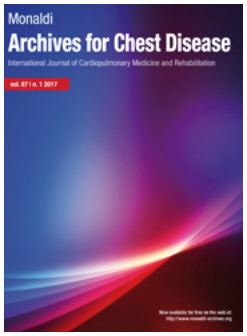

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Clinico-etiological profile and treatment outcome of hospitalized diffuse parenchymal lung disease patients: a prospective cohort study

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Abstract

Diffuse parenchymal lung disease (DPLD) is a group of more than 200 pulmonary diseases that affect the alveoli, pulmonary interstitium, and/or small airways. DPLD patients often present in the outpatient department and inpatient department with acute/subacute worsening in their symptoms. These worsenings are due to a variety of causes that include acute exacerbations (AE), bacterial/viral/fungal infections, pneumothorax, pulmonary thromboembolism, or cardiac compromise. However, regardless of the type of underlying DPLD and the etiology of acute worsening when AE develops, it poses serious difficulties for patients, families, doctors, and the medical system. The current study was performed to evaluate the clinical presentation, etiological factors, and hospital course of DPLD patients presenting with acute/subacute worsening in their respiratory symptoms. A total of 39 hospitalized DPLD patients were recruited as per the inclusion and exclusion criteria. On admission, all relevant investigations were done, and the patients were evaluated thoroughly. All these patients were managed as per standard guidelines with regular monitoring. Based on the clinical course, treatment outcome was categorized as improved (discharged from hospital) or shifted to intensive care unit/mechanical ventilation and improved or died. The mean age of the study subjects was 57.95±11.7 years. The most common symptom reported in the study was dyspnea, followed by cough and fever. The most common etiology observed in the study, leading to hospital admission in DPLD patients, was respiratory infections and AE, followed by cardiac diseases. Out of the total 39 hospitalized DPLD patients, 13 patients required invasive mechanical ventilation, whereas 26 patients (66.7%) were managed with oxygen support/non-invasive ventilation/high-flow nasal oxygen. The univariate logistic analysis showed that patients with diabetes, pedal edema, idiopathic pulmonary fibrosis, regional wall motion abnormalities, and cardiac causes of acute clinical worsening were significant risk factors for the need for mechanical ventilation. On performing multivariate regression, none of the variables was an independent significant risk factor of mechanical ventilation. It is recommended to actively undertake monitoring and treating DPLD in conjunction with managing various concomitant illnesses, which is vital for improving outcomes and lowering the risk of acute clinical worsening and respiratory compromise.

Key words: diffuse parenchymal lung disease, mechanical ventilation, acute exacerbation, infections, hospitalization, treatment outcomes, mortality.

Introduction

Diffuse parenchymal lung disease (DPLD) is a cluster of pulmonary disorders that affect the alveoli, pulmonary interstitium and/or small airways [1]. The term "interstitial lung disease" (ILD), though misleading, is often used interchangeably with DPLD. It is marked by varying degree of interstitial fibrosis and inflammation [2]. Two major symptoms are progressive dry cough and dyspnea and diagnosis integrates clinical, radiological and histopathological data. DPLD is broadly classified into two categories, one with known etiology and the other comprising idiopathic disorders. DPLD patients often present with acute/subacute worsening in their symptoms. These deteriorations are attributed to diverse etiologies that comprise acute exacerbations, bacterial/viral/fungal infections, pneumothorax, pulmonary thrombo-embolism or cardiac compromise.

Acute exacerbations of DPLD are characterized by rapid respiratory decline and new radiological anomalies, and it contributes significantly to morbidity and mortality of such patients [3]. There may be substantial hypoxemia and respiratory failure, necessitating admission to the critical care unit and assisted ventilation [4]. Management broadly includes corticosteroids, other immunosuppressants, antifibrotics and sometimes a combination of these [5].

Apart from acute exacerbations, the course of DPLDs is also complicated by the occurrence of lower respiratory tract infections (LRTI's) and pneumonia due to bacteria, viruses or fungi leading to hospital admissions due to acute worsening [6].

DPLD can be associated with various complications, like the development of Secondary Spontaneous Pneumothorax with an incidence rate of 2-20% in IPF patients [7]. Pulmonary embolism can also complicate DPLD. Studies have been conducted on the vascular anomalies associated with DPLDs demonstrating aberrant angiogenesis, elevated angiogenic chemokines, and abnormalities of the capillary endothelium [8].

