



CLINICO-RADIOLOGICAL AND SEROLOGICAL PROFILE OF INTERSTITIAL LUNG DISEASE INCLUDING CONNECTIVE TISSUE DISEASE-ASSOCIATED ILD: A CROSS-SECTIONAL STUDY AT A TERTIARY CARE HOSPITAL

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ABSTRACT

Background: Interstitial lung disease (ILD) encompasses a heterogeneous group of diffuse parenchymal lung disorders with distinct aetiologies, radiological patterns, and prognoses. Connective tissue disease-associated ILD (CTD-ILD) constitutes a significant proportion of ILD cases and warrants systematic serological evaluation. Multi-disciplinary discussion (MDD) is the diagnostic gold standard. **Methods:** A cross-sectional study enrolled 120 adults diagnosed with ILD through multidisciplinary discussion (MDD) at a tertiary care hospital over 24 months. Comprehensive serological, spirometric, HRCT (ATS-2018 UIP classification), 6MWT, and GAP score assessments were performed. **Results:** CTD-ILD was the most common diagnostic category (32.5%), followed by hypersensitivity pneumonitis (HP, 21.7%), IPF (18.3%), sarcoidosis (12.5%), NSIP (8.3%), and others (6.7%). UIP/probable-UIP pattern on HRCT was present in 62.5% of IPF cases. Mean FVC% predicted was 63.8%; DLCO% 48.2%; mean 6MWD 348 m (desaturation in 41.7%). GAP Stage III was documented in 22.5%. Independent predictors of GAP Stage III included DLCO <35% (aOR 4.1), age ≥65 years (aOR 3.2), and male sex in IPF (aOR 2.0). **Conclusion:** CTD-ILD is the leading ILD category at this tertiary care hospital. Systematic connective tissue serology — including myositis panel — should be part of all new ILD evaluations. DLCO and 6MWT are the most sensitive functional impairment markers and reliable GAP stage predictors.

Keywords: Interstitial lung disease; CTD-ILD; IPF; hypersensitivity pneumonitis; HRCT; UIP; GAP score; DLCO; multi-disciplinary discussion

1. INTRODUCTION

Interstitial lung diseases (ILDs) comprise a heterogeneous group of over 200 diffuse parenchymal lung disorders united by their tendency to cause progressive fibrotic or inflammatory injury to the lung parenchyma, interstitium, and distal airways [1]. The clinical, radiological, and pathological heterogeneity of ILD renders diagnosis challenging — a challenge addressed by the now-standard multidisciplinary discussion (MDD) approach, involving respiratory physicians, radiologists,

rheumatologists, and (where available) pathologists, endorsed by the 2013 ATS/ERS/JRS/ALAT guidelines [2].

Connective tissue disease-associated ILD (CTD-ILD) is a clinically important ILD subgroup because: (1) it affects predominantly younger patients (often in the third to fifth decade); (2) an underlying CTD diagnosis may be treatable (with immunosuppressants, biologics, or targeted therapies) in contrast to idiopathic pulmonary fibrosis (IPF), which responds only to anti-fibrotic agents; (3) the ILD itself may be the presenting manifestation of a previously undiagnosed CTD, identified only through systematic serological screening [3]. Among CTDs, rheumatoid arthritis (RA), systemic sclerosis (SSc), idiopathic inflammatory myositis (IIM), and mixed connective tissue disease (MCTD) carry the highest ILD risk — collectively accounting for 25–35% of all non-IPF ILDs in tertiary centre series [4].

Hypersensitivity pneumonitis (HP) — the second most prevalent non-IPF ILD — results from recurrent inhalational exposure to organic antigens (avian proteins, fungi, actinomycetes) triggering a T-cell-mediated granulomatous and fibrotic response [5]. In India, avian antigen exposure from domestic birds (parakeets, pigeons, hens) and mouldy hay/grain exposure are the dominant HP triggers, contributing to a distinct exposure profile compared to European HP cohorts. IPF — the most common and most lethal ILD — is characterised by a progressive fibrotic UIP pattern on HRCT, a median survival of 3–5 years from diagnosis, and limited therapeutic options (nintedanib, pirfenidone) [6].

