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ORIGINAL ARTICLES

COVID-19 outcomes in hospitalized patients with underlying connective tissue disease-related interstitial lung disease vs. idiopathic interstitial pneumonia: a nationwide analysis 2019-2020

El Sharu H[1], Haddaden M[2], Singh S[1], Romero Noboa M[3], Mubaydeen T[4], Alqalyoobi S[5], Sabha M[6]

ABSTRACT

Background: In the context of the COVID-19 pandemic, understanding the influence of pre-existing Interstitial Lung Disease (ILD) on patient outcomes is crucial. This study aimed to compare the impact of COVID-19 on patients with Idiopathic Interstitial Pneumonia (IIP) versus Connective Tissue Disease-related ILD (CTD-ILD) in terms of mortality, length of hospital stay (LOS) and Intensive Care Unit (ICU) admission.
Methods: The National Inpatient Sample (NIS) database for 2019-2020 identified adult patients hospitalized with COVID-19 and either IIP or CTD-ILD. Patient demographics, comorbidities, and outcomes were analyzed.
Results: Among 1,010,030 COVID-19 hospitalizations, 11,030 had ILD, with 1,105 associated with CTD. Although both IIP and CTD-ILD groups had higher mortality rates than non-ILD patients, there was no significant difference in mortality between CTD-ILD and IIP groups. The odds ratio for mortality was 0.78 (95% CI 0.50-1.2, p = 0.3) for CTD-ILD compared to IIP patients and 1.54 (95% CI 1.03-2.31, p = 0.03) for CTD-ILD compared to non-ILD patients.
Conclusion: This study underscores the importance of considering ILD subtypes in predicting COVID-19 outcomes. Despite demographic and comorbidity differences, mortality rates were comparable between CTD-ILD and IIP patients. Further research is needed to explore underlying mechanisms contributing to mortality in different ILD subtypes and the impact of specific rheumatological diseases and treatments on COVID-19 outcomes.

Keywords: COVID-19; Connective Tissue Disease; Connective Tissue-related Interstitial Lung Disease; Interstitial Lung Disease.

KEY MESSAGES

- Both IIP and CTD-ILD groups had significantly higher COVID-19 mortality rates than non-ILD patients, but there was no significant mortality difference between the CTD-ILD and IIP groups;
- This study highlights the variation in COVID-19 mortality among the IIP and CTD-ILD groups, which may be influenced by the disease process itself or the medications used for treatment;
- Patients with CTD-ILD and IIP both faced high mortality and complication rates when hospitalized with COVID-19, underscoring the vulnerability of these populations during respiratory infections;

INTRODUCTION

In the complex world of Coronavirus disease 2019 (COVID-19), where pre-existing health conditions play a key role in predicting outcomes, interstitial lung disease (ILD) emerges as a critical factor that might be influencing patients' prognosis. ILD has a prevalence of 199.7 per 100,000 persons in the United States and encompasses a category of fibroinflammatory conditions that impact the alveolar interstitium within the lungs, resulting in alveolar damage and thickening of the interstitium[1]. If not promptly addressed, it will lead to the progression of symptoms such as cough, breathlessness, and eventually respiratory failure that might be fatal[2].

[1] Department of Internal Medicine, East Carolina University Brody School of Medicine, Greenville, NC; [2] Department of Pulmonary Medicine and Critical Care, The University of Oklahoma, Oklahoma City, OK; [3] Department of Rheumatology, University of Alabama at Birmingham, Birmingham, AL; [4] Department of Internal Medicine, King Hussein Cancer Center, Amman, Jordan; [5] Department of Pulmonary Medicine and Critical Care, East Carolina University Brody School of Medicine, Greenville, NC; [6] Department of Rheumatology, University Hospitals, Cleveland, OH

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Correspondence to Husam El Sharu
E-mail: elsharuh22@ecu.edu

ILDs can be broadly categorized into idiopathic interstitial pneumonia (IIP), connective tissue disease-related ILD, exposure-related ILD, medication-induced ILD, and others. Over 200 causes have been identified leading to ILDs[3] The most common type of IIP is Idiopathic pulmonary fibrosis (IPF), which affects men more than women and carries high morbidity and mortality[4]. IPF adjusted prevalence is estimated to range from 0.33 to 2.51 cases and 2.40 to 2.98 cases per 10,000 persons in Europe and North America, respectively[5].