DPLD patients often present with cor-pulmonale during the later course of their disease and are at an increased risk of Pulmonary hypertension (PAH), coronary artery disease (CAD), congestive heart failure (CHF), and cardiac arrhythmias which can lead to acute worsening and hospital admission. The burden of disease is significantly impacted by cardiovascular impairment, driven by the harmful trifecta of right heart failure, pulmonary hypertension, and increased pulmonary vascular resistance (PVR) [9].

This study aimed to evaluate the clinical presentation, etiological factors, hospital course and outcome of DPLD patients. Only hospitalized patients were included to ensure access to

complete clinical records, imaging, and laboratory work-up, enabling accurate diagnosis and outcome evaluation.

Existing literature describes a variety of causes that can lead to hospital admission in DPLD patients. Irrespective of the type of underlying DPLD and the etiology of acute deterioration, manifestation of an acute worsening presents a large burden for patients and the doctors. However, the data on the topic is sparse with no major studies aiming to evaluate various causes together and comprehensively.

While previous studies have evaluated the clinical spectrum of DPLDs, most are from Western countries. There is a noteworthy deficiency of all-inclusive information on the clinico-etiological profile and outcomes of DPLD patients from India and other low- and middle-income countries (LMICs), where disparities in environmental exposure and treatment practices may impact disease presentation and prognosis. The scarcity of region-specific evidence contributes to a global knowledge gap and deters the development of context-appropriate clinical guidelines for these populations.

With different genetic makeup and varied environmental/occupational impacts, the results from this geographical region might be different from the Western data. Hence this study was performed to evaluate clinical presentation, etiological factors, and hospital course of DPLD patients presenting with acute/subacute worsening in their respiratory symptoms.

Materials and Methods

Study setting, design and duration

This cohort study was conducted in a tertiary care institute in north Indian region over a period of one and a half years. Patients with diffuse parenchymal lung disease who were admitted to the ward due to acute worsening in their respiratory symptoms were consecutively enrolled. Diffuse parenchymal lung disease was diagnosed based on clinical, radiological, and histopathological criteria as per the latest guidelines [1]. Patients were enrolled after obtaining written informed consent.

Study design: Cohort study

Study duration: One and half years

Sample size

It was estimated based on a 65% anticipated prevalence of dyspnea among patients with diffuse parenchymal lung disease (DPLD), as reported in prior studies [10]. Using a single proportion formula for sample size estimation, with a 95% confidence level (Z = 1.96) and an absolute precision (margin of error) of 15%, the minimum required sample size was calculated as 39 patients

$$n = \frac{Z^2 \cdot p \cdot (1-p)}{d^2} = \frac{(1.96)^2 \times 0.65 \times 0.35}{(0.15)^2} \approx 39$$

This sample size was also deemed sufficient to explore clinically relevant associations between dyspnea, comorbidities, cardiac involvement, etiology of acute worsening, and mechanical ventilation requirement in hospitalized DPLD patients.

Patient Selection: Patients of DPLD admitted in the Pulmonary Medicine Ward due to acute worsening of symptoms were consecutively recruited. Potential confounders such as age, smoking status, occupational exposure, and baseline disease severity were recorded to adjust for their influence in the analysis. Missing data were minimal due to prospective data collection and thorough follow up of the patients during their hospital stay. In cases of incomplete information, patients were excluded from the specific analysis.

Inclusion criteria:

- Adult patients (age > 18 years) of either gender.
- Patients with a confirmed diagnosis of DPLD based on clinical, radiological, and/or histopathological criteria [2].
- Patients admitted to the ward due to acute worsening of respiratory symptoms, defined as new or worsening dyspnea, cough, hypoxemia, or radiological deterioration compared to baseline [3].

Exclusion criteria:

- Patients with other chronic respiratory diseases (e.g., COPD, bronchial asthma, active or previously treated pulmonary tuberculosis) that could confound clinical presentation.
- Patients with a confirmed diagnosis of primary lung malignancy.

Excluding these conditions helped isolate the effects and outcomes related specifically to DPLD and its acute worsening, avoiding overlap with diseases that could independently lead to similar respiratory compromise.

