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ORIGINAL RESEARCH

Correlation Between Serum Inflammatory Factor Level Changes and Disease Severity in Patients with Chronic Obstructive Pulmonary Disease Complicated by Tuberculosis

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Background: The coexistence of chronic obstructive pulmonary disease (COPD) and tuberculosis (TB) complicates diagnosis and treatment, increasing disease burden and mortality. The correlation between serum inflammatory factors and disease severity and prognosis in COPD patients with TB remains unclear.

Methods: This retrospective study included 200 participants treated at the Affiliated Hospital of Hebei University from December 2020 to December 2022: 80 patients with COPD and TB, 40 with COPD alone, 40 with TB alone, and 40 healthy controls. Serum levels of tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), interferon-γ (IFN-γ), soluble IL-2 receptor (sIL-2R), and C-reactive protein (CRP) were compared across groups and correlated with disease severity and prognosis in COPD patients with TB.

Results: Serum levels of TNF-α, IL-6, IFN-γ, sIL-2R, and CRP were significantly higher in the COPD with TB group compared to all other groups ($P<0.05$). In this group, elevated levels of these markers were associated with increased disease severity and poorer prognosis ($P<0.05$). Correlation analysis showed positive associations between inflammatory cytokine levels and disease severity, and negative associations with prognosis ($P<0.05$).

Conclusion: Serum inflammatory markers may help assess disease severity and prognosis in COPD patients with TB. However, due to the observational design, causality cannot be inferred. Further prospective, multi-center studies are required to validate these findings before clinical application.

Keywords: chronic obstructive pulmonary disease, tuberculosis, inflammatory factors, disease condition, prognosis

Background

Chronic obstructive pulmonary disease (COPD) is a chronic inflammatory disease of the lungs caused by progressive obstruction of the airways because of smoking and inhalation of particulate matter.[1] The incidence rate of COPD has continued to increase in the recent years globally and is currently ranked third among the leading causes of death worldwide.[1,2] Tuberculosis (TB) is a deadly infectious disease of the respiratory system caused by *Mycobacterium tuberculosis*. The latest epidemiological data has reported up to 10 million new TB cases and 1.5 million TB-related deaths each year.[3,4] Compared to the healthy subjects, the risk of developing TB is about three times higher in the COPD patients; moreover, chronic and recurrent inflammation caused by TB further worsens COPD by exacerbating emphysema and promoting macrophage dysfunction.[5,6] Therefore, early diagnosis and evaluation of COPD complicated with TB is of great significance.

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The levels of Th1 and Th2 cells in the peripheral blood are closely related with the onset and progression of COPD complicated with TB. Th1 cells promote granuloma formation and inhibit mycobacterial proliferation, whereas Th2 cells promote opposite effects.[7,8] Th1 and Th2 cells secrete cytokines such as TNF-α, IL-6, IFN-γ, and sIL-2R.[8–10] The serum levels of CRP, a common acute phase reactive protein, are aberrantly increased during inflammation.[9,10] However, CRP is a nonspecific inflammatory marker, and its elevation can be observed in various inflammatory conditions, including infections, autoimmune diseases, and tissue injury.[11] Therefore, while CRP levels can reflect the overall inflammatory burden in COPD patients complicated with TB, they may not provide specific information regarding the underlying pathophysiology. Changes in the serum levels of TNF-α, IL-6, IFN-γ, sIL-2R, and CRP have not been well studied in COPD patients complicated with TB. Moreover, their association with COPD complicated with TB has not been confirmed in clinical practice. Future studies should explore more specific biomarkers to better understand the inflammatory mechanisms in these patients.[12]

In this study, we analyzed whether the serum levels of TNF-α, IL-6, IFN-γ, sIL-2R, and CRP were useful biomarkers for the diagnosis and prognosis of COPD patients complicated with TB and potential therapeutic targets. We postulated that our findings would provide a reference for the clinicians to evaluate treatment strategy and prognosis of COPD complicated with TB during the preliminary stages of the disease.

Methods

Study Participants

This single-center retrospective observational study was conducted at the Hebei University Affiliated Hospital for patients that received treatment between December 2020 and December 2022 and included a cohort consisting of 80 patients with COPD complicated with TB, 40 patients with COPD alone, 40 patients with TB alone, and 40 healthy individuals undergoing physical examinations (ratio of 2:1:1:1).

The inclusion criteria were as follows: (1) Satisfied the COPD diagnostic criteria according to the COPD diagnostic guidelines of the Global Initiative for the Prevention and Treatment of Chronic Obstructive Pulmonary Disease (GOLD);[13] (2) The diagnostic criteria for TB refer to the "WS 288-2017 diagnosis of tuberculosis" formulated by the National Health and Health Commission of the People's Republic of China. TB diagnosis was based on microbiological confirmation (sputum smear/culture or molecular diagnostics like PCR) supplemented by clinical and radiological evidence;[14] (3) Availability of complete clinical data; (4) Availability of the laboratory indicator testing records. It is important to note that, due to the retrospective design of this study, detailed lung function tests (eg, FEV1/FVC and FEV1% predicted values) were not available for assessing COPD severity. Furthermore, information regarding the precise usage and adherence to COPD-related medications was not systematically collected within our cohort. The exclusion criteria were as follows: (1) Patients with other respiratory system diseases such as pulmonary embolism, bronchiectasis, interstitial lung disease, or lung tumors; (2) Patients with other serious systemic diseases such as heart failure, liver disease, and kidney disease; (3) Patients with systemic inflammatory diseases such as rheumatoid arthritis or systemic lupus erythematosus; (4) Patients with malignant tumors; (5) Patients with infectious diseases.