Connective tissue diseases (CTDs) are also well-known to cause ILD[6]. The prevalence of ILD is up to 91% in systemic sclerosis (SSc); 80% in dermatomyositis/polymyositis; 67% in mixed connective tissue disease (MCTD); 58% in rheumatoid arthritis (RA), 27% in Sjogren syndrome (SS), and up to 13% in systemic lupus erythematosus (SLE). Non-specific interstitial pneumonia (NSIP) is frequently identified as the prevailing histopathological pattern in CTD-ILD[7,8].

Huang *et al.* and his team were the first to report the clinical characteristics of COVID-19 among patients with preexisting ILD. They found that patients with preexisting ILD who acquired severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection exhibited more complications than those without ILD. It was hypothesized that significantly higher levels of neutrophils, monocytes, and interleukins (IL)-8, IL-10, and IL-1β could have contributed to the increased symptomatology in the ILD group[9]. Li *et al.* also proposed that the increase in incidence and mortality in ILD patients infected with COVID-19 could be attributed to the increased expression of angiotensin-converting enzyme (ACE)-2 receptors on host cells to which the viral surface spike proteins bind[10].

Distinct ILD subtypes may respond differently to COVID-19, emphasizing the need for a nuanced understanding of their contributions to mortality and morbidity. Drake *et al.* revealed that patients who had COVID-19 and IPF face a higher risk of death than non-IPF ILD patients. Among non-IPF ILDs, Hypersensitivity Pneumonitis (HP) and RA-related ILD were associated with higher mortality, while other CTD-ILDs and sarcoidosis were linked to lower mortality rates[11].

This study aims to compare hospitalized patients with underlying IIP to CTD-ILD who acquired SARS-CoV-19 infection to further our understanding of the impact of COVID-19 on the different types of ILDs in terms of mortality, length of stay (LOS), and Intensive care unit (ICU) admission. To achieve this, we conducted a nationwide 2019-2020 analysis utilizing the expansive National Inpatient Sample (NIS).

METHODS

Data source

The study was conducted using the NIS database for 2019-2020. This data was developed by The Agency for Healthcare Research and Quality to aid in healthcare cost and utilization projects[12]. NIS is the largest publicly available inpatient database in the United States. The patients' data in this database are de-identified and considered part of the public record, and it is being assessed periodically to ensure accuracy[13]. Accordingly, Institutional Review Board approval for this study was not required. The large sample size is ideal for rare diseases such as ILD, and it contains over 100 clinical elements drawn from 35 million weighted admissions annually, representing 20% of hospital admissions in the United States. It includes clinical and nonclinical variables for each hospital stay, including up to 40 discharge diagnoses using the International Classification of Diseases, Tenth revision (ICD-10).

Study population

Using the NIS predefined variables, we identified the patient's age, gender, race, and insurance. We also used the Charlson Comorbidity Index (CCI) to determine the comorbidity burden of common co-morbid conditions that can affect outcomes[14]. We identified subjects ≥ 18 years with any IIP defined by (ICD-10 codes: J84.112, J84.113, J84.114, J84.115, J84.116, J84.117, J84.9, J84.09, J84.10, J84.111, and J84.89). CTD were identified such as SLE (ICD-10 codes: M32.1, M32.8, and M32.9), DM (ICD-10 codes: M33.1, M33.2, and M33.9), SSc (ICD-10 codes: M34), SS (ICD-10 codes: M35.0), MTCD (ICD-10 codes: M35.1 and M35.9), RA (ICD-10 codes: M05, M06.0, M06.2, M06.3, M06.4, M06.8, and M06.9) and Granulomatosis with polyangiitis (ICD-10 code: M31.3). We excluded patients with any code related to secondary causes that might lead to ILD, such as exposure-related ILD, including radiation, inorganic dust, and chemicals and medication-induced ILD. (ICD-10 codes: J60, J61, J62, J63, J64, J65, J66, J67, J68, J69, and J70). Additionally, we excluded conditions that might confound the results, including lung transplant (ICD-10 codes in supplementary material), and Goodpasture's disease (ICD-10 code: M31.0). A description of the data extraction is shown in Figure 1. Further codes are described in the Supplementary Table.

