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Impact of comorbid pulmonary disease on COVID-19 disease severity and outcome: a retrospective cohort study

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Abstract

Background Identifying patients with comorbid pulmonary disease may guide prognosis and aid in developing strategies regarding who would benefit the most from vaccines. This study was designed to clarify the influence of comorbid lung disease on COVID-19 severity and outcome.

Methods This is a retrospective cohort analysis of 587 COVID-19 patients. The clinical, laboratory, and imaging data and comorbidities as reported by the patients were obtained from the Kasr Alainy Hospital medical records. Also, data regarding whether the patient is hospitalized or not, the length of hospital stay, complications, and mortality are gathered from the records.

Results The patients' mean ages are 51 ± 15 years (63.9% are males with the remaining 36.1% which are females). Patients with chronic comorbid pulmonary diseases represented 113 patients among the whole study population. with the COPD being 11.4%. Patients with comorbid lung diseases associated or not with other comorbidities were at higher risk of acquiring severe COVID-19 and had higher complication and mortality rates compared to patients without comorbidities (*p-value* < *0.001*). Patients with preexisting diabetes, hypertension, COPD, and chronic kidney disease have a significantly higher risk of severe infection (*p-value* < *0.001*, *0.001*, *0.001*, < *0.001*), complications (*p-value 0.038*, *0.005*, < *0.001*, < *0.001*), and mortality (*p-value 0.021*, *0.001*, < *0.001*, < *0.001*), respectively.

Conclusion This study provides a better understanding of COVID-19 patients with comorbid lung disease and highlights the importance of the data deduced from our study and similar studies in aiding the designation of vaccination programs for those patients if needed.

Keywords Comorbidities, Comorbid lung disease, COPD, COVID-19, Vaccines

Background

The pandemic of coronavirus disease (COVID-19) has seriously struck those with underlying comorbidities [1]. This substantial group of patients with chronic comorbidities is at higher risk of acquiring a more severe COVID-19 and are more prone to rapid deterioration as well as unfavorable disease outcomes including the development of complications and death [2].

It is of note that the majority of hospitalized COVID-19 patients have self-reported a minimum of one underlying chronic health condition, with hypertension, diabetes, malignancy, and chronic obstructive pulmonary disease (COPD) being the most commonly reported comorbidity [3].

Patients with any comorbid lung condition especially COPD have a higher risk for severe illness and are likely to have a worse prognosis and poor outcomes such as

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ARDS leading to an increased risk of mortality. The risk of SARS-CoV-2 infection and mortality in COPD patients is observed to be fourfold exceeding patients without COPD [2, 4]. Accordingly, it is of particular importance to identify COVID-19 patients with underlying comorbid pulmonary disease, especially patients with COPD. Mucus overproduction, systemic inflammation, and bacterial colonization, in addition to inhaled steroid intake, and smoking status are all acknowledged factors contributing to weakening immune responses in those patients [5].

Knowledge gathered concerning this susceptible group of patients with poor pulmonary reserve is still limited regarding their vulnerability to COVID-19 infection and its effect on its course. So, the authors of this research aim to identify the influence of COVID-19 on patients with comorbid lung disease regarding disease severity and outcome, hopefully aiding the medical sector while developing policies regarding those who would benefit the most from the vaccines.

Methods

Study design and participants

This is a retrospective cohort study of 587 SARS-CoV-2-infected patients identified with real-time polymerase chain reaction swabs, seeking medical help at the Kasr Al-Ainy Hospital, an authorized center to treat COVID-19 patients between June 1, 2020, and June 30, 2021.

COVID-19 severity is determined via the World Health Organization (WHO) classification as mild, moderate, severe, and critical with mild and moderate being the non-severe forms of the disease. The defining criteria for mild, moderate, severe, and critical COVID are as follows: mild in patients demonstrating clinically no signs of consolidation and hypoxemia, moderate COVID-19 in those with signs of consolidation but still no hypoxemia, and severe in those with signs of severe consolidation, with signs of severe respiratory distress, or tachypnea more than 30 breaths/min or their saturation of oxygen on room air is less than 90%, whereas critical infection in patients in need of life support measures as mechanical ventilation and/or vasopressors in their management [6].

