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Review Article

Clinical characteristics and outcome of COVID-19 patients with chronic pulmonary diseases

Shimaa Nour Morsi, Hamdy Ali Mohammadien, Abdellah H K AlMostafa Mahmoud El Sayed

[1-] Department of Chest disease and Tuberculosis, Faculty of Medicine, Sohag University, Egypt.

Background: Chronic respiratory diseases (CRDs) consisted of different diseases with largely heterogeneous pathophysiology and more detailed analysis is required to fully explain the link between different categories of CRDs and the outcomes of COVID 19.

Patients and methods: A cohort study of 150 patients with confirmed COVID 19 infection and CRD admitted to isolation unit of Sohag university hospital during the period from May 2020 to May 2023.Patients were divided into COPD, ILD, bronchiectasis and asthma groups. All groups were compared as regard demographic data, comorbidities, laboratory and radiological findings, severity and outcome

Results: The study population was divided into four groups: bronchial asthma group (n=28), bronchiectasis group (n=40), COPD group (n=51) and ILD group (n=31). Neutrophils and NLR were significantly higher in bronchiectasis group, COPD group and ILD group than bronchial asthma group (P value<0.05). Severe cases were significantly higher in COPD group than other groups (P value<0.001). The worst prognosis was in COPD group and the best was in asthma group. Bronchiectasis and current smoking increased the odds for mortality by about 5 and 6 times respectively

Conclusion:

Chronic respiratory diseases have a potent impact on COVID 19 severity and outcome. Severity of infection and mortality were the highest in COPD cases. The absence of significant association between bronchial asthma and increased risk or poor prognosis of COVID-19. Factors associated with higher mortality included bronchiectasis as subtype of CRD, current smoking, the association of DM and CKD as comorbidities, low O2 saturation, high D-dimer and high HCO3 values.

Keywords: COVID 19, chronic respiratory disease, COPD, ILD and predictors.

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Corresponding Author: **Shimaa Nour Morsi** **E.mail**: shimaanour@med.sohag.edu.eg

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Background

investigations. Also we excluded cases that refused to participate in the study.

All the cases were subjected to the following:

A. Medical history: including age, sex, body mass index (BMI), smoking, comorbidities e.g. Diabetes mellitus (DM), hypertension (HTN), ischemic heart disease (IHD), chronic kidney disease (CKD) and malignancy, presenting manifestations e.g. (fever, sneezing, anosmia, sore throat, dry cough, dyspnea, fatigue, myalgia, arthralgia, vomiting or diarrhea) and duration of symptoms.

B. Clinical assessment including:

A. General examination: vital signs including (pulse, blood pressure, respiratory rate and temperature) and signs of respiratory distress

B. local examination: including chest examination (Inspection, palpation, percussion, auscultation), cardiologic examination and abdominal examination**.**

C. Investigations including:

1- Laboratory investigations:

- **Complete blood count (CBC):** white blood cells, neutrophils, lymphocytes, Neutrophil-Lymphocyte ratio (NLR), hemoglobin and platelets**.**
- **Inflammatory markers:** C-reactive protein (CRP), serum ferritin, D-dimer, ESR and LDH.
- **Blood coagulation profile**: prothrombin time (PT), prothrombin concentration (PC) and International normalization ratio (INR).
- **Liver function tests:** Alanine transaminase (ALT), Aspartate aminotransferase (AST), serum albumin and total bilirubin.
- **Renal function tests:** blood urea and serum creatinine,**.**
- **Serum electrolytes:** sodium (Na+), potassium (K+) and ionize calcium (Ca++).
- **Real-time reverse-transcriptase polymerase chain reaction (RT-PCR):** It was done to all patients after collection of nasopharyngeal swabs as recommended by World Health Organization. **(5)**

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.

The severe acute respiratory syndrome corona-virus 2 (SARS-CoV-2) that produced the coronavirus disease 2019 (COVID-19) pandemic has resulted in a high rate of morbidity and mortality over the world. Research shows that at least one COVID-19 related comorbidity affects 75% of hospitalized COVID-19 patients. (1)

Individuals with interstitial lung diseases (ILDs), asthma, chronic obstructive pulmonary disease (COPD), pulmonary hypertension, sarcoidosis, cystic fibrosis (CF), chronic respiratory failure (CRF), pulmonary hypertension, and sarcoidosis were among the first to be identified as being at risk of developing severe forms of COVID-19 (2).

It is true that COVID-19 causes a range of respiratory symptoms, from dyspnea and cough to acute respiratory distress syndrome (ARDS) in its most severe form.(3, 4)

The aim of our study is to declare the clinical characteristics and factors associated with high morbidity and mortality among different categories of chronic respiratory diseases (CRDs) associated with COVID 19.

Patients and methods:

It is a cohort study which included 150 cases with confirmed COVID 19 infection who were admitted at Sohag University Hospital's isolation unit between May 2020 and May 2023. Informed consent was taken from the patient or his family if the patient was unconscious. 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:

Our study included cases more than 16 years confirmed to have COVID 19 infection either with Positive RT-PCR for SARS-CoV-2 and/or computed tomography (CT) chest scan according to WHO interim guidance.**(5)**

The included cases were divided into four groups: bronchial asthma (n=28), bronchiectasis (n=40), COPD (n=51) and interstitial lung disease (n=31).

