Am J Transl Res 2025;17(12):9715-9726
www.ajtr.org /ISSN:1943-8141/AJTR0168896

Original Article

Expression and clinical significance of IL-17 and its receptor in bacterial pneumonia before and after treatment

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Received September 19, 2025; Accepted December 1, 2025; Epub December 15, 2025; Published December 30, 2025

Abstract: Objectives: To investigate the expression of serum Interleukin-17 (IL-17) and its receptor IL-17R in patients with bacterial pneumonia and their diagnostic value for severe bacterial pneumonia. Methods: In this retrospective analysis, 172 patients diagnosed with bacterial pneumonia were included and categorized into the severe (n = 61) and non-severe (n = 111) groups. Serum concentrations of IL-17, IL-17R, procalcitonin (PCT), and high-sensitivity C-reactive protein (hs-CRP) were measured using ELISA upon admission and after antibiotic treatment. ROC curves were drawn to assess the diagnostic performance of influencing factors, correlation analyses were performed to explore relationships among biomarkers, and logistic regression to identify independent risk factors. Results: Before treatment, patients with severe bacterial pneumonia demonstrated significantly higher levels of IL-17, IL-17R, PCT, and hs-CRP compared to non-severe patients (all $P < 0.001$). All biomarkers decreased significantly after treatment in severe group (all $P < 0.05$). IL-17 and IL-17R showed good accuracy in identifying severe disease (AUC = 0.808 and 0.777, respectively) and were positively correlated with PCT and hs-CRP (all $P < 0.05$). Multivariate analysis identified IL-17, IL-17R, PCT, and hs-CRP as independent risk factors for severe bacterial pneumonia. Conclusions: IL-17 and IL-17R are elevated in bacterial pneumonia, demonstrating close association with disease severity and conventional markers. Their decline after treatment indicates therapeutic effectiveness. These cytokines show diagnostic potential and could help monitor disease progression and treatment response. Future research should confirm these findings in larger cohorts and investigate their interactions with other inflammatory pathways.

Keywords: Interleukin-17, interleukin-17 receptor, bacterial pneumonia, expression, clinical value

Introduction

Pneumonia is a major global health concern with substantial clinical impact. Bacterial infections represent a leading etiology, contributing considerably to both the incidence and adverse outcomes of the disease [1]. Among infectious diseases, bacterial pneumonia is highly prevalent and carries a significant risk of mortality, largely due to its tendency to progress to severe illness [2]. Common pathogens, such as Staphylococcus aureus, Streptococcus pneumoniae, and Haemophilus influenzae, more frequently affect vulnerable groups, including children and the elderly, largely owing to their weaker immune function [3-5]. Accurate and timely diagnosis, effective antimicrobial treatments, and continuous evaluation of treatment response are critical for improving patient outcomes with bacterial pneumonia [6, 7].

The development of bacterial pneumonia is associated with the host inflammatory response triggered by invading bacteria [8, 9]. After bacterial infection, inflammatory mediators are released. If this local inflammation is not effectively controlled, it may progress to a systemic inflammatory response, which may go beyond the direct effects of the bacteria.

In recent years, interleukin-17 (IL-17) has been recognized as a key pro-inflammatory cytokine involved in host defense. IL-17 is mainly produced by Th17 cells, gamma delta T cells, and

https://doi.org/10.62347/AHPX9239

innate lymphoid cells (ILCs), and plays an essential role in protecting the host against extracellular bacteria and fungi. However, dysregulated IL-17 has been associated with many inflammatory and autoimmune diseases [10, 11]. IL-17 exerts its biological effects by binding to its specific receptor IL-17R, which is expressed in a wide range of cell types, including epithelial cells and myeloid cells [12]. This binding triggers a series of signaling pathways that lead to the production of proinflammatory cytokines, chemokines, antibacterial peptides, and mitochondrial generators. Together, these mediators promote the recruitment of neutrophils and other immune effector cells to infection sites, strengthening local antimicrobial defense [13, 14]. Thus, IL-17 signaling is essential for coordinating both innate and adaptive immune responses at mucosal surfaces, including the respiratory tract [14, 15]. Exploring the relationship between IL-17/IL-17R and established biomarkers may provide a better understanding of the inflammatory features of bacterial pneumonia.

Although the role of IL-17 in lung immunity and inflammation is well established in the context of human bacterial pneumonia, the specific clinical significance of IL-17 and its receptors has not been fully elucidated in terms of expression dynamics, diagnostic potential, and associations with established biomarkers and patient outcomes. Although dynamic-object model studies have demonstrated the involvement of IL-17 in the pathogenesis of pneumonia [16], and some clinical studies have also noted elevated IL-17 levels in severe pneumonia [13, 14], comprehensive analyses of IL-17 and IL-17R expression before and after treatment remain lacking, particularly in well-defined cohort studies comparing patients with bacterial and non-bacterial pneumonia. Understanding whether IL-17/IL-17R levels can distinguish bacterial pneumonia from other pneumonia types, predict treatment response, or serve as independent risk factors may greatly improve clinical management.