Methodology

All selected patients of DPLD were enrolled after taking informed written consent. The study was conducted after approval from the institute's ethics committee. Detailed history and clinical examination was done including history of underlying DPLD (duration and type of symptoms and progression), environmental and occupational exposures and smoking history. On admission these patients were evaluated using pulse oximetry, arterial blood gas analysis, chest x-ray PA view, electrocardiogram (ECG), echocardiography, routine blood investigations, high resolution computed tomography of thorax and other special tests. Etiological diagnoses of their acute presentation (like acute exacerbation, pneumonia, cardiac compromise, pulmonary embolism, pneumothorax, etc.) were made as per clinic-radiological parameters and investigations [1,3,6,7]. All these patients were managed as per standard guidelines with regular monitoring [5].

After satisfactory improvement, these patients were discharged from the hospital. Based on the clinical course, treatment outcome was categorized as improved (discharged from hospital) or shifted to ICU/mechanical ventilation and improved or died. Percentage distribution of different etiologies and treatment outcomes was measured. Also, clinical parameters and hospital course among patients with different etiologies was compared.

Statistical analysis

Continuous data was summarized as mean ± SD or median (interquartile range) as appropriate and categorical variables were presented as n (%). Comparison of continuous and categorical variables between the 2 groups was done using student T test/Mann-Whitney test and Chi square test/Fischer exact test, respectively. Univariate and multivariate cox proportional hazard regression was used to find out significant risk factors of mechanical ventilation. Data analysis was done by SPSS 25.0 software. P value <0.05 was taken as significant for all statistical tests.

Results

The mean age of the study subjects was 57.95 + 11.7 years. Among the patients, 64.10% were females, while 35.90% were males. Most common DPLD encountered was IPF (38.46%). The mean duration of DPLD among the study subjects was 2.98 ± 1.98 years. The most common

symptom reported was dyspnea, followed by cough and fever (Table 1). Hypertension was the most common co-morbidity encountered, followed by diabetes and CAD. Eleven patients (28.21%) had a history of environmental exposure, whereas 9 (23.08%) were ever smokers and 6 patients (15.38%) had history of occupational exposure. Reticulations and tractional bronchiectasis were the most common findings observed on CT chest (32 and 29 cases). Honeycombing was seen in 21 and consolidation in 15 cases. Ground glass opacity was detected in 13 cases, and pneumothorax in 1 case. 2 D echocardiography revealed pulmonary hypertension in 26 cases and new onset RWMA in 4 cases. The most common etiology leading to hospital admission in DPLD patients was respiratory infections and acute exacerbation, followed by cardiac diseases (Figure 1).

Majority of patients were treated with IV antibiotics (38 cases) and steroids were given in 27 cases. Out of 39 hospitalized DPLD patients, 13 patients required invasive mechanical ventilation whereas 26 patients (66.7%) were managed with oxygen support/NIV/HFNO. Twenty patients were shifted to ICU for monitoring and for requirement of NIV/HFNO and mechanical ventilation support. Out of these, 10 were managed with NIV/HFNO and 13 needed mechanical ventilation. Unfortunately, 3 cases resulted in mortality.

Among the study subjects, 16 patients were discharged on domiciliary oxygen support. It was observed that participants with pre-existing co-morbidities were more prone to require mechanical ventilation. Prevalence of diabetes ($p=0.39$) and hypothyroidism ($p=0.035$) was significantly higher in patients managed with mechanical ventilation as compared to those managed with NIV/HFNO/oxygen support. Pedal edema was significantly more common in patients requiring mechanical ventilation ($p=0.002$). The current study observed that patients with IPF were associated with a greater need for mechanical ventilation, as compared to individuals with non-IPF ($p=0.36$). Those patients managed with mechanical ventilation had significantly higher rates of Pulmonary hypertension ($p=0.001$). The mean LVEF was significantly lower in the mechanical ventilation group ($p=0.018$) (Table 2).

There was no statistically significant correlation between the two most common etiologies leading to hospitalisation (acute exacerbation and respiratory infections) with the requirement of mechanical ventilation. However, cardiac causes (MI/Heart failure/DCMP) were significantly higher in the mechanical ventilation group (Table 2). The univariate logistic analysis showed that patients with diabetes, pedal edema, IPF, RWMA and cardiac cause of acute clinical worsening were significant risk factors of need of mechanical ventilation (Table 3). On performing multivariate regression, none of the variable was independent significant

risk factor of mechanical ventilation. Notably, cardiac cause was a strong predictor despite small absolute numbers (5 in the MV group vs. 0 in the non-MV group), which limits interpretability and should be viewed with caution. Pulmonary hypertension also emerged as a risk factor with an extremely wide confidence interval (OR = 45.90, 95% CI: 0.448–4694.896). This indicates that while PH may be associated with MV requirement, the statistical precision is poor, due to small sample size of the study.