Exclusion Criteria:

Cases excluded from our study included non-confirmed cases of COVID-19 infection either with PCR or by radiological and laboratory

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 analyzed by ANOVA (F) test with post hoc test (Tukey). Qualitative variables were presented as frequency and percentage (%) and were analyzed utilizing the Chi-square test. All variables were included in a model of Binomial Logistic Regression for predictors of survival analysis. Every variable was tested separately with univariate regression and those variable with significant were included in the logistic regression. ROC curve analysis was done to estimate whether having asthma, COPD, Bronchiectasis or ILD would affect the prognosis of the patients as the condition was estimated "death". A two tailed P value ≤ 0.05 was considered statistically significant.

Results:

Our study included 150 cases of COVID 19 with CRDs divided into four groups according to type of pulmonary disease: bronchial asthma group included 28 cases, bronchiectasis group included 40 cases, COPD group included 51cases and ILD group included 31 cases.

Comparison between the four groups as regard demographic data and comorbidities was illustrated in **table 1**.

- **Arterial blood gases (ABG) test:**

It was done to detect PH, PaCo2, PaO2, O2 saturation and 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).

2. Radiological examination:

Computerized tomography (CT) chest scans: to confirm the diagnosis of pneumonia and its probability to be due to COVID 19 according to CO-RADS (the COVID-19 reporting and data system) classification [(6)].

According to WHO classification, COVID-19 infection was categorized into mild, moderate or severe infection. Mild COVID-19 defines as respiratory symptoms without evidence of pneumonia or hypoxia, while moderate or severe infection defined as presence of clinical and radiological evidence of pneumonia. In moderate cases, SpO2 ≥90% on room air while one of the following was required to define the severe cases: respiratory rate >30 breaths/min or SpO2 <90% on room air [(5)].

Treatment protocol followed the recommendat-ions of the Egyptian Ministry of Health and Population Management, which was approved by the scientific COVID-19 committee of Faculty of Medicine, Sohag University [(7)]. Plus management of the associated chronic chest disease.

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

	Bronchial asthma group (n=28)	**Bronchiectasis group (n=40)**	**COPD group (n=51)**	**ILD group (n=31)**	P value
Age (years) Mean ± SD	55.8 ± 14.39	59.6 ± 15.64	56.9 ± 16.8	54.5 ± 19.1	0.613
Sex Male	13 (46.43%)	18 (45%)	28 (54.9%)	13 (41.94%)	0.659
Female	15 (53.57%)	22 (55%)	23 (45.1%)	18 (35.29%)	
BMI (kg/m^2) Mean ± SD	32.7 ± 11.78	34.8 ± 11.55	34.9 ± 11.83	31.2 ± 11.9	0.484
Smoking Non-smoker	15 (53.57%)	23 (57.5%)	13 (25.49%)	6 (19.35%)	
Ex-smoker	5 (17.86%)	9 (22.5%)	11 (21.56%)	6 (19.35%)	0.001*
Current	8 (28.57%)	8 (20%)	27 (52.94%)	19 (37.25%)	
Comorbidities DM	5(17.9 %)	9(22.5 %)	22(43.1 %)	12(38.7 %)	
Hypertension	9(32.1 %)	10(25.0 %)	17(33.3 %)	11(35.5 %)	
IHD	8(28.6 %)	11(27.5 %)	5(9.8 %)	2(6.5 %)	0.045
CKD	4(14.3 %)	6(15.0 %)	2(3.9 %)	1(3.2 %)	
Malignancy	2(7.1 %)	4(10.0 %)	5(9.8 %)	5(16.1 %)	

*Significant as P value ≤0.05, ANOVA (F) test with post hoc test (Tukey), X^2: Chi square test. **BMI**: Body mass index, **DM**: Diabetes mellitus, **IHD**: Ischemic heart disease and **CKD**: Chronic kidney disease.

Age, sex and BMI were insignificantly different among the four groups. Smoking was significantly higher in COPD group (P value =0.001). Comorbidities were significantly different among the four groups (P value =0.04), the incidence of DM and hypertension was higher in COPD group , while the incidence of IHD and CKD was higher in bronchiectasis group and malignancy was detected more in COPD and ILD groups.

Table 2

Table 2: Comparison between the studied groups a regard presenting symptoms and its duration.

