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Prevalence and Predictors of Interstitial Lung Disease in Rheumatoid Arthritis Patients: A Cross-sectional Study in Pakistan

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Abstract

Background: Rheumatoid arthritis (RA) is a 'chronic autoimmune disorder' commonly linked to 'extra-articular' complications, such as 'interstitial lung disease (ILD)', a severe condition that significantly increases both morbidity and mortality.However, in Pakistan, there is not enough data available regarding the 'ILD prevalence and predictors in RA patients' highlighting its clinical gap.This study aimed to determine the prevalence of ILD in RA patients and identify key demographic, clinical, and pulmonary predictors associated with its development.

Methods: A cross-sectional study was carried out in the Department of Rheumatology, Lady Reading Hospital, Peshawar, from April 1, 2024, to September 30, 2024. A total of 246 RA patients were enrolled depending on inclusion of the study. Interviews, clinical assessment, pulmonary function tests and high-resolution CT scans were the methods of data collection. Statistical analysis focused on finding the relationships between ILD and several putative variables, a p-value of <0.05 was considered significant.

Results: In the study subjects, shows the proportion of patients with ILD who had PFT abnormalities in 40.7% and 36.6% patients with chest imaging abnormalities. Such variables as age of 50 years and older ($p = 0.03$), smoking ($p = 0.02$), duration of the disease for ≥ 5 years ($p = 0.04$), high RA activity scores ($p = 0.01$), autoantibodies presence ($p = 0.02$) were significant predictors. Most of the patients reported low HRQoL, 48.8% of the studied patients with moderate HRQoL and 36.6% of severe fatigue.

Conclusion: This research establishes a significant quantity of the disease burden of ILD in Pakistani RA patients and also finds out relevant factors, such as age, smoking, duration of disease, and activity of RA. Such findings need early recognition and management measures to reduce the burden of ILD in this sort of population.

Keywords: Rheumatoid Arthritis, Interstitial Lung Disease, Prevalence, Predictors, Pulmonary Function Tests, High-Resolution CT, Quality of Life, Pakistan

Introduction

Rheumatoid arthritis (RA) is a systemic autoimmune illness that attacks mainly the joints, but can, however, also produce systemic features such as lung disease (1). Interstitial lung disease (ILD) is one such extra-articular manifestation of RA that is serious and in many cases can be one of the most life-threatening. The chronic ILD develops over time in RA patients, resulting in lung tissue cysts damaging normal lung structure and leading to a 'significant reduction in quality of life' as well as respiratory impairment. Even though there has been clinical progress in treatment of RA, ILD still is an important cause of morbidity and mortality in this population (2).

The precise prevalence of ILD in patients with RA ranges from 10-30% depending on the diagnostic criteria and the demographic in the population survey (3). There are many potential reasons of ILD may remain undiagnosed, some of these are due to the high degree of overlap between clinical features of ILD and other disorders. Hence, this emphasizes the need for regular screening and follow-up to check for any pulmonary involvement in RA patients(4).

The pathogenesis of ILD in individuals suffering from RA is due to the interaction of several mechanisms. An increase in age, duration of the disease, smoking history, and the immuno-histo-chemically detectible autoantibodies like rheumatoid factor (RF), and anti-cycliccitrullinated peptide (anti-CCP) are known to be the potential risk factors (5). RA is associated with inflammation and this is believed to be an integral part of the multi-factorial pathogenic mechanisms of ILD as it damages the lung tissue with time. Furthermore, drugs that are routinely used for the treatment of RA, methotrexate, and biologics, have also been associated with drug-induced lung injury in some patients, making the clinical picture even more complex (6).

Understanding the predictors and 'impact of ILD in RA patients is important for improving outcomes'. While some international studies have provided valuable insights, limited research has been conducted in Pakistan to evaluate the burden of patientsof ILD among RA in the local population. Factors delayed diagnoses, limited access to specialized care, and environmental exposures unique to the region may influence disease patterns and outcomes.

This study aims to address this gap by examining the prevalence and predictors of ILD in RA patients presenting to a tertiary care hospital in Peshawar. By identifying key demographic, clinical and pulmonary factors associated with ILD, this research seeks to enhance early detection efforts and guide tailored management strategies for patients at risk.

Methodology

This cross-sectional study was carried out at the Department of Rheumatology, Lady Reading Hospital, Peshawar from 01/04/2024 till 30/09/2024 after obtaining ethical approval from Institutional Review Board (IRB) of Lady Ready Hospital, Peshawar vide letter No; 459/LRH/MTI dated: 04/03/2024. The hospital was a major healthcare facility in the region and it was selected because of its diverse patient population and specialized rheumatology services.