Discussion

A total of 39 diagnosed cases of DPLD were enrolled in the current study. This study showed that age and gender did not affect the clinical course and treatment outcome of hospital course of DPLD patients. Participants with pre-existing co-morbidities were more prone to require mechanical ventilation. Patients with IPF were associated with a greater need for mechanical ventilation, as compared to individuals with non-IPF. There was no statistically significant correlation between etiology of acute respiratory worsening leading to hospital admission with the requirement of mechanical ventilation. However, cardiac causes were significantly higher in the mechanical ventilation group.

In this study, females outnumbered males (64.1%), which could be due to predominance of CTD-ILDs in the present study that are more common in females [11].

All study subjects admitted with acute clinical worsening had dyspnea at the time of presentation. The severity of dyspnea was evaluated by using the Modified Medical Research Council Scale (mMRC) [12]. Majority of patients had mMRC Grade 4 (87.18%) dyspnea at the time of presentation. Emergence of it can be explained by amalgamation of multiple factors which consists of underlying lung pathology, dysfunction of respiratory muscles, poor gas exchange and psychological influence. Cough (89.74%) was the second most common symptom. Majority of patients had dry cough. Although the precise causes of cough in AE-DPLD are not entirely known, they may include airway inflammation, airway cough receptor irritation, and hypersensitivity of the cough reflex. It may also be attributed to inflammatory processes and increased rigidity of lung parenchyma associated with AE. Fever and anorexia were the third most common clinical symptoms observed, followed by chest pain which was seen in 12.82% cases. Some participants with CTD-ILD also presented with joint pain . These clinical presentations are supported by several studies which showed that dyspnea, cough, fever and flu-like symptoms as among the common symptoms encountered during acute worsenings [11,13,14].

Common clinical signs seen were end-inspiratory fine crackles on auscultation (76.92%), clubbing, tachypnoea and pedal edema. The mean oxygen saturation under room air was 81 ± 4 %. These findings were in coherence with a study which demonstrated end-inspiratory crackles and clubbing as the commonest signs in ILD [15].

Findings observed in the HRCT chest were reticulations (94.12%) and tractional bronchiectasis (85.29%), followed by honeycombing which were suggestive of increased diffuse alveolar damage and progressive fibrosis, compared to prior scans of the same participants. Pneumothorax (2.94%) was observed in a patient with CTD-ILD. These CT scan findings were validated by various other studies [16-18].

In the present study, most common DPLD encountered was IPF (38.46%) followed by CTD-ILD, Idiopathic NSIP, Hypersensitivity pneumonitis, Sarcoidosis and Cryptogenic organizing pneumonia. These findings were similar to a retrospective cohort study which also showed a higher prevalence of IPF (60%), followed by CTD-ILD (18%) and the rest were IIP other than IPF [18]. The present study also evaluated the etiologies of acute clinical worsening in DPLD patients leading to admission. The most common causes of admission in the study observed were infection (43.59%) and acute exacerbation (38.46%) of DPLD. Five patients had cardiac etiology including heart failure, new onset CAD and DCMP. Additionally, one case each was admitted with pneumothorax and pulmonary embolism. J.W. Song et al. reported in their study that AE-ILD was the most common cause of respiratory deterioration in DPLD patients, followed by respiratory infections and heart failure [19]. Likewise, a retrospective study conducted on hospitalized fibrosing interstitial lung disease patients, observed that AE-ILD is the most common of acute clinical worsening followed by infections and cardiovascular causes [20]. In our study respiratory infections were most common cause followed by AE-ILD. This difference in etiology of acute worsening can be due to difference in demographic data and because of difference in sample size.

