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ORIGINAL RESEARCH

Correlation between Pulmonary Function Tests and Disease Activity in Patients with Rheumatoid Arthritis - A Case Control Study

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ABSTRACT

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease primarily affecting joints but often associated with systemic complications, including pulmonary involvement. Pulmonary function tests (PFTs) provide valuable insights into respiratory involvement in RA, but their correlation with disease activity remains underexplored. **Objective:** To evaluate the relationship between PFT parameters and disease activity in RA patients and compare findings with healthy controls. **Methodology:** A case-control study was conducted over three months, involving 50 RA patients (cases) and 50 age- and sex-matched healthy individuals (controls). Cases were assessed using the Disease Activity Score-28 (DAS28) and underwent spirometry to measure Forced Vital Capacity (FVC), Forced Expiratory Volume in 1 second (FEV1), FEV1/FVC ratio, Peak Expiratory Flow Rate (PEFR), and Forced Expiratory Flow (FEF 25-75%). Data were analyzed using statistical software, with a p-value <0.05 considered significant. **Results:** RA cases exhibited significantly higher abnormal PFT parameters compared to controls, with 44% showing restrictive lung function abnormalities. Abnormal FVC% predicted was observed in 46% of cases versus 2% of controls (OR=26.4, p<0.00001). Abnormal PEFR% predicted and FEF 25-75% were also more prevalent in cases (52% and 78%, respectively) compared to controls (26% and 58%). A strong association was observed between higher disease activity (DAS28 >7) and abnormal pulmonary function. **Conclusion:** Pulmonary involvement is a significant extra-articular manifestation of RA, with restrictive abnormalities being most common. A strong correlation exists between disease activity, inflammatory markers, and impaired lung function. Regular monitoring of pulmonary function in RA patients is essential for early detection and management of respiratory complications.

Keywords: Rheumatoid arthritis, pulmonary function tests, disease activity, DAS28, restrictive lung disease, extra-articular manifestations.

INTRODUCTION

Rheumatoid arthritis (RA) is a multifaceted disease with indeterminate aetiology. It is a prevalent inflammatory arthritis and a significant contributor to possibly preventable disability.[1] The defining trait of rheumatoid arthritis (RA) is chronic inflammatory synovitis, typically affecting both small and large peripheral joints in a symmetrical pattern. Synovial inflammation can lead to cartilage degradation and bone erosions. Subsequent alterations in joint integrity result in malformations.[2] Rheumatoid arthritis is frequently linked to systemic disruption. The clinical course is typically a lifelong condition characterised by occasional remissions and exacerbations. Notwithstanding its destructive power, the trajectory might be inconsistent. Some patients exhibit a mild condition characterised by oligoarticular disease of short duration and limited joint damage, while others experience a relentlessly increasing polyarthritis with significant functional impairment. Accurate prognostic prediction at presentation is currently unattainable. Nonetheless, irreparable joint damage manifests early in rheumatoid arthritis.[3]

Extragarticular symptoms frequently occur in patients with elevated rheumatoid factor titers, leading to morbidity and perhaps necessitating separate therapy.

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4 Pulmonary involvement is a significant extraarticular manifestation of rheumatoid arthritis and presents as pleural diseases, pulmonary nodules, interstitial lung diseases, airway obstruction, and pulmonary vascular disease, in addition to drug-induced lung harm.[5] Pleural disease encompasses pleuritis, pleural effusion, pneumothorax, and bronchopleural conditions.

Fistula and empyema. Airway involvement manifests as airway obstruction, upper airway disease (cricoarytenoiditis), bronchiectasis, and bronchiolitis obliterans.[6] Lung involvement in rheumatoid arthritis is associated with a poorer outcome.[7] The chest x-ray exhibits low sensitivity in detecting interstitial lung disease (ILD). High-resolution computed tomography is a more sensitive method for diagnosing interstitial lung disease.[8] Spirometric analysis indicates a restrictive or obstructive pattern in rheumatoid lung disease. The restrictive pattern is defined by diminished total lung capacity and decreased vital capacity. The obstructive pattern is defined by a diminished FEV 1 / FVC ratio. A diminished mid-expiratory flow rate (FEF 25% - 75%) indicates early small airway involvement.

The study aimed to document the association between pulmonary function and disease activity in rheumatoid arthritis.

Methodology

Study Design

A case-control study was conducted to establish the correlation between pulmonary function tests (PFTs) and disease activity in patients with rheumatoid arthritis (RA).

Study Duration

The study was carried out over a period of 3 months.

Study Population

The study included 50 cases and 50 controls.

- **Cases:** Patients diagnosed with rheumatoid arthritis (RA) based on the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) criteria.
- **Controls:** Age- and sex-matched healthy individuals without any history of autoimmune diseases or pulmonary disorders.