Therefore, this study aims to investigate the dynamic changes in serum IL-17 and IL-17R levels before and after treatment in a well-defined cohort of patients with bacterial pneumonia, and to evaluate their correlation with established inflammatory biomarkers, diagnostic performance, and their value as independent risk factors. By elucidating the clinical relevance of IL-17 signaling in bacterial pneumonia, this study aims to provide valuable insights to improve diagnosis, monitor treatment outcomes, and ultimately optimize patient care.

Materials and methods

Case selection

A retrospective analysis was conducted on 172 patients with bacterial pneumonia who were treated with conventional antibiotics at The First Affiliated Hospital of Ningbo University between May 2021 and January 2024. Based on standard clinical severity criteria for pneumonia [17], the patients were divided into the severe (n = 61) and non-severe (n = 111) group. Severe pneumonia was diagnosed when patients met one major criterion, or at least three minor criteria. The major criteria comprised the need for invasive mechanical ventilation or septic shock necessitating vasopressor support. The minor criteria included a respiratory rate ≥ 30 breaths/minute, PaO_2/FiO_2 ratio ≤ 250 mmHg, multilobar infiltrates on chest imaging, confusion/disorientation, blood urea nitrogen (BUN) ≥ 20 mg/dL, leukopenia (WBC < 4,000 cells/mm^3), thrombocytopenia (platelets < 100,000 cells/mm^3), core temperature < 36°C, or hypotension demanding aggressive fluid resuscitation. Non-severe pneumonia was characterized by the absence of major criteria and fewer than three minor criteria.

Inclusion criteria: ① Age ≥ 18 years; ② Clinical diagnosis of bacterial pneumonia supported by radiographic evidence and microbiological confirmation; ③ Completion of a full course of conventional antibiotic therapy consistent with international guidelines for the management of bacterial pneumonia [18]; ④ Availability of complete medical records, including detailed clinical characteristics, laboratory results (especially inflammatory biomarkers), and follow-up data before and after treatment.

Exclusion criteria: ① Coexisting significant pulmonary comorbidities, such as active tuberculosis, lung cancer, interstitial lung disease, bronchiectasis, or cystic fibrosis; ② Presence of other active malignancies or severe systemic

immune disorders, including uncontrolled HIV infection, autoimmune diseases requiring immunosuppressive therapy, or primary immunodeficiency syndromes; ③ Concurrent infections other than bacterial pneumonia (e.g., viral, fungal, or parasitic infections) that may confound inflammatory biomarker interpretation; ④ Pregnancy or lactation; ⑤ Recent use of immunomodulatory agents (e.g., corticosteroids, biologics) within 4 weeks prior to enrollment; ⑥ History of organ transplantation or ongoing immunosuppressive therapy.

Ethical statement

The study adhered to the ethical guidelines of the Declaration of Helsinki. Informed consent was waived by the Ethics Committee owing to the retrospective nature of the research. The protocol was approved by the Institutional Review Board (IRB)/Ethics Committee of The First Affiliated Hospital of Ningbo University.

Data collection

Clinical and laboratory data were extracted from electronic health records. A standard case report form (CRF) was utilized for this purpose which was designed following international guidelines for critical care documentation. The data collected covered patient sex, age, body mass index (BMI), smoking history, comorbidities such as hypertension, diabetes, and hyperlipidemia, vital signs at admission, complete blood counts, markers of liver and kidney function, and various inflammatory biomarkers.

Detection methods

Sample collection: Fasting veinous blood sample (5 mL) was collected from each patient within 24 hours of hospital admission and within five days after initiating antibiotic therapy. All phlebotomy procedures were conducted under aseptic conditions. Blood samples were placed into serum separation tubes and allowed to clot at room temperature for 30 minutes. Following the clotting, the samples were centrifuged at 3,000 rpm for 10 minutes to obtain serum. The resulting serum was then aliquoted into sterile microtubes and promptly stored at -80°C to preserve sample integrity until subsequent laboratory analysis.

Whole blood analysis: Complete blood count (CBC) and differential analysis of fresh whole blood samples were performed using a fully automated hematology analyzer (Sysmex XN-1000 Sisen Meikang Corporation Japan). Parameters, including white blood cell count, along with the proportions of neutrophils, lymphocytes, monocytes, and eosinophils, were recorded. Internal quality control procedures were followed in accordance with manufacturer guidelines.

Serum analysis: Serum levels of IL-17, IL-17R, procalcitonin (PCT), and high-sensitivity C-reactive protein (hs-CRP) were quantitatively determined using commercially available enzyme-linked immunosorbent assay (ELISA) kits. Serum levels of IL-17 and IL-17R were quantified with human ELISA kits (R&D Systems, USA) in accordance with the supplier's protocols. PCT levels were assessed via immunofluorescence assay (Jiangsu Relia Biotechnology Co., Ltd., China), and hs-CRP was detected using immunoturbidimetry (Beijing Lidman Biochemical Co., Ltd., China).