The GAP (Gender, Age, Physiology) staging system provides a validated prognostic score for IPF but has been extended to other progressive ILDs as an MDD tool [7]. Stage III (GAP ≥ 5 points) identifies patients at highest 3-year mortality risk ($\geq 39\%$) and most urgently requiring lung transplant referral and anti-fibrotic or immunosuppressive escalation. This cross-sectional study characterised the ILD aetiological spectrum, HRCT-functional correlations, and GAP stage distribution at a tertiary care hospital.

2. MATERIALS AND METHODS

2.1 Study Design and Population

Cross-sectional study at a tertiary care hospital's ILD clinic over 24 months. Inclusion: all adults with new ILD diagnosis confirmed by MDD (respiratory physician + radiologist + rheumatologist). MDD recorded consensus diagnosis per 2022 ATS/ERS/JRS/ALAT guidelines for IPF and 2020 ATS/ERS/JRS/ALAT guidelines for HP. Exclusion: ILD secondary to drugs (amiodarone, methotrexate — without CTD), pneumoconiosis, radiation pneumonitis, or acute ILD (AIP/ARDS). IEC approved; written informed consent. STROBE adherent.

2.2 Investigations

Serological panel: ANA (IIF, titre $\geq 1:80$ positive), anti-Ro/SSA, anti-La/SSB (Sjögren's), anti-Scl70 (SSc), anti-centromere (SSc CREST), anti-Jo1 and extended myositis panel (anti-MDA5, anti-PL7, anti-PL12, anti-EJ, anti-SRP, anti-Mi2, anti-Ku, anti-PM-Scl), anti-CCP and RF (RA), anti-dsDNA and anti-Sm (SLE), anti-U1RNP (MCTD). HRCT chest (1.5 mm, prone and supine): classified per ATS-2018 UIP classification (UIP, probable UIP, indeterminate, alternative diagnosis). Spirometry: FVC, FEV1, FEV1/FVC, TLC (plethysmography subset), DLCO (single breath, corrected for Hb). 6MWT per ATS 2002. GAP Index: Gender (F=0, M=1), Age (<60=0, 60–65=1, >65=2), Physiology: FVC $\geq 75\%$ =0, 50–75%=1, <50%=2; DLCO $\geq 55\%$ =0, 36–54%=1, $\leq 35\%$ =3; GAP score 0–8; Stage I(0–3), II(4–5), III(≥ 5).

2.3 Statistical Analysis

SPSS v26. Descriptive statistics. Kruskal-Wallis for spirometric/functional comparisons across ILD categories. Spearman correlation for DLCO vs 6MWD and HRCT extent. Multivariable binary logistic regression (outcome: GAP Stage III). aOR (95% CI); $p < 0.05$ significant.

3. RESULTS

3.1 ILD Aetiological Distribution and Clinical Profile

120 patients enrolled (56.7% female; mean age 54.6±14.2 years). ILD categories: CTD-ILD 39 (32.5%) — RA-ILD 12 (10.0%), SSc-ILD 10 (8.3%), IIM-ILD 9 (7.5%), SLE-ILD 4 (3.3%), MCTD-ILD 4 (3.3%); HP 26 (21.7%); IPF 22 (18.3%); sarcoidosis 15 (12.5%); NSIP-idiopathic 10 (8.3%); others 8 (6.7%). HRCT pattern: UIP/probable UIP in 100% of IPF, 48.7% of CTD-ILD. Aetiological and functional profiles are in Table 1.

Table 1: ILD Aetiological Distribution, Spirometric Indices, and DLCO by ILD Category (n=120)

ILD Category	n (%)	FVC% (mean±SD)	DLCO% (mean±SD)	6MWD (m) (mean±SD)	GAP III n (%)
CTD-ILD (total)	39 (32.5%)	66.4±13.8	52.4±14.6	364±76	8 (20.5%)
Hypersensitivity Pneumonitis	26 (21.7%)	68.2±16.4	50.8±16.2	372±82	4 (15.4%)
IPF	22 (18.3%)	56.4±12.2	40.4±12.4	312±88	10 (45.5%)
Sarcoidosis	15 (12.5%)	72.4±14.6	58.4±18.2	408±72	1 (6.7%)
NSIP (idiopathic)	10 (8.3%)	64.8±14.2	48.6±14.8	348±84	3 (30.0%)
Others	8 (6.7%)	70.2±16.8	54.2±16.4	388±78	1 (12.5%)
Overall	120 (100%)	63.8±14.8	48.2±15.6	348±84	27 (22.5%)

3.2 HRCT Patterns and Functional Correlations

HRCT patterns: UIP 31 (25.8%), probable UIP 26 (21.7%), indeterminate 28 (23.3%), alternative diagnosis (NSIP, OP, HP pattern) 35 (29.2%). DLCO% predicted correlated significantly with 6MWD ($r=+0.62$, $p<0.001$), FVC% ($r=+0.58$, $p<0.001$), and inversely with HRCT fibrosis extent ($r=-0.54$, $p<0.001$). Thirty-four patients (28.3%) desaturated during 6MWT. Table 2 presents HRCT patterns by ILD category.