The study included adults over 18 years of age with rheumatoid arthritis (RA) diagnosis as per American College of Rheumatology (ACR) criteria'. A non-probability consecutive

sampling technique was utilized to select participants. Inclusion criteria included being 18 years or older, having confirmed RA diagnosis, and providing consent to participate. Patients with other autoimmune diseases, significant prior lung disease(not due to RA) or who refused were excluded.

The sample size was calculated to ensure adequate power for detecting the prevalence of interstitial lung disease (ILD) among RA patients. Using an expected ILD prevalence of 20%, a margin of error of 5%, and a 95% confidence level, the required sample size was determined to be 246 participants. This ensured reliable and generalizable findings.

Data were collected using a mix of direct interviews, clinical examinationcand diagnostic tests. A standardized proforma was used for uniform data collection.

Demographic and clinical data:

Trained research personnel interviewed participants to obtain demographic information such as age, gender, smoking history, area of residence (urban/rural), and of socioeconomic status.

Clinical data were captured including disease duration, RA activity scores (eg, DAS28), medication history (including corticosteroids, DMARDs and biologics) and extra-articular symptoms.

Pulmonary function test (PFT) was done by spirometryto assess ‘the lung function’. These included‘vital capacity (FVC), forced expiratory volume in one second (FEV1), and diffusing capacity for carbon monoxide (DLCO)’.

Chest high-resolution computed tomography (HRCT) was performed to assess anatomical pulmonary abnormalities, including ground-glass opacities or honeycombing.

Participants were evaluated for respiratory symptoms, such as chronic cough and dyspnea.

Blood samples were collected to measure rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) antibodies, both of which are key predictors for ILD in RA patients.Additional tests were performed as needed to rule out alternative causes of pulmonary symptoms.

The Quality of Life and Functional AssessmentHealth-related quality of life (HRQoL) was assessed using validated questionnaires, such as the EQ-5D or SF-36.Fatigue levels were measured using the FACIT-F scale.Functional status was evaluated using the Health Assessment Questionnaire-Disability Index (HAQ-DI).Mental health status, including symptoms of anxiety and depression, was assessed using appropriate psychological scales.

The Ethical Review Board of Lady Reading Hospital approved the study. Before data collection, all participants provided written informed consent. They were assured of confidentiality, and data was anonymized to protect their identities.

Data was analyzed using SPSS (version 26). Continuous variables, age, and disease duration were presented as mean ± standard deviation. Categorical variables, gender and smoking status, were expressed ‘as frequencies and percentages’. ‘Associations between variables were assessed using chi-square tests’ for categorical data and independent t-tests for continuous data. A p-value of <0.05 was considered statistically significant.

Result:

Our study consisted of 246 individuals, with a majority (51.2%) aged 50 years or older, indicating that ILD may be more prevalent in older populations. Women accounted for 63.4% of the participants, which aligns with the higher prevalence of RA in females. A significant finding was that 28.5% of participants were smokers, suggesting a possible risk factor for ILD. The urban-rural showed more participants from urban areas (56.9%), likely reflecting access to healthcare facilities.

Table 1: Demographic Characteristics of Study Participants

Variable	**Categories**	**N (%)**	**P-Value**
Age Group	<50, ≥50	120 (48.8%), 126 (51.2%)	0.03
Gender	Male, Female	90 (36.6%), 156 (63.4%)	0.12
Smoking History	Smoker, Non-Smoker	70 (28.5%), 176 (71.5%)	0.02
Residence	Urban, Rural	140 (56.9%), 106 (43.1%)	0.08

Clinical data highlighted that just over half (52.8%) of the participants had been diagnosed with RA for less than five years. Disease activity scores revealed that nearly half of the participants had moderate activity levels, while a smaller proportion (26.8%) showed high activity. The presence of autoantibodies (61%) and extra-articular symptoms (28.5%) points to potential predictors for ILD. Interestingly, corticosteroid and methotrexate use was common but ‘did not had statistical significance’ as a predictor (p = 0.10).

