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Original Article

Impact and predictors of severity of COVID 19 infection in patients with chronic pulmonary diseases: A single center study

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Abstract:

Background: The severity and prognosis of the COVID-19 pandemic are impacted by chronic illnesses that coexist with it.

Patients and methods: A cohort of 301 patients hospitalized to Sohag University Hospital between May 2020 and May 2023 who had a confirmed COVID-19 infection. There were two groups of patients: group 1 included cases with chronic respiratory diseases (CRD) and group 2 included cases without CRD. Both groups were compared as regard demographic data, comorbidities, laboratory and radiological findings, severity and outcome.

Results: Group 1 included 150 cases. The need for non- invasive ventilation (NIV) and mechanical ventilation was more in group 1 ($p \leq 0.001$). Severe cases and mortality were more detected in group 1 ($p \leq 0.001$). Following multiple logistic regression analyses, predictors of severity in cases with CRD included factors related to symptoms as headache and prolonged duration of symptoms (Odd ratio 1.166, CI 1.088 - 1.249) , factors related to laboratory investigations including high neutrophil count, lymphopenia, increase neutrophil lymphocyte ratio (NLR), high serum ferritin and LDH(Odd ratio 1.006, CI 1.004 - 1.008), increase PaCO2, increase HCO3 (Odd ratio 0.883, CI 0.793 - 0.982) and the need for O2 inhalation in management .

Conclusion: Coexistence of CRD and COVID 19 is accompanied by higher disease severity and mortality. Predictors of severity in CRD cases with COVID 19 include headache and prolonged duration of symptoms, high neutrophil count, lymphopenia, increase NLR, high serum ferritin and LDH, increase PaCO2, increase HCO3 and need for O2 inhalation in management.

Keywords: COVID 19, chronic respiratory disease, mortality, comorbidity and prognosis.

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Introduction:

There has been a global outbreak of the COVID-19 virus. The Chinese COVID-19 epidemic was designated as a public health emergency of worldwide concern by the World Health

Organization on January 30, 2020.[1] and on March 11, 2020. [2] it was classified as a crisis all over the world. Comorbidities are prevalent and strongly associated with the likelihood that a patient with COVID-19 will need invasive or non-invasive ventilatory support (NIV), be hospitalized in the intensive care unit (ICU), or died [3.4]. Following diabetes and cardiovascular disease, chronic respiratory disease (CRD) has the third-highest fatality ratio among the comorbidities.[5] Patients with CRD are considered to be at risk of developing severe forms of COVID-19 infection due to their limited physiological reserve.[6]

This study is intended to detect the relationship between COVID 19 and chronic lung diseases and the predictors of severe infection in this category of patients.

Materials and methods:

The current study is a cohort study which included 301 cases with confirmed COVID 19 infection who were admitted to the Sohag University Hospital's isolation unit between May 2020 and May 2023. Every patient received an explanation of the purpose of our study. The patient or his family members gave their consent. The study was approved by the Medical Research Ethics Committee, and it was registered under the Institutional Review Board registration number Soh-Med-21-10-22.

Inclusion criteria:

Every patient enrolled in this study met the requirements listed below for inclusion:

Patients > 16 years old with confirmed diagnosis to have COVID-19 infection according to World Health Organization interim guidance : [7]

- Positive RT-PCR for SARS-CoV-2 and/or
- Computed tomography (CT) chest scan showing findings of pneumonia according to CO-RADS classification [8].

The research sample was split up into two groups:

Group 1: SARS-CoV-2 COVID-19 infected patients (150) with CRD. Chronic respiratory disorders were diagnosed when a patient's medical history and results from investigations, such as X-rays, CT scans or previous pulmonary function tests were documented and support the diagnosis. It was subdivided into 4 groups:

A. Bronchial asthma. (n=28)
B. COPD. (n=51)
C. Interstitial lung disease. (n=31)
D. Bronchiectasis. (n=40)

Group 2: Patients with confirmed diagnosis to have COVID-19 infection without CRD (151).

Exclusion Criteria:

Study participants were considered ineligible if:

- Those who are not confirmed to have COVID-19 infection with PCR or by radiological and laboratory investigations.
- Those who refused to give consent.