Patient, hospital characteristics, and outcomes

Baseline patient demographics (age, race, and sex) and relevant comorbidities (smoking, respiratory failure, asthma, chronic obstructive pulmonary disease

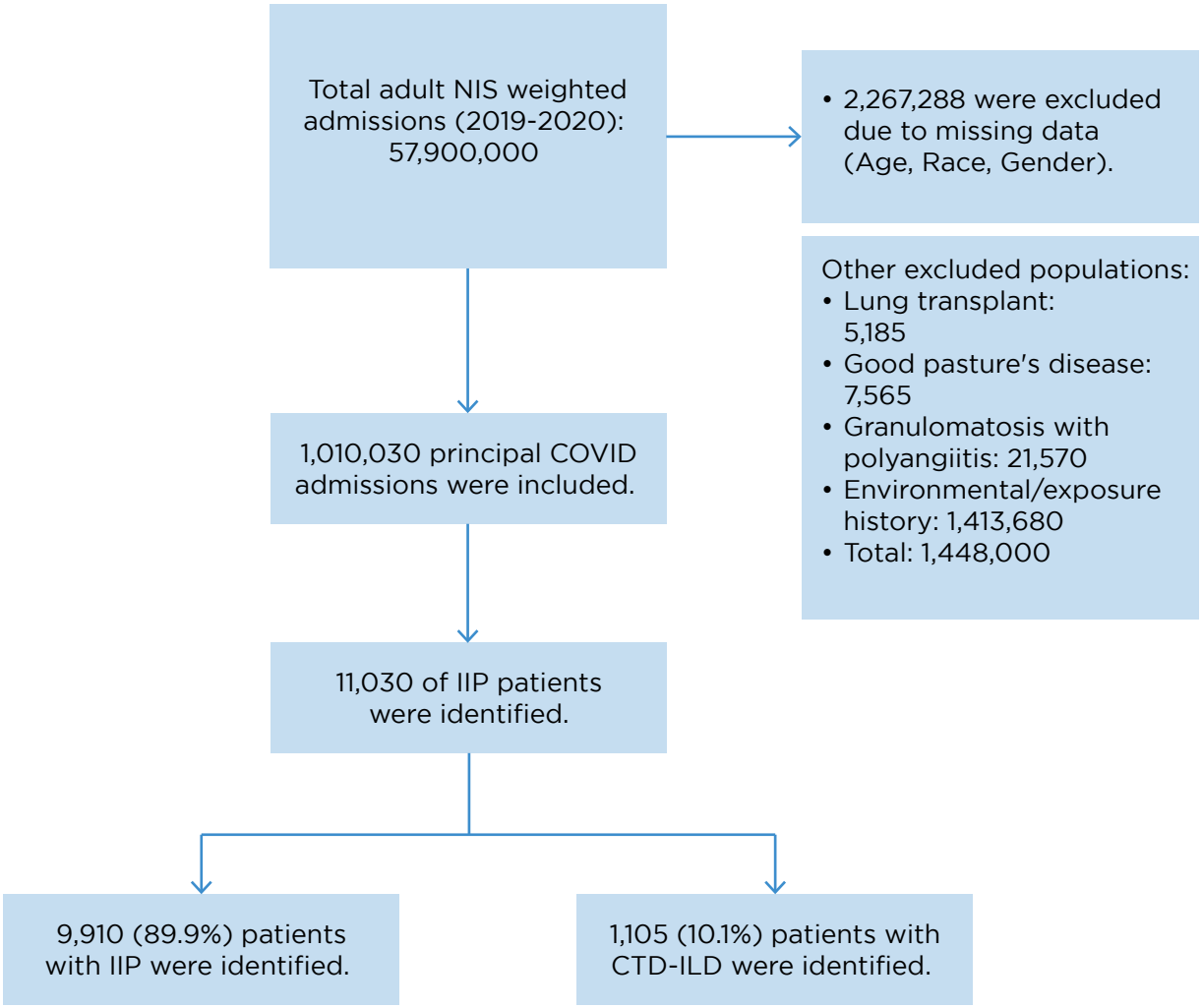

Figure 1. How the data were extracted and the numbers of each group category

(COPD), congestive heart failure, and pulmonary embolism) were extracted (Table I). Interquartile income and CCI were also extracted (Table I). The primary outcome was in-hospital mortality. Secondary outcomes, including LOS, total hospital charges, and ICU admission, are included in Table II.

Statistical analysis

The analysis was performed using STATA, version 14.2. Univariate and multivariate analyses were used for each appropriate variable. Covariates in the multivariate model included demographics such as age, gender, race, zip code, hospital location and setting, hospital region, and hospital size. Additional comorbidities included hypertension, pneumonia, heart failure, oxygen use, respiratory failure, COPD, obstructive sleep apnea, frailty, tobacco use, and pulmonary embolism. The comorbidities were selected based on univariate logistic screen analysis and a careful review of previous literature.[15,16] Univariate logistic screen analysis assessed crude Odds Ratio (OR) for secondary outcomes. Variables associated with the outcome of interest with p-value <0.2% were only included in the second logistic regression model. While unadjusted p-values were not reported for univariate models, adjusted p-values were reported for multivariate models.

RESULTS

Population characteristics

Between 2019 and 2020, 57.9 million adult admissions

were recorded in the NIS, of which 1,010,030 weighted records with a principal diagnosis of COVID-19 met the inclusion and exclusion criteria. Subjects <18 years and specific patient populations (lung transplant patients, exposure-related ILD, medication-induced ILD, and Goodpasture's disease) were excluded. In the study sample, 11,030 patients had ILD, of which 1,105 (10.1%) were associated with CTD.