However, it should be noted that this study was limited by its single-center retrospective design, which may restrict the generalizability of the findings. This limitation may introduce potential selection bias. Prospective multi-center studies involving diverse patient populations are needed to validate and generalize our findings. Additionally, potential confounding variables such as smoking status, comorbidities, and medication use were not controlled for in this study, which could potentially influence the results.

Assessment of Inflammatory Indicators

We collected 4 mL of fasting venous blood on the morning after admission. The blood samples were centrifuged at 2500 r/min for 15 min, and the supernatant was harvested and used as serum. The serum levels of TNFα, IL-6, IFNγ, sIL-2R, and CRP were measured using the enzyme-linked immunosorbent assay (ELISA).

It is important to acknowledge that the measurement of serum inflammatory factors was performed at a single time point, which may not capture the dynamic changes of these inflammatory markers over time.

Assessment of the Severity of COPD Complicated with TB Patients

Based on the imaging examination, the severity of COPD complicated with TB was assessed as follows: (1) Mild: single lobe involvement without obvious cavity; (2) Moderate: ≥2 lung lobes involved in a single lung and presence of cavities with a diameter <4 cm; (3) Severe: Both lungs are significantly affected and presence of multiple cavities.

Prognostic Evaluation of COPD Patients Complicated with TB

Based on the clinical symptoms and imaging data analysis, prognosis of COPD patients complicated with TB was categorized as follows: (1) Good prognosis: significantly mild clinical symptoms; absence of acute attacks; negative results for the TB pathogen test, including sputum smear, culture, or molecular biological identification (eg, PCR); and absence or reduced pore area based on imaging examination; (2) Poor prognosis: patients exhibiting persistent clinical symptoms, reduced lung function (FEV1 decline ≥10%), recurrent acute exacerbations, or progression on imaging examination after 6 months were categorized as having a poor prognosis.

Statistical Analysis

The statistical data was analyzed using SPSS version 26.0 (IBM Corp, Armonk, NY, USA). The Shapiro Wilk test was used for assessing normal distribution. The continuous variables are represented as mean ± standard deviation (SD) or median and interquartile range (IQR). One-way analysis of variance (ANOVA) was used to evaluate the statistical significance of differences between groups for the continuous variables. Subsequently, pairwise comparisons were performed using the LSD method. Kruskal Wallis *H*-test was used to compare the statistical differences between the four groups for the variables that showed non-normal distribution. Subsequently, pairwise comparisons were performed using the Nemenyi test. Categorical variables are represented as frequencies and percentages. The differences in the categorical variables between the four groups were evaluated using the Chi-square test or Fisher's exact test. Two-sided *p*-value less than 0.05 was considered statistically significant. Spearman correlation analysis was performed to determine if the serum levels of TNF-α, IL-6, IFN-γ, sIL-2R, and CRP were associated with the severity and prognosis of COPD complicated with TB. $P<0.05$ was considered statistically significant.

Results

Baseline Characteristics

This study included 200 participants (127 males and 73 females) with an age range of 35–73 years and an average age of 55.21 ± 8.65 years. There were four categories of participants, including 80 patients with COPD complicated with TB, 40 patients with TB alone, 40 patients with COPD alone, and 40 healthy patients undergoing physical examination. Among the 80 patients with COPD complicated with TB, 25 showed mild symptoms, 28 showed moderate symptoms, and 27 showed severe symptoms. After 6 months of follow-up, 21 cases showed poor prognosis and 59 cases showed good prognosis. The participant screening and selection process is shown in Figure 1. As shown in Table 1, there were no significant differences between the four groups regarding clinical data.

Serum Levels of Inflammatory Factors are Higher in COPD Patients Complicated with TB

Our data showed statistically significant differences in the serum levels of TNF-α, IL-6, IFN-γ, sIL-2R, and CRP between the four groups. The serum levels of TNF-α, IL-6, IFN-γ, sIL-2R, and CRP were significantly higher in the COPD patients complicated with TB compared to the other three groups ($P<0.05$) (Figure 2).

