

Hormonal harmony disrupted: hypothyroidism and diabetes mellitus in interstitial lung disease. An observational study

Manju Bala,¹ Akhlesh Rajpoot,¹ Dinesh Chandra Punera,¹ Suyash Singh Rathore²

¹Department of Respiratory Medicine, Soban Singh Jeena Government Institute of Medical Science and Research, Almora, Uttarakhand;

²Department of Pulmonary Medicine, All India Institute of Medical Sciences, Rishikesh, Uttarakhand, India

Correspondence: Akhlesh Rajpoot, Department of Respiratory Medicine, Soban Singh Jeena Government Institute of Medical Science and Research, Almora, Uttarakhand, India.
Tel.: +91-7696575848.
E-mail: akhileshrajpoot855@gmail.com

Key words: ILD, COPD, hypothyroidism, diabetes mellitus, GERD.

Contributions: MB, AR, concepts, design, definition of intellectual content, literature search, data acquisition, data analysis, statistical analysis, manuscript preparation, editing, and review; DCP, concepts, design, definition of intellectual content, literature search, manuscript preparation, editing, and review; SSR, concepts, design, definition of intellectual content, literature search. All the authors have read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Conflict of interest: the authors declare that they have no competing interests, and all authors confirm accuracy.

Ethics approval and consent to participate: this study followed ethical standards set by the institutional and national research committee, as well as the 1964 Helsinki Declaration and its later amendments. Approval was obtained from the Institute's Ethics Committee of SSJGIMSR Almora, IRB-EC/NEW/INST/2022/1921.

Informed consent: taken.

Patient consent for publication: not applicable.

Availability of data and materials: available from the corresponding author upon request.

Funding: none.

Acknowledgments: the authors thank all the patients who participated in this study for their valuable consent.

Received: 13 February 2024.

Accepted: 24 April 2024.

Early view: 23 July 2025.

Publisher's note: all claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article or claim that may be made by its manufacturer is not guaranteed or endorsed by the publisher.

©Copyright: the Author(s), 2024

Licensee PAGEPress, Italy

Monaldi Archives for Chest Disease 2025; 95:2956

doi: 10.4081/monaldi.2024.2956

This article is distributed under the terms of the Creative Commons Attribution-NonCommercial International License (CC BY-NC 4.0) which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author(s) and source are credited.

Abstract

Interstitial lung disease (ILD) and chronic obstructive pulmonary disease (COPD) are chronic respiratory diseases that affect the lungs and airways. ILD encompasses approximately 200 different conditions with known and unknown causes. Various comorbidities, such as cardiovascular, psychological, obstructive sleep apnea, and gastrointestinal disorders, are often associated with them. However, little is known about the relationship and prevalence of hypothyroidism and diabetes mellitus (DM) in ILD and COPD. Therefore, understanding these connections is crucial for proper treatment. This cross-sectional, prospective observational study was conducted at a tertiary care hospital in North India. After obtaining informed consent, we consecutively enrolled 100 patients with ILD and 100 patients with COPD who reported to the Respiratory Medicine Outpatient Department. We collected demographic, clinical, and medical data from the patients and conducted appropriate statistical analysis to determine the prevalence of hypothyroidism and DM in patients with ILD. ILD patients exhibit a significantly higher prevalence of hypothyroidism (24% vs. 4%) and DM (24% vs. 4%) compared to those with COPD ($p < 0.05$). Additionally, the study showed that ILD patients also had a significantly higher prevalence of self-reported gastroesophageal reflux disease (30%), had a higher body mass index, and consulted a pulmonologist earlier than COPD patients after the onset of symptoms ($p < 0.05$). Therefore, it is important to screen for hypothyroidism and DM in ILD patients due to their high prevalence and potential impact on disease progression and management. Additionally, evidence suggests a bidirectional relationship between these conditions, making it essential to screen patients with hypothyroidism and DM for ILD if there is any suspicion. These screening measures could contribute to the early detection and management of these comorbidities, thereby improving the overall outcome for ILD patients.

Introduction

Chronic respiratory disease (CRD) is a group of lung and airway conditions that includes chronic obstructive pulmonary disease (COPD), asthma, allergic bronchopulmonary aspergillosis (ABPA), interstitial lung disease (ILD), occupational lung diseases, and more. It is the third leading cause of death worldwide in 2019 and is associated with a significant burden and cost [1,2]. A proper understanding of chronic respiratory disease and its associated comorbidities is essential for its management and treatment. COPD and ILD are complex respiratory conditions with overlapping and distinct characteristics that various comorbidities can worsen. COPD is a progressive lung disease primarily characterized by chronic bronchitis and emphysema, leading to airflow limitation