Symptoms	Bronchial asthma group (n=28)	Bronchiectasis group (n=40)	COPD group (n=51)	ILD group (n=31)	P value
Fever	19 (67.86%)	32 (80%)	38 (74.51%)	26 (83.87%)	0.476
Sore throat	8 (28.57%)	13 (32.5%)	13 (25.49%)	8 (25.81%)	0.887
Cough	17 (60.71%)	27 (67.5%)	37 (72.55%)	25 (80.65%)	0.375
Chest pain	8 (28.57%)	10 (25%)	14 (27.45%)	9 (29.03%)	0.981
Dyspnea	17 (60.71%)	28 (70%)	29 (56.86%)	22 (70.97%)	0.469
Headache	5 (17.86%)	1 (2.5%)	5 (9.8%)	3 (9.68%)	0.201
Malaise	2 (7.14%)	7 (17.5%)	10 (19.61%)	8 (25.81%)	0.307
Fatigue	8 (28.57%)	13 (32.5%)	13 (25.49%)	8 (25.81%)	0.887
Arthralgia	0 (0%)	4 (10%)	3 (5.88%)	2 (6.45%)	0.402
Myalgia	3 (10.71%)	3 (7.5%)	5 (9.8%)	4 (12.9%)	0.900
Duration of symptoms (days) Mean ± SD	10.6 ± 5.14	14.6 ± 4.78	15.4 ± 5.27	14.2 ± 4.73	**<0.001***
	P1	**0.008***	**<0.001***	**0.034***	
	P2		0.871	0.984	
	P3			0.699	

*Significant as P value≤0.05, ANOVA (F) test with post hoc test (Tukey), X^2: Chi square test, **P1:P** value compared to Bronchial asthma group, **P2:P** value compared to Bronchiectasis group, **P3:P** value compared to COPD group.

showed the comparison between the studied groups as regard the presenting symptoms; it was insignificantly different among the studied groups. Duration of symptoms was significantly longer in bronchiectasis group, COPD group and ILD group than bronchial asthma group (P1: P value 0.008, P2: P value <0.001, P3: P value 0.034). The longest duration of symptoms was detected in COPD group and the shortest duration was detected in bronchial asthma group (P value <0.001**Table3**

Table 3: Comparison between the studied groups as regard severity of COVID 19 according to Co-RADS score of chest CT at admission.

Chest CT at admission	Bronchial asthma group (n=28)	Bronchiectasis group (n=40)	COPD group (n=51)	ILD group (n=31)	P value
CO-RADS 1	0 (0%)	0 (0%)	0 (0%)	0 (0%)	----
CO-RADS 2	0 (0%)	0 (0%)	0 (0%)	0 (0%)	----
CO-RADS 3	0 (0%)	0 (0%)	0 (0%)	0 (0%)	----
Co-RADS 4	13 (46.43%)	15 (37.5%)	25 (49.02%)	13 (41.94%)	0.752
Co-RADS 5	15 (53.57%)	25 (62.5%)	26 (50.98%)	18 (58.06%)	**<0.001***

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

showed the comparison between the studied groups as regard chest CT findings at admission, Co-RADS 5 was significantly higher in bronchiectasis and ILD than other groups (P value <0.001). **Table 4**

Table 4: Comparison between the studied groups as regard laboratory investigations.

Variable	Bronchial asthma group (n=28)	Bronchiectasis group (n=40)	COPD group (n=51)	ILD group (n=31)	P value
Hb (g/dl) Mean ± SD	13.1 ± 3.35	12.9 ± 3.3	12.4 ± 3.51	12.9 ± 4.06	0.841
WBCs (x109/L) Mean ± SD	12.9 ± 5	13.4 ± 4.79	12 ± 4.13	14.3 ± 4.91	0.180
Neutrophils (x109/L) Mean ± SD	5.6 ± 2.79	8.9 ± 3.42	8.2 ± 2.82	8.4 ± 1.92	**<0.001***
	P1	**<0.001***	**<0.001***	**0.001***	
	P2		0.656	0.863	
	P3			0.994	
Lymphocytes (x109/L) Mean ± SD	1.4 ± 0.44	1.3 ± 0.35	1.2 ± 0.45	1.2 ± 0.36	0.129
NLR Mean ± SD	4.7 ± 3.29	7.6 ± 3.56	8.1 ± 4.07	7.8 ± 2.91	**<0.001***
	P1	**0.007***	**<0.001***	**0.007***	
	P2		0.913	0.997	
	P3			0.977	
PLT (x109/L) Mean ± SD	273 ± 137.88	325.5 ± 126.94	285.3 ± 119.92	296.4 ± 118.8	0.320
CRP (ng/mL) Mean ± SD	79.6 ± 39.11	80.5 ± 40.31	80.2 ± 36.27	71.1 ± 36.25	0.704
Serum ferritin (ng/mL) Mean ± SD	458.1 ± 202	492.1 ± 232.63	410.9 ± 214.63	410.8 ± 212.99	0.269
D-dimer (ng/mL) Mean ± SD	3645.5 ± 2975.25	5352 ± 3257.72	4358.8 ± 3122	4593.8 ± 2692.74	0.148
LDH (U/L) Mean ± SD	552.2 ± 126.71	510.8 ± 154.84	509.1 ± 147.01	503.2 ± 114.87	0.511
ALT (U/L) Mean ± SD	44.5 ± 17.94	43.5 ± 17.4	48.8 ± 17.38	42.9 ± 16.4	0.371
AST (U/L) Mean ± SD	33.7 ± 12.51	33.3 ± 12.05	31.2 ± 12.88	30 ± 11.7	0.567
Na+ (mmol/L) Mean ± SD	136.2 ± 8.12	135.8 ± 9.96	135 ± 9	134.5 ± 8.82	0.883
K+ (mmol/L) Mean ± SD	4 ± 0.86	4.2 ± 0.8	4.1 ± 0.78	4 ± 0.81	0.733
Ca++ (mmol/L) Mean ± SD	1 ± 0.24	1.2 ± 0.28	1.1 ± 0.27	1 ± 0.24	**0.032***
	P1	0.236	0.774	0.841	
	P2		0.665	**0.026***	
	P3			0.218	
Prothrombin time (sec) Mean ± SD	14.6 ± 2.48	14.8 ± 2.41	15.3 ± 2.42	14.8 ± 2.27	0.620
Prothrombin concentration (mg/L) Mean ± SD	1 ± 0.17	0.9 ± 0.17	0.9 ± 0.16	1 ± 0.17	0.217
INR Mean ± SD	1.2 ± 0.17	1.3 ± 0.19	1.2 ± 0.17	1.2 ± 0.16	0.700