Data collection

By referring to the hospital records, the extracted data from hospital medical records included patients' demographics, presenting symptoms, comorbidities as reported by the patient on admission and confirmed by the patient's previous medical records, oxygen saturation, laboratory results on admission including CBC (complete blood count), CRP (C-reactive protein) with titer, ferritin, and D-dimer, chest radiological findings upon admission. Also, data regarding whether the patient is hospitalized or not, ICU (intensive care unit) admitted or not, and the length of hospital stay, as well as the development of complications and mortality, is gathered from the medical records.

Comorbidities are sorted based on the system affected, and this permits grouping of chronic pulmonary diseases and merging them all into a single category.

The study population is initially categorized based on the presence or absence of comorbidities and then subcategorization of patients with comorbidities into three groups: group 1: patients with comorbid lung disease not associated with other comorbidities, group 2: patients with comorbid lung disease associated with other comorbidities, and group 3: patients with comorbidities other than comorbid lung disease.

Statistical analysis

The Statistical Package for Social Science version 24 is used for the analysis of data. Mean and standard deviation are used for the numerical variables, while frequencies and percentages are applied for categorical ones. Analysis of variance (ANOVA) is used to compare between groups. Post hoc test is applied for normally distributed quantitative variables, while the Kruskal–Wallis test and Mann–Whitney test were used for non-normally distributed quantitative variables. For comparing categorical data, a chi-square (χ^2) test was performed. *P*-values less than 0.05 were considered statistically significant.

Ethics approval

This research is revised by the institutional review board and accepted by the research ethics committee, at Cairo University (no. 101–2022) dated 24 December 2022. The policy of data confidentiality is firmly followed.

Results

Demographics of the studied patients

This research included 587 COVID-19 patients. Their mean age is 51 ± 15 years. The study included 375 males (63.9%) and 212 females (36.1%). Four-hundred thirty-five (74.1%) had nonsevere SARS-CoV-2 infection, and 152 (25.9%) had a severe and critical infection. Three-hundred sixty-four (62%) patients were hospitalized, and the length of hospital stay was 8 ± 4 days. One-hundred fifty (25.5%) patients needed intensive care unit (ICU) admission (Table 1).

Table 1 Demographics and clinical characteristics of the study population

(*n* = 587)		
Age (mean ± SD)		51 (± 15)
Gender (*n*, %)	Males	375 (63.9%)
	Females	212 (36.1%)
The severity of COVID-19 infection (*n*, %)	Non-severe	435 (74.1%)
	Severe and critical	152 (25.9%)
Site of admission (*n*, %)	Not hospitalized	223 (38%)
	Ward	214 (36.5%)
	ICU	150 (25.5%)
Duration of hospital stay (mean ± SD)		8 (4)
Occurrence of complications (*n*, %)	Yes	84 (14.3%)
	No	503 (85.7%)
Complications (*n*, %)	Invasive mechanical ventilation	66 (11.2%)
	ARDS	36 (6.1%)
	Pulmonary embolism	6 (1%)
	Secondary bacterial lower respiratory tract infection	40 (6.8%)
	Septic shock	16 (2.7%)
	Acute kidney injury	22 (3.7%)
	Hepatic encephalopathy	1 (0.2%)
Mortality (*n*, %)		58 (9.9%)
Laboratory data (median, IQR)		
TLC (/cmm)		6.5 (4.57–10.15)
Lymphocytes count (/μL)		1.4 (0.9–2.1)
Platelets (/μL)		250 (197–325)
CRP (mg/L)		39 (11–96)
Ferritin (ng/mL)		334 (126–896)
D-dimer (μg/mL)		0.6 (0.3–1.1)

SD standard deviation, *TLC* total leucocyte count, *CRP* reactive protein, *ARDS* acute respiratory distress syndrome, *ICU* intensive care unit

Patients with chronic comorbid pulmonary diseases represented 113 patients among the whole study population as shown in Table 2.