Patients with CTD-ILD had a mean age of 70.4 years compared to 71.9 years in patients with IIP ($p < 0.001$). Female representation in the CTD-ILD group was significantly higher compared to the IIP group, 63.9% vs. 38.1%, respectively ($p < 0.001$).

The CTD-ILD group had a similar proportion of white patients (60.1% versus 61.8%) but a significantly higher proportion of African American patients (19.5% versus 14.2%, $p < 0.001$) compared to the IIP group. Table 1 outlines patient characteristics among three groups: patients without ILD, patients with CTD-ILD and patients with IIP.

Subgroup characteristic analysis

There were no significant differences in most of the comorbidities between the CTD-ILD group and the IIP

TABLE I. Patient characteristics among the 3 groups: patients without ILD, patients with CTD-ILD, and patients with IIP

	Non-LLD n= 1,010,030	CTD-ILD n= 1105	IIP n= 9910	The P value of the ILD group (CTDILD and IIP) compared to the Non-ILD group
Patient characteristics				
Age, mean years	64.4	70.4	71.9	<0.001
Female (%)	47.2%	63.9%	38.1%	<0.001
Race				<0.001
White	52.2%	60.1%	61.1%	
African American	18.2%	19.5%	14.2%	
Hispanic	20.8%	13.2%	15.%	
Asian or Pacific	3.2%	2.0%	3.1%	
Native American	1%	1.2%	1.2%	
Charlson comorbidity index				<0.001
0	28.5%	1.2%	14.5%	
1	28.3%	19.9%	24.2%	
2	16.2%	19.3%	21.9%	
> 3	26.9%	56.8%	41.8%	
Median (IQR)				<0.001
Household income Q1 (%)	34.2%	29.1%	31.4%	
Household income Q2 (%)	27.2%	27.9%	26.4%	
Household income Q3 (%)	21.9%	25.4%	22.3%	
Household income Q4 (%)	16.2%	17.5%	19.7%	
Comorbidities				
HF	15%	23.5%	23.8%	<0.001
aOR	REF	0.57 (p <0.001)	0.94 (p =0.23)	
Oxygen Use	3.7%	18.1%	15.6%	<0.001
aOR	REF	3.6 (p <0.001)	1.7 (p <0.001)	
Respiratory Failure	57%	70.5%	70.1%	<0.001
aOR	REF	1.54 (p =0.008)	1.55 (p <0.001)	
COPD	12.5%	19.9%	24.5%	<0.001
aOR	REF	.79 (p =0.22)	1.21 (p <0.001)	
Frailty	13.8%	22.6%	22.7%	0.002
aOR	REF	2.56 (p =0.003)	2.53 (p <0.001)	
Pulmonary Embolism	27.7%	31.1%	46.9%	<0.001