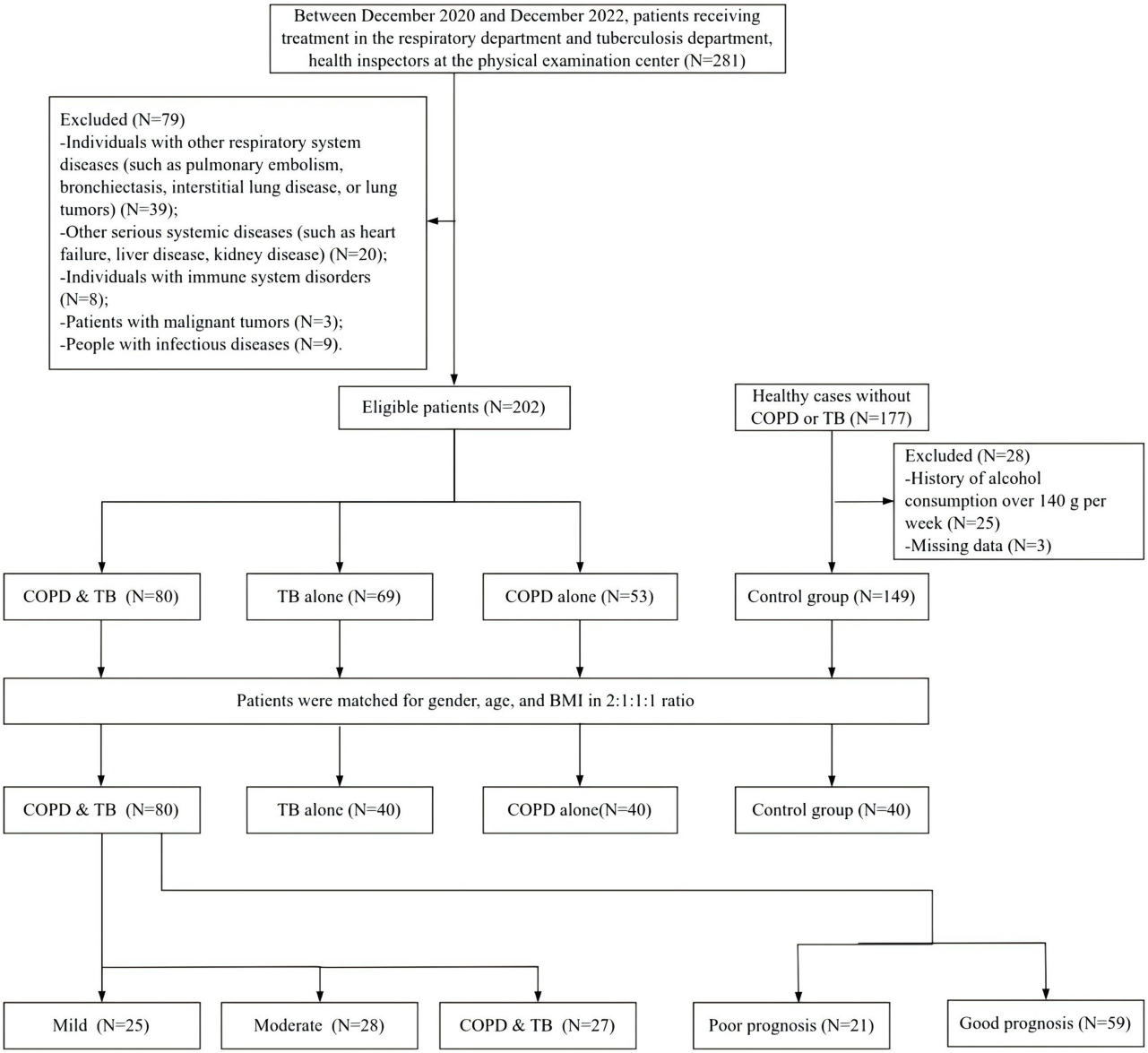

Figure 1 Diagram of participant screening and selection process.

Comparison of Serum Inflammatory Factor Levels in Patients with Different Degrees of COPD Complicated with TB

Among the 80 COPD patients complicated with TB, we identified 25 mild cases, 28 moderate cases, and 27 severe cases. The serum levels of TNF-α, IL-6, IFN-γ, sIL-2R, and CRP increased proportionately with higher severity of COPD ($P<0.05$) (Figure 3). Supplementary Figure 1 illustrates the correlation between these inflammatory markers and disease severity, showing a positive correlation with the disease progression.

Table 1 Comparison of Clinical Data Between the Four Participant Groups

Parameters	Health Group (n=40)	COPD Group (n=40)	TB Group (n=40)	COPD & TB Group (n=80)	F/χ^2	P
Male (yes), n (%)	26 (65.0)	24 (60.0)	29 (72.5)	48 (60.0)	2.071	0.558
Age (years), mean±SD	54.53±7.56	56.33±8.66	53.25±8.22	55.96±9.31	1.194	0.313
BMI (kg/m^2), mean±SD	23.92±2.41	23.65±3.05	22.93±2.86	24.04±3.54	1.203	0.310
Smoke (yes), n (%)	26 (65.0)	25 (62.5)	24 (60.0)	44 (55.0)	1.328	0.723
Drink (yes), n (%)	21 (52.5)	14 (35.0)	19 (47.5)	29 (36.3)	4.191	0.242

Abbreviations: COPD, chronic obstructive pulmonary disease; SD, standard deviation; TB, tuberculosis.