The following was administered to the patients:

A. A comprehensive medical history from patients or their family members, encompassing:

1) Age, sex and body mass index (BMI).
2) Smoking.
3) Comorbidities (Diabetes mellitus, hypertension, ischemic heart disease, chronic kidney disease, malignancy).
4) Presenting manifestations: (fever, sneezing, sore throat, dry cough, dyspnea, fatigue, myalgia, arthralgia, anosmia, vomiting or diarrhea) and duration of symptoms.

B. A comprehensive clinical assessment that includes:

A. General examination:

- Vital signs: (Pulse, blood pressure, respiratory rate, temperature)
- Signs of respiratory distress

B. local examination:

- Chest examination (Inspection, palpation, percussion, auscultation)
- Cardiologic examination.
- Abdominal examination.

C. Investigations including:

I. Laboratory investigations:

1) **Complete blood count (CBC)**: white blood cells, lymphocytes, Neutrophil Lymphocyte ratio (NLR), hemoglobin, platelets.

2) **Inflammatory markers:** C-reactive protein (CRP), serum ferritin, D-dimer, Erythrocyte sedimentation rate (ESR), Lactate dehydrogenase (LDH).

3) **Blood coagulation profile**: prothrombin time (PT), prothrombin concentration (PC), activated partial thromboplastin time (aPTT), International normalization ratio (INR).

4) **Liver function tests**: Alanine transaminase (ALT), Aspartate aminotransferase (AST), serum albumin, total bilirubin.
5) **Renal function tests**: serum creatinine, blood urea.
6) **Serum electrolytes**: sodium (Na+), potassium (K+) and ionize calcium (Ca++).
7) **Real-time reverse-transcriptase polymerase chain reaction (RT-PCR):**

Done for all the patients to detect the virus in specimens collected through nasopharyngeal swabs as recommended by World Health Organization [(7)].

The nasal swab samples were collected from the patients and then put in tubes containing virus preservation solutions so that the virus's genetic material can be retrieved.

The used methods are basic local alignment search tool (BLAST) and fast protein comparison (FASTA), the patient was confirmed positive when there was a match in between.

8) Arterial blood gases (ABG) test:

Arterial blood gases analysis was done to detect PH, PaCo2, PaO2, SaO2, HCO3. The samples were obtained with a needle and syringe slightly heparinized, freshly drawn and bubble free then analyzed using automated blood gases analyzer (ABL800FLEX blood gas analyzer, radiometer, USA).

II. Radiological examination:

Computerized tomography (CT) chest scan:

It was done (using 16 slice Toshiba ALEXION) for all patients to confirm the diagnosis of pneumonia and its probability to be due to SARS-CoV-2 according to CO-RADS (the COVID-19 reporting and data system) classification [(8)].

Severity of covid-19 disease was assessed according to WHO classification.[(9)]

- **Mild illness:**
  Symptomatic, showing no signs of hypoxia or viral pneumonia

- **Moderate illness:**
  Pneumonia with clinical signs of pneumonia (fever, cough, dyspnea, tachypnea) but no evidence of severe pneumonia, and SpO2 ≥ 90% on room air)

- **Severe illness:**
  Severe pneumonia: Clinical signs of pneumonia (fever, cough, dyspnea, tachypnea) plus one of the following; respiratory rate greater than 30 breaths per minute, significant respiratory distress, or SpO2 lower than 90% on room air.

- **Critical disease**:
  Acute Respiratory distress syndrome (ARDS) with onset within 1 week of clinical insult (i.e., pneumonia) or new or worsening respiratory symptom.

Management of patients included in the study was according to severity of COVID 19 plus management of the associated CRD [(7)].

Statistical analysis:

Statistical analysis was done by SPSS v27 (IBM©, Chicago, IL, USA). Shapiro-Wilks test and histograms were used to evaluate the normality of the distribution of data. Quantitative parametric data were presented as mean and standard deviation (SD) and were analysed by ANOVA (F) test with post hoc test (Tukey). Quantitative nonparametric variables were presented as median (IQR) and compared between the two groups utilizing Mann-Whitney U test. Qualitative variables were presented as frequency and percentage (%) and were analysed utilizing the Chi-square test. A two tailed P value ≤ 0.05 was considered statistically significant.

Results:

There were 301 patients in our study. They were divided into two groups: 150 patients made up group 1 of COVID-19 patients with CRD and 151 patients made up group 2 of COVID-19 patients without CRD.