aOR= adjusted odds ratio; COPD: chronic obstructive pulmonary disease; CTD: Connective Tissue Disease; CTD-ILD: Connective Tissue Disease related Interstitial Lung disease; HF: Heart failure; ILD: Interstitial Lung disease; IIP: Idiopathic Interstitial Pneumonia.

TABLE II. Subgroup analysis for each specific CTD subset rate in patients with ILD vs. without ILD

CTD Subtype	No ILD (%)	ILD (%)
MCTD Overlap	0.03	0.09
Sjögren's Syndrome	0.09	0.28
Scleroderma	0.05	0.39
Dermatomyositis	0.03	0.21
Rheumatoid Arthritis (RA)	1.92	3.77
Systemic Lupus Erythematosus (SLE)	0.54	0.82
ANCA-Associated Vasculitis (AAV)	0.05	0.22
Total proportion	2.72	5.78

group. However, compared to patients with IIP, patients with CTD-ILD had lower odds of having concomitant heart failure (aOR of 0.56, 95% CI 0.37-0.84, p=0.005). Patients with IIP had significantly higher odds of having COPD when compared to the non-ILD group (aOR of 1.21, 95% CI 1.11-1.32, p<0.001). In contrast, patients with CTD-ILD had no significant difference in having COPD when compared to the non-ILD group (aOR of 0.79, 95% CI 0.87-1.32, p=0.022) but had significantly lower odds of COPD when compared to the IIP group (aOR of 0.59, 95% CI 0.40-0.87, p<0.001).

Primary outcome

Mortality

Among COVID-19 patients without ILD, 108,430 estimated deaths (10.7%) occurred, whereas those with ILD had 2435 estimated deaths (22.0%). Patients with CTD-ILD and IIP exhibited comparable mortality rates, with 205 (18.5%) deaths compared to 2230 (22.4%) deaths, which was also reflected in multivariate analysis with an aOR of 0.78 (95% confidence interval [CI] 0.50-1.2, p=0.3) after adjusting for the previously described comorbidities. However, when comparing CTD-ILD and IIP groups to the non-ILD group, patients with CTD-ILD and IIP had higher odds of mortality (aOR of 1.54, 95% CI 1.03-2.31, p=0.03) and (aOR of 1.50, 95% CI 1.36-1.65, p<0.001), respectively.

On combined analysis of ILD patients overall (CTD-ILD and IIP) to their non-ILD counterparts, males exhibited higher odds of mortality, with an aOR of 1.26 (95% CI 1.20-1.31, p<0.001). Similarly, white Americans had higher odds of mortality compared to African Americans, with an aOR of 1.22 (95% CI 1.15-1.29, p<0.001).

Also, ICU admission was associated with the highest in-hospital mortality (aOR of 3.20, 95% CI 2.96-3.45, p<0.001), followed by chronic respiratory failure (aOR of 1.93, 95% CI 1.83-2.02, p<0.001), and pneumonia (aOR 1.68, 95% CI 1.56-1.82, p-value < 0.001). Heart failure, frailty, and pulmonary embolism were also associated with statistically significant increased odds of mortality (p<0.001). Table II summarizes predictors of increased odds of inpatient mortality.