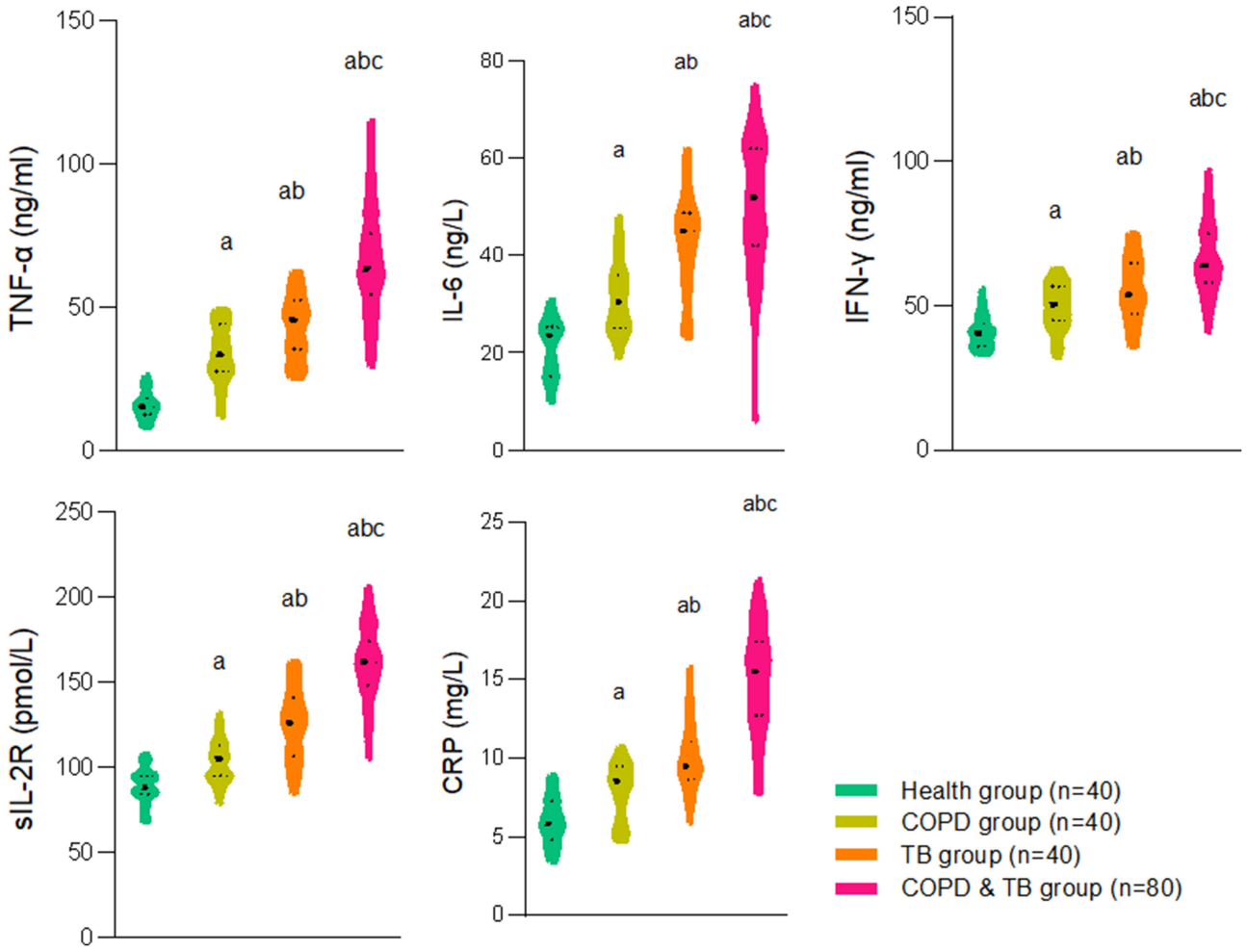

Figure 2 Distribution of serum levels of TNF-α, IL-6, IFN-γ, sIL-2R, and CRP between the four groups.
Notes: [a]*P*<0.05, compared with the healthy group; [b]*P*<0.05, compared with the COPD group; [c]*P*<0.05, compared with the TB group.
Abbreviations: COPD, Chronic obstructive pulmonary disease; TB, Tuberculosis; TNF-α, Tumor necrosis factor-α; IL-6, Interleukin-6; IFN-γ, Interferon -γ; sIL-2R, soluble IL-2 receptor; CRP, C-reactive protein.

Comparison of Serum Inflammatory Factor Levels in COPD Complicated with TB Patients with Good and Poor Prognosis

At the 6-month follow-up of 80 COPD patients complicated with TB, 59 patients showed good prognosis or improvement, whereas 21 patients showed poor prognosis or worsening of COPD. It should be emphasized that, due to the retrospective design of this study, detailed data regarding the treatment regimens and adherence to anti-tuberculosis and COPD medications were not systematically collected. Our data showed that the serum levels of TNF-α, IL-6, IFN-γ, sIL-2R, and CRP were significantly higher in patients with poor prognosis compared to those with good prognosis (P<0.05) (Figure 4). Supplementary Figure 2 provides a further illustration of the correlation between inflammatory markers and disease prognosis, showing a negative correlation with better prognosis outcomes.

Correlation Analysis Between Serum Inflammatory Cytokine Levels and the Severity and Prognosis of COPD Complicated with TB

According to the Spearman correlation analysis results, serum levels of TNF-α, IL-6, IFN-γ, sIL-2R, and CRP showed positive correlation with the severity of COPD complicated with TB and negative correlation with the disease prognosis (P<0.05) (Table 2).

