Experience of severe and critical COVID-19 in interstitial lung disease patients

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Abstract

Background

Since the first case of severe COVID-19, its effect on patients with previous interstitial lung disease (ILD) has been uncertain. We aimed to describe baseline clinical characteristics in ILD patients hospitalized by several or critical COVID and compare mortality during hospitalization.

Methods

We studied patients with ILD plus COVID-19 and a control group, matched by age, 1:2 ratio of patients with COVID-19 without chronic lung disease. On admission, laboratory tests and sociodemographic variables we evaluated. We classified patients as severe or critically ill and compared baseline characteristics and mortality in each group. Additionally, we performed a sub-analysis of patients who died versus survivors.

Results

41 patients and 82 controls were analyzed. We found differences in the ILD group, women 65 versus 33% ($p < 0.001$); lower leukocytes (9 ± 6 versus 11 ± 7, $p = 0.01$), lower neutrophils (8 ± 5 vs 10 ± 6, $p = 0.02$). Also, higher mortality in the ILD plus critical COVID-19 group (63 vs. 33%, $p = 0.007$). Patients who died had higher BMI (28 ± 6 vs. 25 ± 4kg/m2, $p = 0.05$), less extended hospital stay (20 ± 17 vs. 36 ± 27 days, $p = 0.01$), and less days of evolution (9 ± 7 vs. 16 ± 16, $p = 0.05$).

Conclusions

We found higher mortality in patients with ILD plus critical COVID-19. Higher BMI and comorbidities were present in the non-survivors. The most common presented ILD was secondary to autoimmune diseases.

Background

Since 2002, there have been three outbreaks reported secondary to coronavirus [1]. On December 31, 2019, in the province of Hubai in Wuhan, China, reported for the first time pneumonia of non-identified etiology. In January 7, 2020, the molecule of Severe Acute Respiratory Syndrome Coronavirus − 2 was identified. The cases increased progressively until it officially declared a pandemic on March 11, 2020 **[2].**

The most common symptoms described in the study of Xiabo et al. were fever in 97–100% of the cases, cough (75–78%), dyspnea (60–66%), and malaise (20–44%) [3]. According to Zunyou Wu et al., the clinical presentation varied with age. 81% of the cases of severe COVID-19 will present a mild disease, 14% severe, and 5% will be critically ill [4]. Xiabo Yang et al. defined critically ill patients as those who

required admission to the intensive care unit with mechanical ventilation or a requirement of FiO2 of at least 60% [5]. There have been settled risk factors for presenting a severe clinical course of the disease, among others, male gender, age > 60 years, type 2 diabetes, systemic high blood pressure, obesity, low income, chronic kidney disease, and chronic obstructive pulmonary disease [4]. Patients with comorbidities have 12 times more risk of death secondary to severe COVID-19 and six times more risk of requiring hospitalization [6].

Tomographic patterns reported in severe COVID-19 varied from patches to diffuse patterns of ground glass opacities of subpleural predominance that progressed at 1–3 weeks to consolidations and occasionally crazy paving, even in asymptomatic patients [7]. Despite this, some patients presented tomographic changes associated with Organizing Pneumonia three weeks after the initial presentation of the disease [8]. Consequently, some questions have been raised about the implications of severe COVID-19 in the pulmonary interstitium.

In this context, it has been disputed the impact of severe COVID-19 on patients with interstitial lung diseases (ILD). Multiple questions arose that we will enunciate in three main points: 1) The diagnostic approach of new patients during the pandemic. 2) the follow-up visits of the known patients with ILD, and 3) the therapeutic approach of the ILD patients with severe COVID-19 [9]. Some authors have developed studies to describe mortality in this group of patients.