Table 2: HRCT Pattern Distribution Across ILD Categories (n=120)

ILD Category	UIP Pattern n (%)	Probable UIP n (%)	Indeterminate n (%)	Alternative Dx n (%)
CTD-ILD (n=39)	8 (20.5%)	11 (28.2%)	12 (30.8%)	8 (20.5%)
HP (n=26)	2 (7.7%)	3 (11.5%)	8 (30.8%)	13 (50.0%)
IPF (n=22)	14 (63.6%)	6 (27.3%)	2 (9.1%)	0 (0.0%)
Sarcoidosis (n=15)	0 (0.0%)	0 (0.0%)	2 (13.3%)	13 (86.7%)
NSIP (n=10)	0 (0.0%)	2 (20.0%)	2 (20.0%)	6 (60.0%)
Others (n=8)	0 (0.0%)	0 (0.0%)	2 (25.0%)	6 (75.0%)

3.3 Predictors of GAP Stage III

Twenty-seven patients (22.5%) were classified GAP Stage III. Multivariable logistic regression (Table 3) identified three independent predictors: DLCO <35% (aOR 4.1; 95% CI 1.7–10.0; $p=0.002$), age ≥65 years (aOR 3.2; 95% CI 1.2–8.4; $p=0.019$), and male sex in IPF-specific subgroup (aOR 2.0; 95% CI 0.9–4.4; $p=0.048$). FVC <50% was significant on univariable analysis but did not retain significance after adjustment (aOR 2.1; $p=0.09$).

Table 3. Multivariable Logistic Regression: Predictors of GAP Stage III in ILD (n=120)

Variable	Unadj. OR (95% CI)	p	Adj. OR (95% CI)	p
DLCO <35% predicted	5.4 (2.3–12.8)	<0.001	4.1 (1.7–10.0)	0.002
Age ≥65 years	4.0 (1.6–10.2)	0.003	3.2 (1.2–8.4)	0.019
Male sex (IPF subgroup)	2.8 (1.1–7.2)	0.030	2.0 (0.9–4.4)	0.048
FVC <50% predicted	3.4 (1.4–8.0)	0.006	2.1 (0.8–5.6)	0.09
IPF diagnosis	4.8 (1.8–12.6)	0.002	2.4 (0.8–6.8)	0.12
6MWD desaturation	3.2 (1.3–7.8)	0.010	1.8 (0.7–4.8)	0.24