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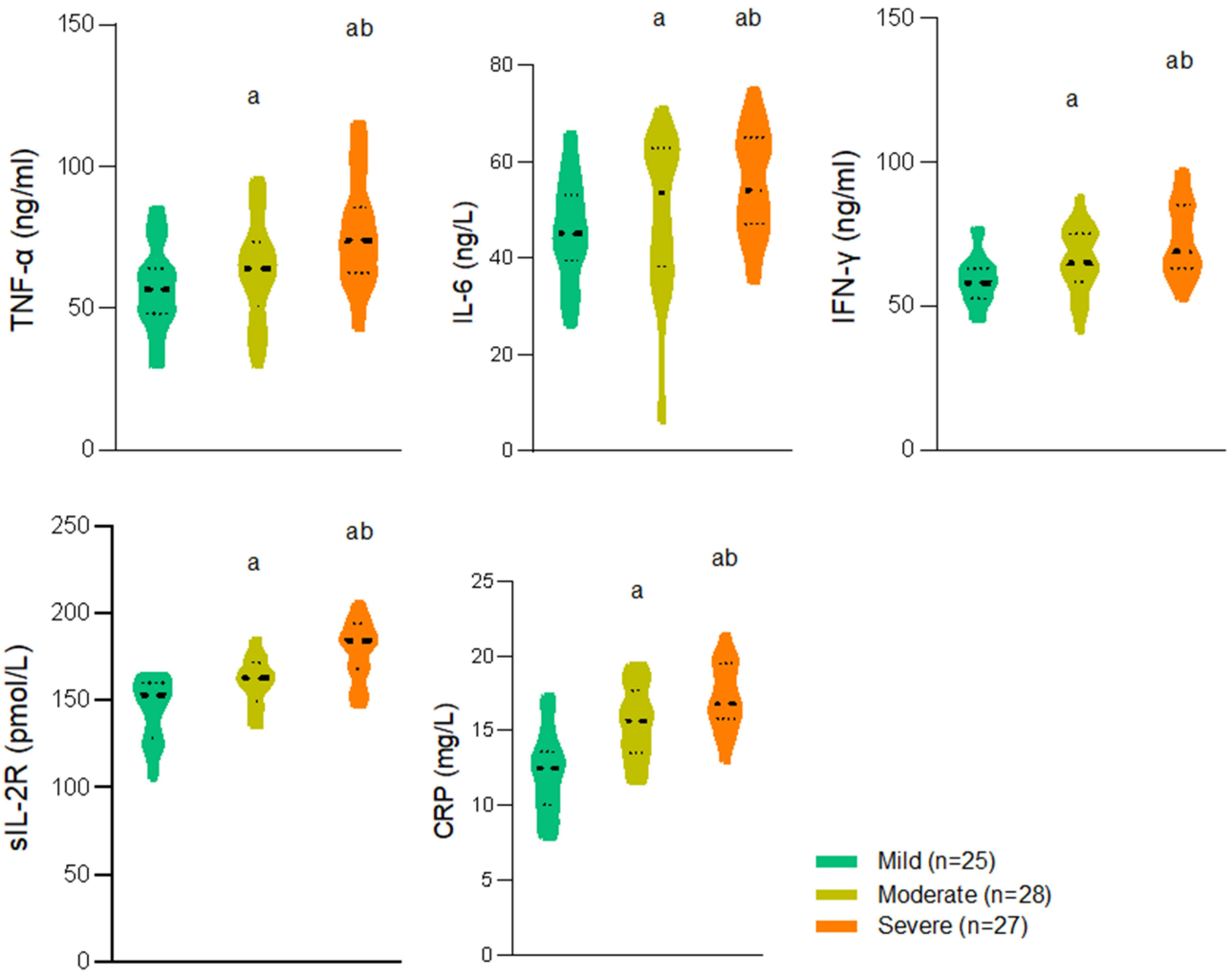

Figure 3 Serum levels of inflammatory cytokines in patients with different severity of COPD complicated with TB.
Notes: [a]*P*<0.05, compared with mild patients; [b]*P*<0.05, compared to moderate patients.
Abbreviations: COPD, chronic obstructive pulmonary disease; TB, Tuberculosis; TNF-α, Tumor necrosis factor-α; IL-6, Interleukin-6; IFN-γ, Interferon-γ; sIL-2R, soluble IL-2 receptor; CRP, c-reactive protein (CRP).

Discussion

This study showed that the serum levels of inflammatory factors such as TNF-α, IL-6, IFN-γ, sIL-2R, and CRP were significantly higher in the COPD patients complicated with TB than those in the other three groups and highlighted the severity of COPD. These data suggested that TB significantly affected the severity and prognosis of COPD patients. In recent years, several studies have shown mutual influence between TB and COPD.[6,15] The occurrence and development of COPD is associated with the past history of TB; moreover, the risk of TB is increased by the airflow restriction and long-term chronic inflammation of the respiratory tract in the COPD patients.[6,15,16] Furthermore, COPD patients complicated with TB show varying degrees of inflammation responses. Therefore, the correlation between relevant inflammatory indicators and severity of diseases can provide a practical reference for the diagnosis and treatment of human diseases.[6,8,16] Coitinho et al[17] reported that the cell-mediated inflammation response via natural killer cells, T lymphocytes and macrophages played a significant role in the inflammation response against TB. Macrophages present specific antigens of *Mycobacterium tuberculosis*, engulf the mycobacterium through lysosomal fusion, and kill the mycobacterium by generating cytotoxic free radicals and other cytokines.[16,17] Several studies have also shown that cytotoxic T cells, $CD8^+$ cells, $CD4^+$ cells, and gamma cells play important roles in the onset and progression of COPD; moreover, inflammation imbalance is a common feature in COPD patients.[18] The incidence rate of TB is higher in the

