A, et al. Heparin-binding protein in lower airway samples as a biomarker for pneumonia. Respir Res. 2021;22(1):1–4.

7. Li S, Xu Y, Wu Y, Huang H, Sun C, Xu S, et al. Heparin-Binding Protein: A Prognostic Biomarker Associated with Severe or Complicated Community-Acquired Pneumonia in Children. J Inflamm Res. 2023;321–31.

8. Turnier JL, Anderson MS, Heizer HR, Jone PN, Glodé MP, Dominguez SR. Concurrent respiratory viruses and Kawasaki disease. Pediatrics. 2015;136(3):e609–14.

9. Fisher J, Linder A. Heparin-binding protein: a key player in the pathophysiology of organ dysfunction in sepsis. J Intern Med. 2017;281(6):562–74.

10. Zhu W, Yuan SS, Li J, Huang CB, Lin H, Liao B. A first computational frame for recognizing heparin-binding protein. Diagnostics. 2023;13(14):2465.

11. Xiao X, Hong Y, Wang S, Ma M, Xu Z. Diagnostic value of plasma heparin-binding protein and the heparin-binding protein-to-albumin ratio in patients with community-acquired Pneumonia: a retrospective study. BMC Infect Dis. 2023;23(1):777.

12. Huang C, Zhang C, Zhang J, Zhang L, Mo Y, Mo L. Heparin-binding protein in critically ill children with severe community-acquired pneumonia. Front Pediatr. 2021;9:759535.

13. Mishra H, Balanza N, Francis C, Zhong K, Wright J, Conroy AL, et al. Heparin-binding protein stratifies mortality risk among Ugandan children hospitalized with respiratory distress. In: Open Forum Infectious Diseases. Oxford Academic; 2024;11(7):386.

14. Fan J, Luo H, Zhang X, Duan W, Zhao X, Xie B, et al. Application of heparin-binding protein in severe adenovirus pneumonia. Chinese J Appl Clin Pediatr. 2021;1389–1393.

15. Kaukonen KM, Linko R, Herwald H, Lindbom L, Ruokonen E, Ala-Kokko T, et al. Heparin-binding protein (HBP) in critically ill patients with influenza A (H1N1) infection. Clin Microbiol Infect. 2013;19(12):1122–8.

16. Fisher J, Kahn F, Wiebe E, Gustafsson P, Kander T, Mellhammar L, et al. The dynamics of circulating heparin-binding protein: implications for its use as a biomarker. J Innate Immun. 2022;14(5):447–60.

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