Group 1 was subdivided into 4 subgroups: COPD (51), bronchiectasis (40), ILD (31) and bronchial asthma (28) as shown in **figure 1**.

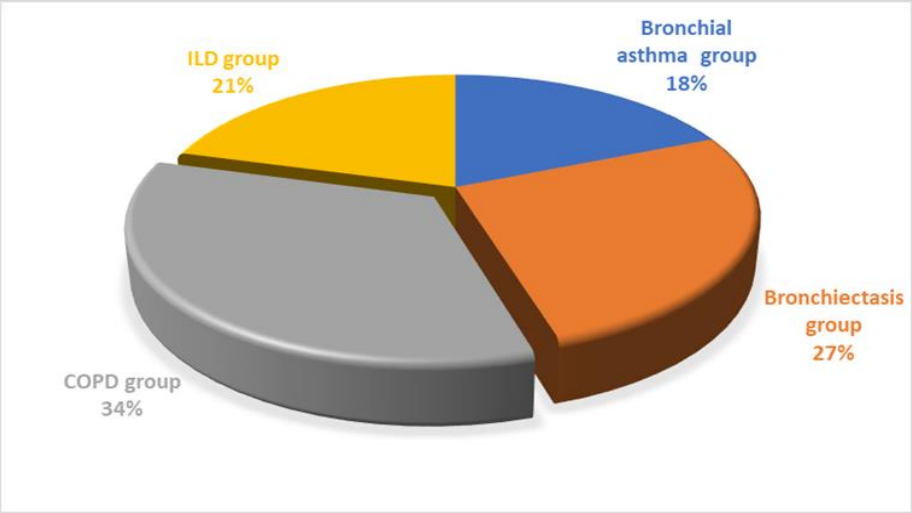

Figure 1: Classification according to type of pulmonary disease of group 1 patients

Table 1 showed the comparison between the two groups as regard demographic parameters. Age and sex were insignificantly different between both groups. BMI and smoking were significantly higher in group1 (P value <0.001). The two groups were compared as regard comorbidities, hypertension, ischemic heart disease (IHD) and malignancy were more detected in group 1(P value <0.005)

Table 1: Comparison between the studied groups as regard demographic data and comorbidities.

Variable		**Group 1 (n=150)**	**Group 2 (n=151)**	**P value**
Age (years)	Mean ± SD	55.25 ± 17.33	51.56 ± 17.42	0.067
	Range	19 - 82	21 - 87	
Sex	Male	72 (48%)	68 (45.03%)	0.606
	Female	78 (52%)	83 (54.97%)	
BMI (kg/m^2)	Mean ± SD	33.71 ± 11.74	29.7 ± 7.99	<0.001*
	Range	15.6 - 55.8	14 - 58	
Smoking	Non-smoker	57 (38%)	129 (85.43%)	<0.001*
	Ex-smoker	31 (20.67%)	0 (0%)	
	Current smoker	62 (41.33%)	22 (14.57%)	
Comorbidities	DM	48 (32%)	40 (26.49%)	0.293
	Hypertension	47 (31.33%)	30 (19.87%)	0.023*
	IHD	26 (17.33%)	10 (6.62%)	0.004*
	CKD	13 (8.67%)	14 (9.27%)	0.854
	Malignancy	16 (10.67%)	7 (4.64%)	0.049*

*Significant as P value ≤0.05, T: unpaired t. test, X^2: Chi square test. **BMI**: Body mass index, **DM**: Diabetes mellitus, **IHD**: Ischemic heart disease and **CKD**: Chronic kidney disease.

Table 2 showed the comparison between the presenting symptoms in the two groups. Symptoms including fever, sore throat, chest pain and fatigue were significantly more in group 1(P value <0.05). Duration of symptoms was significantly longer in group1 (P value <0.001).

Table 2: Comparison between the studied groups as regard symptoms and duration of symptoms.