*Significant as P value≤0.05, ANOVA (F) test with post hoc test (Tukey), **P1:P** value compared to Bronchial asthma group, **P2:P** value compared to Bronchiectasis group, **P3:P** value compared to COPD group, **Hb:** Hemoglobin, **WBCs**: white blood cells, **PLT**: Platelets, **CRP**:C-reactive protein, **LDH**: Lactate dehydrogenase, **ALT**: Alanine Aminotransferase, **AST**: aspartate aminotransferase, **INR**: international normalized ratio.

showed the comparison between the studied groups as regard laboratory findings at admission, neutrophils and NLR were significantly higher in bronchiectasis group, COPD group and ILD group than bronchial asthma group (P value<0.001). Calcium **(Ca++)** was significantly higher in bronchiectasis group than other groups (P value<0.032). **Table 5**

Table 5: Comparison between the studied groups as regard ABG analysis.

Variable	Bronchial asthmagroup (n=28)	Bronchiectasis group (n=40)	COPD group (n=51)	ILD group (n=31)	P value
$PaCO_2$ (mmHg) Mean ± SD	52.7 ± 19.24	55.8 ± 16.09	57.9 ± 16.42	60.1 ± 18.48	0.385
PaO_2 (mmHg) Mean ± SD	63.8 ± 18.81	62.7 ± 17.74	66.5 ± 20.4	60.9 ± 17.79	0.587
HCO_3 (mEq/L) Mean ± SD	20.5 ± 2.81	21.6 ± 4.18	20.9 ± 3.53	22.7 ± 3.31	0.073
O_2 saturation (%) Mean ± SD	89.9 ± 5.6	75.9 ± 10.48	74.5 ± 14.52	76.1 ± 15.34	**<0.001***
	P1	**<0.001***	**<0.001***	**<0.001***	
	P2		0.946	1	
	P3			0.937	

*Significant as P value≤0.05, ANOVA (F) test with post hoc test (Tukey), **P1:P** value compared to Bronchial asthma group, **P2:P** value compared to Bronchiectasis group, **P3:P** value compared to COPD group.

showed the comparison between the studied groups as regard ABG analysis; O_2 saturation was significantly lower in COPD, ILD and bronchiectasis than bronchial asthma group (P value<0.001). While PaCO2, PaO2 and HCO3 values were insignificantly different among the four groups. Table 6

Table 6: Comparison between the studied groups as regard disease severity (According to WHO classification, 2020).

Variable	Bronchial asthma group (n=28)	Bronchiectasis group (n=40)	COPD group (n=51)	ILD group (n=31)	P value
Mild	0 (0%)	0 (0%)	0 (0%)	0 (0%)	-----
Moderate	20 (71.43%)	18 (45%)	17 (33.33%)	17 (54.84%)	**0.01***
Severe	8 (28.57%)	22 (55%)	34 (66.67%)	14 (45.16%)	
	P1	**0.046***	**0.002***	0.281	
	P2		0.284	0.477	
	P3			**0.033***	

*Significant as P value≤0.05, X^2: Chi square test, **P1: P** value compared to Bronchial asthma group, **P2:P** value compared to Bronchiectasis group, **P3:P** value compared to COPD group.

showed the comparison between the studied groups as regard distribution of disease severity according to WHO classification (2020), severe cases were significantly higher in COPD group than other groups (P value<0.01). **Table 7**

Table 7: Comparison between the studied groups as regard the needed O_2 therapy, NIV and MV.

