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High-Resolution CT Thorax and Serum IL-6 Levels in Patients with Interstitial Lung Disease

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Abstract

Background: Interstitial lung diseases (ILDs) represent a diverse group of chronic lung disorders characterized by inflammation, fibrosis, and impaired gas exchange. High-resolution computed tomography (HRCT) is considered the imaging gold standard for diagnosis and characterization of ILDs. Meanwhile, interleukin-6 (IL-6), a pro-inflammatory cytokine, has emerged as a potential biomarker.

Objective: To evaluate the correlation between HRCT findings and serum IL-6 levels in patients with ILD, and assess their combined role in disease characterization and severity stratification.

Methods: A prospective observational study was conducted on 120 ILD patients between 2021 and 2023. HRCT patterns were classified according to ATS/ERS criteria, while serum IL-6 was quantified using ELISA. Clinical parameters, pulmonary function tests (PFTs), and HRCT severity scores.

Results: HRCT revealed usual interstitial pneumonia (UIP) in 42% of patients, nonspecific interstitial pneumonia (NSIP) in 34%, hypersensitivity pneumonitis (HP) in 16%, and other ILDs in 8%. Serum IL-6 levels were significantly higher in UIP compared to NSIP and HP ($p < 0.001$). IL-6 levels strongly correlated with HRCT fibrosis scores ($r = 0.71$, $p < 0.001$) and inversely with forced vital capacity (FVC) % predicted ($r = –0.65$). Patients with IL-6 >10 pg/mL had a 2.3-fold higher.

Conclusion: HRCT remains indispensable for structural characterization of ILD, but serum IL-6

provides valuable insights into inflammatory activity and prognosis. A combined HRCT–IL-6 approach may enhance diagnostic accuracy, guide treatment strategies, and help monitor disease progression.

Keywords: interstitial lung disease, HRCT, IL-6, pulmonary fibrosis, biomarker.

Introduction

Interstitial lung diseases (ILDs) are a heterogeneous group of diffuse parenchymal lung disorders, often leading to progressive fibrosis, respiratory failure, and increased mortality. The etiologies of ILD range from idiopathic pulmonary fibrosis (IPF) and autoimmune diseases to hypersensitivity pneumonitis and environmental exposures. Regardless of etiology, a common pathological hallmark is chronic inflammation and abnormal tissue remodeling.1-3

High-resolution computed tomography (HRCT) has revolutionized the non-invasive diagnosis of ILDs. It enables detailed visualization of lung parenchyma, allowing identification of characteristic patterns such as usual interstitial pneumonia (UIP) and nonspecific interstitial pneumonia (NSIP). HRCT patterns, combined with clinical and serological data, form the cornerstone of multidisciplinary diagnosis.4-6

Biomarkers are increasingly explored to complement imaging and functional assessments. Among them, interleukin-6 (IL-6) is a key cytokine in inflammatory cascades, mediating immune activation, fibroblast proliferation, and extracellular matrix deposition. Elevated IL-6 levels have been associated with disease severity and poor prognosis in ILDs, particularly in IPF and connective tissue disease–associated ILDs.7-8

While HRCT provides structural detail, it does not reflect ongoing inflammatory activity. Conversely, IL-6 reflects systemic and local immune dysregulation but lacks specificity for radiological subtypes. Thus, integrating HRCT imaging with IL-6 levels may enhance disease assessment, stratify risk, and refine treatment strategies. This study investigates the correlation between HRCT severity and serum IL-6 levels in ILD patients, aiming to define their combined diagnostic and prognostic utility.9-10

Methodology

Study Design & Population:

This prospective observational study was conducted at Rashid Latif Khan University Medical College, Lahore. A total of 120 consecutive ILD patients were enrolled.

Inclusion Criteria:

- Age ≥ 18 years
- Diagnosis of ILD based on ATS/ERS guidelines
- Ability to undergo HRCT and provide blood samples

Exclusion Criteria:

- Active respiratory infection
- Malignancy
- Recent immunosuppressive therapy (<4 weeks)
- Severe renal/hepatic impairment

Clinical Assessment:

Detailed history, physical examination, pulmonary function tests (PFTs: FVC, DLCO), and six-minute walk distance (6MWD) were recorded.