Thomas Drake et al. reported a multicentric European study to evaluate the impact of severe COVID-19 in patients with ILD, reporting a mortality of 49% vs. 35% without lung diseases (p = 0.013). 84% of the patients in the group ILD and 79% of the control group received supplementary oxygen through high-flow oxygen devices. The group that did not receive high-flow nasal oxygen devices had better survival than those that received them (93% vs. 75%) **[10].** In 2021 in Korea, Lee et al. did a national cohort study of patients with severe COVID-19 (n = 8070) and controls from the same geographic area with a relation of 1:15 without a diagnostic of severe COVID-19 (n = 121,050) from January 1 to May 30, 2020. They evaluated the number of patients with ILD in both groups and found that patients with ILD had a more significant probability of having severe COVID-19, in comparison with the rest of the population (0.8 versus 0.4% p = < 0.001), of presenting a more severe presentation of the disease (OR 2.23, IC 95% 1.24–4.01) and of dying (13.4% vs. 2.8%, p = < 0.001) **[11].** Laure Gallay et al. reported that patients with idiopathic lung fibrosis had higher risk of death secondary to severe COVID-19 than other interstitial lung diseases (35% vs. 19%, p = 0.04) **[12].** Duut N. carried out a retrospective study in a tertiary care hospital in India with 30 patients and obtained a mortality of 35.7%, however, they did not have a control group. **[13].** Wang Y. et. Al. performed a meta-analysis, where they characterized a higher mortality rate in patients with (pooled effect = 1.26 [95% CI: 1.09–1.46) and higher disease (pooled effect = 1.34 [95% CI: 1.16–1.55) **[14].**

Given that the Instituto Nacional de Enfermedades Respiratorias (INER) is a reference center of interstitial lung diseases in Mexico and, during the pandemic has been a center of exclusive attention for severe and critically severe COVID-19, this study aimed to describe baseline clinical characteristics and the ILD more

frequently presented in patients hospitalized by several or critical COVID and compare mortality during hospitalization.

Materials and Methods

Study population

We included all patients admitted to the hospital with a confirmed diagnosis of COVID-19, defined with a positive PCR swab test to SARS-CoV2, with a severe or critical presentation, and who had an ILD diagnosis previously in our Institute. The control group was randomized among patients hospitalized without respiratory diseases but with confirmed severe COVID-19 matched by age with a 1:2 ratio.

We defined severe or critical COVID-19 as reported in severe COVID-19 Treatment Guidelines:

*Severe Illness: Individuals who have SpO2 < 94% on room air at sea level, the ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO2/FiO2) < 300 mm Hg, respiratory rate > 30 breaths/min, infiltrates in computed tomography > 50%.

*Critical Illness: Individuals who have respiratory failure, septic shock, and multiple organ dysfunction [15].

At admission, all the patients underwent computed tomography, laboratory tests with inflammatory biomarkers, and a complete clinical chart including comorbidities, smoking history, and physical exploration. Patients with incomplete medical records or patients with mild or severe COVID-19 disease that did not require hospitalization were excluded. All the information was obtained from electronic medical records.

We classified patients into four groups: patients with ILD plus severe or critically ill and patients without previous respiratory disease plus severe or critically ill (controls); we performed a comparison between baseline characteristics and mortality in each group. Finally, we performed a sub-analysis of the patients with previous ILD who died versus the survivors.

Ethics and Consent

This study was approved by the Investigation and Bioethics Committee of the National Institute of Respiratory Diseases (C20-21), all methods were carried out in accordance with relevant guidelines and regulations (we follow up declaration of Helsinki). The results obtained guaranteed the protection of individual rights and maintained confidentiality; we obtained informed consent from all patients.

Statistical analysis

We performed a normality test with the Kolmogorov-Smirnov test. The descriptive data were presented as frequency, percentages, and mean and standard deviation. Comparison between groups was performed with Fisher- exact test in the case of qualitative variables and U-Mann-Whitney in the quantitative

variables. We used the statistical program GraphPad Prism V8. P-values < 0.05 were considered statistically significant.

Results

We studied a total of 41 ILD plus COVID-19 patients in our center and 82 patients with COVID-19 without chronic respiratory diseases. The mean age in both groups was over 60 years old. We found a difference in gender in the ILD group with more women in the control group, (65% versus 33%, p = 0.0005). We did not find any difference in comorbidities (type 2 diabetes, systolic high blood pressure, and smoking history), basal oxygen saturation, length of hospital stay, or evolution days. Leukocytes were significantly higher in the control group than in the ILD group (11 ± 7 vs. 9 ± 6, p = 0.01), caused by higher neutrophils (10 ± 6 vs. 8 ± 5, p = 0.02). CRP and procalcitonin levels had a trend; they were more elevated in the control group compared to ILD patients. Table 1