Variable		Bronchial asthma group (n=28)	Bronchiectasis group (n=40)	COPD group (n=51)	ILD group (n=31)	P value
O_2 mask	**Yes**	20 (71.43%)	35 (87.5%)	40 (78.43%)	22 (70.97%)	0.295
	No	8 (28.57%)	5 (12.5%)	11 (21.57%)	9 (17.65%)	
NIV	**Yes**	13 (46.43%)	24 (60%)	30 (58.82%)	15 (48.39%)	0.557
	No	15 (53.57%)	16 (40%)	21 (41.18%)	16 (31.37%)	
MV	**Yes**	3 (10.71%)	6 (15%)	9 (17.65%)	5 (16.13%)	0.876
	No	25 (89.29%)	34 (85%)	42 (82.35%)	26 (50.98%)	

*Significant as P value≤0.05, X^2: Chi square test, **NIV**: Non-invasive ventilation, **MV**: mechanical ventilation

showed the comparison between the studied groups as regard the utilized O2 therapy, NIV and MV. There was no significant difference in the type of used O_2 therapy, NIV and MV among the studied groups. **Table 8**

Table 8: Comparison between the studied groups as regard the duration of hospital stay and prognosis

Variable		Bronchial asthma group (n=28)	Bronchiectasis group (n=40)	COPD group (n=51)	ILD group (n=31)	P value
Hospital stays (days)	Mean ± SD	7.6 ± 2.81	7.9 ± 2.96	7.5 ± 2.38	7.7 ± 3.41	0.907
Prognosis	Improved	22 (78.57%)	21 (52.5%)	22 (43.14%)	10 (32.26%)	**0.003***
	Died	6 (21.43%)	19 (47.5%)	29 (56.86%)	21 (41.18%)	
	P1		**0.041***	**0.004***	**0.006***	
	P2			0.404	0.098	
	P3				0.359	

*Significant as P value≤0.05, ANOVA (F) test with post hoc test (Tukey), X^2: Chi square test, **P1:P** value compared to Bronchial asthma group, **P2:P** value compared to Bronchiectasis group, **P3:P** value compared to COPD group.

showed the comparison between the studied groups as regard the duration of hospitalization, it was insignificantly different among the four groups. As regard Prognosis, improved cases were significantly higher in bronchial asthma group than other groups (P value=0. 003), while died cases in hospital were significantly higher in COPD group than other groups (P value=0. 004) **Table 9**

Table (9): Comparison between improved and died cases during hospitalization.

Variable	Improved cases (75 pt.)	Died cases (75 pt.)	P value
Age (years)*	57.4± 15.5	56.4± 7.6	0.72
Gender			
Male	39(52)	33(44)	0.41
Female	36(48)	42(56)	
Smoking			
Non-smoker	44(58.7)	25(33.3)	**0.003**
Ex-smoker	9(12.0)	22(29.3)	
Current smoker	22(29.3)	28(37.3)	
Comorbidity			
DM	21(28.0)	27(36.0)	
Hypertension	22(29.3)	25(33.3)	**0.045**
IHD	17(22.7)	9(12.0)	
CKD	10(13.3)	3(4.0)	
Duration of symotoms(days)*	13.6± 5.57	14.6±4.89	0.24
Chest Ct on admission			
CORAD 4	30(40)	36(48)	0.32
CORAD 5	45(60)	39(52)	
Type of CRD:			
Bronchial Asthma	22 (29.3)	6 (8)	
Bronchiectasis	21(28)	19 (25.3)	**0.002**
COPD	22(29.3)	29 (38.7)	
ILD	10 (13.3)	21(28)	

T: Student t test, **CRD**: chronic respiratory disease. X2: Chi square test

showed the comparison between improved patients (75 cases) and those who died in hospital as regard age, sex, smoking status, presence of comorbidity, duration of symptoms, chest CT findings at admission and the type of CRD. It illustrated that, the type of CRD disease was significantly related to poor outcome as mortality rate was higher in COPD group followed by ILD group then bronchiectasis group and finally bronchial asthma group (P value=0. 002). Age, sex, duration of symptoms and chest CT findings at admission were insignificantly different between improved and died cases in hospital. Smoking significantly affect the poor outcome and death as current smokers and Ex- smokers were higher in died cases than improved cases (P

value=0. 04). The presence of comorbidity was significantly related to poor outcome as died cases had high incidence of DM and hypertension than improved cases (P value=0. 045). **Table (10)**

Table (10): Comparison between improved and died patients during hospitalization as regard laboratory finding.

Variable	Improved cases (75 pt.)	Died cases (75 pt.)	P value
Hb (g/dl)	12.8± 3.47	12.7± 3.6	0.89
WBCs (x109/L)	13.2± 4.69	12.9±4.68	0.68
Neutrophils (x109/L)	6.36± 2.51	9.59± 2.64	**< .001**
Lymphocytes (x109/L)	1.47± 0.348	1.02±0.341	**< .001**
Neutrophil-Lymphocyte ratio	4.55± 1.94	10± 3.08	**< .001**
PLT(x109/L)	281± 120	311± 130	0.14
CRP(ng/mL)	76.4± 37.4	80.2± 38.2	0.54
Serum Ferritin (ng/mL)	432± 200	451± 235	0.58
D-dimer(ng/mL)	3957± 2874	5122±3176	**0.02**
LDH(ng/mL)	511± 142	522± 137	0.62
AST (U/L)	33.8± 11.6	30.1± 12.8	0.05
ALT(U/L)	43.1± 16.5	47.6± 17.9	0.11
Na+ (mmol/L)	136± 8.62	135± 9.42	0.63
K+ (mmol/L)	4.15± 0.811	4.02±0.791	0.33
Ca++ (mmol/L)	1.1± 0.284	1.03± .252	0.11
Prothrombin time (sec)	14.6± 2.41	15.2± 2.34	0.11
Prothrombin concentration (mg/L)	0.944± 0.169	0.919±0.168	0.37
INR	1.23± 0.18	1.24± 0.166	0.82
SO2 (%)	80.2± 13.7	75.9± 13.3	**0.05**
PaCo2(mmHg)	54.9±18.9	58.8±15.5	0.17
PaO2(mmHg)	62.5± 18.9	65.2± 18.8	0.38
HCO3(mEq/L)	20.8± 3.28	21.9± 3.84	**0.049**
Hospital stay (days)	7.8± 3.04	7.52± 2.61	0.54