Secondary outcomes

Length of Stay and Hospital Charges

COVID-19 patients with no reported ILD had a mean LOS of 7.2 days. Unsurprisingly, IIP and CTD-ILD groups had statistically significant higher LOS of 14.1 days versus 9.8 days (p<0.001), respectively. Similarly, patients without ILD had a mean hospital charge of $75,608, while patients with IIP and CTD-ILD had statistically significant higher charges of $171,003 and $107,189 (p<0.001).

ICU admission

When compared to the non-ILD group, patients with CTD-ILD and IIP had a statistically significant difference in ICU admission (aOR of 2.10, 95% CI 1.55-3.01, p<0.001) versus (aOR of 3.20, 95% CI 2.96-3.45, p<0.001). However, patients with CTD-ILD had no significant difference in ICU admission compared to the IIP group. Table III highlights the outcome differences between patients without ILD, patients with CTD-ILD, and patients with IIP.

DISCUSSION

This study examined outcomes among COVID-19 hospitalizations across patients without ILD versus patients with ILD, subdivided into IIP and CTD-ILD groups. Mortality rates, LOS, total charges, and ICU admission were markedly higher in the ILD group compared to the non-ILD group. Both the CTD-ILD and IIP groups exhibited elevated mortality rates (18.5% and 22.4%, respectively) in contrast to the non-ILD group (10.7%).

TABLE III. Predictors of mortality in patients with ILD overall compared to non-ILD patients

Predictors associated with mortality	Adjusted Odds Ratio	P Value
Female	Reference	Reference
Male	1.26	<0.001
Pneumonia	1.68	<0.001
Heart Failure	1.09	<0.001
Chronic Respiratory Failure	1.93	<0.001
Frailty	1.30	<0.001
Pulmonary Embolism	1.34	<0.001
Intensive Care Unit Admission	3.20	<0.001

TABLE IV. Primary and Secondary outcomes in 3 groups: patients without ILD, patients with CTD-ILD, and patients with IIP

	No ILD n= 1,010,030	CTD-ILD n= 1105	IIP n= 9910	P value	CTD-ILD vs. IIP
Primary outcome					
In-hospital mortality	10.7%	18.5%	22.4%	<0.001	p value= 0.30
aOR	REF	1.54	1.50	<0.001	
Secondary outcomes					
Mean Length of stay (days)	7.2	9.8	14.1	<0.001	
Adjusted co-efficient	REF	0.89 (p=0.12)	4.4 (p <0.001)		-3.1, CI; -4.4 - -1.7, p<0.001).
Mean Hospital Charges ($)	$75,608	$107,189	$171,003	<0.001	
Adjusted co-efficient	REF	$7,864 (p=0.39)	$57,419 (p <0.001)		-35688.37 (p=0.008)
ICU admission	9%	14.9%	16.7%	<0.001	
aOR	REF	2.16 (p <0.001)	3.20 (p <0.001)		p value= 0.23

aOR: adjusted odds ratio; CTD: Connective Tissue Disease; CTD-ILD: Connective Tissue Disease related Interstitial Lung disease; ILD: Interstitial Lung disease; IIP: Idiopathic Interstitial Pneumonia

However, when comparing patients with CTD-ILD to those with IIP, differences in mortality and ICU admission were not observed. Interestingly, patients with CTD-ILD experienced shorter LOS and lower total hospital charges than IIP patients. In addition to mortality, patients with ILD had higher comorbidities, including heart failure, COPD, respiratory failure, and PE. Compared to IIP, patients with CTD-ILD had similar comorbidities except for lower odds of having concomitant heart failure and COPD. To the best of our knowledge, this is the first study to describe the effect of COVID-19 specifically on patients with CTD-ILD, comparing them to other types of ILD and non-ILD patients.

Only a few studies have examined the effect of COVID-19 on ILD. A case-control study done in South Korea on 8,070 patients found that patients with ILD, including patients with IIP and CTD-ILD, were more susceptible to catching COVID-19 with an aOR of 2.02 compared to non-ILD patients. As previously mentioned, this is likely due to the increased expression of Angiotensin Converting Enzyme-2 and specific integrins, which facilitate COVID-19 entry into the body[17].