Statistical methods

Data were analyzed using SPSS 22.0 (IBM Corp., USA). Normally distributed continuous data were reported as mean ± standard deviation (SD) and compared between groups using independent t-tests; non-normally distributed data were analyzed with the Mann-Whitney U test. Categorical variables were expressed as counts and percentages and compared using chi-square or Fisher's exact tests. Within-group comparisons before and after treatment were made using paired t-tests or Wilcoxon signed-rank tests based on data distribution. ROC curves were plotted to assess the diagnostic value of IL-17 and IL-17R for bacterial pneumonia, with AUC, sensitivity, and specificity calculated. Correlations between IL-17, IL-17R, and established inflammatory markers (PCT and hs-CRP) were evaluated using Pearson or Spearman methods, depending on the normality of the data distribution. Variables with $P < 0.10$ in univariate analysis were included in the multivariate logistic regression model to identify independent risk factors for bacterial pneumonia. Results were expressed as odds ratios (OR) with 95% confidence intervals (CI). Subgroup analyses were performed to compare IL-17 and

Table 1. Comparison of baseline information between the two groups [n (%)]

Clinical Characteristics	Non-Severe Group (n = 111)	Severe Group (n = 61)	t/χ^2	*p*-value
Sex [n (%)]			0.203	0.652
Male	64 (57.66)	33 (54.10)		
Female	47 (42.34)	28 (45.90)		
Age (years)	51.34 ± 9.28	59.47 ± 8.93	5.57	< 0.001
BMI (kg/m²)	24.17 ± 3.62	22.84 ± 4.13	2.195	0.030
Smoking History [n (%)]			4.775	0.029
Yes	48 (43.24)	37 (60.66)		
No	63 (56.76)	24 (39.34)		
Diabetes [n (%)]			2.518	0.113
Yes	21 (18.92)	18 (29.51)		
No	90 (81.08)	43 (70.49)		
Hypertension [n (%)]			4.013	0.045
Yes	39 (35.14)	31 (50.82)		
No	72 (64.86)	30 (49.18)		
Hyperlipidemia [n (%)]			0.695	0.404
Yes	28 (25.23)	19 (31.15)		
No	83 (74.77)	42 (68.85)		
Admission Vital Signs				
Heart Rate (beats/min)	88.52 ± 12.37	90.14 ± 13.85	0.791	0.430
Respiratory Rate (breaths/min)	22.45 ± 3.26	24.58 ± 3.91	3.814	< 0.001
Systolic BP (mmHg)	132.67 ± 16.54	129.83 ± 18.22	1.038	0.301
Oxygen Saturation (%)	96.52 ± 1.87	96.18 ± 2.14	1.07	0.286

BMI: Body Mass Index.

IL-17R levels between patients with Gram-positive and Gram-negative bacterial infections, and between antibiotic-sensitive and antibiotic-resistant cases, using independent t-tests or Mann-Whitney U tests as appropriate. A *p*-value < 0.05 was considered statistically significant.

Results

Baseline demographic and clinical characteristics

Significant differences were observed in age, BMI, smoking history, and hypertension between the severe and non-severe groups (all P < 0.05). Specifically, the severe group demonstrated older age (59.47 ± 8.93 vs. 51.34 ± 9.28 years, P < 0.001), lower BMI (22.84 ± 4.13 vs. 24.17 ± 3.62 kg/m^2, P = 0.030), higher proportion of smokers (60.66% vs. 43.24%, P = 0.029), and more hypertension cases (50.82% vs. 35.14%, P = 0.045). As expected, the severe group also presented with a significantly higher respiratory rate at admission (24.58 ± 3.91 vs. 22.45 ± 3.26 breaths/min, P < 0.001). No significant differences were found in sex, diabetes, or hyperlipidemia (all P > 0.05) (**Table 1**).

Comparison of peripheral blood leukocyte profiles and biochemical indicators between the two groups before and after treatment

As shown in **Table 2**, before treatment, the severe group exhibited significantly higher WBC counts, monocyte percentages, neutrophil percentages, Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), and creatinine levels, along with significantly lower lymphocyte and eosinophil percentages compared to the non-severe group (all P < 0.001). After treatment, most parameters improved and showed no significant differences between groups except for lymphocyte count, ALT, AST, and creatinine, which remained higher in the severe group (all P < 0.05).