Management of study participants varied depending upon the clinical status of patient at the time of presentation, presence of co-morbid conditions, etiology of acute clinical worsening leading to hospital admission and various other factors. Out of 39 patients, 16 were managed in ward while 23 patients required ICU admission for monitoring, need of NIV/HFNO support and mechanical ventilation. Thirteen patients required mechanical ventilation. Patients were treated with IV antibiotics, steroids, anti-fibrotics, and other immunosuppressants depending on the type of DPLD and the cause of admission. These treatment strategies were consistent with those followed in various other studies [5,21]. The in-hospital mortality in our study was

7.69%. The most common underlying DPLD leading to mortality was IPF and the most common immediate cause of worsening was pneumonia.

Treatment outcome was studied in patients who required mechanical ventilation and those who did not. It was observed that need for mechanical ventilation was associated with higher morbidity and mortality, as compared to patients managed on NIV/ oxygen support only. Similar results were obtained in a study performed in DPLD patients hospitalized due to acute respiratory worsening [18].

It was observed that participants with pre-existing co-morbidities were more prone to require mechanical ventilation. Prevalence of diabetes (46.15% vs. 11.54%, p = 0.039) and hypothyroidism (30.77% vs. 3.85%, p = 0.035) was significantly higher in patients managed with mechanical ventilation as compared to those managed with NIV/oxygen support. This finding was similar to a study conducted to see the influence of various co-morbid conditions affecting survival in IPF patient [22]. In contrast to the present study, a prospective cohort study found that presence of OSA and GERD were associated with poor outcome in hospitalized ILD patients due to acute worsening [23]. Another study demonstrated that presence of CAD in patients with DPLD was associated with worse outcome [24]. This difference in results could be due to variations in the prevalence of these comorbidities in the geographical regions. In general, concomitant conditions like CAD, GERD, hypothyroidism, diabetes and hypertension can worsen preexisting lung pathology making patients more vulnerable for respiratory infections and decrease respiratory muscle performance, which can cause abrupt clinical deterioration. These findings highlight that proactively monitoring and treating ILD in conjunction with managing these coexisting illnesses is crucial for improving outcomes and lowering the risk of acute clinical worsening and respiratory compromise.

Cardiac evaluation through screening 2D Echo demonstrated poor outcome in those with PH, RWMA and/or low LVEF, posing a higher chance of requiring mechanical ventilation thus emphasising the importance of scrutinizing every DPLD patient presenting with acute worsening, for presence of acute cardiac decompensation. Management of cardiac co-morbidities does not per-se alter the course of primary disease, i.e. DPLD, but has shown to significantly reduce morbidity and hence socio-economic burden of the disease [25].

The most common etiology causing acute clinical worsening in DPLD patients observed in our study was respiratory infections, followed by AE-ILD and cardiac diseases. Patients admitted due to respiratory infections or AE had almost similar hospital course. No significant difference was observed in both conditions with requirement of mechanical ventilation and both were

associated with poor treatment outcome. However, it was observed that patients with cardiac diseases were significantly higher in the mechanical ventilation group. Similarly, a study demonstrated that cardiovascular causes were more fatal as compared to AE in non-IPF patients [20]. Different studies in the past have concluded that patients with AE had longer duration of hospitalization and increased need for mechanical ventilation resulting in poor outcome compared to respiratory infections [18,20,26]. This difference in results in the studies maybe due to sample size variation, clustering of one type of patient profile, demographic variation, or because of selection bias at the time of study.

The current study showed that IPF was associated with a greater need for mechanical ventilation, as compared to individuals with non-IPF. Of those requiring mechanical ventilation, 61.54% belonged to IPF group. Also, mortality was higher in IPF patients. Results of previous studies also validate these findings [11,18,20]. In comparison with other DPLDs, IPF shows rapid progression, resulting in a continuous loss in lung function. This already aggressive disease course is significantly accelerated in AE-IPF, which causes respiratory compromise and rapid deterioration. It is difficult to predict and treat acute worsening of IPF since the underlying mechanisms are not well studied. Also, different studies have shown that incidence of AE is higher in IPF patients than compared to other ILDs [18,27,28].

DPLDS are pulmonary diseases with a chronic incapacitating course. Acute worsenings due to infections, acute exacerbations (AE) and other factors like cardiac causes or complications like SSP or pulmonary embolism are detrimental in the clinical course of ILDs. Early recognition of patients who are more susceptible to acute worsenings are of paramount importance before the onset of severe respiratory failure so that treatment can be tailored as per the cause leading to less morbidity and improved survival.