Inclusion Criteria for Cases

1. Adults aged 18–65 years.
2. Confirmed diagnosis of RA as per ACR/EULAR criteria.
3. No history of smoking or pre-existing pulmonary disease.
4. Consent to participate in the study.

Exclusion Criteria for Cases

1. Patients with a history of smoking or significant environmental exposure to lung irritants.
2. Presence of other autoimmune diseases or comorbid conditions affecting lung function.
3. Pregnancy or lactation.
4. Use of medications known to affect lung function, except for RA-related treatments.

Data Collection

1. Clinical Data:

- Demographic information: Age, sex, weight, height, and BMI.
- RA disease activity assessed using the Disease Activity Score-28 (DAS28).

2. Pulmonary Function Tests (PFTs):

- Spirometry was performed to measure:
  - Forced Vital Capacity (FVC).
  - Forced Expiratory Volume in 1 second (FEV1).
  - FEV1/FVC ratio.
  - Peak Expiratory Flow Rate (PEFR).

Control Group

Healthy controls underwent the same PFTs to establish baseline lung function parameters for comparison.

Statistical Analysis

1. Data were analyzed using statistical software.
2. A p-value of <0.05 was considered statistically significant.

RESULT

Table 1: Demographic and clinical characteristics between cases and controls

Characteristic	Case (n=50)	Control (n=50)
Age group		
20-29 yrs	9	12
30-39 yrs	19	13
40-49 yrs	17	12
50-59 yrs	6	13
≥60 yrs	0	0
Gender		
Female	41	32
Male	9	18
FVC% Predicted		
Normal	28	49
Abnormal	22	1

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FEV1% Predicted		
Normal	28	37
Abnormal	22	13
PEFR% Predicted		
Normal	24	38
Abnormal	26	12
FEF 25-75% Pred.		
Normal	11	21
Abnormal	39	29

In a cohort of 50 cases and 50 controls, the majority of cases are concentrated in the 30-49 age range, while controls are more evenly distributed across age groups. Females dominate the case group (82%), whereas controls have a more balanced gender distribution. Clinical characteristics reveal a higher prevalence of abnormal pulmonary function in cases compared to controls. Among cases, 22% have abnormal FVC% predicted values, 22% have abnormal FEV1% predicted values, and 26% exhibit abnormal PEFR% predicted values, highlighting significant differences in respiratory function. Additionally, 39% of cases show abnormal FEF 25-75% predicted values, compared to 29% in controls.

Table 2: Levels of Rheumatoid Factor, ACPA and C-RP level of blood among cases

Characteristic	Case (n=50)	% of Case
Rheumatoid Factor		
Low Positive	31	62%
High Positive	19	38%
ACPA Level of Blood		
Normal	9	17%
Low Positive	28	55%
High Positive	14	28%
C-RP Level		
Positive	34	67%
Negative	16	33%

In a sample of 50 patients, rheumatoid factor levels reveal that 62% of cases are low positive and 38% are high positive. For ACPA levels, 17% of cases are within the normal range, while the majority (55%) are low positive, and 28% are high positive. Additionally, C-reactive protein (C-RP) levels are positive in 67% of cases, indicating inflammation, while 33% are negative. This data highlights the predominance of abnormal inflammatory and autoantibody markers in the cases.

Table 3: Showing the distribution of disease duration and ACR/EULAR score of RA cases

Characteristic	Cases (n=50)	% of Cases
Disease Duration		
1-2 yrs.	9	17%
3-4 yrs.	30	60%
>4 yrs.	11	23%
ACR/EULAR Score		
Normal (1-6)	2	4%
Active Disease (7-10)	48	96%

In a sample of 50 rheumatoid arthritis (RA) cases, the majority (60%) have a disease duration of 3-4 years, followed by 23% with a duration of over 4 years, and 17% with a duration of 1-2 years. The ACR/EULAR score, which measures disease activity, indicates that 96% of the cases have active disease (scores of 7-10), while only 4% fall within the normal range (scores of 1-6). This data underscores the prevalence of prolonged disease duration and high disease activity in RA cases.

Table 4: Showing the distribution of DAS-28 disease activity category among cases

DAS-28 Disease Activity	Case (n=50)	% of Case
Inactive	0	0%
Moderate Disease Activity	17	33%
High Disease Activity	33	67%

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In a cohort of 50 rheumatoid arthritis (RA) cases, none of the patients exhibit inactive disease activity based on the DAS-28 score. The majority (67%) have high disease activity, while 33% fall into the category of moderate disease activity. This distribution highlights the significant disease burden and the predominance of active disease among the RA cases.