Table 1
Demographic data and clinical characteristics

Variable	ILD plus COVID-19 (n = 41)	COVID-19 (n = 82)	p-value
Age, IQR (years)	65 (57–75)	64 (59–72)	0.8
Gender, women (%)	27 (65)	27 (33)	0.0005
BMI, IQR (kg/m2)	27	28 (25–32)	0.3
Type 2 diabetes, (%)	8 (20)	25 (30)	0.13
Systemic high blood pressure (%)	14 (34)	32 (39)	0.3
Smoking status (%)	14 (34)	24 (29)	0.3
Complete vaccination (%)	6 (14)	7 (9)	0.2
Oxygen saturation at rest, ± IQR (%)	71 (62–85)	65 (54–80)	0.13
Days of evolution, ± IQR	10 (6–15)	10 (7–13)	0.7
Leukocytes absolute number, ± IQR (10^3/mm^3)	9 (6–12)	11 (8–14)	0.01
Neutrophiles absolute number, ± IQR (10^3/mm^3)	8 (5–10)	10 (6–12)	0.02
Lymphocytes absolute number, ± IQR (10^3/mm^3)	0.8 (0.3-1)	0.8 (0.5–1)	0.1
CRP, ± IQR (mg/dL)	15 (8–22)	19 (11–25)	0.06
Procalcitonin, ± IQR (ng/dL)	0.6 (0.06–0.4)	0.7 (0.1–0.5)	0.09
Ferritin, ± IQR (ng/mL)	1246 (445–1687)	1592 (588–2202)	0.1
Fibrinogen, ± IQR (mg/dL)	639 (472–750)	698 (600–750)	0.1
D-Dimer, IQR (µg/mL)	3.6 (0.6–3.7)	4 (0.7-3)	0.9
BMI: body mass index, CRP: C-reactive protein, ILD: interstitial lung diseases, IQR: interquartile range			

3.1 Oxygen requirements and hospital outcomes

During their hospital stay, 24 (57%) ILD patients and 72 (88%) patients in the control group required invasive mechanical ventilation (IMV), 11 (27%) patients in the ILD group and 8 (10%) in the control group required high flow nasal cannula and 6 (14%) ILD patients and 2 (2%) in the control group required only low flow oxygen devices,without significant differences in either groups. As a trend, nineteen patients (45%) in the ILD group died during their hospital stay vs. 25 (30%) in the control group. Table 2

Table 2
Outcomes and oxygen requirements

Variable	ILD plus COVID-19 (n = 41)	COVID-19 (n = 82)	p-value
IMV, %	24 (57)	72 (88)	0.0003
HFNC, %	11 (27)	8 (10)	0.01
SFC/SM, %	6 (14)	2 (2)	0.01
Death, %	19 (45)	25 (30)	0.06

IMV: invasive mechanical ventilation, HFNC: high Flow nasal cannula, SFC: simple Flow cannula, SM: simple mask, ILD: interstitial lung disease

Furthermore, we obtained the type of ILD diagnosis in the patients with COVID-19: 31 patients with connective tissue related to interstitial lung disease, three had idiopathic pulmonary fibrosis, two had fibrotic hypersensitivity pneumonia, one alveolar proteinosis, four patients presented combined syndromes and one drug induced nonspecific interstitial pneumonia. Figure 1

3.2 Differences between groups of Critical and Severe COVID-19

When we analyzed patients according to their clinical severity into severe COVID-19 and critical COVID-19 in both groups, we detected that the critical group included 27 patients with ILD and 72 patients in the control group; while 14 patients in the ILD group were classified inthe severe COVID-19 group compared to only ten patients from the control group were classified as severe. Significant differences were observed in gender in the critical group, with a predominance of women compared to the control group (n = 17, 63% versus n = 22, 31%, p = 0.003). A trend in higher lymphocytes in the control group (ILD: 0.7 ± 0.7 vs control: 0.8 ± 0.5, p = 0.07). The ILD with critical COVID-19 had significantly higher mortality than the control group (63% vs. 33%, p = 0.007). Table 3.