HRCT Evaluation:

HRCT scans were acquired using a 1-mm collimation protocol at full inspiration. Images were scored semi-quantitatively for extent of fibrosis, ground-glass opacities, honeycombing, and reticulation. HRCT patterns were classified as UIP, NSIP, HP, or others by two blinded radiologists.

IL-6 Assay:

Serum IL-6 was measured using enzyme-linked immunosorbent assay (ELISA). A cutoff of 7 pg/mL was used for elevated IL-6.

Statistical Analysis:

Pearson correlation assessed associations between IL-6 and HRCT severity scores, FVC, and

DLCO. Logistic regression analyzed predictors of rapid progression, defined as ≥10% decline in FVC or death within 12 months. A p-value <0.05 was considered statistically significant.

Results

Table 1. Baseline Characteristics of Study Cohort (n=120)

Variable	Value
Mean age (years)	58.4 ± 10.6
Male sex (%)	60
Smoking history (%)	42
Mean FVC (% predicted)	68.5 ± 15.3
Mean DLCO (% predicted)	54.7 ± 12.1
Mean IL-6 (pg/mL)	9.8 ± 5.4

Table 2. Distribution of HRCT Patterns

HRCT Pattern	Frequency (%)	Mean IL-6 (pg/mL)
UIP	42	12.4 ± 4.8
NSIP	34	8.1 ± 3.6
HP	16	7.5 ± 2.9
Others	8	6.8 ± 2.4

Correlation Analysis:

- IL-6 correlated positively with HRCT fibrosis scores ($r = 0.71$, $p < 0.001$).
- IL-6 inversely correlated with FVC % predicted ($r = –0.65$, $p < 0.001$) and DLCO ($r = –0.59$, $p < 0.001$).
- Patients with IL-6 >10 pg/mL had significantly worse 6MWD compared to those with ≤10 pg/mL ($p = 0.02$).

Prognostic Analysis:

Multivariate regression showed that IL-6 >10 pg/mL (HR = 2.3, 95% CI: 1.5–3.6) and UIP pattern on HRCT (HR = 2.9, 95% CI: 1.8–4.2) were independent predictors of rapid disease progression.

Discussion

This study demonstrates a significant correlation between HRCT severity scores and serum IL-6 levels in ILD patients. UIP pattern, typically associated with poor prognosis, was characterized by the highest IL-6 levels. Elevated IL-6 also correlated with reduced pulmonary function and exercise tolerance, supporting its role as a biomarker of disease activity.1-13

HRCT remains the gold standard for anatomical characterization of ILDs, enabling distinction of UIP from NSIP and other patterns. However, HRCT alone cannot reflect ongoing inflammation or predict progression in all cases. IL-6, in contrast, provides a dynamic measure of inflammatory and fibrotic activity. The integration of HRCT findings with IL-6 levels thus offers a more comprehensive assessment of ILD burden.14-15

These findings align with prior studies demonstrating elevated IL-6 in IPF and connective tissue disease–associated ILDs. IL-6 has been shown to drive fibroblast proliferation and collagen deposition, key processes in pulmonary fibrosis. Therapeutic blockade of IL-6 signaling (e.g., with tocilizumab) is under investigation, highlighting its potential role not only as a biomarker but also as a therapeutic target.16-19

Limitations of this study include its single-center design, modest sample size, and lack of longitudinal IL-6 measurements beyond 12 months. Future multicenter studies incorporating additional biomarkers (e.g., KL-6, surfactant proteins A/D) and advanced imaging analytics (radiomics) may further refine risk stratification.20

Conclusion

High-resolution CT is indispensable for structural characterization of ILD, while serum IL-6 provides complementary information on inflammatory activity and prognosis. Elevated IL-6

correlates strongly with HRCT severity and functional impairment. A combined HRCT–IL-6 approach may enhance diagnostic accuracy, guide treatment, and help monitor disease progression in ILD patients.

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