Timely identification of clinical worsenings could lead to earlier hospitalization, lower clinical threshold for antibiotic therapy, and faster and probably more extensive diagnostic work-up and decisions for treatment in the right clinical setting. This study gave detailed evidence on the clinical and etiological profile of patients with acute worsening of DPLDs. The outcome of these patients along with the factors predicting the outcomes as shown in the results will help in early detection of at risk patients who require more intensive treatment.

Limitations

The study had a few limitations. Due to smaller sample size, the distribution of participants among different types of DPLD was unequal (15 IPF, 24 non-IPF) which reduced power for

subtype comparisons. Predicting the exact course and outcome and extrapolating the findings onto general population is difficult. The study's sample size, while adequate for descriptive analysis and initial comparisons, is insufficient for robust multivariate modeling. Only 13 patients in the cohort required mechanical ventilation, limiting the number of outcome events available for multivariate logistic regression. This reduced the statistical power to detect independent predictors and increased the risk of overfitting the model. Therefore, the results of the multivariate analysis should be interpreted with caution and viewed as exploratory. Future studies with larger sample sizes and more outcome events are essential to validate these associations.

Conclusions

The present study validated that both underlying DPLD and aetiology of the acute clinical worsening are strong predictors of disease morbidity and mortality in DPLD patients requiring hospitalization. IPF was the most common type of DPLD observed in our study, having increased requirement of mechanical ventilation. Important risk factors observed in present study requiring mechanical ventilation and resulting in poor treatment outcome were patients with diabetes, pedal edema, RWMA, IPF and cardiac diseases. These comorbidities can worsen preexisting lung pathology making patients more vulnerable for respiratory infections and decrease respiratory muscle performance, which can cause abrupt clinical deterioration. It is emphasised that prudent screening for presence of any infections, comorbidities and cardiac diseases should be undertaken in DPLD patients and steps taken for their management as they impact the prognosis and morbidity of such patients. Consequently, identification of the factors that envisage the probability of adverse events will help in devising the most effectual preemptive measures to be taken., hence, enhancing the survival of DPLD patients. However, further studies with larger sample size are needed to validate these findings.

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Table 1. Data on demographics, clinical features, co-morbidities and clinical variables of hospitalized DPLD patients.

Variables	n=39
Age (years)	57 ± 11.7 years
Gender (male/female)	14/25
Type of DPLD(IPF/Non-IPF)	15/24
Duration of illness	2.98 ± 1.98 years
Dyspnea (yes/no)	39/00
Cough (yes/no)	35/4
Fever (yes/no)	19/20
Pulmonary hypertension (yes/no)	26/13
Managed with invasive mechanical ventilation (yes/no)	13/26
Patient managed in ICU (yes/no)	23/16
Discharge on domicillary oxygen support (yes/no)	16/23

DPLD, diffuse parenchymal lung disease; IPF, idiopathic pulmonary fibrosis.

Table 2. Association of co-morbidities, type of DPLD and etiology of acute respiratory worsening in DPLD patients leading to admission with the requirement of mechanical ventilation.

Variable	Requirement of mechanical ventilation	No requirement of mechanical ventilation	p
Hypertension	7 (53.85%)	12 (46.15%)	0.651§
Diabetes	6 (46.15%)	3 (11.54%)	0.039*
CAD	2 (15.38%)	2 (7.69%)	0.589*
GERD	0 (0%)	2 (7.69%)	0.544*
Hypothyroidism	4 (30.77%)	1 (3.85%)	0.035*
Pedal edema	5 (38.46%)	0 (0%)	0.002*
IPF v/s non IPF	8/5 (61.54/38.46%)	7/9 (26.92/73.08%)	0.036§
PH	13 (100%)	13 (50%)	0.001*
RWMA	3 (23.08%)	1 (3.85%)	0.099*
ILD exacerbation (disease progression)	3 (23.08%)	12 (46.15%)	0.295*
Respiratory infection	5 (38.46%)	12 (46.15%)	0.648§
Cardiac (MI / heart failure / DCMP) cause of admission	5 (38.46%)	0 (0%)	0.002*

DPLD, diffuse parenchymal lung disease; CAD, coronary artery disease; GERD, gastroesophageal reflux disease; PH, pulmonary hypertension; IPF, idiopathic pulmonary fibrosis; RWMA, regional wall motion abnormality; ILD, interstitial lung disease; MI, myocardial infarction; DCMP, dilated cardiomyopathy.