Student t-test was used

illustrated the comparison between improved cases (75 cases) and those who died during hospitalization as regard the laboratory findings. It showed that

As regard CBC findings, neutrophils were significantly higher (P value<0.001) while lymphocytes were significantly lower (P value<0.001) in died cases than improved cases. Neutrophil-Lymphocyte ratio (NLR) was significantly higher in died cases than improved (P value<0.001). As regard inflammatory markers, D dimer was significantly higher in died cases than improved cases (P value=0.02).Comparison between died and improved cases as regard ABG analysis, showed higher level of HCO3 in died cases than improved (P value =0.04) and SO2 was significantly lower in died cases (P value =0.05). **Table (11)**

Table (11): Binomial logistic regression for predictors of hospital mortality in the studied population.

	95% Confidence Interval				
Predictor	**E**	**Lower**	**Upper**	**P value**	**Odds ratio**
Bronchia Asthma	-0.84	-3.31	1.61	0.5	0.42
Bronchiectasis	1.77	-0.24	3.78	0.048	5.87
Smoking "current smoker"	1.82	-0.201	3.83	0.04	6.16
Diabetes Mellitus	-3.69	-7.71	0.31	0.042	0.02
Chronic kidney disease	-5.45	-10.36	-0.55	0.029	0.004
Neutrophils (x109/L)	-0.073	-1.16	1.01	0.89	0.92
Lymphocytes (x109/L)	0.159	-7.25	7.57	0.96	1.17
Neutrophil-Lymphocyte Ratio	-1.44	-2.95	0.055	0.059	0.23
D-dimer (ng/mL)	-3.73	-6.94	-5.16	0.023	0.99
AST(U/L)	0.045	-0.021	0.11	0.181	1.04
HCO3(mEq/L)	-0.27	-0.54	-0.011	0.041	0.75
O2 saturation (%)	0.048	-0.008	0.11	0.09	1.049
NIV	0.89	-0.62	2.42	0.24	2.45

Model fit measures: R^2 0.71

illustrated the binomial logistic regression analysis for predictors of mortality in the studied population. It showed that the presence of bronchiectasis in association with COVID 19 is associated with higher risk of mortality (Odd ratio 5.87, 95% CI -0.24 to 3.78). Current smokers are at higher risk of mortality in the studied population (Odd ratio 6.16, 95% CI -0.201 to 3.83).The presence of comorbidities was one of the predictors of mortality in our study; DM (Odd ratio 0.02, 95% CI -7.71 to 0.31) and CKD (Odd ratio 0.004, 95% CI -10.36 to -0.55) were more detected in died cases. High level of D dimer was one of the predictors of mortality (Odd ratio 0.99, CI 95% -6.94 to -5.16). High level of HCO3 was associated with higher mortality (Odd ratio 0.75, CI 95% -0.54 to -0.011). In the Odds ratio analysis, having bronchiectasis and current smoking increased the odds for mortality by about 5 and 6 times respectively. For those significant predictors, the ROC curve analysis showed Accuracy of 0.92, Specificity of 0.93, Sensitivity of 0.9 and AUC of 0.98 "**figure 1**"

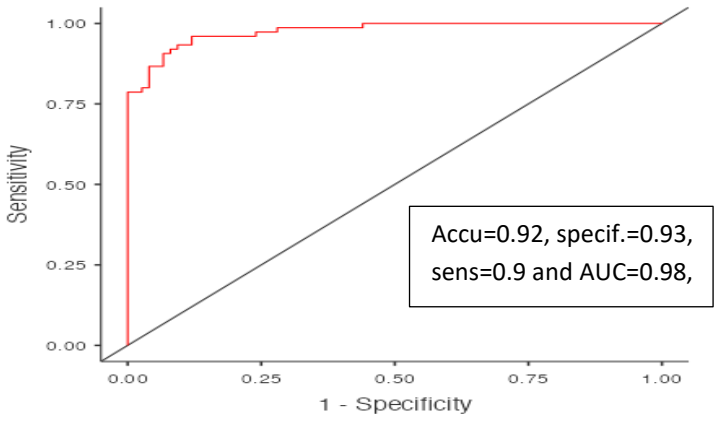

Figure (1) : the ROC curve analysis for the significant predictors for hospital mortality

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Review Article

Discussion:

The COVID-19 outbreak posed a significant obstacle to scientific research on CRDs, whose impact has also been significant worldwide. There is growing worry that individuals with a history of CRDs may be more vulnerable to a severe COVID-19 infection, which could result in mortality.