and respiratory symptoms [3]. ILD refers to a group of diverse lung conditions that cause gradual scarring and fibrosis of the lung's parenchyma [4]. Over 200 entities fall under this category, leading to dyspnoea, reduced life expectancy, and a gradual decline in the ability to exercise [5]. The availability of high-resolution computed tomography (HRCT) scans of the thorax has increased the recognition of ILD [6]. ILD can be caused by exposure to some substances, radiation, medication side effects, and connective tissue diseases (CTD). Idiopathic pulmonary fibrosis (IPF), pulmonary sarcoidosis, cryptogenic organizing pneumonia, and eosinophilic pneumonia are examples of ILD cases with unknown causes. CTDs associated with ILD, which include rheumatoid-associated ILD (RA-ILD) and systemic sclerosis-associated ILD (Ssc-ILD), are a group of disorders characterized by inflammation and scarring of the lungs that occur alongside CTD. The treatment involves managing the underlying CTD and addressing ILD symptoms, often requiring immunosuppressive therapy. However, ILD and COPD patients often suffer from concurrent diseases such as pulmonary hypertension (PH), systemic hypertension (HTN), diabetes mellitus (DM), hypothyroidism, gastroesophageal reflux disease (GERD), coronary artery disease (CAD), obstructive sleep apnea (OSA), osteoporosis, and mental health comorbidities. It is crucial to manage comorbidities to enhance the well-being and prognosis of patients, as they have a significant impact on clinical outcomes. Therefore, understanding the complex interplay of these comorbidities in ILD and COPD is vital for providing comprehensive patient care. The bidirectional relationship between ILD and various comorbidities necessitates a multidisciplinary approach that includes pulmonologists, cardiologists, rheumatologists, endocrinologists, and other health professionals. However, literature is scarce on the possible association of ILD with hypothyroidism and DM. To address this unmet need, we investigated the relationship between ILD with hypothyroidism and DM.

Materials and Methods

Study design and sample size

This cross-sectional, prospective observational study was conducted over one year at a tertiary care hospital in northern India with the approval of the institutional review board. After obtaining informed consent, 100 patients with ILD and 100 patients with COPD, both newly diagnosed and under treatment, were consecutively enrolled in the study from the respiratory medicine outpatient department. ILD was diagnosed using a multidisciplinary approach, including clinical, radiological, and pathological features [7,8]. COPD was diagnosed based on the diagnostic criteria of the Global Initiative for Chronic Obstructive Lung Disease [3].

The study excluded patients who were under 18 years of age, refused to provide their informed consent, were not competent enough to complete the questionnaires, had a psychiatric illness before being diagnosed with ILD/COPD, showed apparent memory deficits on clinical assessment, had organicity (like delirium or dementia) or malignancy, or were critically ill.

Methodology

Then all the patients with ILD and COPD underwent a thorough clinical evaluation, including arterial blood gas analysis, complete blood count, renal function tests, liver function tests, thyroid function tests (thyroid stimulating hormone, free triiodothyronine, free thyroxine), fasting blood glucose, postprandial blood glucose, 6-minute walk test, spirometry and dual-energy x-ray absorptiometry

scan. The diagnosis of hypothyroidism and DM was made as per the established guidelines [9,10]. The diagnosis of self-reported GERD was made by using the symptom-based (heartburn, regurgitation, epigastric pain, nausea, disturbed sleep, and need for additional medications for these symptoms) 6-item GERD questionnaire [11]. Anemia was diagnosed with hemoglobin levels less than 13 grams per deciliter (<13 gm/dL) in adult males and less than 12 gm/dL in adult females (non-pregnant and non-lactating) as per the established criteria by the World Health Organization [12]. The cardiologist diagnosed PH using a transthoracic echocardiogram. This diagnosis of PH was based on a combination of factors, including tricuspid regurgitant velocity, right ventricular size, interventricular septal function, fluctuations in the diameter of the inferior vena cava during the respiratory cycle, systolic right atrial area, the pattern of systolic flow velocity, early diastolic pulmonary regurgitant velocity, and the diameter of the pulmonary artery [13]. The diagnosis of osteoporosis was made according to the World Health Organization guidelines, where a T-score greater than 2.5 is used to diagnose osteoporosis [14]. Psychological illness was diagnosed based on the score of the self-administered Hospital Anxiety and Depression Scale [15]. All the patients were given all the necessary information before conducting the tests.

Statistical analysis

The statistical analysis was done using the computer-based Statistical Package for Social Sciences, version 22.0 (SPSS 22.0, IBM, Armonk, NY, USA). Quantitative variables were summarized as mean \pm standard deviation (SD) or median (interquartile range), and qualitative variables as frequency/percentage. Unpaired student *t*-test and Chi-square test were used, as appropriate, to compare continuous and nominal variables between ILD and COPD patients. A *p*-value of <0.05 was considered statistically significant with a confidence interval of 95%.