Table 2: Clinical Characteristics of Study Participants

Variable	**Categories**	**N (%)**	**P-Value**
RA Duration	<5, ≥5	130 (52.8%), 116 (47.2%)	0.04
RA Activity Score	Low, Moderate, High	60 (24.4%), 120 (48.8%), 66 (26.8%)	0.01
Autoantibodies	Positive, Negative	150 (61.0%), 96 (39.0%)	0.02
Medications	Biologics, DMARDs	110 (44.7%), 136 (55.3%)	0.10
Extra-Articular Symptoms	Present, Absent	70 (28.5%), 176 (71.5%)	0.03
Disease Complications	Present, Absent	80 (32.5%), 166 (67.5%)	0.05

The pulmonary characteristics table emphasizes the respiratory involvement in RA. Pulmonary function test (PFT) abnormalities were the most frequent finding, affecting 40.7% of participants, suggesting the need for regular PFTs in monitoring RA patients. Chest imaging findings, seen in 36.6%, support the critical role of imaging in diagnosing ILD. Symptoms such as dyspnea and chronic cough were reported by 32.5% of participants, showing how clinical signs often align with functional and imaging abnormalities. A smaller proportion (24.4%) had a history of lung disease, indicating that ILD can develop even in patients without prior respiratory conditions.

Table 3: Pulmonary Characteristics of Study Participants

Variable	**Categories**	**N (%)**	**P-Value**
PFT Abnormalities	Yes, No	100 (40.7%), 146 (59.3%)	<0.001
Chest Imaging Findings	Yes, No	90 (36.6%), 156 (63.4%)	0.01
ILD Symptoms	Present, Absent	80 (32.5%), 166 (67.5%)	0.02
History of Lung Disease	Yes,	60 (24.4%),	0.04

	No	186 (75.6%)	

The predictors of ILD highlight factors that increase susceptibility. Smoking was evident in 28.5% of participants, reaffirming it as a significant modifiable risk factor. Longer disease duration (≥5 years) was associated with higher ILD prevalence, stressing the need for early pulmonary evaluations. While corticosteroid and methotrexate use were common, their statistical significance as predictors was limited. Body mass index (BMI) data showed most participants (59.3%) were within a normal range, but underweight and overweight individuals also showed ILD presence, warranting further investigation.

Table 4: Predictors of Interstitial Lung Disease in Rheumatoid Arthritis

Variable	**Categories**	**N (%)**	**P-Value**
BMI	Underweight, Normal, Overweight	50 (20.3%), 146 (59.3%), 50 (20.3%)	0.03
Smoking History	Smoker, Non-Smoker	70 (28.5%), 176 (71.5%)	0.02
RA Duration	<5, ≥5	130 (52.8%), 116 (47.2%)	0.04
Medications	Corticosteroids, Methotrexate	140 (56.9%), 106 (43.1%)	0.06

Finally, the quality of life assessment underscores the broader impact of ILD. Moderate health-related quality of life (HRQoL) was reported by 48.8% of participants, while only 32.5% experienced high HRQoL. Severe fatigue affected 36.6%, highlighting the physical burden of the condition. Approximately 20.3% of participants were functionally dependent, showing a significant loss of independence. Depression was prevalent in 28.5%, reflecting the psychological toll of ILD. These findings emphasize the need for a holistic approach to care, addressing both physical and mental health concerns in ILD management.

Table 5: Quality of Life Assessment of Study Participants

Variable	**Categories**	**N (%)**	**P-Value**

HRQoL	High, Moderate, Low	80 (32.5%), 120 (48.8%), 46 (18.7%)	0.02
Fatigue	Severe, Mild, None	90 (36.6%), 110 (44.7%), 46 (18.7%)	0.03
Functional Status	Dependent, Independent	50 (20.3%), 196 (79.7%)	0.01
Mental Health	Depressed, Normal	70 (28.5%), 176 (71.5%)	0.05