Variable		Group 1 (n=150)	Group 2 (n=151)	P value
Symptoms	Fever	115 (76.67%)	86 (56.95%)	<0.001*
	Sore throat	42 (28%)	20 (13.25%)	0.002*
	Cough	106 (70.67%)	96 (63.58%)	0.190
	Chest pain	41 (27.33%)	16 (10.6%)	<0.001*
	Dyspnea	96 (64%)	82 (54.3%)	0.087
	Headache	15 (10%)	8 (5.3%)	0.125
	Malaise	27 (18%)	19 (12.58%)	0.192
	Fatigue	42 (28%)	12 (7.95%)	<0.001*
	Arthralgia	9 (6%)	3 (1.99%)	0.075
	Myalgia	15 (10%)	9 (5.96%)	0.196
Duration of symptoms (days)	Mean ± SD	14.06 ± 5.25	7.36 ± 3.84	<0.001*
	Range	5 - 23	2 - 27	

*Significant as P value ≤0.05, X^2: Chi square test

Chest CT findings at admission were significantly different between both groups. Chest CT on admission including Co-RADS 1 and Co-RADS 3 were significantly higher in group2 (P value <0.001) and Co-RADS 5 was significantly higher in group1 (P value<0.001) as shown in **Figure 2.**

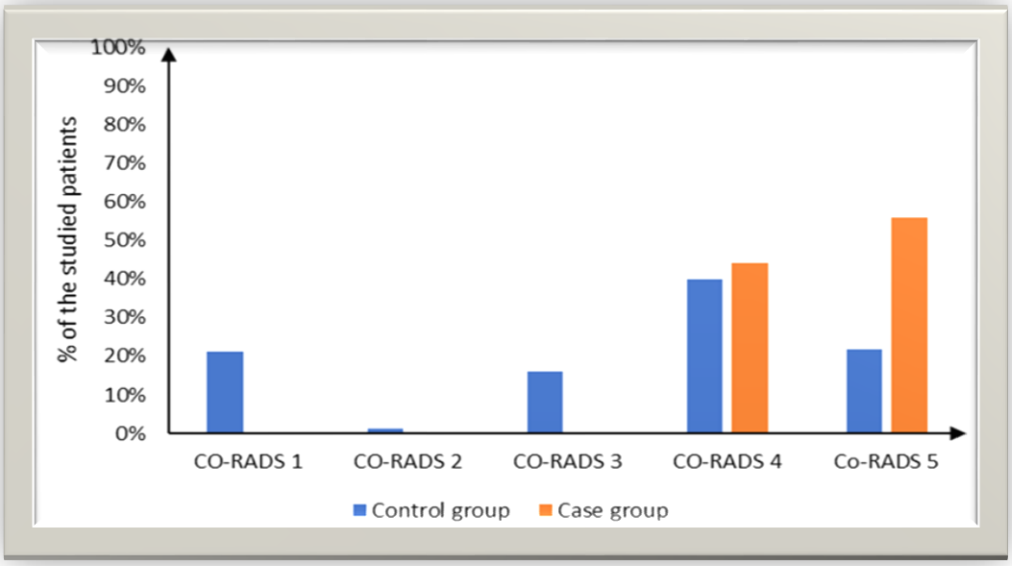

Figure 2: Chest CT on admission of the studied groups

Table 3 demonstrated the comparison as regard the Laboratory findings between both groups at admission. Hemoglobin (Hb), platelets, neutrophils, Neutrophil Lymphocyte ratio (NLR), ALT, AST and D-dimer were significantly higher in group1 (P value <0.001 for all). Lymphocytes (P value = 0.009), prothrombin time (P value = 0.003), prothrombin concentration (P value <0.001) and INR (P value <0.001) were significantly higher in group 2.

Table 3: Comparison between the studied groups as regard laboratory findings.