Dynamics of serum and established inflammatory biomarkers in response to treatment

As shown in **Table 3**, before treatment, the severe group had significantly higher levels of

Table 2. Comparison of peripheral blood leukocyte profiles and biochemical indicators between the two groups before and after treatment

Clinical Indications	Time	Non-Severe Group (n = 111)	Severe Group (n = 61)	t-value	*p*-value
WBC count (×10^9 cells/L)	Before	8.91 ± 2.08	13.86 ± 3.42	10.305	< 0.001
	After	8.74 ± 2.13	9.23 ± 2.37***	1.377	0.170
Monocyte count (%)	Before	6.82 ± 1.74	8.93 ± 2.16	6.987	< 0.001
	After	6.91 ± 1.68	7.12 ± 1.81***	0.75	0.454
Neutrophil count (%)	Before	62.38 ± 8.47	78.64 ± 9.23	11.667	< 0.001
	After	63.11 ± 7.92	65.29 ± 8.14***	1.708	0.089
Lymphocyte count (%)	Before	28.47 ± 6.12	16.83 ± 5.47	12.377	< 0.001
	After	27.96 ± 5.88	25.74 ± 6.33***	2.308	0.022
Eosinophil count (%)	Before	2.33 ± 0.87	1.26 ± 0.64	9.186	< 0.001
	After	2.28 ± 0.82	2.07 ± 0.79***	1.621	0.107
ALT (IU/L)	Before	26.43 ± 8.72	38.67 ± 12.44	6.819	< 0.001
	After	25.89 ± 7.93	29.14 ± 9.26***	2.42	0.017
AST (IU/L)	Before	24.76 ± 7.18	36.92 ± 10.57	8.023	< 0.001
	After	23.84 ± 6.92	27.63 ± 8.41***	3.18	0.002
Creatinine (μmol/L)	Before	78.34 ± 16.27	92.46 ± 21.83	4.422	< 0.001
	After	76.89 ± 15.64	84.17 ± 18.92*	2.708	0.007

WBC: White Blood Cell; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; *P < 0.01, ***P < 0.001 compared to before treatment.

Table 3. Comparison of serum levels of IL-17, IL-17R, PCT, and hs-CRP between the two groups before and after treatment

Clinical Indications	Time	Non-Severe Group (n = 111)	Severe Group (n = 61)	t-value	*p*-value
IL-17 (pg/mL)	Before	12.38 ± 3.27	46.72 ± 11.83	22.205	< 0.001
	After	13.01 ± 3.41	18.93 ± 5.26***	7.930	< 0.001
IL-17R (pg/mL)	Before	215.47 ± 48.36	487.62 ± 112.74	17.968	< 0.001
	After	208.93 ± 46.58	278.41 ± 67.35***	7.170	< 0.001
PCT (ng/mL)	Before	0.18 ± 0.07	3.87 ± 1.26	22.836	< 0.001
	After	0.16 ± 0.06*	0.94 ± 0.38***	16.040	< 0.001
hs-CRP (ng/mL)	Before	8.42 ± 2.73	65.39 ± 21.47	20.627	< 0.001
	After	7.89 ± 2.64	22.16 ± 8.93***	12.198	< 0.001

IL-17: Interleukin-17; IL-17R: Interleukin-17 Receptor; PCT: Procalcitonin; hs-CRP: High-Sensitivity C-Reactive Protein. *P < 0.05, ***P < 0.001 compared to before treatment.

IL-17, IL-17R, PCT, hs-CRP compared to the non-severe group (all P < 0.001). After treatment, biomarker levels decreased significantly in the severe group (all P < 0.001). In the non-severe group, only PCT decreased significantly after treatment (P < 0.05), while IL-17, IL-17R, and hs-CRP did not show significant changes. Following treatment, all biomarker levels remained significantly higher in the severe group compared to the non-severe group (all P < 0.001).

Logistic regression analysis for risk factors of bacterial pneumonia

Univariate analysis revealed that several variables significantly associated with bacterial pneumonia risk (**Table 4**), including older age (OR = 1.073, 95% CI: 1.025-1.103, P = 0.001), smoking history (OR = 2.307, 95% CI: 1.203-4.424, P = 0.012), hypertension (OR = 1.861, 95% CI: 1.012-3.422, P = 0.045), higher respiratory rate (OR = 1.115, 95% CI: 1.028-1.209,

Table 4. Univariate logistic regression analysis of risk factors for severe bacterial pneumonia