Results

The mean age of the ILD cohort ($n=100$) was 56.22 (SD 9.05) years (range 36-76 years) with a predominance of males ($n=56$, 56%), and the mean duration of ILD symptoms was 12.72 (SD 10.16) months (range 2-48 months). However, at presentation, COPD patients ($n=100$) were older than patients with ILD (63.48 vs. 56.22 years; $p=0.009$) and had more duration of symptoms before consultation with a pulmonologist as compared to ILD (30.26 vs. 12.72 months; $p<0.001$), respectively. Patients with ILD also had lesser exposure to noxious matters, higher body mass index (BMI), a higher percentage (%) predicted forced expiratory volume in one second (FEV1), and a lower % predicted forced vital capacity (FVC) as compared to COPD patients (Table 1). In the ILD cohort, only 22 (22%) patients were above 65 years of age, and 18 (82%) patients of this subgroup were diagnosed with IPF.

The study cohort had various comorbidities as depicted in Table 2. 58 (58%) patients of ILD and 52 (52%) patients of COPD had at least one comorbidity. The most common comorbidities observed in ILD patients were GERD [30% ($n=30$, male 16, female 14)], HTN [28% ($n=28$, male 16, female 12)], type 2 DM [24% ($n=24$, male 14, female 10)], and hypothyroidism [24% ($n=24$, male 18, female 6)]. Among the 24 patients who were diagnosed with hypothyroidism in the ILD cohort, 6 (25%) exhibited the presence of thyroid peroxidase antibody. Out of these 6, 3 patients were found to have CTD-ILD, 2 patients were diagnosed with sarcoidosis, and the remaining one was found to have UIP pattern on the HRCT of the

chest. Other comorbidities observed in patients with ILD were osteoporosis [22% (n=22, male 9, female 13)], followed by psychological illness [18% (n=18, male 10, female 8)], PH [16% (n=16, male 9, female 7)], dyslipidemia [14% (n=14, male 8, female 6)],

CAD (8%), anemia (6%) and polycythemia (4%). Out of 100 (70 newly diagnosed and 30 under treatment) patients with ILD, only 7 (7%) patients were on oral steroids, and one of these 7 patients was diagnosed with type 2 DM.

Table 1. Association of baseline characteristics of interstitial lung disease and chronic obstructive lung disease patients.

Characteristics		ILD (n=100)	COPD (n=100)	p
Age (years)	Mean	56.22	63.48	0.009*
	Median	58.60	64.16	
	SD	9.05	6.82	
Gender – male, n (%)	56 (56)	66 (66)	0.305	
Duration of symptoms (months)	Mean	12.72	30.26	0.0001*
	Median	6.10	12.80	
	SD	10.16	23.80	
Cough present, n (%)	76 (76)	68 (68)	0.373	
Dyspnea (mMRC grade)	Mean	2.26	2.18	0.061
	Median	2.10	2.20	
	SD	1.20	1.12	
Exposure/ever smokers, n (%)	70 (70)	100 (100)	0.0001*	
Chullah, n (%)	34 (34)	46 (46)	0.221	
Old PTB, n (%)	12 (12)	4 (4)	0.140	
LTOT, n (%)	6 (6)	18 (18)	0.065	
Systemic steroid use, n (%)	7 (7)	3 (3)	0.097	
SaO ₂ (%)	Mean	94.72	93.16	0.093
	Median	96.0	94.40	
	SD	3.70	5.35	
BMI (kg/m ²)	Mean	25.11	23.28	0.006*
	Median	25.13	23.37	
	SD	3.40	3.14	
% predicted FEV ₁	Mean	69.34	60.98	0.003*
	Median	67.50	61.20	
	SD	15.20	12.20	
% predicted FVC	Mean	62.94	78.34	0.0001*
	Median	61.50	79.80	
	SD	15.11	12.46	
6-MWD (meters)	Mean	299.38	288.42	0.499
	Median	313.20	294.60	
	SD	100.11	54.84	

ILD, interstitial lung disease; COPD, chronic obstructive lung disease; SD, standard deviation; mMRC, modified medical research scale; PTB, pulmonary tuberculosis; LTOT, long-term oxygen therapy; SaO₂, arterial oxygen saturation; BMI, body mass index; kg/m², kilograms per square meter; FEV₁, forced expiratory volume in first second; FVC, forced vital capacity; 6-MWD, 6-minute walk distance; *significant p-value at a confidence interval of 95.

Table 2. Association of various comorbidities between interstitial lung disease and chronic obstructive lung disease.