Variable		Group 1 (n=150)	Group 2 (n=151)	P value
Hb (mg/dl)	Mean ± SD	12.76 ± 3.52	11.14 ± 2.05	<0.001*
	Range	7.1 - 18.9	3.4 - 15.6	
WBCs (x10^9/L)	Mean ± SD	13.03 ± 4.67	11.76 ± 6.66	0.058
	Range	5.7 - 22	2.1 - 40.9	
Neutrophils (x10^9/L)	Mean ± SD	9.97 ± 6.73	7.97 ± 3.04	0.001*
	Range	1.2 - 38	2 – 15	
Lymphocytes (x10^9/L)	Mean ± SD	1.24 ± 0.41	1.55 ± 1.39	0.009*
	Range	0.58 - 1.9	0.2 - 12.3	
NLR	Mean ± SD	7.29 ± 3.76	0.23 ± 0.37	<0.001*
	Mean ± SD	1.11 - 18.75	0.03 - 3.84	
Platelets (x10^9/L)	Mean ± SD	296.01 ± 125.31	224.95 ± 106.25	<0.001*
	Range	117 - 551	8 - 461	
CRP (ng/mL)	Range	78.3 ± 37.71	83.1 ± 42.47	0.302
	Mean ± SD	5.7 - 139.5	10 - 200	
Serum ferritin (ng/mL)	Range	441.35 ± 217.73	446.35 ± 372.44	0.887
	Mean ± SD	88 - 800	39 - 1500	
D-dimer (ng/mL)	Median (IQR)	4167	700	<0.001*
	Range	1913-6987.75	450-2800	
LDH (U/L)	Range	516.37 ± 139.28	546.1 ± 255.01	0.211
	Mean ± SD	257 - 750	140 - 980	
ALT (U/L)	Range	45.36 ± 17.3	32.46 ± 13.89	<0.001*
	Mean ± SD	14 - 75	8 - 55	
AST (U/L)	Range	31.95 ± 12.32	21.16 ± 7.33	<0.001*
	Mean ± SD	13 - 55	8 - 33	
Na+ (mmol/L)	Mean ± SD	135.34 ± 9.01	133.55 ± 9.37	0.091
	Range	121 - 149	110 - 167	
K+ (mmol/L)	Mean ± SD	4.09 ± 0.8	4.18 ± 1.12	0.424
	Range	2.9 - 5.6	2.2 - 8.4	
Ca++ (mmol/L)	Mean ± SD	1.07 ± 0.27	1.11 ± 0.24	0.170
	Range	0.7 - 1.5	0.6 - 1.8	
Prothrombin time (sec)	Mean ± SD	14.94 ± 2.39	17.73 ± 11.06	0.003*
	Range	11 - 18.9	10.4 - 141	
Prothrombin concentration (%)	Mean ± SD	0.93 ± 0.17	9.05 ± 25.77	<0.001*
	Range	0.65 - 1.2	0.23 - 128	
INR	Mean ± SD	1.24 ± 0.17	1.45 ± 0.56	<0.001*
	Range	1 - 1.57	0.85 - 3	

*Significant as P value ≤0.05, T: unpaired t. test and Mann-Whitney U test. **Hb**: hemoglobin, **NLR**: Neutrophil lymphocyte ratio, **ALT**: alanine transaminase, **AST**: aspartate aminotransferase, **CRP**: C-reactive protein, **LDH**: Lactate dehydrogenase, **INR**: international normalized ratio.

Table 4 showed that PaO_2 and O_2 saturation at admission were significantly lower in group1 but $PaCO_2$ was significantly higher in group 1(P value <0.001).

Table 4: Comparison between the studied groups as regard the parameters of ABG.

Variable		Group 1 (n=150)	Group 2 (n=151)	P value
PaO_2 (mmHg)	Mean ± SD	54.68 ± 15.54	63.83 ± 18.83	<0.001*
	Range	28 - 97	30 - 80	
$PaCO_2$ (mmHg)	Mean ± SD	56.84 ± 17.33	33.03 ± 10.38	<0.001*
	Range	27 - 87	15 - 50	
O_2 saturation (%)	Mean ± SD	86.68 ± 10.33	78.09 ± 13.62	<0.001*
	Range	57 - 99	52 - 97	
HCO_3 (mEq/L)	Mean ± SD	21.38 ± 3.6	21.27 ± 3.23	0.784
	Range	16 - 33	10 - 25	

***Significant as P value ≤0.05, T: unpaired t. test**

Table 5 showed that disease severity according to WHO was significantly more in group 1 than in group2 (P value <0.001).

Table 5: Comparison between the studied groups as regard disease severity (According to WHO classification**)**.

	Group 1 (n=151)	Group 2 (n=150)	P value
Mild	0 (0%)	55 (36.42%)	**<0.001***
Moderate	72 (48%)	42 (27.81%)	
Severe	78 (52%)	54 (35.76%)	

***Significant as P value ≤0.05, X^2: Chi square test**

Table 6 demonstrated the comparison between the studied groups as regard the utilized O2 therapy, NIV and MV. O_2 mask with reservoir, NIV and MV were significantly different between both groups (P value <0.001). The use of O_2 mask with reservoir was significantly higher in group2 while NIV and MV were higher in group1.