Factors	Coefficient	SE	Wald	OR (95% CI)	*P* value
Age (years)	0.061	0.018	11.482	1.073 (1.025-1.103)	0.001
BMI (kg/m^2)	-0.116	0.041	7.987	0.890 (0.821-0.965)	0.005
Smoking History	0.836	0.332	6.337	2.307 (1.203-4.424)	0.012
Hypertension	0.621	0.310	4.016	1.861 (1.012-3.422)	0.045
Respiratory Rate (breaths/min)	0.109	0.042	6.742	1.115 (1.028-1.209)	0.009
WBC count (×10^9 cells/L)	0.283	0.057	24.638	1.327 (1.186-1.485)	< 0.001
Monocyte count (%)	0.191	0.072	7.042	1.210 (1.051-1.393)	0.008
Neutrophil count (%)	0.154	0.023	44.826	1.167 (1.114-1.222)	< 0.001
Lymphocyte count (%)	-0.181	0.031	33.871	0.834 (0.785-0.887)	< 0.001
Eosinophil count (%)	-1.018	0.191	28.394	0.361 (0.248-0.525)	< 0.001
ALT (IU/L)	0.066	0.017	15.058	1.068 (1.033-1.104)	< 0.001
AST (IU/L)	0.081	0.018	20.284	1.084 (1.046-1.123)	< 0.001
Creatinine (μmol/L)	0.027	0.008	11.391	1.027 (1.011-1.043)	0.001
IL-17 (pg/mL)	0.132	0.019	48.211	1.141 (1.099-1.185)	< 0.001
IL-17R (pg/mL)	0.008	0.002	16.000	1.008 (1.004-1.012)	< 0.001
PCT (ng/mL)	1.041	0.173	36.207	2.833 (2.019-3.976)	< 0.001
hs-CRP (ng/mL)	0.840	0.142	34.928	2.317 (1.753-3.062)	< 0.001

OR: Odds Ratio; CI: Confidence Interval; SE: Standard Error; BMI: Body Mass Index; WBC: White Blood Cell; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; IL-17: Interleukin-17; IL-17R: Interleukin-17 Receptor; PCT: Procalcitonin; hs-CRP: High-Sensitivity C-Reactive Protein.

Table 5. Multivariate logistic regression analysis of risk factors for severe bacterial pneumonia

Factors	Coefficient	SE	Wald	OR (95% CI)	*P* value
Age (years)	0.061	0.022	7.691	1.063 (1.018-1.110)	0.006
Smoking History	0.629	0.359	3.073	1.876 (0.928-3.793)	0.080
IL-17 (pg/mL)	0.133	0.034	15.290	1.142 (1.068-1.221)	< 0.001
IL-17R (pg/mL)	0.083	0.028	8.782	1.087 (1.028-1.149)	0.003
PCT (ng/mL)	1.042	0.186	31.422	2.834 (1.970-4.084)	< 0.001
hs-CRP (ng/mL)	0.840	0.145	33.517	2.318 (1.742-3.083)	< 0.001

OR: Odds Ratio; CI: Confidence Interval; SE: Standard Error; IL-17: Interleukin-17; IL-17R: Interleukin-17 Receptor; PCT: Procalcitonin; hs-CRP: High-Sensitivity C-Reactive Protein.

P = 0.009), and elevated inflammatory markers such as WBC (OR = 1.327, 95% CI: 1.186-1.485, P < 0.001), neutrophil % (OR = 1.167, 95% CI: 1.114-1.222, P < 0.001), IL-17 (OR = 1.141, 95% CI: 1.099-1.185, P < 0.001), IL-17R (OR = 1.008, 95% CI: 1.004-1.012, P < 0.001), PCT (OR = 2.833, 95% CI: 2.019-3.976, P < 0.001), and hs-CRP (OR = 2.317, 95% CI: 1.753-3.062, P < 0.001). In contrast, higher BMI (OR = 0.890, 95% CI: 0.821-0.965, P = 0.005), lymphocyte % (OR = 0.834, 95% CI: 0.785-0.887, P < 0.001), and eosinophil % (OR = 0.361, 95% CI: 0.248-0.525, P < 0.001) were protective.

After adjusting for confounders, multivariate analysis confirmed that age (OR = 1.063, 95% CI: 1.018-1.110, P = 0.006), IL-17 (OR = 1.142, 95% CI: 1.068-1.221, P < 0.001), IL-17R (OR = 1.087, 95% CI: 1.028-1.149, P = 0.003), PCT (OR = 2.834, 95% CI: 1.970-4.084, P < 0.001), and hs-CRP (OR = 2.318, 95% CI: 1.742-3.083, P < 0.001) were independent risk factors (**Table 5**). Smoking history approached but did not achieve statistical significance (OR = 1.876, 95% CI: 0.928-3.793, P = 0.080), which may be due to insufficient sample size or residual confounding not fully adjusted in the model.