Comorbidities		ILD (n=100)	COPD (n=100)	p
Comorbidity, n (%)		58 (58)	52 (52)	0.546
Hypertension, n (%)		28 (28)	20 (20)	0.349
Type 2 diabetes mellitus, n (%)		24 (24)	4 (4)	0.004*
Hypothyroidism (n=24)	Anti-TPO positive (n=6)	24 (24)	4 (4)	0.004*
	Anti-TPO negative (n=18)			
CAD, n (%)		08 (08)	4 (04)	0.401
GERD, n (%)		30 (30)	12 (12)	0.027*
Pulmonary hypertension, n (%)		16 (16)	10 (10)	0.372
Psychological illness, n (%)		18 (18)	14 (14)	0.338
Osteoporosis, n (%)		22 (22)	16 (16)	0.345
Dyslipidemia, n (%)		14 (14)	10 (10)	0.349
Anemia, n (%)		6 (6)	3 (3)	0.307
Polycythemia, n (%)		4 (4)	8 (8)	0.169

ILD, interstitial lung disease; COPD, chronic obstructive lung disease; TPO, thyroid peroxidase antibody; CAD, coronary artery disease; GERD, gastroesophageal regurgitation disease; *significant p-value at a confidence interval of 95.

In patients with COPD, the most common comorbidities were HTN [20% (n=20, male 12, female 8)], followed by osteoporosis [16% (n=16, male 6, female 10)], psychological illness [14% (n=14, male 7, female 7)], GERD [12% (n=12, male 7, female 5)], PH [10% (n=10, male 6, female 4)], dyslipidemia [10% (n=10, male 6, female 4)], polycythemia [8% (n=8, male 5, female 3)], type 2 DM [4% (n=4, male 1, female 3)], hypothyroidism (4%, n=4, male 1, female 3), CAD (4%), and anemia (3%). The prevalence of hypothyroidism, type 2 DM, and GERD was significantly higher in patients with ILD than in patients with COPD (Table 2).

In Figure 1, a comparison of different comorbidities in patients with ILD and COPD is presented. The distribution of sub-categories of ILD is shown in Figure 2, where the highest proportion is made up of IPF [26% (n=26, male 22, female 4)] and sarcoidosis [26% (n=26, male 12, female 14)], followed by RA-ILD [22% (n=22, male 10, female 12)], hypersensitivity pneumonitis [18% (n=18, male 11, female 7)], Ssc-ILD [4% (n=4, female 4)] and nonspecific interstitial pneumonia [4% (n=4, male 1, female 3)]. Figure 3 illustrates the distribution of hypothyroidism, type 2 DM, and GERD in the sub-categories of ILD. About 46% (n=12) of patients with CTD-ILD had hypothyroidism, followed by sarcoidosis (n=6, 23%) and IPF (n=6, 23%) (Figure 3). Almost 90% of diabetic patients in the ILD cohort belong to sarcoidosis (n=8), CTD-ILD (n=8), and IPF (n=6) (Figure 3). Similarly, about 80% (n=24) of GERD patients in the ILD cohort belong to sarcoidosis (n=7), IPF (n=8), and CTD-ILD (n=9) groups (Figure 3).

Discussion

The present study revealed that the average age of the ILD patients was significantly lower (56.22 vs. 63.48; $p=0.009$) than

COPD patients (Table 1). This could be because 70% of the ILD patients in the study cohort had non-IPF ILD (Figure 2), which generally affects middle-aged adults, and this finding is consistent with the previous studies [8,16]. Patients with ILD consulted a pulmonologist earlier than patients with COPD after the onset of symptoms (12.72 vs. 30.26; $p<0.001$) (Table 1). This may be due to the more severe symptoms experienced by ILD patients, such as intractable coughing, which is difficult to manage by a general physician. Patients with ILD had a significantly higher BMI of 25.11 compared to COPD patients with a BMI of 23.28 ($p=0.006$). The higher weight of ILD patients could be attributed to the presence of hypothyroidism and type 2 DM [17,18]. Patients with ILD also had a higher %FEV1 but a lower %FVC than COPD patients (Table 1). This difference in %FEV1 and %FVC could be because COPD patients tend to have preserved or higher FVC and experience more decline in FEV1. ILD and COPD are both chronic respiratory disorders that can lead to various comorbidities, resulting in significant morbidity and mortality in affected patients [19,20]. The present study showed a significantly higher prevalence of hypothyroidism, type 2 DM, and self-reported GERD in ILD patients as compared to COPD patients ($p<0.05$) (Table 2). However, data are scarce on the possible association of ILD with hypothyroidism and DM [21,22].

In our study, hypothyroidism was found in 24% of ILD patients, which was significantly higher than the hypothyroidism in COPD patients (4%; $p=0.004$). Although it is not clear how ILD may cause hypothyroidism. However, it is possible that chronic inflammation in ILD can influence the function of the thyroid gland through its impact on the hypothalamic-pituitary-thyroid axis, leading to hypothyroidism. This hypothesis is supported by a case series of two patients who suggested a link between hypothyroidism and radiological ILD, which improved with thyroxine replacement therapy for hypothyroidism and returned to a euthyroid state [23].