In our study, we are concerned with illustration of the clinical characteristics and factors associated with high morbidity and mortality among different categories of CRDs associated with COVID 19 to allow the proper management of population at risk and improve outcome. The study population included 150 cases of COVID 19 with CRDs and it was divided into four groups: bronchial asthma (n=28), bronchiectasis (n=40), COPD (n=51) and ILD (n=31).

According to our study, most of the cases were in COPD group and smoking was significantly higher in COPD group than other groups. Smoking, which represents the most important risk factor for COPD, is also an established risk factor for COVID-19 infection. The meta-analysis of patients with COVID-19 found that 7.63% of the patients were smokers. [8] Further work investigating the effect of COPD and smoking in patients with severe COVID-19 infection showed that smokers were 1.98 times more likely to have severe infection as compared with nonsmokers. In the same meta-analysis, there was a 4.38-fold increased risk of severe COVID-19 in patients with COPD. [9]

In our study as regard comorbidities, DM was detected in 48 cases, HTN in 47 cases, IHD in 26 cases, CKD in 13 cases and malignancy in 16 cases. Incidence of DM and hypertension was higher in COPD group, while the incidence of IHD and CKD was higher in bronchiectasis group and malignancy was detected more in COPD and ILD group.

For those who are 50 years of age or older, hypertension (HTN) is the most prevalent condition **[10].** Following COVID-19 infection, individuals with cardiovascular disease (CVD), such as HTN, have a higher risk of hospitalization, according to epidemiological research **[11].** According to a study by **Wu C et al., (2020)**, the most common comorbidities (8%) among patients infected with COVID-19 were hypertension (30%) and coronary heart disease (20%). [12] Increased Ang-II levels in COVID-19-infected hypertensive patients cause vasoconstriction, which subsequently exacerbates the hypertension situation. [13]

In a clinical study by **Guan W j et al., (2020),** out of a group of 52 COVID-19 patients receiving intensive care, 32 of them died, and the most common underlying comorbidity in these cases was diabetes . [14] In the same study, 140 COVID-19 hospitalized patients in Wuhan revealed that diabetes (12.1%) was the second most common comorbidity after hypertension. [14]

Numerous research investigations have documented elevated mortality among COVID-19 patients who had diabetes, which may be linked to hyperglycemia. Diabetes-related hyperglycemia facilitates the non-enzymatic glycosylation of lung collagen and elastin by advanced glycation end products. This reduces lung elasticity and lowers pulmonary capillary blood volume and diffusing capacity, all of which have an impact on the patient's overall prognosis. [15] Hyperglycemia, even for a short while, can change immune cell activity **[16].** Patients with diabetes may be more vulnerable to cytokine storms, according to a research by **Webb Hooper M et al., (2020)** [17] .This could become even more heightened in reaction to a stimulus, as in individuals infected with COVID-19.

In our study, there was no difference in the presenting manifestations between the studied groups of CRD but the duration of symptoms was significantly longer in the groups of bronchiectasis, COPD and ILD than bronchial asthma. The longest duration of symptoms was detected in COPD group which may be attributed to that patient can not differentiate between symptoms related to their chronic underlying symptoms, or COPD acute exacerbation from manifestations of COVID 19 plus the presence of

multiple comorbidities in the COPD group cases. Testing for SARS-CoV-2 should be taken into consideration if there is a suspicion of COVID-19 [18].

According to our study, the comparison between the studied groups as regard chest CT findings at admission revealed that Co-RADS 5 was significantly higher in bronchiectasis and ILD than other groups which can be explained by the pathology of the underlying category of CRD. 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 [19].

In our study, as regard ABG analysis; O_2 saturation was significantly lower in COPD, ILD and bronchiectasis than bronchial asthma group while PaCO2, PaO2 and HCO3 were insignificantly different among the four groups. There was no significant difference as regard the need for O_2 therapy, NIV and MV among the studied groups

The comparison between the studied groups as regard the laboratory findings revealed that neutrophils and NLR were significantly higher in Bronchiectasis group, COPD group and ILD group than Bronchial asthma group, which indicated that severity of infection is less in bronchial asthma group than other groups. COPD group showed the highest severity of COVID 19 infection and the worst prognosis which may be explained by the pathophysiological changes of the lungs resulting from the effect of COPD, effect of smoking which was high in this category of CRD and the associated highest incidence of comorbidities.