Diagnostic performance of serum IL-17 and IL-17R for bacterial pneumonia severity

The utility of IL-17 and IL-17R in assessing disease severity was evaluated through ROC cur-

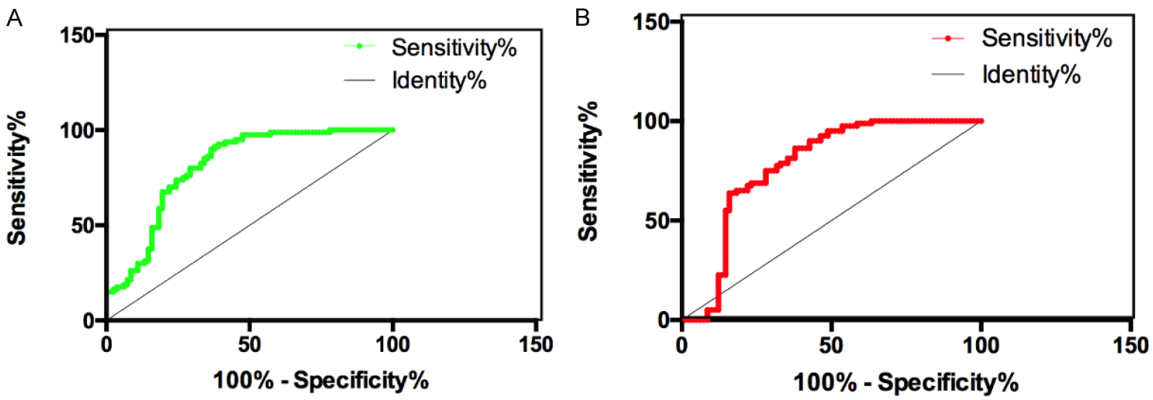

Figure 1. Receiver operating characteristic (ROC) curve analysis of serum IL-17 and IL-17R for diagnosing severe bacterial pneumonia. A: ROC curve for IL-17. B: ROC curve for IL-17R.

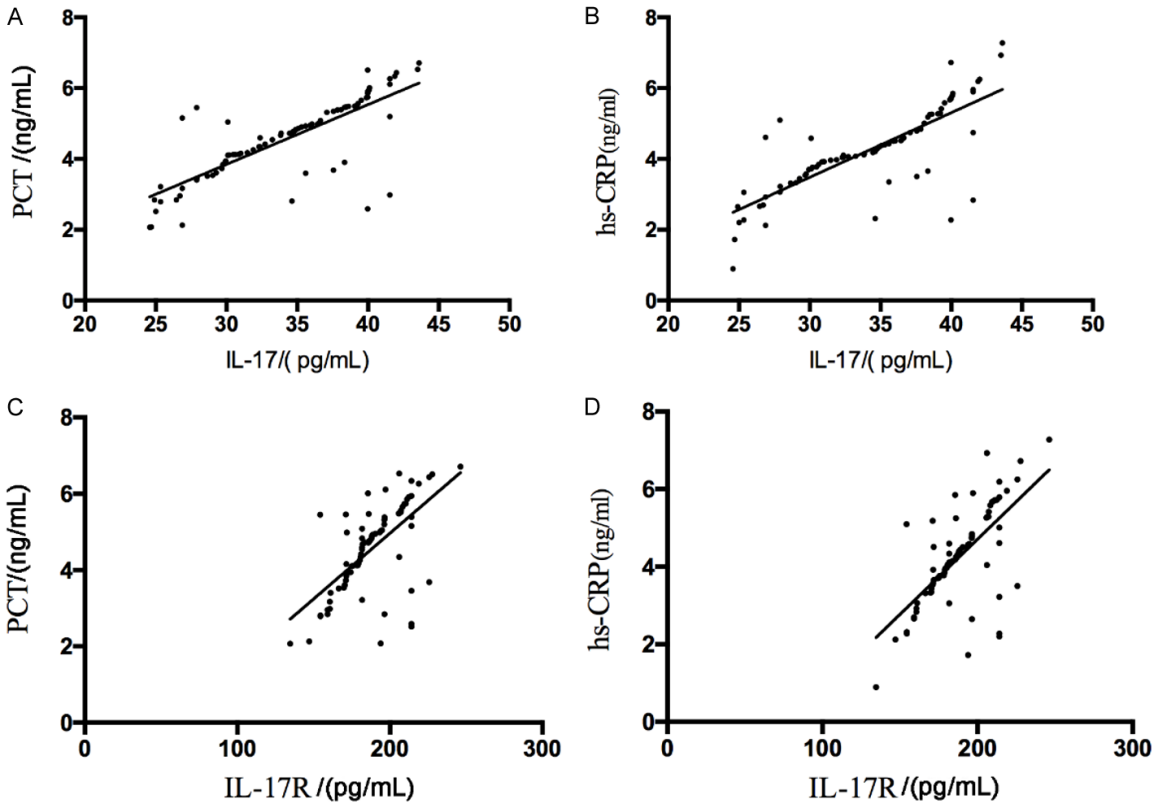

Figure 2. Correlation analysis of serum IL-17, IL-17R with PCT and hs-CRP. A: Serum IL-17 showed a significant positive association with PCT; B: IL-17 was positively correlated with hs-CRP; C: A positive correlation was observed between IL-17R and PCT; D: IL-17R demonstrated a significant positive relationship with hs-CRP. IL-17: Interleukin-17; IL-17R: Interleukin-17 Receptor; PCT: Procalcitonin; hs-CRP: High-Sensitivity C-Reactive Protein.

ve analysis, using the severe group as the positive condition. For IL-17, the area under the curve (AUC) was 0.808, with a sensitivity of 78.75% and a specificity of 70.73%. For IL-17R, the AUC was 0.777, with a sensitivity of 73.75% and a specificity of 71.75% (**Figure 1**).