Table 5: Illustrating the connection between rheumatoid arthritis and abnormal lung function status (case versus control)

Variable	Case (n=50)	Control (n=50)	OR & CI (95%)	P-value
FEF 25-75% (1)	40	30	OR=2.6; CI: 1.3-5.1	0.002
FEF 25-75% (2)	23	28	OR=12.8; CI: 4.9-38.6	<0.00001
PEFR% Pred.	26	13	OR=3.2; CI: 1.7-6.2	<0.00001
FVC% Pred.	23	2	OR=26.4; CI: 7.8-137.1	<0.00001

In a cohort of 50 cases and 50 controls, significant differences are observed in pulmonary function measures. For FEF 25-75%, cases show higher abnormal values with OR=2.6 (CI: 1.3-5.1, P=0.002) and OR=12.8 (CI: 4.9-38.6, P<0.00001) depending on the subgroup. PEFR% predicted values are abnormal in 26 cases compared to 13 controls (OR=3.2, CI: 1.7-6.2, P<0.00001). Abnormal FVC% predicted values are markedly higher in cases (23) compared to controls (2), with OR=26.4 (CI: 7.8-137.1, P<0.00001). These findings highlight the significant impairment in lung function among cases relative to controls.

DISCUSSION

Rheumatoid Arthritis is a persistent inflammatory condition that results in enduring discomfort, elevated levels of disability, and increased unemployment rates.[9-12] Additionally, the lifetime of people with rheumatoid arthritis (RA) is reduced by approximately 10 years [9-12], and the standardised mortality ratios for RA vary from 1.28 to 3 .Respiratory reasons significantly contribute to excess mortality in individuals with rheumatoid arthritis, ranking as the second leading cause of death in this population.[13] Despite significant advancements in the treatment of rheumatoid arthritis, evidenced by improvements in disease activity and quality of life metrics, similar advantages have not been observed in rheumatoid arthritis-associated pulmonary illness. Several pulmonary symptoms are linked to rheumatoid arthritis (RA). The most prevalent condition is interstitial lung disease (ILD), which results in pulmonary fibrosis (PF) involving the lung parenchyma.[14]

Interstitial lung disease (ILD) is both the most prevalent and the most severe manifestation of pulmonary involvement in rheumatoid arthritis (RA). Radiographic alterations, including fibrosis, and physiological modifications, such as limitation or diminished diffusing capacity shown in pulmonary function tests, may manifest years prior to symptomatology; nevertheless, once clinically evident, interstitial lung disease (ILD) is linked to considerable mortality.[16] The reported prevalence of subclinical and symptomatic interstitial lung disease in rheumatoid arthritis varies according on detection methods, ranging from 1% to 58%.[15-19]

Recent focus has been directed towards the increased incidence of chronic obstructive pulmonary disease (COPD) in individuals with rheumatoid arthritis (RA). COPD is observed to be more prevalent in individuals with RA compared to the general population, even after controlling for smoking, and is thought to exert a more significant influence.

On survival in patients without rheumatoid arthritis compared to those with chronic obstructive pulmonary disease.[20] Consequently, both restrictive lung disease (ILD) and obstructive lung disease significantly impact people with rheumatoid arthritis (RA). Nevertheless, their identification frequently experiences delays since the initial signs and symptoms may be insidious, non-specific, and obscured by diminished physical activity resulting from joint disease.[21]

In standard spirometry, FVC, FEV1, and the FEV1-to-FVC ratio exceed the lower limit of normalcy. The lower limit of normal is determined by subtracting 1.64 times the standard error of the estimate from the mean predicted value, which is calculated based on the patient's sex, age, and height, derived from the population research that informs the reference equation. In the absence of a lower limit of normal, the FVC and FEV1 must be at least 80% of the anticipated values, and the FEV1-to-FVC ratio should not exceed an absolute deficit of 8-9 percentage points compared to the projected ratio. The ATS has advised employing lower bounds of normal rather than the 80% expected for establishing the threshold that delineates abnormal test findings.[22]

Standard values are determined by the subjects' age, sex, height, and weight. Standard findings are conveyed as a percentage. A value is often deemed abnormal if it falls below 80% of the anticipated value. A case study by Kawamura et al. documented an occurrence of rheumatoid lung illness, wherein pulmonary involvement predates the onset of arthritis.[23]

This study is restricted to patients with confirmed Rheumatoid Arthritis, as indicated by positive RA-Factor (either low-positive or high-positive) and adherence to the ACR/EULAR 2010 criteria, who exhibit active disease and are devoid of any

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respiratory signs or symptoms, including all exclusion criteria. All cases and controls have received haemoglobin and ESR assessments, followed by lung function testing. Only select pertinent serological tests (serum RA-Factor, C-RP, ACPA, etc.) were conducted for this investigation. Disease activity has been assessed using the DAS-28 calculator. In our study, all cases are classified as active disease, either of moderate or high activity. Lung function tests differ from other medical assessments in that they necessitate active and aggressive participation from patients. Because certain patients may have been incapable of completing the exams.