A review conducted by Fukihara *et al.* and a meta-analysis by Ouyang *et al*. discussed how a preexisting ILD affects the severity and prognosis of COVID-19 infection based on previous studies. It was found that preexisting ILD consistently exacerbated various outcomes of the COVID-19 clinical trajectory, such as mortality, LOS, and admission rates to the ICU. The Mortality Hazard Ratio, ranging from 1.47 to 1.6, mirrored the findings from our study. Moreover, resembling our research, other studies identified similar aggravating prognostic factors, including advanced age, male gender, and the necessity for long-term oxygen therapy[18,19].

Drake *et al.* investigated the outcomes of 161 patients with COVID-19 and ILD across Europe, which showed that there is a mortality difference among the ILD subtype[11]. IPF patients had a higher risk of death compared to non-IPF ILD patients. Among non-IPF ILDs, HP and RA-related ILD were associated with higher mortality, while other CTD-ILDs and sarcoidosis were associated with lower mortality. Notably, there was no detailed description of the included CTDs in the study. Our findings align with Drake *et al.* regarding overall ILD mortality but differ in that our CTD-ILD population, analyzed as a single group, had significantly higher odds of mortality compared to non-ILD patients, similar to IIP. These variations in results might be explained by the different sample size and cohort composition. Additionally, unlike Drake *et al.*, we observed differences in length of hospital stay (LOS), which may be due to variations in healthcare systems and management approaches. Similar to our study, a retrospective study done by Besteiro *et al.*, those who studied the impact of COVID-19 on different types of ILD, showed no statistical difference in mortality in patients who had COVID-19 and IPF versus COVID-19 and CTD-ILD, 34.8% versus 30%, p = 0.979)[20].

We hypothesize that the increased mortality observed in the ILD group compared to the non-ILD group is due to chronic inflammatory changes in patients with ILD, a finding supported by multiple studies. In our study, 70% of the ILD population had concomitant chronic respiratory failure, compared to 57% in the non-ILD

group ($p<0.001$), which may also contribute to the mortality difference between these groups. The lack of disparity in mortality between the CTD-ILD and IIP groups is likely multifactorial, influenced by the type and prognosis of the disease and the medications used for CTD. Additionally, patients with various forms of CTD-ILD respond differently to COVID-19 for unknown reasons, which might affect our pooled analysis. In our study, we did not sub-stratify ILD patients according to the type of CTD when comparing aOR.

It is also noteworthy that CTD patients are typically on immunosuppressants, which can significantly alter mortality rates. For instance, patients infected with COVID-19 who are on chronic prednisone >20mg daily have shown worsened mortality[21–23]. Corticosteroids have been widely used in severe COVID-19 due to their ability to attenuate excessive immune responses. Bahsoun *et al.* suggested that in severe COVID-19 cases, where the infection progresses to the pulmonary phase, corticosteroids may provide benefit by downregulating immune-mediated lung injury and mitigating the cytokine storm. However, corticosteroids have significant dose- and duration-dependent adverse effects, making CTD patients more susceptible to their drawbacks[24].

Whereas Tocilizumab and mycophenolate mofetil were found to reduce mortality and prevent mechanical ventilation rates in ILD patients with COVID-19.[25] Tocilizumab, an IL-6 receptor antagonist, plays a critical role in mitigating cytokine-driven inflammation. Although IL-6 levels were not directly measured, Mushtaq *et al.* reported that tocilizumab administration led to a reduction in inflammatory markers, including CRP, ferritin, LDH, D-dimer, and NLR, particularly in patients who showed clinical improvement and were subsequently discharged[26].

The strength of our study lies in the use of the NIS, as it is a large inpatient database representative of all U.S. hospitalizations. This allows us to report COVID-19 hospitalization in non-ILD, IIP, and CTD-ILD rarity. We performed an adjusted odds ratio to evaluate mortality in these three groups adjusted to various common comorbid conditions. The limitations of our study include the use of ICD-10 billing codes where human error in diagnosing and coding can't be excluded, and that the NIS doesn't provide us with information with respect to disease severity, other comorbidities, or therapeutic modalities used. Additionally, we performed a pragmatic pooling of the CTD patients, which might interfere with the results.