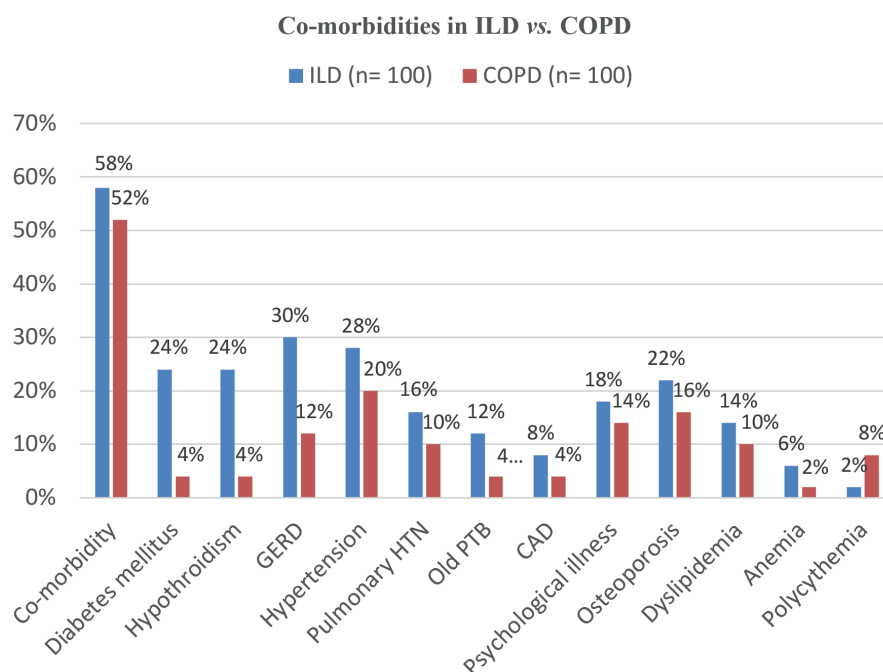


Figure 1. Bar diagram showing percentage (%) of different comorbidities in interstitial lung disease and chronic obstructive lung disease patients. GERD, gastroesophageal regurgitation disease; PTB, pulmonary tuberculosis; CAD, coronary artery disease.

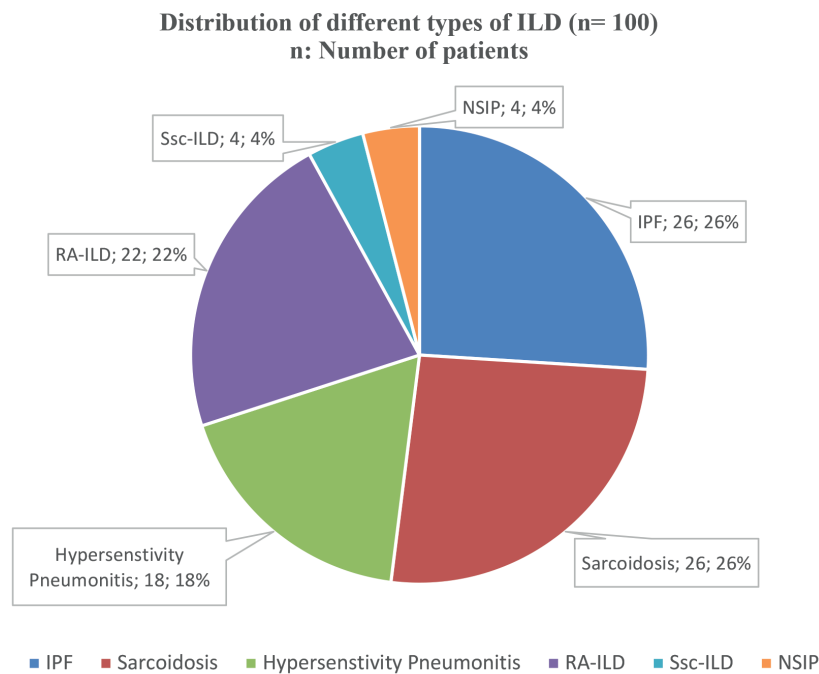


Figure 2. Pie chart showing the distribution of different types of interstitial lung disease (ILD). Ssc-ILD, sclerosis-associated ILD; NSIP, nonspecific interstitial pneumonia; RA-ILD, rheumatoid-associated ILD; IPF, idiopathic pulmonary fibrosis.