Frequency of comorbidities among the whole study population

Hypertension represented the most common comorbidity in our patients 157 (26.7%), followed by diabetes (25.4%), then obesity (15.5%), and COPD (11.4%). The distribution of other comorbidities among the whole study group is shown in Table 2.

Characteristics of patients with comorbid pulmonary disease associated or not with other comorbidities as compared to patients without comorbidities concerning the severity of COVID-19

Patients with comorbid chronic lung disease associated or not with other comorbidities had a significantly higher COVID-19 severity when compared to patients without comorbidities ($p < 0.001$) (Fig. 1) (Table 3).

Characteristics of patients with comorbid pulmonary disease associated or not with other comorbidities as compared to patients without comorbidities concerning the frequency of complications

Patients with comorbid chronic lung disease associated or not with other comorbidities had a statistically significant higher frequency of complications in comparison to patients without comorbidities ($P < 0.001$). ARDS and mechanical ventilation, chest infection, and acute kidney injury were significantly higher in patients with comorbid chronic lung disease associated or not with other comorbidities as compared to patients without comorbidities ($p\ 0.003$, $p < 0.001$, $p < 0.001$, $p < 0.001$) (Fig. 1) (Table 3).

Characteristics of patients with comorbid pulmonary disease associated or not with other comorbidities as compared to patients without comorbidities concerning mortality

Patients with comorbid chronic lung disease associated or not with other comorbidities had a significantly

Table 2 Frequency of comorbidities among the whole study population

(*n* = 587) (*n*, %)		
Comorbidities	**With**	353 (60.1%)
	Without	234 (39.9%)
Type of comorbidity		
Autoimmune diseases		16 (2.7%)
Obesity		91 (15.5%)
Endocrinal diseases	Diabetes	149 (25.4%)
	Thyroid disease[a]	10 (1.7%)
Chronic lung disease		113 (19.2%)
Bronchial asthma		21 (3.6%)
COPD		67 (11.4%)
Bronchiectasis		1 (0.2%)
Pulmonary hypertension		23 (3.9%)
ILD		3 (0.5%)
OSA		2 (0.3%)
Venous thromboembolism[b]		6 (1%)
Chronic liver disease		11 (1.9%)
Chronic renal disease		21 (3.6%)
Cardiovascular diseases	Coronary artery disease	35 (6%)
	Hypertension	157 (26.7%)
Malignancy		15 (2.6%)
Neurological disorders	Parkinson disease	2 (0.3%)
	Multiple sclerosis	1 (0.2%)
	Epilepsy	1 (0.2%)

COPD chronic obstructive pulmonary disease, *OSA* obstructive sleep apnea, *ILD* interstitial lung disease, [a]eight hypothyroid and two hyperthyroid patients, [b]one patient with DVT 2 months before COVID, one patient with chronic sagittal sinus thrombosis, four patients with chronic thromboembolism

higher mortality rate when compared to patients without comorbidities ($p < 0.001$) (Fig. 1) (Table 3).

Characteristics of patients with comorbid pulmonary disease associated or not with other comorbidities as compared to patients without comorbidities concerning laboratory data

Patients with comorbid chronic lung disease (CLD) associated or not with other comorbidities had significantly higher CRP, ferritin, and d-dimer serum levels when compared to patients without comorbidities (*p 0.003*, *p 0.003*, $p < 0.001$) respectively. Other labs showed no significance as outlined in Table 3.

Characteristics of patients with different comorbidities concerning the severity of infection, complications, and mortality

Patients with preexisting diabetes, hypertension, COPD, and chronic kidney disease have a significantly higher risk of severe and critical infection (*p-value* < 0.001, *0.001*, *0.001*, < 0.001, respectively), complications (*p-value 0.038*, *0.005*, < 0.001, < 0.001, respectively), and mortality (*p-value 0.021*, *0.001*, < 0.001, < 0.001, respectively). On the contrary, other comorbidities such as autoimmune, hepatic or thyroid diseases, bronchial asthma, pulmonary hypertension (PHTN), and malignancy did not show significant severity of infection, complications, and mortality (Table 4).