Table 6: Comparison between the studied groups as regard the needed O_2 therapy, NIV and MV**.**

Variable	Group 1 (n=150)	Group 2 (n=151)	P value
O_2 mask	117 (78%)	106 (70.2%)	0.122
O_2 mask with reservoir	10 (6.67%)	21 (13.91%)	<0.001*
NIV	82 (54.67%)	10 (6.62%)	<0.001*
MV	23 (15.33%)	0 (0%)	<0.001*

***Significant as P value ≤0.05, X^2: Chi square test**

Hospital stay was significantly longer in group1 (P value <0.001). Regarding prognosis, improved cases were significantly higher in group 2 while mortality was significantly higher in group1 (P value <0.001) **(Table 7)**.

Table 7: Comparison between the studied groups as regard the duration of hospital stay and prognosis

Variable		Group 1 (n=150)	Group 2 (n=151)	P value
Hospital stay (days)	Mean ± SD	7.66 ± 2.83	6.21 ± 2.77	<0.001*
	Range	4 - 19	2 - 15	
Prognosis	Improved	75 (50%)	139 (92.05%)	<0.001*
	Died	75 (50%)	12 (7.95%)	

***Significant as P value ≤0.05, T: unpaired t. test, X^2: Chi square test**

Table 8 showed the multivariate regression analysis to predict factors associated with increase severity of COVID 19 in cases with CRD. As regard presenting symptoms, Presence of headache and prolonged duration of symptoms were considered predictors of severity (P value 0.015 and <0.001 respectively). Regarding laboratory investigations, increase number of neutrophils, lymphopenia, increase NLR, high serum ferritin and LDH, increase PaCO2 (P value <0.001 for all) and increase HCO3 (P value <0.022) were considered predictors of severity and poor outcome. Finally, need for O2 inhalation in management was considered predictor of severity (P value <0.001)**.**

Table 8: Multivariate regression analysis of all parameters for prediction of COVID 19 severity in cases with CRD:

Variables	Odds ratio	95% CI	P
Age (years)	1.002	0.983 - 1.021	0.844
Sex	0.603	0.300 - 1.210	0.155
Smoking	0.498	0.166 - 1.490	0.213
Fever	1.046	0.394 - 2.773	0.929
Sore throat	0.332	0.098 - 1.116	0.075
Cough	0.499	0.180 - 1.378	0.180
Chest pain	3.290	0.960 - 11.270	0.058
Dyspnea	1.889	0.812 - 4.389	0.139
Headache	0.139	0.028 - 0.676	**0.015***
Malaise	0.326	0.090 - 1.173	0.086
Fatigue	1.325	0.370 - 4.737	0.665
Arthralgia	0.979	0.145 - 6.563	0.982
Myalgia	1.272	0.337 - 4.785	0.722
Duration of symptoms (days)	1.166	1.088 - 1.249	**<0.001***
Hb (mg/dl)	1.020	0.922 - 1.129	0.698
WBCs ($x10^9$/L)	0.986	0.916 - 1.059	0.697
Neutrophils ($x10^9$/L)	1.098	1.003 - 1.201	**0.043***
Lymphocytes ($x10^9$/L)	0.258	0.135 - 0.490	**<0.001***
NLR	0.807	0.725 - 0.896	**<0.001***
Platelets ($x10^9$/L)	0.999	0.996 - 1.002	0.612
CRP (ng/mL)	1.005	0.995 - 1.013	0.305
Serum ferritin (ng/mL)	1.003	1.001 - 1.004	**<0.001***
D-dimer (ng/mL)	1.000	0.9999 - 1.0001	0.858
LDH (U/L)	1.006	1.004 - 1.008	**<0.001***
ALT (U/L)	1.002	0.982 - 1.020	0.879
AST(U/L)	0.995	0.967 - 1.023	0.728
Na+ (mmol/L)	0.989	0.952 - 1.026	0.559
K+ (mmol/L)	1.277	0.840 - 1.942	0.252
Ca++ (mmol/L)	1.752	0.417 - 7.347	0.443
Prothrombin time (sec)	0.997	0.958 - 1.037	0.897
Prothrombin concentration (%)	1.022	0.987 - 1.058	0.207
INR	1.239	0.413 - 3.706	0.702
PaO_2 (mmHg)	0.994	0.975 - 1.013	0.542
PCO_2 (mmHg)	0.942	0.913 - 0.971	**<0.001***
O_2 saturation (%)	0.980	0.946 - 1.013	0.233
HCO_3 (mEq/L)	0.883	0.793 - 0.982	**0.022***
O2 mask	18.935	6.039 - 59.365	**<0.001***
O_2 mask with reservoir	2920.000	-----	0.998
NIV	2.293	0.789 - 6.662	0.127
MV	3.044	0.599 - 15.452	0.179
Hospital stays (days)	0.946	0.822 - 1.086	0.431