Correlations between serum IL-17, IL-17R and established inflammatory biomarkers in bacterial pneumonia

As shown in **Figure 2**, significant positive correlations were observed between IL-17 and

Table 6. Comparison of serum levels of IL-17 and IL-17R between patients stratified by bacterial pathogen type and antibiotic susceptibility

Subgroup	N	IL-17 (pg/mL)	*P* value	IL-17R (pg/mL)	*P* value
By Pathogen Type					
Gram-positive bacteria	110	28.91 ± 10.34	< 0.001	312.18 ± 87.45	< 0.001
Gram-negative bacteria	62	35.24 ± 12.56		385.47 ± 98.63	
By Antibiotic Susceptibility					
Antibiotic-sensitive	115	26.55 ± 9.67	< 0.001	305.92 ± 84.16	< 0.001
Antibiotic-resistant	57	38.72 ± 11.89		401.33 ± 102.74	

PCT ($r = 0.776$, $P < 0.05$), IL-17 and hs-CRP ($r = 0.783$, $P < 0.05$), IL-17R and PCT ($r = 0.626$, $P < 0.05$), and IL-17R and hs-CRP ($r = 0.659$, $P < 0.05$).

Subgroup analysis of IL-17 and IL-17R levels by bacterial pathogen and antibiotic susceptibility

We further compared the serum levels of IL-17 and IL-17R across these clinically relevant subgroups, as detailed in **Table 6**. Serum IL-17 and IL-17R levels were significantly higher in patients with Gram-negative bacterial infections compared to those with Gram-positive infections ($P < 0.001$). Similarly, patients with antibiotic-resistant infections had notably elevated IL-17 and IL-17R levels compared to antibiotic-sensitive cases ($P < 0.001$). These findings suggest that IL-17 and IL-17R levels vary based on the bacterial pathogen type and antibiotic susceptibility status.

Discussion

Bacterial pneumonia represents a prevalent respiratory condition. Distinguishing bacterial pneumonia from other types of pneumonia is of great significance for guiding appropriate treatment and improving patient prognosis [19]. At present, clinical diagnosis relies primarily on bacterial culture and identification. However, this culture process usually takes about 3 days, making it unsuitable for rapid diagnosis and potentially delaying early treatment [20, 21]. Increasing evidence indicates that excessive release of inflammatory cytokines contributes greatly to the development of bacterial pneumonia [22, 23].

In this research, we assessed the dynamic changes in serum levels of IL-17, IL-17R, and other inflammatory markers including PCT and hs-CRP in patients with bacterial pneumonia, stratified by disease severity, both before and after treatment. The results indicated that pretreatment levels of IL-17, IL-17R, PCT, and hs-CRP were markedly elevated in the severe bacterial pneumonia group compared to the non-severe group. After treatment, the levels of these markers decreased significantly in the severe group, whereas in the non-severe group, only PCT showed a significant decline. Notably, despite the post-treatment reductions, all biomarker levels remained significantly higher in the severe group compared to the non-severe group. Our findings show elevated serum IL-17 and IL-17R levels in bacterial pneumonia, suggesting a contributory role in disease pathogenesis. The marked decline of these cytokines after treatment further underscores their value in evaluating disease severity and tracking therapeutic efficacy.

Studies have elucidated the molecular mechanisms underlying IL-17/IL-17R signaling in inflammatory responses [24, 25]. Upon ligand-receptor binding, IL-17/IL-17R engagement activates key downstream signaling pathways including NF-κB and MAPK, which drive the transcription of proinflammatory cytokines and chemokines [26, 27]. This signaling cascade enhances neutrophil recruitment to infection sites by upregulating chemokines such as CXCL1, CXCL2, and CXCL8, and promotes the secretion of antimicrobial peptides like β-defensins and S100 proteins, which are critical for mucosal host defense [28-30]. For instance, IL-17 has been shown to induce granulopoiesis and neutrophil mobilization via G-CSF, reinforcing its role in controlling bacterial load and tissue inflammation [31]. These mechanistic insights highlight how IL-17/IL-17R axis activation contributes to both protective immunity and pathological inflammation in bacterial pneumonia. While most current studies on IL-17

have focused on its expression in rat models of pneumonia [32, 33], clinical research on IL-17 and its receptor in human subjects remains limited. Previous investigation [34] reported elevated IL-17 expression in rat models of severe pneumonia, which is consistent with our observations. To further evaluate the value of IL-17 and IL-17R in assessing the severity of bacterial pneumonia, ROC analysis was performed, revealing that both biomarkers exhibit good sensitivity with comparable AUC values, supporting their utility in distinguishing severe from non-severe cases. Nevertheless, given the currently limited body of evidence on the diagnostic significance of IL-17 and IL-17R in bacterial pneumonia, we additionally conducted correlation analyses between these markers and already established inflammatory indicators such as PCT and hs-CRP.