Table 3
Demographic data and clinical characteristics of patients with critical COVID-19

Variable	Critical COVID-19 ILD group (n = 27)	Critical COVID-19 Control group (n = 72)	p-value
Age, years ± IQR	62 (55–69)	65 (60–71)	0.3
Women Gender (%)	17 (63)	22 (31)	0.003
BMI, ± IQR, (kg/m2)	27 (25–29)	29 (25–32)	0.4
Type 2 diabetes, (%)	6 (22)	19 (26)	0.4
Systemic high blood pressure (%)	8 (30)	28 (39)	0.2
Complete vaccination (%)	5 (19)	6 (8)	0.1
Oxygen saturation, ± IQR	70 (61–82)	64 (52–78)	0.2
Days of evolution, ± IQR (#)	11 (7–16)	10 (7–13)	0.7
Leukocytes absolute number, ± IQR (10^3/mm^3)	10 (7–13)	12 (8–14)	0.1
Neutrophiles absolute number, ± IQR (10^3/mm^3)	9 (6–12)	10 (6–13)	0.3
Lymphocytes absolute number, ± IQR (10^3/mm^3)	0.7 (0.3-1)	0.8 (0.5-1)	0.07
CRP, ± IQR (mg/dL)	18 (11–24)	19 (11–26)	0.5
Procalcitonin, ± IQR (ng/mL)	0.8 (0.07–0.6)	0.6 (0.1–0.6)	0.6
Ferritin, ± IQR (ng/mL)	1325 (449–1693)	1628 (669–2190)	0.2
Fibrinogen, ± IQR (mg/dL)	705 (677–779)	713 (624–776)	0.7
D-Dimer, ± IQR (µg/dL)	5 (0.8–4.8)	4.1 (0.7–3.5)	0.3
Dead (%)	17 (63)	24 (33)	0.007
BMI: body mass index, CRP: C-reactive protein, ILD: interstitial lung diseases, IQR: interquartile range			

In the severe COVID-19 group, there was a significant difference in CRP, which was higher in the control group in comparison to the ILD group (9 ± 4 vs. 14 ± 6, p = 0.01) and a trend in comorbidities: more patients in the control group had type 2 diabetes (14% vs. 50%, p = 0.07) and more patients in the ILD group smoked (57% vs. 20%, p = 0.07). There was no significant difference in mortality in the severe group. Table 4

Table 4
Demographic data and clinical characteristics of patients with severe COVID-19

Variable	COVID-19 ILD group (n = 14)	COVID-19 Control group (n = 10)	p-value
Age, (years) ± IQR	70.85 (66–80)	61 (46–74)	0.1
Women gender, (%)	10 (71)	5 (50)	0.4
BMI, ± IQR, (kg/m2)	27 (24–29)	26 (22–29)	0.8
Type 2 diabetes, (%)	2 (14)	5 (50)	0.07
Systemic high blood pressure (%)	6 (43)	4 (40)	1
Smoking (%)	8 (57)	2 (20)	0.07
Complete vaccination (%)	4 (29)	1 (10)	0.2
SpO2, IQR (%)	73 (63–88)	76 (71–86)	0.9
FiO2, IQR (%)	25 (21–30)	21 (21)	0.1
Days of evolution, IQR	8 (6–8)	10 (6–14)	0.4
Leukocytes absolute number, ± IQR (10^3/mm^3)	7 (6–9)	9 (6–11)	0.2
Neutrophiles absolute number, ± IQR (10^3/mm^3)	6 (4–8)	8 (5–9)	0.2
Lymphocytes absolute number, ± IQR (10^3/mm^3)	0.9 (0.4–1.1)	0.7 (0-5-0.9)	0.9
CRP, ± IQR (mg/dL)	9 (7–11)	14 (12–18)	0.01
Procalcitonin, ± IQR (ng/mL)	0.1 (0.06-0-17)	0.9 (0.07–0.2)	0.4
Ferritin, ± IQR (ng/mL)	1034 (425–1427)	1341 (469–1829)	1
Fibrinogen, ± IQR (mg/dL)	500 (451–528)	586 (534–646)	0.06
D-Dimer, ± IQR (µg/dL)	1.4 (0.4–1.6)	3 (0.4–2.7)	0.88
Dead (%)	2 (14)	1 (10)	0.6

BMI: body mass index, SpO2: oxygen saturation, CRP: C-reactive protein, ILD: interstitial lung diseases, IQR: interquartile range

We performed a sub-analysis to compare the clinical, sociodemographic, and laboratory findings among the patients with ILD who died vs. the survivors. The patients who died had a higher BMI compared to the ones who survived (28 ± 5 vs. 26 ± 5, p = 0.02), without other differences in the other variables, including vaccination status. Table 5.