Discussion

Several comorbid diseases increase the severity and risk of mortality in COVID-19 [7]. The presence of diabetes, hypertension, malignancies, cardiovascular

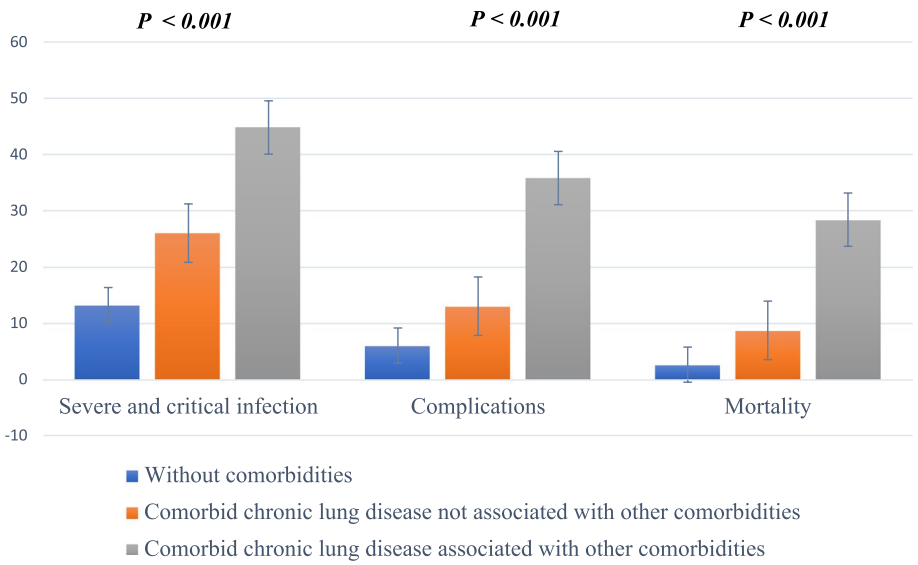

Fig. 1 Comparative statistical analysis between COVID-19 patients without comorbidities and patients with comorbid chronic lung disease associated or not with other comorbidities regarding the severity of COVID-19 and outcome

Table 3 Comparative statistical analysis between COVID-19 patients without comorbidities and patients with comorbid chronic lung disease associated or not with other comorbidities

		Without comorbidities (*n* = 234)	Comorbid chronic lung disease (*n* = 113)		*p*-value
			Not associated with other comorbidities (*n* = 46)	Associated with other comorbidities (*n* = 67)	
Age (mean ± SD)		44 ± 14	46 ± 17	62 ± 12	< 0.001
Gender (*n*, %)	**Males**	157 (67%)	29 (63%)	54 (80%)	0.07
	Female	77 (33%)	17 (37%)	13 (20%)	
The severity of COVID-19 infection (*n*, %)	**Non-severe**	203 (86.7%)	34 (74%)	37 (55.2%)	< 0.001
	Severe and critical	31 (13.2%)	12 (26%)	30 (44.8%)	
ICU admission (*n*, %)		31 (13.2%)	12 (26%)	30 (44.8%)	< 0.001
Duration of hospital stay (mean ± SD)		6 ± 2.6	8 ± 4	9 ± 5	< 0.001
Occurrence of complications (*n*, %)		14 (6%)	6 (13%)	24 (35.8%)	< 0.001
Complications (*n*, %)	Invasive MV	7 (3%)	5(10.8%)	20 (29.8%)	< 0.001
	ARDS	6 (2.6%)	2 (4.3%)	9 (13.4%)	0.003
	Pulmonary embolism	1 (0.43%)	0 (0%)	2 (3%)	0.144
	Chest infection	8 (3.4%)	1 (2.2%)	12 (18%)	< 0.001
	Septic shock	3 (1.3%)	1 (2.2%)	4 (6%)	0.060
	Acute kidney injury	2 (0.9%)	1 (2.2%)	10 (15%)	< 0.001
	Hepatic encephalopathy	0 (0%)	0 (0%)	0 (0%)	0.326
Outcome (*n*, %)	Survival	228 (97.4%)	42 (91.3%)	48 (71.6%)	< 0.001
	Mortality	6 (2.6%)	4 (8.7%)	19 (28.4%)	
Laboratory data (median, IQR)					
TLC (/cmm)		5.8 (4.2–8.5)	6 (4–9)	7.4 (4.5–11.7)	0.08
Lymphocyte count (/μL)		1.5 (0.92–2.1)	1.5 (0.95–2.1)	1.2 (1–1.6)	0.14
Platelets (/μL)		249 (207–319)	229 (180–320)	235 (181–285)	0.13
CRP (mg/L)		18 (5–79)	26 (9–77)	45 (17–171)	0.003
Ferritin (ng/mL)		260 (67–670)	287 (106–590)	518 (213–1237)	0.003
D-dimer (μg/mL)		0.5 (0.3–0.8)	0.5 (0.3–1)	0.8 (0.5–2)	< 0.001

