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RESEARCH ARTICLE

Decoding Interstitial Pneumonia with Autoimmune Features (IPAF): Lack of Association with Common Systemic Diseases and COVID-19 in Interstitial Lung Disease (ILD) Patients

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Abstract: ***Background:*** Interstitial Pneumonia with Autoimmune Features (IPAF) is a subcategory of interstitial lung disease (ILD) with autoimmune characteristic, but not meeting any criteria of a specific connective tissue disease (CTD). Little Indian data on the prevalence and determinants of IPAF exist. This paper seeks to determine the epidemiology and possible risk factors of IPAF in a South Indian tertiary care hospital. ***Aim and Objectives:*** To establish the prevalence of IPAF in the ILD patients, to define the possible risk factors, and to identify the correlation between clinical variables and IPAF. ***Methods:*** The cross-sectional analytical cross-sectional study aimed to be done in the Department of General Medicine, Sree Balaji Medical College & Hospital, Chennai, between July 2023 and January 2025. A total of 50 patients with ILD were selected and assessed by the ERS/ATS 2015 criteria. Data was collected in the form of clinical history, serological examination and HRCT chest results. The analysis was conducted by the use of open Epi 3.0 Chi-square test was used and p was set at 0.05. ***Findings:*** The average age of the participants was 54.04 years of age with a standard deviation of 10.15 years (35 years to 75 years old). The majority of respondents (64%) had the age of 41 years to 60. 34% of the patients had a history of COVID-19 infection. The rates were 32 and 34 percent respectively with diabetes mellitus and hypothyroidism. Nonetheless, such independent variables as age, gender, previous COVID infection, diabetes, hypothyroidism did not significantly influence the presence of IPAF ($p > 0.05$). ***Conclusion:*** IPAF is also found between ILD patients in the tertiary care cohort, but other common comorbidities of the system and previous infections were not significantly associated. These facts indicate that the IPAF can occur without the conventional systemic risk factors, and it is necessary to conduct specific clinical, serological, and radiological examination to make an accurate diagnosis.

Keywords: Interstitial Lung Disease (ILD), Interstitial Pneumonia with Autoimmune Features (IPAF), Autoimmunity, NSIP, Risk Factors, ERS/ATS Criteria

INTRODUCTION

Interstitial lung diseases (ILDs) represent a diversified category of conditions that has diverse ranges of lung inflammation as well as fibrosis. One of them, Interstitial Pneumonia with Autoimmune Features (IPAF), first described by the European Respiratory Society (ERS) and American Thoracic Society (ATS) in 2015[1], is used to describe patients with Interstitial Pneumonia who exhibit autoimmune features without meeting the criteria of a connective tissue disease (CTD) [2].

IPAF has uneven distributions all over the world and the most reported radiological pattern is NSIP (Nonspecific Interstitial Pneumonia). Nevertheless, there is a dearth of Indian literature and even regional variations in the expression of autoimmune diseases may affect the prevalence and determinants of IPAF [3].

The current research was conducted among ILD patients in a tertiary care hospital in Chennai, and it was aimed to assess the possible risk factors like age, previous COVID-19 infection, diabetes mellitus, and hypothyroidism.

MATERIAL AND METHODS

Study Title: A Study of Prevalence and Risk Factors of Interstitial Pneumonia with Autoimmune Features (IPAF) among Interstitial Lung Disease (ILD) Patients in a Tertiary Care Hospital.

Study Design: Hospital-based prospective analytical study.
Study Setting: Department of General Medicine, Sree Balaji Medical College & Hospital, Chennai, Tamil Nadu.
Study Period: A period of 18 months, from July 2023 to January 2025.
Study Population: Fifty patients with a diagnosis of ILD attending outpatient and inpatient services in Sree Balaji Medical College and Hospital, Chennai, were included.

Inclusion Criteria:

- Radiological evidence of Interstitial Pneumonia in HRCT chest.
- Application of ERS/ATS 2015 criteria for IPAF classification.

Exclusion Criteria:

- Patients not willing to participate in the study.
- Patients meeting the diagnosis of Connective Tissue Disease.
- Patients under 18 years of age.

Data Collection:

- **Demographic data:** Age and gender of the patient.
- **Clinical history:** Past infections (COVID-19), systemic diseases (diabetes mellitus and hypothyroidism).
- **Clinical examination:** Clinical domain of IPAF criteria - Distal digital fissuring, Distal digital tip ulceration, Polyarticular morning joint stiffness, Palmar telangiectasia, Raynaud's phenomenon, Unexplained digital edema, Gottron's sign
- **Investigations**: HRCT chest, serological tests (ANA, anti-Ro, others).