Table 5
Demographic data and clinical characteristics of dead and survivors ILD patients with COVID-19

Variable	ILD plus COVID-19 dead (n = 19)	ILD plus COVID-19 survivors (n = 22)	p-value
Gender, women, SD (%)	14 (73)	13 (59)	0.2
BMI, IQR (kg/m2)	**28 (26–31)**	**26 (23–28)**	**0.02**
Type 2 diabetes, (%)	5 (26)	3 (13)	0.2
Systemic high blood pressure (%)	8 (42)	7 (30)	0.3
Smoking (%)	5 (26)	9 (39)	0.2
Complete vaccination(%)	2 (10.5)	4 (18)	0.4
Days of hospital stay, IQR	19 (11–28)	24 (13–27)	0.4
Days of evolution, SD	8 (5–11)	12 (6–19)	0.3
Leukocytes absolute number, ± IQR (10^3/mm^3)	9 (7–11)	9 (6–12)	0.9
Neutrophiles absolute number, ± IQR (10^3/mm^3)	8 (6–9)	8 (4–11)	0.9
Lymphocytes absolute number, ± IQR (10^3/mm^3)	0.7 (0.3–0.8)	0.8 (0.4–1.2)	0.4
CRP, ±SD (mg/dL)	16 (11–23)	14 (8–20)	0.6
Procalcitonin, ± IQR (ng/mL)	1 (0.07–0.9)	0.2 (0.05–0.3)	0.2
Ferritin, ± IQR (ng/mL)	1098 (430–1668)	1422 (662–1591)	0.4
Fibrinogen, ± IQR (mg/dL)	646 (438–763)	632 (474–714)	0.7
D-Dimer, ± IQR (µg/dL)	2.87 (1–5)	4.2 (0.3–3.6)	0.09

BMI: body mass index, DD: D dimer, CRP: C-reactive protein, ILD: interstitial lung diseases, IQR: interquartile range

Finally, we classified the survivors and dead patients in the ILD patients into severe and critical COVID-19 and performed the same analysis. The severe COVID-19 group consisted of 2 patients in the dead group and 12 in the survivor group. We did not find any significant differences in the baseline characteristics between groups. The critical COVID-19 group was made up of 17 non-survivors and ten survivors. The BMI was significantly higher in the non-survivors group (28 ± 6 vs 25 ± 4, p = 0.05). The length of stay and days of evolution was significantly longer in the survivors' group (20 ± 11 vs 36 ± 24, p = 0.01; 9 ± 7 vs 16 ± 16, p = 0.05). Table 6

Table 6
Demographic data and clinical characteristics of dead versus survivors ILD patients with critical COVID-19

Variable	ILD plus critical COVID-19 dead (n = 17)	ILD plus critical COVID-19 survivors (n = 10)	p-value
Age, IQR	12 (70)	5 (50)	0.3
Gender, women, IQR (%)	28 (25–31)	25 (23–27)	0.2
BMI, IQR (kg/m2)	4 (24)	2 (20)	0.05
Type 2 diabetes, (%)	7 (41)	1 (10)	0.6
Systemic high blood pressure (%)	3 (18)	3 (30)	0.09
Smoking (%)	2 (12)	3 (30)	0.3
Complete vaccination(%)	20 (12–29)	36 (18–46)	0.2
Days of hospital stay, IQR	9 (5–12)	16 (7–23)	0.01
Days of evolution, IQR	140 (93–172)	176 (130–242)	0.05
PaO2/FiO2, IQR	9 (8–11)	12 (6–14)	0.2
Leukocytes absolute number, ± IQR (10^3/mm^3)	8 (6–9)	10 (6–13)	0.2
Neutrophiles absolute number, ± IQR (10^3/mm^3)	0.7 (0.3–0.9)	0.6 (0.3-1)	0.2
Lymphocytes absolute number, ± IQR (10^3/mm^3)	17 (12–23)	19 (10–25)	0.9
CRP, ± IQR (mg/dL)	1 (0.1–1.3)	0.4 (0.04–0.5)	0.6
Procalcitonin, ± IQR (ng/mL)	1207 (449–1688)	1561 (429–2085)	0.2
Ferritin, ± IQR (ng/mL)	681 (656–771)	736 (686–956)	0.8
Fibrinogen, ± IQR (mg/dL)	3 (1–5)	7 (0.4-4)	0.6
D-Dimer, ± IQR (µg/dL)	4 (24)	2 (20)	0.6
BMI: body mass index, SD: standard deviation, DD: D dimer, CRP: C-reactive protein, ILD: interstitial lung diseases			

Discussion

Diverse risk factors have been described with severe forms of COVID-19 disease, including obesity, type 2 diabetes, systemic high blood pressure, chronic obstructive pulmonary disease, male gender, and having

60 years or more. Due to the this characteriztics, it has been questioned the impact of severe COVID-19 infection on interstitial lung diseases.