Existing literature suggests that bacterial infections trigger substantial PCT release, which in turn amplifies the production of proinflammatory factors [35, 36]. Consequently, PCT is considered a reliable indicator of the intensity of systemic inflammation. Similarly, hs-CRP, known for its sensitivity to infections, also increases markedly during bacterial invasion [37]. Our correlation analysis revealed positive associations among IL-17, IL-17R, PCT, and hs-CRP, indicating that IL-17 and its receptor IL-17R may serve as potential indicators of bacterial infections. Huangfu et al. [38] suggested that IL-17 contributes to pathogen clearance by stimulating lymphocytes and other immune cells to secrete chemotactic proteins, thereby enhancing neutrophil recruitment and local immunity. Sanchez Sanchez et al. [39] described a synergistic interaction between IL-17 and interferon, generating a potent inflammatory signal that promotes neutrophil recruitment. The potential functional cooperation of IL-17/IL-17R with conventional biomarkers (PCT, hs-CRP) in bacterial pneumonia remains unclear. Clarifying these interactions will be essential for a more comprehensive understanding of the integrated inflammatory response and should be a focus of subsequent investigations.

Our multivariate analysis identified elevated levels of IL-17, IL-17R, PCT, and hs-CRP as independent risk factors for severe bacterial pneumonia. This finding implies that increased concentrations of these biomarkers may not only reflect heightened inflammatory activity but also help indicate a bacterial etiology of pneumonia, vacillating appropriate therapeutic strategies. Our subgroup analysis revealed IL-17 and IL-17R levels were significantly higher in patients with Gram-negative bacterial infections and in those with antibiotic-resistant strains. This suggests that the IL-17/IL-17R axis may be more activated in certain types of bacterial infections, potentially reflecting differences in pathogen-associated molecular patterns or host immune responses. The interplay between IL-17/IL-17R and virulence factors of common pathogens such as Streptococcus pneumoniae and Staphylococcus aureus may influence disease severity and host immune activation. For example, pneumococcal surface adhesins and staphylococcal superantigens can modulate IL-17 production by stimulating Th17 cells and innate lymphocytes, thereby amplifying local inflammation and neutrophil influx [40, 41]. This interaction may explain the elevated IL-17/IL-17R levels observed in infections caused by Gram-negative and antibiotic-resistant bacteria in this study, as these pathogens often possess distinct virulent profiles that potently trigger IL-17-mediated immunity. Further research is needed to delineate how specific bacterial components directly or indirectly regulate IL-17/IL-17R signaling and whether targeting these pathways could ameliorate disease progression. These findings highlight the potential of IL-17 and IL-17R as biomarkers for distinguishing between Gram-positive and Gram-negative infections and for identifying antibiotic resistance, which could inform targeted therapy and improve clinical management.

Despite the promising findings, this study has several limitations that should be acknowledged. First, as a single-center retrospective study conducted at a tertiary hospital in Eastern China, the potential for selection bias cannot be excluded. The geographic and clinical setting may limit the generalizability of our findings to other regions or healthcare environments. Future multi-center studies involving diverse populations are warranted to validate our results. Second, key clinical outcomes, such as length of hospital stay, duration of mechanical ventilation, 30-day readmission or mortality, were not assessed in this study. The associ-

ation between IL-17/IL-17R levels and patient prognosis remains to be established. Future research should incorporate these clinical endpoints to better evaluate the prognostic value of these biomarkers. Third, the absence of non-bacterial pneumonia control groups (viral or fungal pneumonia) and healthy individuals limits the ability to establish specific diagnostic thresholds for bacterial infections. Future studies should incorporate such control groups to better ascertain the diagnostic specificity of these biomarkers. Finally, no functional assays were performed to determine the precise role of the elevated IL-17/IL-17R axis. Therefore, future prospective, multi-center studies with larger cohorts are needed to validate these findings and to further investigate local pulmonary expression, underlying mechanisms, and the combined diagnostic value of IL-17/IL-17R with traditional biomarkers.

Conclusion

Serum levels of IL-17 and IL-17R are significantly elevated in patients with bacterial pneumonia, particularly in severe cases. These cytokines exhibit good diagnostic accuracy and are positively correlated with traditional inflammatory markers PCT and hs-CRP. Furthermore, multivariate analysis identified both IL-17 and IL-17R as independent risk factors for server bacterial pneumonia. These findings suggest that IL-17 and its receptor play a significant role in the host immune response to bacterial pulmonary infection and hold potential as valuable biomarkers for assessing disease severity and monitoring therapeutic efficacy in bacterial pneumonia.

Disclosure of conflict of interest

None.

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