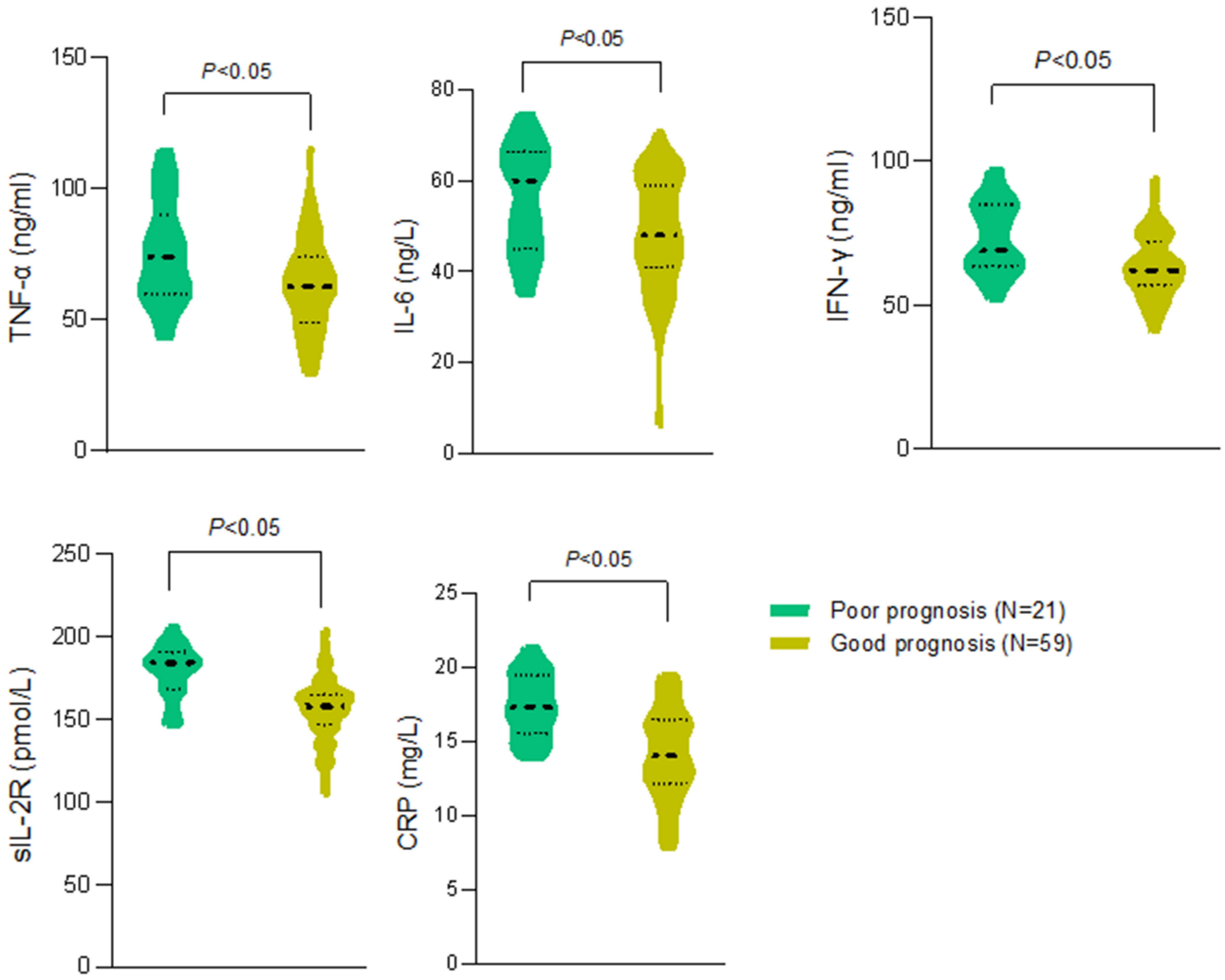

Figure 4 Serum levels of inflammatory factors in COPD patients complicated with TB categorized according to their prognostic outcomes.
Abbreviations: COPD, chronic obstructive pulmonary disease; TB, Tuberculosis; TNF-α, Tumor necrosis factor-α; IL-6, Interleukin-6; IFN-γ, Interferon-γ; sIL-2R, soluble IL-2 receptor; CRP, c-reactive protein.

COPD patients than in the healthy people because pathogenetic mechanisms of COPD and TB are similar.[18,19] Jiang et al[20] identified two distinct groups of $CD4^+$cells, namely, Th1 and Th2 cells. Th1 cells produce cytokines such as IL-2, IL-12, IF -γ, and TNF-β, which promote cellular inflammation responses. Th2 cells produce cytokines such as IL-9, IL-4, IL-5, IL-10, and IL-13, which play an important role in the humoral inflammation response of the body by enhancing proliferation and activation of eosinophils and mast cells. Therefore, monitoring the serum levels of the above indicators is essential for accurately evaluating the status of inflammation function in the body.

Table 2 Results of the Spearman Correlation Analysis

Parameters		TNF-α	IL-6	IFN-γ	sIL-2R	CRP
Degree of illness	*ρ*	0.414	0.320	0.464	0.654	0.636
	P	<0.001	0.004	<0.001	<0.001	<0.001
Disease prognosis	*ρ*	−0.268	−0.262	−0.346	−0.527	−0.476
	P	0.016	0.019	0.002	<0.001	<0.001

Abbreviations: TNF-α, tumor necrosis factor-α; IL-6, interleukin-6; IFN-γ, interferon -γ; sIL-2R, soluble IL-2 receptor; CRP, c-reactive protein.

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The levels of inflammatory factors in COPD patients complicated with TB showed an increasing trend as the condition worsened. This indicated that the inflammatory factors such as TNF-α, IL-6, IFN-γ, sIL-2R, and CRP played significant roles in the pathological process of COPD and TB, and were important disease markers for COPD and TB. However, this study did not compare these inflammatory markers against existing clinical assessment tools such as lung function tests or symptom-based evaluations. Future studies should explicitly compare the predictive value of these inflammatory markers with established clinical assessments to determine their additional clinical benefit. Previous studies have also shown that inflammatory reactions result in varying degrees of bronchial stenosis, which subsequently cause incomplete bronchial obstruction and adversely affect ventilation.[21] Oh et al[22] also reported that higher levels of inflammatory factors in COPD patients complicated with TB were associated with increased severity of the disease. This was consistent with the results of our study. The alveolar interstitium is damaged by repeated respiratory tract infections and gets detached from the bronchi and the surrounding lung parenchyma, thereby weakening the respiratory function.[21,22] Therefore, TB can significantly reduce pulmonary function of the COPD patients and increase their inflammatory index.