Further studies are needed to evaluate the multifactorial reasons behind the lack of difference in mortality between CTD-ILD and IIP. Future analysis should stratify CTD-ILD according to its specific rheumatological disease, such as systemic sclerosis, rheumatoid arthritis, or lupus, as these might exhibit distinct COVID-19 outcomes. Additionally, considering pulmonary involvement pattern and extent, fibrosis status, and treatment regimen could provide more nuanced insights instead of generalizing it.

CONCLUSION

This study highlights the need to consider ILD subtypes in predicting COVID-19 outcomes. While mortality rates for CTD-ILD and IIP patients hospitalized with COVID-19 were comparable, both were significantly higher than for non-ILD patients. The findings call for further research to uncover the mechanisms driving these outcomes and the specific impact of various rheumatological diseases and treatments on COVID-19 mortality and morbidity. Addressing these factors could enhance patient management and therapeutic strategies.

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SUPPLEMENTARY MATERIAL

TABLE I. Major idiopathic interstitial pneumonias and their international Classification of Diseases (ICD) codes for ninth and tenth editions that are abstracted in this study

	ICD-10 codes
Idiopathic pulmonary fibrosis	J84.112
Idiopathic nonspecific interstitial pneumonia	J84.113
Acute interstitial pneumonia	J84.114
Respiratory bronchiolitis–interstitial lung disease	J84.115
Cryptogenic organizing pneumonia	J84.116
Desquamative interstitial pneumonia	J84.117
Nonspecific codes for interstitial lung diseases	J84.9 J84.09 J84.10 J84.111 J84.89

TABLE II. Diagnoses abstracted using Elixhauser Comorbidity Software

Diagnoses abstracted using Elixhauser Comorbidity Software	Obesity, CHF, Pulmonary circulation disease, Chronic renal disease, Liver disease, Solid tumor w/o metastasis, Metastatic cancer, Rheumatoid arthritis, Diabetes mellitus and Hypothyroidism.

TABLE III. International Classification of Diseases (ICD) codes for ninth and tenth editions that are abstracted in this study

Diagnoses	ICD 10 codes		
Smoking:			
Current	F17.200	F17.201	F17.203
	F17.208	F17.209	F17.210
	F17.211	F17.213	F17.218
	F1.7219	Z72.0	
Previous	Z87.891		
Dependence on long-term oxygen	Z99.81		
Respiratory failure:			
Acute respiratory failure	J96.00	J96.01	J96.02
Acute on Chronic respiratory failure	J96.20	J96.21	J96.22
Chronic respiratory failure	J96.10	J96.11	J96.12
Unspecified respiratory failure	J96.90	J96.91	J96.92
Chronic obstructive lung disease	J44.0	J44.1	J44.9
Obstructive sleep apnea	G47.33		
Gastroesophageal reflux disease	K21.0	K21.9	
Frailty	R54		
Low body mass index (<20)	Z68.1		
New pulmonary embolism	I26.01	I26.02	I26.09
	I26.90	I26.92	I26.93
	I26.94	I26.99	
Any history of lung transplant	Z94.2	Z94.3	Z48.24
	Z48.280		
Procedures			
Lung transplant	0BYC0Z0	0BYC0Z1	0BYC0Z2
	0BYD0Z0	0BYD0Z1	0BYD0Z2
	0BYF0Z0	0BYF0Z1	0BYF0Z2
	0BYG0Z0	0BYG0Z1	0BYG0Z2
	0BYH0Z0	0BYH0Z1	0BYH0Z2
	0BYJ0Z0	0BYJ0Z1	0BYJ0Z2
	0BYK0Z0	0BYK0Z1	0BYK0Z2
	0BYL0Z0	0BYL0Z1	0BYL0Z2
	0BYM0Z0	0BYM0Z1	0BYM0Z2