Unlike previously published studies, we observed that our population was made up of significantly more women than men, which we believe is associated with the fact that our ILD group was made up mainly of ILD secondary to autoimmune diseases, which are more common in women. Compared to the study by Drake et al., [11]. who reported that the most frequent ILD was IPF (42% of the cases), it was only 7% of the cases in our study. The age of our population was similar to that published in the other studies. Other differences found were lower levels of leukocytes and neutrophils in the ILD group compared to the control group and a trend in inflammatory markers such as lower CRP and procalcitonin in the ILD group vs. the control group. We believe this could be influenced by the chronic use of systemic steroids in the ILD group.

We classified the patients according to their severity according to COVID-19 guidelines [15].since we consider it an essential factor in mortality. Our results agree with previous literature where patients with ILD + critical COVID-19, compared to patients without known pulmonary pathologies (63% vs. 33%, p = 0.007), have higher mortality. In the study by Drake, et. to the. 10, only 3.7% of the patients with ILD and 9% of the controls belonged to this group. We consider that this increase is influenced by the previous structural alterations of the patients that make them a complex group to ventilate, challenging to maintain alveolar protection goals, with a low functional reserve, and difficult to extubate. These findings support the recommendation given by Caro et al. [9] in the ALAT recommendations about not recommending advanced airway management in this group of patients since their mortality is higher than the rest of the population. These data reinforce the importance of individualizing the decision for advanced airway management in patients and prioritizing other modalities of supplemental oxygen support.

We did not find a difference in mortality in the severe-COVID-19 group between patients with ILD and those without known lung diseases, unlike what was reported in other studies. We believe this could be due to the small number of patients with severe COVID-19 evaluated at our institute, as it is a reference center for critically ill COVID-19 patients.

Finally, we decided to compare the differences between the patients who died in the ILD group vs. the survivors. We found a difference in BMI, which was higher in the group of patients who died compared to the survivors (28 ± 8 vs. 26 ± 4, p = 0.02). This result is consistent with what has been published in multiple COVID-19 studies on the influence of BMI on mortality. When classifying the survivors between severe and critical, we found no significant difference in the severe group. While critical group showed a significant difference in BMI. In the group of non survivors showeda trend in suffering more high blood pressure compared to survivors, which has also been described as a risk factor for poor prognosis. Also a difference in the days of evolution of the disease in the non-survivors, who were within the first 14 days of the disease, which we know are the ones with the greatest inflammation. While the survivors were in more

advanced stages of the natural cycle of the disease.. A more extended hospital stay in the group of survivors, which is expected because the non-survivors died in their first days of stay.

Our study has significant limitations; our population is smaller than those reported in other articles, it is a single-center study, and as INER is a reference center for patients with severe or critical COVID-19, we could have lost some patients. Therefore should be taken into account for the conclusions.

The strength of our study is that it opens the doors to be able to reaffirm some previously made experts' recommendations. We compared the ILD group with a randomized group without any lung disease. Moreover, it invites other centers to participate in getting a more significant number of patients. We consider it essential to maintain health measures in this group of patients and vaccination despite not having found a difference in mortality. In the future, we believe it is essential to follow up on the group of patients with ILD + severe COVID-19 to find out the impact on their disease and if having suffered from severe COVID-19 is a risk factor for developing progressive pulmonary fibrosis.

Conclusions

This study increases the knowledge on COVID and is effect on ILD patients. We found higher mortality in the group of ILD patients with critical COVID-19 than in patients without known lung diseases. Higher BMI, systemic high blood pressure, and type 2 diabetes were present in the non-survivors with ILD plus critical COVID-19. The most common presented ILD in our study was secondary to autoimmune diseases.