Statistical Analysis: Data analyzed using OpenEpi 3.0; Chi-square test used for associations; $p < 0.05$ considered significant**.**

RESULTS AND OBSERVATIONS:

- **Age and Gender Distribution: [table 1,2 & figure 1,2]**
  - Mean age: 54.04 ± 10.15 years (range 35–75 years).
  - Majority between 41–60 years, accounting to 64%.
  - Majority of the participants were female – 82%.
- **Past Infection: [table 3 & figure 3]**
  - 34% had a history of COVID-19 infection.
- **Systemic Diseases: [table 4 & figure 4]**
  - Diabetes mellitus: 32%.
  - Hypothyroidism: 34%.
  - Absent systemic disease: 34%.
- **Statistical Findings:**
  - **Independent variables such as age, gender, past COVID-19 infection, diabetes mellitus, and hypothyroidism were not significantly associated with the occurrence of IPAF** in patients with ILD ($p > 0.05$**).**

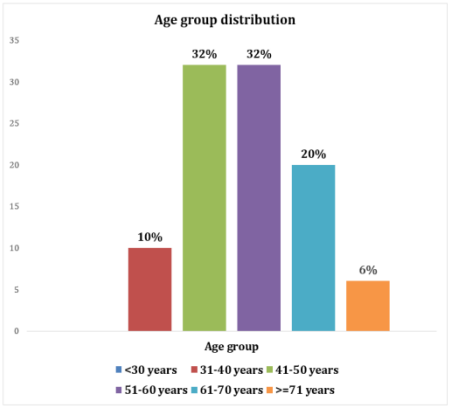
Table 1: Study participants' age distribution (n=50)

Age group	Frequency	Percent
≤ 30 years	0	0
31 – 40 years	5	10.0
41 – 50 years	16	32.0
51 – 60 years	16	32.0
61 – 70 years	10	20.0
> 70 years	3	6.0
Total	50	100.0

- Mean Age (± S.D): 54.04 (± 10.15) years

Minimum: 35 years maximum: 75 years

Figure 1: Age distribution bar diagram



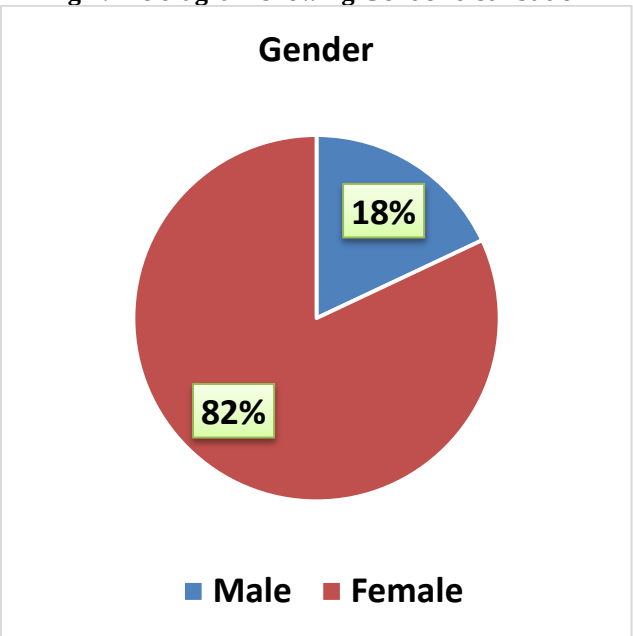
- **Comments:**

  The majority of research participants were in the 41–60 age range.

Table 2: Distribution of genders (n=50)