Table 3. Univariate cox proportional hazard regression to find out significant risk factors of mechanical ventilation.

Variables	Hazards ratio	95% CI for hazards ratio		p
		Lower	Upper	
Hypertension	1.291	.433	3.845	0.647
Diabetes	3.644	1.221	10.875	0.020
CAD	1.505	.333	6.795	0.595
GERD	.045	.000	963.864	0.542
Pedal edema	8.063	2.523	25.770	0.0004
PH	45.876	.448	4694.896	0.105
RWMA	4.261	1.137	15.964	0.031
Type of DPLD				
Non-IPF	1.000			
IPF	3.079	1.003	9.455	0.049
ILD exacerbation (Disease progression)	0.452	0.124	1.649	0.229
Infection	0.681	0.222	2.090	0.501
Cardiac (MI/Heart failure/DCMP)	16.310	3.732	71.280	0.0002

DPLD, diffuse parenchymal lung disease; CAD, coronary artery disease; IPF, idiopathic pulmonary fibrosis; GERD, gastroesophageal reflux disease; PH, pulmonary hypertension; RWMA, regional wall motion abnormality; ILD, interstitial lung disease; IPF:MI, myocardial infarction; DCMP, dilated cardiomyopathy.

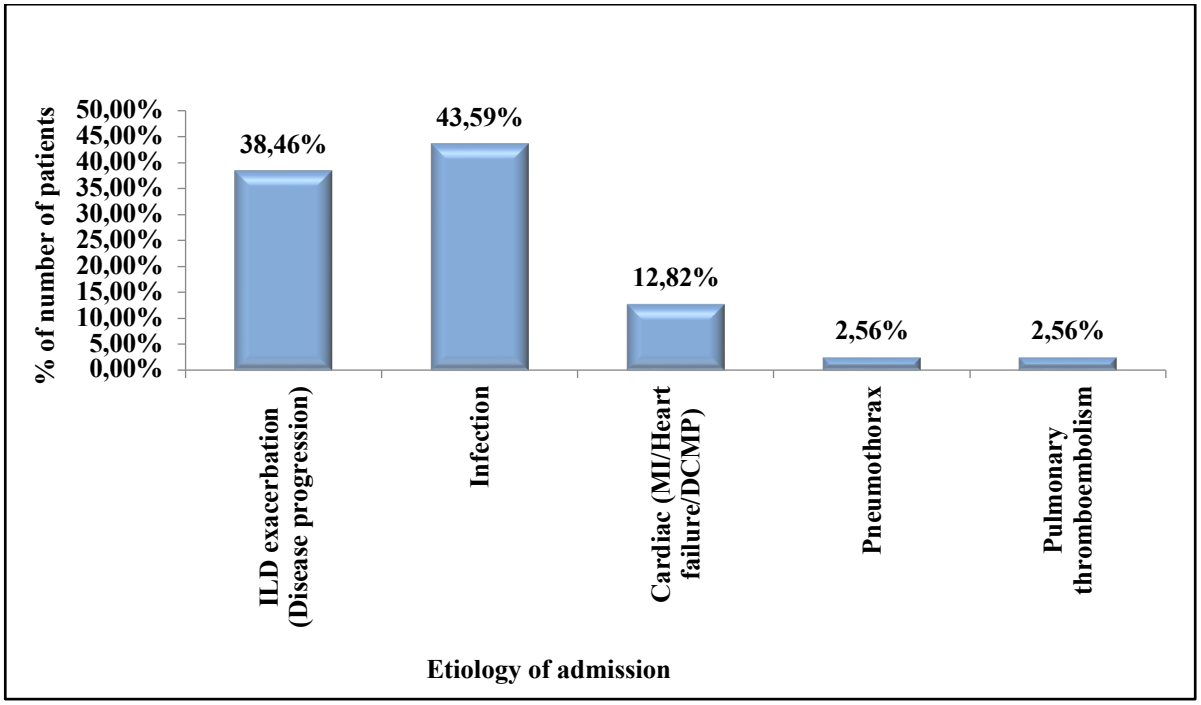

Figure 1. Bar graph showing etiology of acute clinical worsening in diffuse parenchymal lung disease patients.