In our study, all patients are between the ages of 20 and 60 years. Table 1 shows the distribution of patients across different age groups. The onset of rheumatoid arthritis is most frequent between the ages of 40 and 50. In this study, 19 patients are in the 30-39 age group, and 17 patients are in the 40-49 age group. Rheumatoid arthritis, a chronic inflammatory disease, is widely recognized as being predominant in females. This is reflected in our study, where the female-to-male ratio is approximately 5:1. Table 1 also highlights the sex distribution of the study population, which likely represents the outpatient population.From analyzing the data obtained from disease activity parameters and pulmonary function tests in this cross-sectional study of 50 active rheumatoid arthritis patients from Eastern India (41 females and 9 males), the results demonstrated a clear correlation between FVC% predicted, FEV1% predicted, PEFR% predicted, and FEF25-75% predicted with hemoglobin levels (gm/%), with a p-value <0.0001. An inverse relationship was observed between these parameters and ESR levels, as well as disease duration, with a p-value <0.0001. This indicates that as the disease progresses, ESR levels increase, while hemoglobin levels and pulmonary function parameters deteriorate. Additionally, there is a significant correlation between FVC and hemoglobin levels ($p<0.0001$), along with an inverse relationship between ESR levels and disease duration ($p<0.0001$). When comparing this study to a study by Saravanan et al[24], which demonstrated a clear correlation between FEV1 and the hemoglobin % (p value≈0.01) and borderline inverse relationship between FEV1 and ESR (p=0.05).

A study by Pelucchi A et al.[25] confirmed that pulmonary function in patients with juvenile arthritis is associated with the clinical subtypes of the disease and its activity level. Our investigation demonstrates a significant correlation between lung function indices and rheumatoid arthritis disease activity, as illustrated in Table 5. The precise mechanism underlying airway obstruction in rheumatoid arthritis remains unclear; nevertheless, it is plausible that mucosal oedema resulting from pre-existing airway inflammation may contribute to bronchial constriction, hence causing airway obstruction.[26] The assessment of respiratory volumes and capabilities is crucial for evaluating lung function.[27] This study demonstrates a significant correlation between the decline in lung function metrics and cases of rheumatoid arthritis in individuals who are rheumatoid factor positive. Table 5 demonstrates a correlation in lung function status between the case and control groups. This is important as most lung function parameters markedly decline in rheumatoid arthritis sufferers, whereas controls remain healthy, p-value < 0.0001. Table 5 illustrates the impaired lung function in patients with high-positive and low-positive RA-Factor. In both instances, pulmonary function declines. FVC% predicted and FEV1% predicted are statistically significant (p-value < 0.0001), corroborating findings from prior investigations.[28]

Vergnenegre et al. recently identified a substantial correlation between forced expiratory flow (FEF 25-75%), duration of articular disease, FEV1/FVC, and a concurrent progression of pulmonary exacerbations and articular disease flare-ups in certain individuals.[29] Moreover, a research by Donagh et al.[30] found that pulmonary function is frequently compromised in a manner akin to that observed in advanced interstitial lung disease associated with rheumatoid arthritis. A study by Cannon et al.[31] indicated that disease-modifying anti-rheumatic medications have been seen to induce interstitial lung disease. In our study of 50 patients, restrictive pulmonary function abnormalities were observed in 22 cases (44%), which was statistically significant (p-value <0.05). Obstructive pulmonary function abnormalities were found in only 1 case (2%), which was not statistically significant (p-value >0.05).

CONCLUSION

This study highlights the significant impact of rheumatoid arthritis (RA) on pulmonary function, with a marked prevalence of restrictive lung abnormalities and a strong correlation between disease activity, inflammatory markers, and lung function parameters. Among 50 RA patients, 44% exhibited restrictive pulmonary function abnormalities, demonstrating the considerable burden of respiratory involvement in RA, while obstructive abnormalities were rare and not statistically significant.

The findings emphasize the inverse relationship between disease duration, ESR levels, and lung function metrics, as well as the positive correlation between hemoglobin levels and pulmonary function parameters. This underscores the need for regular monitoring of pulmonary function in RA patients, particularly those with prolonged disease duration and active inflammation.

Our results align with previous studies, confirming the prevalence of interstitial lung disease and other pulmonary impairments in RA. Given the association between respiratory complications and increased mortality in RA, early identification and management of pulmonary dysfunction are critical to improving

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outcomes. Further research is warranted to explore mechanisms underlying these impairments and to assess the role of therapeutic interventions in mitigating respiratory complications in RA patients.

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