***Significant as P value≤0.05, CI: Confidence interval**

Discussion:

The impaired lung function in patients with chronic respiratory diseases (CRD), including interstitial lung disease (ILD), bronchial asthma, bronchiectasis, and chronic obstructive pulmonary disease (COPD), is responsible for more vulnerability to respiratory infections. The tendency of COVID-19 virus to impact the respiratory system can make these chronic illnesses worse leading to more severe disease courses and consequences.

Our study cases were divided into two groups: group 1 included 150 cases with SARS-COV-2 and chronic pulmonary disease while group 2 included 151 cases with SARS-COV-2 only without pulmonary disease. The CRDs included COPD in 51patients, bronchiectasis in 40 patients, ILD in 31 patients and bronchial asthma in 28 patients.

Obesity and smoking were associated with most patients in group 1 in the present study. This result was consistent with other research that found significant risk factors, including obesity, smoking, and comorbidities, for poor outcomes in COVID-19 individuals [10,11].

Comorbidities like hypertension, IHD and malignancy were more prevalent in CRD cases in our study. This was in agreement with a study by Kilic H **et al., (2022**) , which demonstrated that

hypertension (n = 113; 48.9%) was the most prevalent comorbidity associated with individuals with chronic lung disease, followed by diabetes mellitus (n = 61; 26.4%) and coronary artery disease (n = 56; 24.2%) (12) .

In our study fever, fatigue, chest pain and sore throat were more common in patients with CRD. Contrary to our findings, **Riou et al. (2021)** reported that symptoms were similar in both groups with the exception of fever, which was substantially more common in individuals without underlying lung illness [(13)].

This can be explained by presence of a small number of cases in the CRD group (40%) in the previous study and also it included two categories of CRD (COPD and bronchial asthma) while our study included 50% of cases with CRD categorized into four groups (COPD, asthma, ILD, bronchiectasis).

Although COVID-19 patients with chronic chest disease expectorated more sputum than COVID-19 patients without the condition (p = 0.002), there was no discernible difference in the clinical appearance of the two groups, according to a study by **Abdelghany et al., (2022).** This could be explained by the small percentage of CRD cases (17.6%) [(14)].

According to our findings, Chest CT Co-RADS 5 on admission was significantly higher in group 2 with CRD (P value<0.05). This observation reflects the different imaging characteristics between COVID-19 and chronic lung diseases. CO-RADS 5 is used when imaging features are highly suggestive of COVID-19. The typical findings in COVID-19 include bilateral, peripheral ground-glass opacities, often with a rounded morphology and involvement of the lower lobes. These features can be quite distinctive compared to other types of lung pathology [(15)].

As regard laboratory findings, hemoglobin (Hb) was higher in CRD group. This can be explained by the presence of chronic hypoxemia in patients with chronic respiratory diseases which stimulates erythropoiesis.

According to our findings, there was a statistically significant difference in D-dimer levels among COVID-19 patients with and without CRD, but not in serum ferritin, CRP, or LDH levels. Ferritin was found to be substantially greater in group 2 than in group 1 cases (p < 0.0001). This agreed with a study by **Abdelghany et al., (2022)**, which showed that COVID-19 patients without CRD had significantly higher serum LDH and D-dimer levels than patients with CRD (p = 0.033 and p = 0.008, respectively) [(14)] .

The neutrophil lymphocyte ratio (NLR) was higher in CRD group according to our findings (P value <0.001). Elevated NLR is linked to increased disease severity and poorer prognosis. This ratio is an easily accessible biomarker that may be used to estimate the severity COVID-19 infection [(16)] .

According to our findings, INR was considerably higher in group 1 patients (P value <0.001). In a research published in 2021, **Pearson et al.** analyzed INR testing volumes and results prior to and during the COVID-19 outbreak. It was observed that, particularly among outpatients, there was a decrease in testing volume and an increase in the percentage of abnormal high INR results. This suggests that the pandemic impacted INR testing, which could lead to suboptimal therapy for patients with conditions such as venous thromboembolism [(17)] .