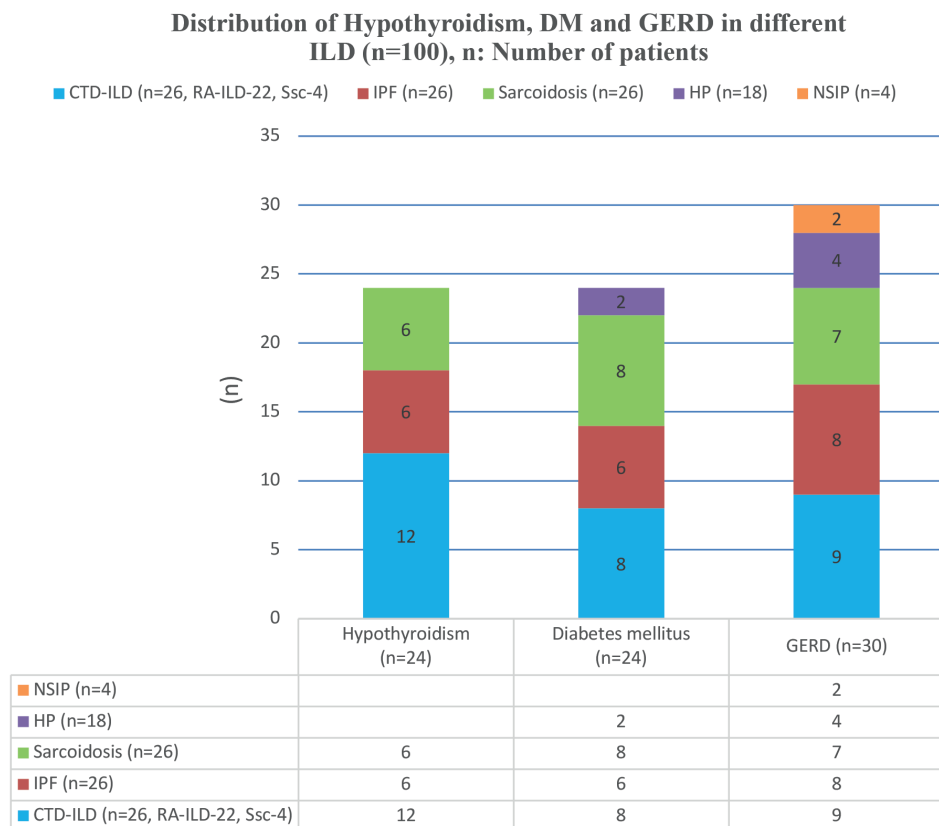


Figure 3. Bar diagram showing the distribution of hypothyroidism, diabetes mellitus (DM), and gastroesophageal regurgitation disease (GERD) in different interstitial lung diseases (ILDs). NSIP, nonspecific interstitial pneumonia; HP, hypersensitivity pneumonitis ; IPF, idiopathic pulmonary fibrosis; CTD-ILD, connective tissue disease-ILD.

Conversely, in a few studies, the induction of a hypothyroid state in mice appears to prevent pulmonary fibrosis associated with systemic sclerosis and accelerate the recovery of liver fibrosis, raising doubt that hypothyroidism itself could contribute to IPF onset or progression [24,25]. Another possible link between hypothyroidism and ILD may be immune dysregulation in ILD, which is supported by the expression of several genes, including *CTLA-4*, *ICOS*, and *CD28*, in patients with ILD [26]. Additionally, the relationship between ILD and hypothyroidism is complex and multifaceted. Hypothyroidism weakens respiratory muscles, reduces lung function, and affects the immune system, leading to the progression of lung damage. Therefore, it is important to regularly check thyroid function in all patients with ILD, and patients with hypothyroidism should be screened for ILD if there is any suspicion.

In the present study, patients with ILD had a significantly higher prevalence of type 2 DM compared to those with COPD (24% vs. 4%, $p=0.004$, as shown in Table 2). This finding corroborates previous studies that have also reported a higher incidence of DM in patients with ILD [22,27]. The etiology of such a correlation might be attributed to the impact of ILD on glucose processing and blood sugar regulation. The chronic inflammation and fibrotic alterations in the lung tissue may lead to systemic inflammation, insulin resistance, and disruption of glucose homeostasis. Furthermore, the hypoxia associated with ILD can exacerbate insulin resistance in patients with coexisting DM. Studies from around the globe have reported a 20% to 32% prevalence of ILD in DM patients due to diabetic-related pneumopathy, also highlighting a bidirectional relationship between these two conditions [28,29]. However, it is important to note that international guidelines on ILD and DM do not mention either DM as a risk factor for ILD, or ILD as a risk factor for DM. These are two separate medical conditions, but they can occur together and affect each other's progression and management. Thus, it is crucial to comprehend the connection between ILD and DM to provide comprehensive care to patients affected by these conditions. While the underlying mechanisms of this association are not completely understood, chronic inflammation and alterations in the blood vessels associated with DM may contribute to the development or aggravation of pulmonary fibrosis [28,29]. Therefore, managing DM in patients with ILD requires coordination among medical professionals, including pulmonologists, endocrinologists, and other healthcare providers, with regular monitoring of blood glucose levels and adjusting diabetes medication to avoid interactions with ILD therapies.