COPD has continuously been linked to a higher chance of unfavorable COVID-19 outcomes [20-24]. Smokers and COPD patients have high expression levels of ACE2 in their small airway epithelium, which suggests that both conditions increase the likelihood of COVID-19 side effects[23-25]. This finding is consistent with a study by **Kilic H et al., (2022)** that found lung cancer, ILD, and COPD to be related to greater mortality [26] In contrast, earlier researchs have found that asthma and bronchiectasis are poorer prognostic variables [27–29]

In patients with COVID-19, bronchiectasis was a risk factor for hospitalization but not for ICU admission or mortality [22], and the Chinese nationwide database [30]. did not reveal any conclusive link between bronchiectasis and the unfavorable outcomes of COVID-19. In contrast to COPD, bronchiectasis is characterized by type 1-skewed airway inflammation; nevertheless, infections with other bacteria, such as Pseudomonas aeruginosa and Haemophilus influenzae, are more common [30].

New evidence suggests that interstitial lung disease is a negative prognostic indicator for individuals diagnosed with COVID-19 [31] The International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC) conducted a study to assess the mortality risk in COVID-19 patients with interstitial lung diseases. The findings revealed that individuals with more severe restriction experienced higher rates of mortality [32].

Individuals with ILD are at a high risk of infection by COVID-19. This increased susceptibility may result from the fact that patients with ILD are more prone to viral infections [33]. which can trigger an inflammatory response in the lung tissues. Additionally, individuals with ILD frequently experience symptoms of dyspnea [34]. which can make it challenging for them to wear masks. The lack of adherence to mask-wearing among ILD patients could potentially raise their risk of COVID-19.

Our study agreed with the previous studies in the absence of significant association between asthma and increased risk or poor prognosis of COVID-19 infection.[22] In spite of finding that respiratory viral infections are major causes of asthma exacerbation.[35] In contrast to our study, a study from Korea including ~220,000 participant revealed a greater susceptibility to contracting SARS-CoV-2 among asthmatic patients (OR, 1.07; 95%CI,1.00–1.15) and developing adverse clinical outcomes (OR, 1.62; 95%CI, 1.01–2.67) compared with those without asthma.[36]

The correlation between asthma and COVID-19 is influenced by the severity of asthma. According to the ISARIC study, individuals with severe asthma were the only cases who showed a notable rise in the risk of mortality when compared to those

without asthma [adjusted hazards ratio, 1.96; 95%CI, 1.25–3.08].[21] In a comprehensive analysis.[37] that examined 18 studies on COVID-19 infection in individuals with comorbid asthma, the researchers discovered that asthma was present in 2.3% (1873/81,319) of patients with severe COVID-19 and in 2.2% (11,796/538,737) of patients with non-severe COVID-19. Notably, data from China **[20]** indicated a relatively low prevalence of asthma among COVID-19 patients, suggesting a potential protective effect mediated by TH2 response in individuals with asthma. It is worth mentioning that COPD is primarily associated with type 1 airway inflammation, whereas asthmatic patients exhibited a reduced expression of angiotensin-converting enzyme 2 (ACE2) due to the prevalence of type 2-skewed inflammation [23].

In our study, the logistic regression analysis showed that predictors of mortality in cases with CRD infected with COVID 19 included the presence of bronchiectasis as a subtype of CRD, current smoking, DM, CKD, low O2 saturation, high D-dimer and high HCO3. The association of bronchiectasis and current smoking increased the odds for mortality by about 5 and 6 times respectively. The findings can help us to give special care to patients with the previous criteria to decrease the mortality rate and improve outcome.

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. Further research is required about severity of asthma exacerbation and comparison between received treatments in different groups of CRD to determine their effect on COVID 19 infection outcome.

Conclusion:

Chronic respiratory diseases have a potent impact on COVID 19 severity and outcome. Severity of infection and mortality were the highest in COPD cases. The absence of significant association between bronchial asthma and increased risk or poor prognosis of COVID-19. Factors associated with higher mortality included bronchiectasis as subtype of CRD, current smoking, the association of DM and CKD as comorbidities, low O2 saturation, high D-dimer and high HCO3 values.

Abbreviations:

COVID-19; the coronavirus disease 2019, **SARS-CoV-2**; severe acute respiratory syndrome coronavirus 2, **CRDs**; chronic respiratory diseases, **CRF**; chronic respiratory failure, **COPD**; chronic obstructive pulmonary disease, **ILDs**; interstitial lung diseases, **CF**; cystic fibrosis, **ARDS**; acute respiratory distress syndrome, **PCR**; Polymerase Chain Reaction, **BMI**; body mass index, **DM**; diabetes mellitus, **CKD**; chronic kidney disease, **ISARIC**; The International Severe Acute Respiratory and Emerging Infection Consortium and **ACE2**; angiotensin-converting enzyme 2.

Declarations:

- **Ethics approval and consent to participate**: The study received its approval by the Sohag Faculty of Medicine's Medical Research Ethics Committee, and it was 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 authors confirm that all data supporting the findings of this study are available within the article, its supplementary material, and upon reasonable request.
- **Competing interests**: The authors declare that they have no conflict of interest
- **Funding**: Non
- **Authors' contributions:** **SN** and **HA** contribute to the conceiving of the study and its design; **MM**, **SN** and **AH** conducted of the study and administrative support and collected clinical data; **SN** conducted data analyses and figures designs. All authors wrote the manuscript. All authors provided clinical input and collected and interpreted the data, read, critically reviewed, and edited the manuscript and approved of the final version.
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