In the current research, PaO2 was substantially lower while PaCO2 was significantly higher in group 1 compared to group 2. O2 saturation (%) was significantly lower (P value <0.001) in group 1. Decreased oxygen saturation in COVID-19-infected cases with CRD is quite concerning since it indicates the combined effects of two serious respiratory disorders. Chronic pulmonary illnesses that already impair lung function; adding a COVID-19 infection can make respiratory distress worse [(18)].

Our findings showed that group 1 patients required NIV and MV more than group 2 (P value <0.001). Consistent with our findings, **Beltramo et al. (2021)** observed a noteworthy rise in the requirement for ICU admission and mortality among patients diagnosed with CRD [19]. Contrary to our findings, **Riou et al. (2021)** noted that CRD was not a risk factor for ICU management [(13)] . Comparable results have been revealed by a recent meta-analysis [(20)].

In our study, group 1 had higher mortality due to more severe cases and associated comorbidities. National investigations carried out in the UK [(21)] . and Sweden [(22)] . have demonstrated a correlation between pulmonary illnesses and an increased risk of mortality and severe illness in SARS-CoV-2 infected cases. In order to determine the effect of underlying medical illnesses on severe COVID-19

outcomes, **Treskova-Schwarzbach et al. (2021)** carried out a comprehensive meta-analysis and discovered that those with a history of chronic lung illnesses had more severe COVID-19 and poor outcome [23] . This was consistent with the research done by **KHAN et al. (2020),** who found that COVID-19 deaths in patients with respiratory illnesses are twice more likely to occur [24]. A study by **Abdelghany et al. (2022)**, in contrast, revealed no appreciable difference in hospital mortality between patients with COVID-19 and concomitant CRD (n = 15; 26.3%) and those without CRD (n = 86 ; 32.3%) (p = 0.347) [14] .

Factors that may lead to an increased risk of COVID-19 infection severity in CRD patients were predicted after performing the multivariate regression analysis in the current study. It contained factors related to symptoms including headache (**Odd ratio** 0.139, **CI** 0.028 - 0.676) and prolonged duration of symptoms (**Odd ratio** 1.166, **CI** 1.088 - 1.249) , factors related to laboratory investigations including high neutrophil count(**Odd ratio** 1.098, **CI** 1.003 - 1.201), lymphopenia(**Odd ratio** 0.258, **CI** 0.135 - 0.490), increase NLR(**Odd ratio** 0.807, **CI** 0.725 - 0.896), high serum ferritin (**Odd ratio** 1.003, **CI** 1.001 - 1.004) and LDH(**Odd ratio** 1.006, **CI** 1.004 - 1.008), increase PCO2 (**Odd ratio** 0.942, **CI** 0.913 - 0.971) and increase HCO3 (**Odd ratio** 0.883, **CI** 0.793 - 0.982) and finally the need for O2 mask in management (**Odd ratio** 18.93, **CI** 6.039 - 59.365).

The limitations in our study included that it was a single center study that may result in different findings than elsewhere and relatively small sample size that may produce imprecise conclusion.

Conclusion:

Coexistence of CRD and COVID 19 is accompanied by higher severity of the disease and mortality. Predictors of severity in CRD cases with COVID 19 include headache and prolonged duration of symptoms, high neutrophil count, lymphopenia, increase NLR, high serum ferritin and LDH, increase PaCO2, increase HCO3 and need for O2 inhalation in management.

Declarations:

- **Ethics approval and consent to participate**: The study was approved by the Medical Research Ethics Committee of the Sohag Faculty of Medicine and registered under the Institutional Review Board registration number Soh-Med-21-10-22.
- **Consent for publication**: Patients' informed written consents were obtained.
- **Availability of data and material**: The study's data are available inside the article and its additional materials, as well as upon reasonable request, according to the authors' confirmation.
- **Competing interests**: Non
- **Funding**: Non
- **Authors' contributions:** MM, SN, and AH carried out the study, provided administrative support, and gathered clinical data; SN carried out data analyses and created the designs. SN and HA also contributed to the project's conception and design. The manuscript was written by all contributors.. Each author read, critically reviewed, revised, and approved the final version of the publication in addition to providing clinical input and collecting and interpreting the data..
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