SD standard deviation, *CLD* chronic lung disease, *ICU* intensive care unit, *ARDS* acute respiratory distress syndrome, *MV* mechanical ventilation, *CRP* C-reactive protein, *TLC* total leucocyte count, *P*-value < 0.05 is considered significant

diseases (CVD), and COPD, besides other comorbid diseases, places COVID-19 patients in a life-threatening situation [8].

It is of vital importance to recognize those at risk of developing severe and critical COVID-19 to implement an efficient strategy to hinder SARS-CoV-2 infection through patient isolation and early vaccination [9]. Researchers still enquire about the relationship between the presence of various comorbidities including chronic pulmonary diseases and the COVID-19 severity and outcome. Hence, the authors of this study tackled this point of research.

In the present study, hypertension is the most common comorbidity in our patients (26.7%), followed by diabetes (25.4%), then obesity (15.5%), COPD (11.4%), pulmonary hypertension (3.9%), and bronchial asthma (3.6%). This percentage is surprisingly striking as one might expect that patients with chronic pulmonary diseases, particularly COPD and asthma, would be at increased risk of COVID-19 owing to their poor pulmonary reserve and greater angiotensin-converting enzyme 2 (ACE2) receptors' expression in their lungs [10]. However, chronic pulmonary diseases are underrepresented in the studies registering comorbidities for patients with COVID-19 as compared to the global estimated prevalence of chronic pulmonary diseases in the general population [11].

Several explanations are postulated. First, this vulnerable community of patients conformed to the general lockdown measures applied during most of the study period as well as following strict preventive procedures leading to a significant reduction in SARS-CoV-2 infection [12]. Also, it is noticed that medications utilized by patients with chronic lung diseases can lessen disease manifestations as was observed in in vitro models that inhaled steroids and bronchodilators suppress viral replication and cytokine production [13].

Consistent with several previous studies, the current study shows that patients with preexisting chronic lung

Table 4 Characteristics of patients with different comorbidities in relation to the severity of COVID-19 infection, complications, and mortality