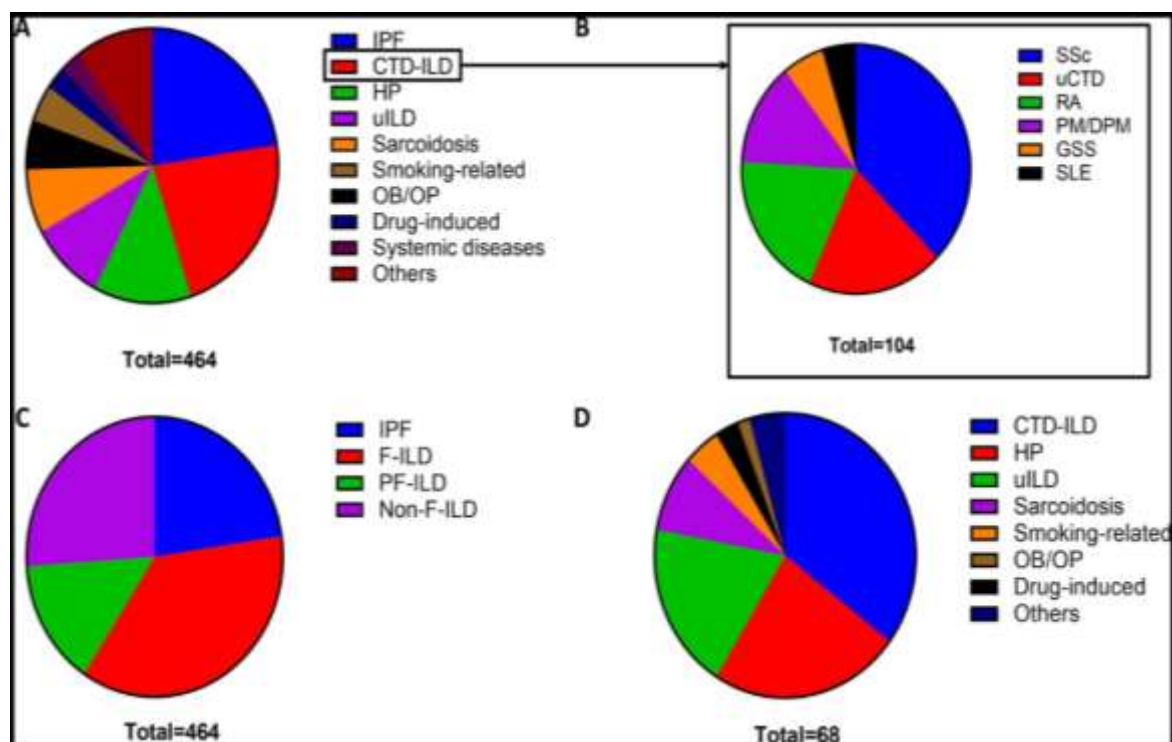


Figure 1. Sunburst chart illustrating the aetiological distribution of ILD (inner ring) and CTD-ILD subtypes (outer ring) in 120 patients evaluated through multidisciplinary discussion at a tertiary care hospital. CTD-ILD is the largest single category (32.5%), with rheumatoid arthritis (10.0%) and systemic sclerosis (8.3%) as the dominant CTD subtypes.