At the 6-month follow-up, serum levels of TNF-α, IL-6, IFN-γ, sIL-2R, and CRP were significantly higher in COPD patients complicated with TB demonstrating poor prognosis compared to those showing good prognosis. This further confirmed the importance of the above-mentioned inflammatory factors in the assessment of COPD complicated with TB and prognosis. However, COPD and TB are heterogeneous diseases involving complex immune responses beyond these inflammatory markers. The current study did not stratify patients based on COPD phenotypes (eg, emphysema-predominant versus chronic bronchitis) or TB subtypes (eg, drug-sensitive versus drug-resistant TB). Future research should include subgroup analyses based on these phenotypes to clarify the specific roles of inflammatory markers in different disease states. Park et al[23] also showed that COPD patients with a history of TB were associated with worse pulmonary function. Therefore, the history of TB is associated with higher severity of COPD and worse prognosis. The main clinical manifestations of COPD complicated with TB include multi shaped lung lesions with calcification, patchy shadows, non-segmental shadows and cavities, pleural effusion, pleural changes, consolidation shadows, and organizing pneumonia-like lesions; CT findings of COPD patients with early TB show the presence of clear and visible solid nodules in the posterior segment of the upper lobe tip and the posterior segment of the lower lobe. Tang et al[12] also reported that patients with pulmonary TB and COPD were associated with elevated levels of serum inflammatory factors, impaired cellular immunity, and a higher severity of inflammatory damage compared to patients with pulmonary TB and COPD. These data were consistent with the results of our study. The strength of our study was that we analyzed healthy individuals as a control group and monitored diverse inflammatory markers, which are routinely examined in the hospitals. Therefore, our research findings are clinically significant and can help guide the examination of COPD patients. The positive correlations observed between serum inflammatory factors and disease severity and prognosis in COPD complicated with TB patients are consistent with known inflammatory mechanisms in these diseases. Elevated cytokine levels, such as TNF-α, IL-6, IFN-γ, and sIL-2R, reflect enhanced Th1 immune responses, which contribute to pulmonary inflammation and tissue injury. Additionally, increased CRP levels represent systemic inflammatory activation, further supporting their association with disease severity. It is important to note, however, that these observed associations do not imply causation, given the observational nature of our study. Although serum inflammatory factors showed significant associations with disease severity and prognosis, their clinical utility as biomarkers has several limitations. These markers are non-specific, influenced by various inflammatory and infectious conditions, potentially limiting their diagnostic specificity for COPD complicated with TB. Further comparative studies are needed to evaluate whether these biomarkers offer superior predictive value compared to established clinical assessments, such as pulmonary function tests, symptom-based assessments, and radiological findings.

This study has several limitations. Firstly, it was a single-center retrospective study, which may introduce selection bias and limit the external validity of our findings. Secondly, potential confounding factors, such as smoking status, comorbidities, and medication use, were not fully controlled, which may affect the interpretation of results. Thirdly, inflammatory markers were measured only at a single time point, which could not reflect the dynamic inflammatory changes over time. Future multi-center, prospective studies with controlled confounding factors and repeated measurements of biomarkers are recommended to validate these preliminary findings.

Conclusions

This study demonstrated that the serum levels of inflammatory cytokines were significantly increased in COPD patients complicated with TB. The magnitude of the increase was closely associated with the severity of disease and prognosis. Our findings suggest that serum inflammatory factors, including TNF-α, IL-6, IFN-γ, sIL-2R, and CRP, may serve as potential biomarkers for disease monitoring and prognosis in COPD patients complicated with TB. Given the limitations of cross-sectional measurements, longitudinal studies with serial biomarker measurements are necessary to confirm these biomarkers' predictive reliability and clinical applicability.

Abbreviations

COPD, chronic obstructive pulmonary disease; TB, tuberculosis; TNF-α, tumor necrosis factor -α; IL-6, interleukin-6; IFN - γ, interferon -γ; sIL-2R, soluble IL-2 receptor; CRP, c-reactive protein; ELISA, enzyme-linked immunosorbent assay; SD, standard deviation; IQR, interquartile range; ANOVA, One-way analysis of variance.

Data Sharing Statement

The data used to provide support for the results of this study can be obtained from the corresponding authors.

Ethics Approval and Consent to Participate

The study was conducted in accordance with the Declaration of Helsinki (as was revised in 2013). The study was approved by Ethics Committee of the Hebei University Affiliated Hospital (Ethics approval number: HBFYLW2024058). The informed consent was waived by the ethics committee due to the observational and retrospective nature of the study. All data were stored securely, and confidentiality was maintained throughout the study.

Consent for Publication

The patients participating in the study all agree to publish the research results.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

All authors declare that they have no conflict of interest.

References

1. Safiri S, Carson-Chahhoud K, Noori M, et al. Burden of chronic obstructive pulmonary disease and its attributable risk factors in 204 countries and territories, 1990–2019: results from the Global Burden of Disease Study 2019. *BMJ*. 2022;378:e069679. doi:10.1136/bmj-2021-069679
2. Yu J, Ni J, Chen X, Fang Y, Fu S. Effect of different doses of Budesonide combined with Tiotropium bromide inhalation on elderly patients with chronic obstructive pulmonary disease. *Pak J Med Sci*. 2024;40(7):1338–1344. doi:10.12669/pjms.40.7.9209
3. Lyon SM, Rossman MD. Pulmonary tuberculosis. *Microbiol Spectr*. 2017;5(1):10–128. doi:10.1128/microbiolspec.TNMI7-0032-2016
4. Liaquat A, Iram S, Hussain S, Yusuf NW, Azeem H. Concomitant presence of culture-proven active pulmonary tuberculosis in patients with chronic obstructive pulmonary disease - A hospital based study. *Pak J Med Sci*. 2015;31(6):1344–1348. doi:10.12669/pjms.316.8166
5. Gai X, Allwood B, Sun Y. Post-tuberculosis lung disease and chronic obstructive pulmonary disease. *Chin Med J*. 2023;136(16):1923–1928. doi:10.1097/CM9.0000000000002771
6. Kayongo A, Nyiro B, Siddharthan T, et al. Mechanisms of lung damage in tuberculosis: implications for chronic obstructive pulmonary disease. *Front Cell Infect Microbiol*. 2023;13:1146571. doi:10.3389/fcimb.2023.1146571