		Severe and critical infection	Complications	Mortality
Autoimmune diseases	With (*n* = 16)	1 (6.25%)	0 (0%)	0 (0%)
	Without (*n* = 571)	151 (26.4%)	84 (14.7%)	58 (10.2%)
	P-value	0.08	0.146	0.38
Obesity	With (*n* = 91)	32 (35.2%)	19 (20.8%)	12 (13.2%)
	Without (*n* = 496)	120 (24.2%)	65 (13.1%)	46 (9.3%)
	P-value	**0.028**	0.052	0.25
Diabetes	With (*n* = 149)	60 (40.3%)	29 (19.5%)	22 (14.7%)
	Without (n = 438)	92 (21%)	55 (12.5%)	36 (8.2%)
	P-value	**< 0.001**	**0.038**	**0.021**
Thyroid disease	With (*n* = 10)	2 (20%)	1 (10%)	1 (10%)
	Without (*n* = 577)	150 (26%)	83 (14.4%)	57 (9.9%)
	P-value	1	1	1
Bronchial asthma	With (*n* = 21)	7 (33.3%)	4 (19%)	3 (14.3%)
	Without (*n* = 566)	145 (25.6%)	80 (14.1%)	55 (9.7%)
	P-value	0.42	0.52	0.45
COPD	With (*n* = 67)	29 (43.2%)	22 (32.8%)	18 (26.8%)
	Without (*n* = 520)	123 (23.6%)	62 (11.9%)	40 (7.7%)
	P-value	**0.001**	**< 0.001**	**< 0.001**
PHTN	With (*n* = 23)	7 (30.4%)	6 (26%)	4 (17.4%)
	Without (*n* = 564)	145 (25.7%)	78 (13.8%)	54 (9.6%)
	P-value	0.612	0.122	0.271
Chronic liver disease	With (*n* = 11)	3 (27.3%)	2 (18.2%)	2 (18.2%)
	Without (*n* = 576)	149 (25.9%)	82 (14.2%)	56 (9.7%)
	P-value	1	0.66	0.29
Chronic renal disease	With (*n* = 21)	13 (62%)	11 (52.4%)	11 (52.4%)
	Without (*n* = 566)	139 (24.6%)	73 (12.9%)	47 (8.3%)
	P-value	**< 0.001**	**< 0.001**	**< 0.001**
Coronary artery disease	With (*n* = 35)	12 (34.3%)	9 (25.7%)	5 (14.3%)
	Without (*n* = 552)	140 (25.4%)	75 (13.6%)	53 (9.6%)
	P-value	0.24	**0.047**	0.38
HTN	With (*n* = 157)	57 (36.3%)	33 (21%)	26 (16.6%)
	Without (*n* = 430)	95 (22%)	51 (11.9%)	32 (7.44%)
	P-value	**0.001**	**0.005**	**0.001**
Malignancy	With (*n* = 15)	7 (46.6%)	4 (26.7%)	3 (20%)
	Without (*n* = 572)	145 (25.3%)	80 (14%)	55 (9.6%)
	P-value	0.07	0.25	0.12

COPD chronic obstructive pulmonary disease, *PHTN* pulmonary hypertension, *HTN* hypertension, *P*-value < 0.05 is considered significant

disease associated or not with other comorbidities have severe and critical COVID-19, ICU admission, and longer hospital stays compared to patients without preexisting comorbidities [14–17].

It is well-known that the frequent coexistence of comorbidities is associated with compromised baseline health conditions contributing to a poor prognosis as compared with no or single comorbidity [17]. The present study reveals that patients with preexisting chronic lung disease associated or not with other comorbidities have more frequent complications compared to patients without comorbidities with ARDS, mechanical ventilation, secondary bacterial infection, and acute kidney injury being the most significant complications.

The current study reveals that the mortality rate is significantly higher in patients with preexisting chronic lung disease associated or not with other comorbidities as compared to those without comorbidities. This echoes the latest report stating that patients with comorbidities such as chronic lung disease or patients with multiple

comorbid diseases have an increased risk of death [18]. This indicates that those patients have sustained lung injury, bronchial hyperactivity, and impaired natural airway immune responses [19].

In our study, the frequency of SARS-CoV-2-infected COPD patients is higher as compared to other comorbid chronic lung diseases. This could be explained by the increase of ACE2 receptors' expression in the epithelial cells mediating viral entry [20]. This finding came in line with Singh et al., who reported that COPD patients have increased COVID-19 susceptibility when compared to other comorbid lung diseases such as asthma and pulmonary hypertension [21].

Our finding that COPD patients present with a more severe infection and with significantly higher rates of complications and mortality is attributed to the lowered antiviral defense mechanisms together with the impaired natural immune responses [22].

The most important limitations of our study are its retrospective nature and the comorbidities being self-reported, so few patients might have missed reporting other comorbid conditions that they were not aware of.

Conclusion

Patients with comorbid pulmonary diseases are susceptible to a more severe COVID-19 with higher complications and mortality rates. Thus, precautions should be directed to limit SARS-CoV-2 infection along with directing future research regarding the usefulness of implementing an annual vaccination program for those patients if needed.