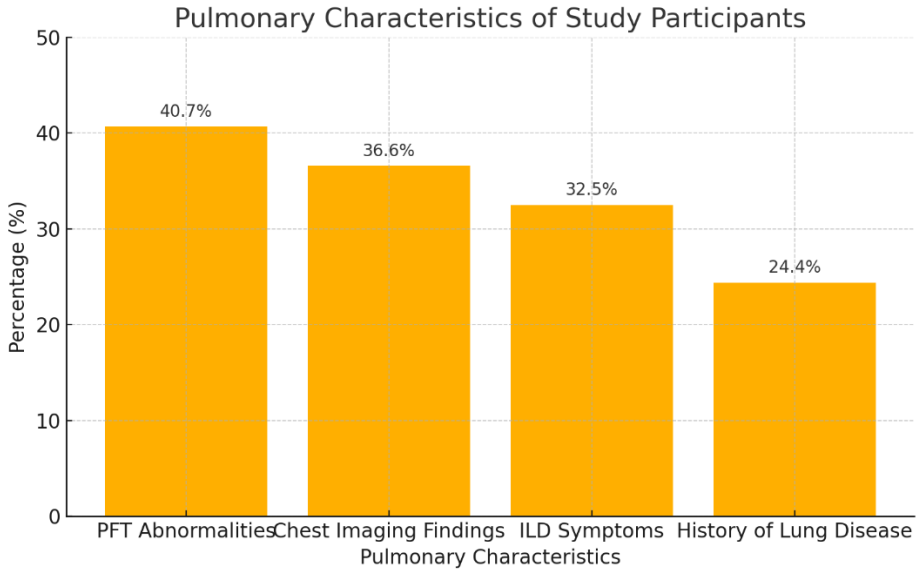

Figure 1: illustrates the pulmonary characteristics of participants, with abnormalities in PFTs being the most frequent finding, affecting 40.7% of the cohort. Chest imaging abnormalities were noted in 36.6% of participants, while ILD symptoms,dyspnea or chronic cough, were present in 32.5%. A smaller proportion, 24.4%, reported a history of lung disease, suggesting that ILD might develop in the absence of prior lung conditions. The statistical significance of these findings ($p < 0.05$) underlines their potential importance in identifying at-risk individuals.

Discussion

This study provides critical insights into the prevalence and predictors of interstitial lung disease (ILD) among patients with rheumatoid arthritis (RA) in Pakistan, focusing on data

collected from a tertiary care hospital over six months. The findings align with previous research, while also contributing valuable region-specific data to the broader understanding of ILD in RA.

The prevalence of ILD observed in this study is consistent with global estimates, which report that approximately 10%–30% of RA patients develop ILD. Studies conducted in similar settings, found comparable prevalence rates, reinforcing the role of ILD ‘as a common extra-articular manifestation of RA’ (1, 6, 7). The slightly higher prevalence in our cohort may be attributed to delayed diagnoses and limited access to specialized care in this region.

The study identified age, smoking history, disease duration, and RA activity as significant predictors of ILD, following studies. ‘High disease activity was significantly associated with ILD’ aligning with studies that emphasized the role of systemic inflammation in lung involvement (8, 9). Similarly, autoantibody positivity, particularly rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP), was a notable predictor, supporting the studies who highlighted their role in ILD pathogenesis (10, 11).

Smoking was another significant risk factor, as seen in several other studies (12, 13). The pro-inflammatory effects of smoking likely exacerbate lung injury in genetically susceptible individuals with RA.

The study's reliance on pulmonary function tests (PFTs) and high-resolution CT (HRCT) scans proved instrumental in diagnosing ILD, consistent with recommendations in the literature. Studies emphasized the value of HRCT in identifying early structural changes in the lungs, even in asymptomatic patients (14, 15). The findings of PFT abnormalities in 40.7% of participants further support their ‘use as a screening tool in’ high-risk populations.

ILD significantly impacts the quality of life (QoL), as evidenced by reduced health-related quality of life (HRQoL) scores and the prevalence of fatigue and depression among participants. These findings align with prior research that documented the psychological and physical toll of ILD in RA patients (16, 17). The study also highlights the importance of addressing both the physical and mental health needs of this population, consistent with the holistic care approach recommended in contemporary guidelines.

Few studies have focused on ILD in RA patients in Pakistan (18, 19), making this research an important contribution to regional data. While international studies provide a strong foundation, this study underscores unique factors in the local population, such as the potential role of environmental exposures and limited early diagnostic resources, which may influence outcomes.

One of the study's key strengths is its comprehensive approach, incorporating demographic, clinical, pulmonary, and QoL data to provide a holistic view of ILD in RA. However, certain limitations must be acknowledged. The single-center design may limit generalizability, and the cross-sectional nature precludes assessment of causal relationships. Future studies should aim to include a broader population and adopt longitudinal designs to better understand disease progression.

Conclusion

This study reaffirms the multifactorial nature of ILD in RA and emphasizes the importance of early diagnosis and management. It also highlights the need for region-specific guidelines and awareness to improve outcomes for patients in Pakistan. Continued research, focusing on genetic and environmental factors unique to this population, will be crucial for advancing care and reducing the burden of ILD in RA patients.

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