7. Liu Y, Ye F, Ma L. The effect of budesonide combined with bifidobacteria and lactobacilli on lung function and gut microbiota of patients with chronic obstructive pulmonary disease. *Pak J Med Sci*. 2024;40(4):695–700. doi:10.12669/pjms.40.4.8514
8. Martynova E, Rizvanov A, Urbanowicz RA, Khaiboullina S. Inflammasome contribution to the activation of Th1, Th2, and Th17 immune responses. *Front Microbiol*. 2022;13:851835. doi:10.3389/fmicb.2022.851835
9. Zhang J, Chen Y, He G, Jiang X, Chen P, Ouyang J. Differential diagnosis of tuberculous and malignant pleural effusions: comparison of the Th1/Th2 cytokine panel, tumor marker panel and chemistry panel. *Scand J Clin Lab Invest*. 2020;80(4):265–270. doi:10.1080/00365513.2020.1728784
10. Lee JM, Han HJ, Choi WK, Yoo S, Baek S, Lee J. Immunomodulatory effects of intraoperative dexmedetomidine on T helper 1, T helper 2, T helper 17 and regulatory T cells cytokine levels and their balance: a prospective, randomized, double-blind, dose-response clinical study. *BMC Anesthesiol*. 2018;18(1):164. doi:10.1186/s12871-018-0625-2
11. Zhang T, Huang WS, Guan W, et al. Risk factors and predictors associated with the severity of COVID-19 in China: a systematic review, meta-analysis, and meta-regression. *J Thorac Dis*. 2020;12(12):7429–7441. doi:10.21037/jtd-20-1743
12. Tang S, Cui H, Yao L, et al. Increased cytokines response in patients with tuberculosis complicated with chronic obstructive pulmonary disease. *PLoS One*. 2013;8(4):e62385. doi:10.1371/journal.pone.0062385
13. Halpin DMG, Criner GJ, Papi A, et al. Global initiative for the diagnosis, management, and prevention of chronic obstructive lung disease. The 2020 GOLD science committee report on COVID-19 and chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2021;203(1):24–36. doi:10.1164/rccm.202009-3533SO
14. Goletti D, Delogu G, Matteelli A, Migliori GB. The role of IGRA in the diagnosis of tuberculosis infection, differentiating from active tuberculosis, and decision making for initiating treatment or preventive therapy of tuberculosis infection. *Int J Infect Dis*. 2022;124 Suppl 1:S12–S19. doi:10.1016/j.ijid.2022.02.047
15. Park YB, Rhee CK, Yoon HK, et al. Revised (2018) COPD clinical practice guideline of the Korean academy of tuberculosis and respiratory disease: a summary. *Tuberc Respir Dis*. 2018;81(4):261–273. doi:10.4046/trd.2018.0029
16. Fan H, Wu F, Liu J, et al. Pulmonary tuberculosis as a risk factor for chronic obstructive pulmonary disease: a systematic review and meta-analysis. *Ann Transl Med*. 2021;9(5):390. doi:10.21037/atm-20-4576
17. Coitinho C, Greif G, Robello C, Laserra P, Willery E, Supply P. Rapidly progressing tuberculosis outbreak in a very low risk group. *Eur Respir J*. 2014;43(3):903–906. doi:10.1183/09031936.00150413
18. Guiedem E, Ikomey GM, Nkenfou C, et al. Chronic obstructive pulmonary disease (COPD): neutrophils, macrophages and lymphocytes in patients with anterior tuberculosis compared to tobacco related COPD. *BMC Res Notes*. 2018;11(1):192. doi:10.1186/s13104-018-3309-6
19. Sehgal IS, Dhooria S, Muthu V, Salzer HJF, Agarwal R. Burden, clinical features, and outcomes of post-tuberculosis chronic obstructive lung diseases. *Curr Opin Pulm Med*. 2024;30(2):156–166. doi:10.1097/MCP.0000000000001026
20. Jiang M, Pang N, Wang J, et al. Characteristics of serum autoantibody repertoire and immune subgroup variation of tuberculosis-associated obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis*. 2023;18:2867–2886. doi:10.2147/COPD.S434601
21. Knox-Brown B, Patel J, Potts J, et al. Small airways obstruction and its risk factors in the Burden of Obstructive Lung Disease (BOLD) study: a multinational cross-sectional study. *Lancet Glob Health*. 2023;11(1):e69–e82. doi:10.1016/S2214-109X(22)00456-9
22. Oh JY, Lee YS, Min KH, et al. Difference in systemic inflammation and predictors of acute exacerbation between smoking-associated COPD and tuberculosis-associated COPD. *Int J Chron Obstruct Pulmon Dis*. 2018;13:3381–3387. doi:10.2147/COPD.S177371
23. Park HJ, Byun MK, Kim HJ, et al. History of pulmonary tuberculosis affects the severity and clinical outcomes of COPD. *Respirology*. 2018;23(1):100–106. doi:10.1111/resp.13147