Abbreviations

- ILD: interstitial lung disease
- COVID-19:
- BMI: body mass index
- CRP: C-reactive protein
- IQR: interquartile range
- IMV: invasive mechanical ventilation
- HFNC: high flow nasal cannula
- SFC: simple flow cannula
- SM: simple mask
- SpO2: oxygen saturation
- DD: D dimer

Declarations

Ethics approval and consent to participate: This study was approved by the Research and Bioethics Committee of the National Institute of Respiratory Diseases (C20-21). The results obtained guaranteed

the protection of individual rights and maintained confidentiality; we obtained informed consent from all patients.

Consent for publication:

Not applicable.

Data availability statement:

All data generated or analysed during this study are included in this published article.

Conflict of interest

The authors declare no conflict of interest.

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- Authors' contributions

The authors confirm contribution to the paper as follows: study conception and design: Ana Karem S. Pruneda, Ivette Buendía-Roldán, Moises Selman; data collection: Ana Karem S. Pruneda, José Omar Barreto-Rodríguez, F. Juárez-Hernández; analysis and interpretation of results: Ana Karem S. Pruneda; draft manuscript preparation: Ana Karem S. Pruneda, Ivette Buendía-Roldán, Moises Selman. All authors reviewed the results and approved the final version of the manuscript.

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Figures

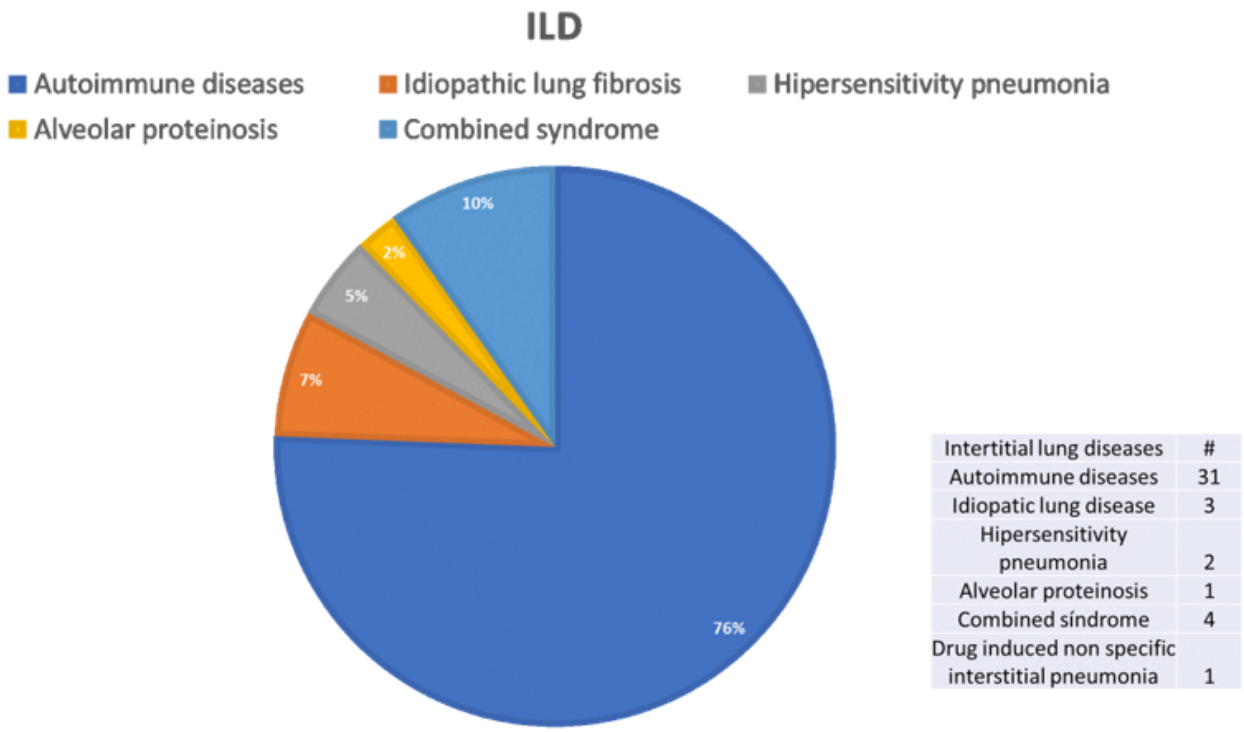

Figure 1

We showed the frequencies of different previous diagnosis in patients with ILD + COVID-19