Gender	Frequency	Percent
Male	9	18
Female	41	82
Total	50	100.0

Fig 2: Pie diagram showing Gender distribution



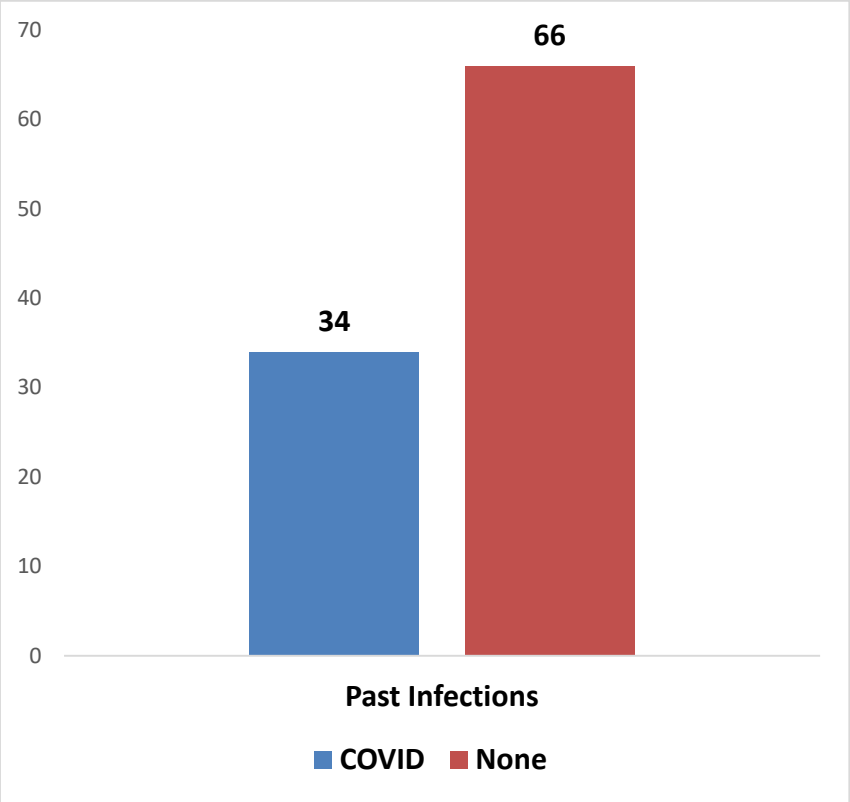
- **Comments:**

  The majority of research participants (82%) were women.

Table 3: Participant distribution in the study as per History of Past COVID infection (n=50)

Past infections	Frequency	Percent
COVID	17	34
None	33	66
Total	50	100.0

Fig. 3: Bar diagram displaying study participant distribution according to past infection history



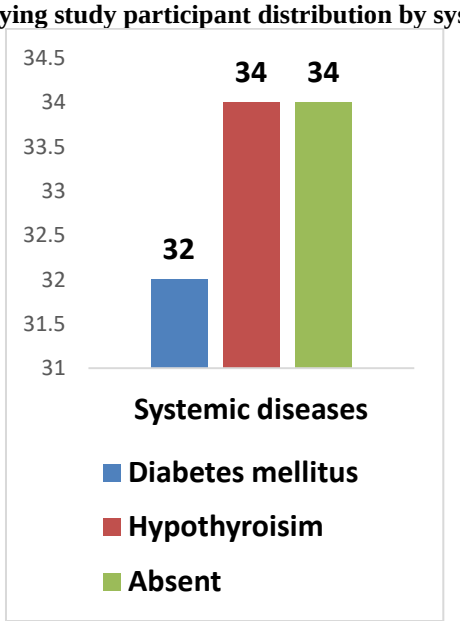
- **Comments:**

34% of the study participants had COVID infections in the past.

Table 4: Study participant distribution by systemic diseases (n = 50)

Systemic diseases	Frequency	Percent
Diabetes mellitus	16	32
Hypothyroidism	17	34
Absent	17	34
Total	50	100.0

Figure 4: Bar diagram displaying study participant distribution by systemic diseases



- **Comments:**
  32% had Diabetes mellitus and 34% had Hypothyroidism

DISCUSSION

Interstitial pneumonia with autoimmune features (IPAF) has been first defined, by European Respiratory Society (ERS)/ American Thoracic Society (ATS) taskforce in 2015, to classify a subgroup of Idiopathic Interstitial Pneumonias (IIP) that have autoimmune features, but do not meet the criteria to be classified as CTD-ILDs [4,5]. The radiologic picture detailed in the IPAF criteria are nonspecific interstitial pneumonia (NSIP), organizing pneumonia (OP), lymphoid interstitial pneumonia (LIP) and NSIP-OP overlap [6,7]. This study assessed the prevalence and determinants of IPAF among ILD patients in a tertiary care hospital in Chennai. The mean age of patients (54 years) and predominance of middle-aged individuals, particularly 5th and 6th decades, align with previous literature describing IPAF as a disease of mid to late adulthood [8,9]. The observed preponderance of female gender (82%) in the study parallels the increased burden of auto-immune diseases on women [10].

Globally, autoimmune diseases often show systemic disease and comorbidity associations, including Diabetes Mellitus and Hypothyroidism among others. But in this study, no statistically significant correlation was observed between IPAF and factors such as age, gender, past history of COVID-19 infection, diabetes mellitus, or hypothyroidism among patients with ILD. This contrasts with some international studies that report associations between autoimmune diseases and interstitial pneumonias, possibly reflecting differences in population genetics, environmental exposures, or sample size limitations [11,12].

The lack of association with systemic comorbidities suggests that IPAF arises through mechanisms distinct from traditional systemic diseases. The lack of significant correlation between systemic diseases and past infection profile with the development of IPAF, gives importance to the fact that a clear panel of comorbidities could not be made for the disease. Importantly, early recognition of IPAF relies on HRCT patterns and serological markers rather than background comorbidities [13,14,15].

CONCLUSION

This study highlights that while IPAF is present among ILD patients in a South Indian tertiary care setting, common systemic diseases (diabetes, hypothyroidism) and past infections (COVID-19) were not significantly associated with IPAF. These results show how important it is to use the same ERS/ATS 2015 criteria for correct IPAF diagnosis, no matter what other risk factors are present.

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