In the present study, the prevalence of self-reported GERD was also significantly higher in ILD patients compared to those with COPD (30% vs. 12%, $p=0.02$) (Table 2). It may be due to secondary progressive pulmonary fibrosis, which can cause negative pressure in the chest, distorting the mediastinal structures and weakening the lower esophageal sphincter. Alternatively, it could be due to more frequent involvement of the esophagus in CTD-ILD [30]. GERD and ILD share a relationship based on the microaspiration of gastric contents into the lungs. This process triggers inflammation and fibrotic responses. It is important to note that chronic microaspiration can worsen ILD and lead to a more rapid decline in lung function. Thus, healthcare providers need to recognize and manage GERD in ILD patients to improve their quality of life and reduce the burden on healthcare systems. Early diagnosis and customized treatment strategies can prevent further complications and improve overall health outcomes.

According to the present study, ILD patients were more likely to have several other health issues, such as cardiovascular disorders, psychological disorders, osteoporosis, dyslipidemia, and anemia, as

compared to COPD patients (Table 2); however, this difference is not statistically significant. These comorbidities can worsen the prognosis and outcomes of ILD patients, especially cardiovascular diseases such as PH, ischemic heart disease, and heart failure. The impaired gas exchange associated with ILD can exacerbate cardiac conditions, making it difficult to manage both systems. A coordinated approach between cardiologists and pulmonologists is essential for managing these conditions simultaneously. The chronic nature of ILD and COPD, combined with the daily functioning challenges, can significantly impact mental health. Consequently, incorporating psychosocial support into the overall management of ILD and COPD is essential to address the holistic well-being of patients. Additionally, ILD and COPD patients have an increased risk of developing osteoporosis due to common factors such as aging, chronic inflammation, and glucocorticoid use [31]. Therefore, managing bone health in these patients requires a careful balance between therapies for these diseases and strategies to prevent and treat osteoporosis. Dyslipidemia is closely associated with both ILD and COPD, although the exact nature of this relationship remains unclear. Managing lipids in this population requires a nuanced approach that considers the potential impact of medications on lung function. Hematological disorders such as anemia and polycythemia are also encountered in these patients. Chronic inflammation and hypoxia contribute to anemia, while chronic lung disease can lead to polycythemia as a compensatory response [32]. Addressing these hematological abnormalities necessitates a tailored approach that considers the underlying mechanisms in each case. Therefore, it is crucial to identify and manage these comorbidities in ILD and COPD patients to improve their overall well-being and potentially slow lung function decline.

Conclusions

The co-occurrence of different comorbidities with ILD creates a challenging scenario. Therefore, whenever dealing with ILD patients, it is crucial to screen for these comorbidities, including hypothyroidism and DM, as they have a significant impact on disease progression and management. It is also important that patients with hypothyroidism and DM should be screened for ILD if there is any suspicion, as there is evidence of a two-way relationship between these conditions. Ensuring that these screening measures are implemented could contribute to the early detection and management of these comorbidities, thereby improving the overall outcome for patients with ILD. However, it should be noted that neither the international guidelines on ILD nor diabetes/hypothyroidism mention diabetes/hypothyroidism as a risk factor for ILD, or *vice versa*, due to insufficient data. Therefore, further studies with larger sample sizes are needed to establish a clearer understanding of ILD with hypothyroidism and DM.

References

1. GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990- 2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* 2020;396:1204-22.
2. Syamlal GBA, Dodd KE. Medical expenditures attributed to asthma and chronic obstructive pulmonary disease among workers- United States, 2011-2015. *MMWR Morb Mortal Wkly Rep* 2020;69:809-14.
3. Global strategy for the diagnosis, management, and prevention