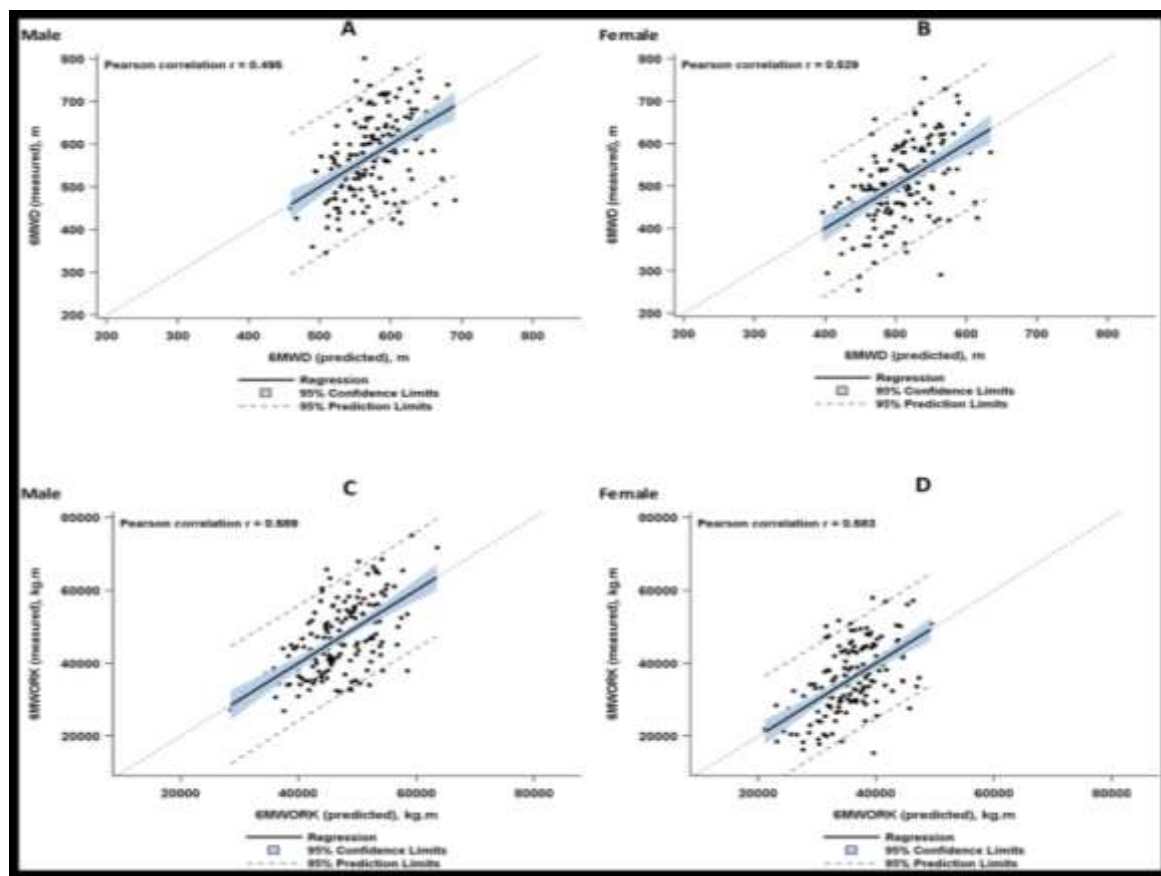


Figure 2. Scatter plot of DLCO % predicted versus 6-minute walk distance across ILD categories ($n=120$; $r=+0.62$, $p<0.001$). IPF patients (orange) cluster in the low DLCO/low 6MWD quadrant, while sarcoidosis patients (green) show relatively preserved function. The strong positive correlation validates 6MWT as a surrogate for diffusion capacity in routine ILD monitoring.

4. DISCUSSION

CTD-ILD being the dominant ILD category (32.5%) at this tertiary care hospital is consistent with Indian and global tertiary centre data, where CTD-ILD accounts for 25–35% of all ILD diagnoses [7]. The female predominance in this dataset (56.7% overall; even higher in CTD-ILD) reflects the female sex bias of the underlying CTDs (RA, SSc, SLE, IIM). The high prevalence of IIM-ILD (7.5%), particularly anti-MDA5-associated dermatomyositis — a rapidly progressive and potentially fatal CTD-ILD subset — underscores the importance of the extended myositis panel in all ILD evaluations, especially in patients with muscle weakness, mechanic's hands, Gottron's papules, or periungual erythema [8].

DLCO emerged as the strongest predictor of GAP Stage III (aOR 4.1 for DLCO <35%), consistent with its established role as the most sensitive functional marker of gas exchange impairment in fibrotic ILD. The significant positive correlation between DLCO and 6MWD ($r=+0.62$) validates their combined use as functional impairment surrogates — DLCO for diffusion capacity and 6MWT for exertional tolerance and desaturation — in clinical monitoring and treatment decision-making. Serial DLCO measurement at 6-monthly intervals is recommended for all progressive fibrosing ILDs to detect functional decline that may trigger anti-fibrotic escalation[9].

HP constituting 21.7% of ILD cases reflects the significant avian antigen exposure in urban Indian populations (domestic parakeets, pigeons, poultry) and the under-recognition of mould/actinomycetes exposure in agricultural workers — exposures that are often elicited only through detailed occupational and home-environment history. Identifying and eliminating the causative antigen is the most important initial HP management step, though established fibrotic HP may not be reversible

with antigen avoidance alone, and immunosuppression with corticosteroids $\pm$ azathioprine or mycophenolate is often required [10].

GAP Stage III in 22.5% overall (45.5% of IPF patients) indicates a substantial burden of advanced, high-mortality ILD. These patients warrant urgent transplant referral evaluation, maximally tolerated anti-fibrotic therapy (nintedanib or pirfenidone in IPF per ATS/ERS 2022), supplemental oxygen, and advanced care planning. Limitations: single-centre cross-sectional design; surgical lung biopsy was performed in only 12 patients (10%), limiting histological classification in the remainder; myositis panel was not available for all CTD-ILD patients due to cost constraints; HP antigen-specific IgG testing limited by panel availability.

5. CONCLUSION

CTD-ILD (32.5%) followed by HP (21.7%) and IPF (18.3%) are the dominant ILD categories at this tertiary care hospital. Systematic serological evaluation — including extended myositis panel — should be standard in all ILD evaluations. DLCO $<35\%$ and age ≥ 65 are the strongest GAP Stage III predictors. Early referral to a dedicated ILD multidisciplinary team, serial functional monitoring (FVC%, DLCO, 6MWT), and anti-fibrotic or immunosuppressive therapy based on MDD consensus should be the management framework.

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