- of COPD. Global initiative for chronic obstructive lung disease (GOLD) 2023. Available from: <http://goldcopd.org>. Accessed on: 30/12/2023.
4. Ryerson CJ, Areal PA, Berkeley J, et al. Depression is a common and chronic comorbidity in patients with interstitial lung disease. *Respirology* 2012;17:525-32.
 5. Du Bois RM. An earlier and more confident diagnosis of idiopathic pulmonary fibrosis. *Eur Respir Rev* 2012;21:141-6.
 6. Raghu G, Chen SY, Hou Q, et al. Incidence and prevalence of idiopathic pulmonary fibrosis in US adults 18–64 years old. *Eur Respir J* 2016;48:179-86.
 7. Raghu G, Remy-Jardin M, Myers JL, et al. Diagnosis of idiopathic pulmonary fibrosis. An official ATS/ERS/JRS/ALAT clinical practice guideline. *Am J Respir Crit Care Med* 2018;198:e44-68.
 8. Travis WD, Costabel U, Hansell DM, et al. An official American Thoracic Society/European Respiratory Society statement: update of the international multidisciplinary classification of the idiopathic interstitial pneumonias. *Am J Respir Crit Care Med* 2013;188:733-48.
 9. Garber JR, Cobin RH, Gharib H, et al. Clinical practice guidelines for hypothyroidism in adults. *Endocr Pract* 2012;18:988-1028.
 10. ElSayed NA, Aleppo G, Aroda VR, et al. Classification and diagnosis of diabetes: standards of care in diabetes-2023. *Diabetes Care* 2023;46:S19-40.
 11. Jones R, Junghard O, Dent J, et al. Development of the GERDQ, a tool for the diagnosis and management of gastroesophageal reflux disease in primary care. *Aliment Pharmacol Ther* 2009;30:1030-8.
 12. Nutritional anemias. Report of a WHO Scientific Group. *World Health Organization Tech Rep Ser* 1968;45:5-37.
 13. Frost A, Badesch D, Gibbs JSR, et al. Diagnosis of pulmonary hypertension. *Eur Respir J* 2019;53:1801904.
 14. Kanis JA. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis: synopsis of a WHO report. *WHO Study Group. Osteoporos Int* 1994;4:368-81.
 15. Snaith RP, Zigmond AS. The hospital anxiety and depression scale. *Br Med J* 1986;292:344.
 16. Dhooria S, Sehgal IS, Agarwal R, et al. (2022) Incidence, prevalence, and national burden of interstitial lung diseases in India: estimates from two studies of 3089 subjects. *PLoS One* 17:e0271665.
 17. Oldham JM, Kumar D, Lee C, et al. Thyroid disease is prevalent and predicts survival in patients with idiopathic pulmonary fibrosis. *Chest* 2015;148:692-700.
 18. Rajpoot A, Garg K, Saini V, Gupta N. Psychological morbidity in interstitial lung disease: a study from India. *Monaldi Arch Chest Dis* 2020;90:1434.
 19. Hill J, Harrison J, Christian D, et al. The prevalence of comorbidity in rheumatoid arthritis: a systematic review and meta-analysis. *Br J Community Nurs* 2022;27:232-41.
 20. Smith MC, Wrobel JP. Epidemiology and clinical impact of major comorbidities in patients with COPD. *Int J Chron Obstruct Pulmon Dis* 2014;9:871-88.
 21. Alzghoul BN, Amer FN, Barb D, et al. Prevalence and characteristics of self-reported hypothyroidism and its association with non-organ-specific manifestations in US sarcoidosis patients: a nationwide registry study. *ERJ Open Res* 2021;7:00754-2020.
 22. Suga T, Sugiyama Y, Kitamura S. Clinical study of patients with idiopathic interstitial pneumonia accompanied by diabetes mellitus. *Nihon Kyobu Shikkan Gakkai Zasshi* 1994;32:1131-5. [Article in Japanese].
 23. George JT, Thow JC, Rodger KA, et al. Reversibility of fibrotic appearance of lungs with thyroxine replacement therapy in patients with severe hypothyroidism. *Endocr Pract* 2009;15:720-4.
 24. Bagnato G, Bitto A, Irrera N, et al. Propylthiouracil prevents cutaneous and pulmonary fibrosis in the reactive oxygen species murine model of systemic sclerosis. *Arthritis Res Ther* 2013;15:R120. Erratum in: *Arthritis Res Ther* 2014;16:406. Retraction in: *Arthritis Res Ther* 2022;24:272.
 25. Bruck R, Weiss S, Traister A, et al. Induced hypothyroidism accelerates the regression of liver fibrosis in rats. *J Gastroenterol Hepatol* 2007;22:2189-94.
 26. Herazo-Maya JD, Noth I, Duncan SR, et al. Peripheral blood mononuclear cell gene expression profiles predict poor outcomes in idiopathic pulmonary fibrosis. *Sci Transl Med* 2013;5:205ra136.
 27. Kim SY, Yoo CG, Lee CT, et al. Incidence and risk factors of steroid-induced diabetes in patients with respiratory disease. *J Korean Med Sci* 2011;26:264-7.
 28. Kopf S, Groener JB, Kender Z, et al. Breathlessness and restrictive lung disease: an important diabetes-related feature in patients with type 2 diabetes. *Respiration* 2018;96:29-40.
 29. Enomoto T, Usuki J, Azuma A, et al. Diabetes mellitus may increase the risk for idiopathic pulmonary fibrosis. *Chest* 2003;123:2007-11.
 30. Margaritopoulos GA, Antoniou KM, Wells AU. Comorbidities in interstitial lung diseases. *Eur Respir Rev* 2017;26:160027.
 31. Aggarwal D, Palta A, Jindal R, et al. Prevalence and predictors of osteoporosis in patients of interstitial lung disease: An observational study from North India. *Indian J Respir Care* 2022;11:353-7.
 32. Babakhanlou R, Verstovsek S, Pemmaraju N, Rojas-Hernandez CM. Secondary erythrocytosis. *Expert Rev Hematol* 2023;16:245-51.