Abbreviations

COVID-19	The coronavirus disease
COPD	Chronic obstructive pulmonary disease
WHO	World Health Organization
ARDS	Acute respiratory distress syndrome
CBC	Complete blood count
CRP	C-reactive protein
ICU	Intensive care unit
CLD	Comorbid chronic lung disease
CVD	Cardiovascular diseases
ACE-2	Angiotensin-converting enzyme 2

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Authors' contributions

SM, shared the conception and the design of the work, drafted the work, and revised it. RE, contributed to the conception and design of the work and shared in writing the manuscript. EH, shared in the acquisition and analysis of data, shared in writing the manuscript, drafted the work, and revised it. HH, shared in patient assessment, data collection, and writing the manuscript. All authors read and approved the final manuscript. HMA, designed the study idea, the acquisition, and analysis of data, shared in writing the manuscript, drafted the work, and revised it.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

The research proposal is revised by the institutional review board and accepted by the research ethics committee, at Cairo University (no. 101–2022). The policy of data confidentiality was firmly followed. The research design followed the conditions of the revised Helsinki Declaration of biomedical ethics. The research ethics committee, at Cairo University, waived the need for informed consent.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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References

1. Li B, Yang J, Zhao F, Zhi L, Wang X, Liu L, Bi Z, Zhao Y (2020) Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. Clin Res Cardiol 109(5):531–538
2. Sanyaolu A, Okorie C, Marinkovic A, Patidar R, Younis K, Desai P, Hosein Z, Padda I, Mangat J, Altaf M (2020) Comorbidity and its impact on patients with COVID-19. SN Compr Clin Med 2(8):1069–1076
3. Malik JA, Ahmed S, Shinde M, Almermesh MH, Alghamdi S, Hussain A, Anwar S (2022) The impact of COVID-19 on comorbidities: a review of recent updates for combating it. Saudi J Biol Sci 29(5):3586–3599
4. Andreen N, Andersson LM, Sundell N, Gustavsson L, Westin J (2022) Mortality of COVID-19 is associated with comorbidity in patients with chronic obstructive pulmonary disease. Infect Dis 14:1–6
5. Toraldo DM, Conte L (2019) Influence of the lung microbiota dysbiosis in chronic obstructive pulmonary disease exacerbations: the controversial use of corticosteroid and antibiotic treatments and the role of eosinophils as a disease marker. J Clin Med Res 11(10):667
6. World Health Organization 2. Clinical management of COVID-19: interim guidance, 27 May 2020. World Health Organization; 2020.
7. Williamson EJ, Walker AJ, Bhaskaran K, Bacon S, Bates C, Morton CE, Curtis HJ, Mehrkar A, Evans D, Inglesby P, Cockburn J (2020) Factors associated with COVID-19-related death using OpenSAFELY. Nature 584(7821):430–436
8. Ejaz H, Alsrhani A, Zafar A, Javed H, Junaid K, Abdalla AE, Abosalif KO, Ahmed Z, Younas S (2020) COVID-19, and comorbidities: deleterious impact on infected patients. J Infect Public Health 13(12):1833–1839
9. Gülsen A, König IR, Jappe U, Drömann D (2021) Effect of comorbid pulmonary disease on the severity of COVID-19: a systematic review and meta-analysis. Respirology 26(6):552–565
10. Leung JM, Niikura M, Yang CW, Sin DD (2020) COVID-19 and COPD. Euro Respir J 56(2):2002108
11. Halpin DMG, Faner R, Sibila O, Badia JR, Agusti A (2020) Do chronic respiratory diseases or their treatment affect the risk of SARS-CoV-2 infection? Lancet Respir Med 8:436–438
12. Beltramo G, Cottenet J, Mariet AS, Georges M, Piroth L, Tubert-Bitter P, Bonniaud P, Quantin C (2021) Chronic respiratory diseases are predictors of severe outcome in COVID-19 hospitalized patients: a nationwide study. Eur Respir J 58(6):2004474
13. Yamaya M, Nishimura H, Deng X, Sugawara M, Watanabe O, Nomura K, Shimotai Y, Momma H, Ichinose M, Kawase T (2020) Inhibitory effects of

glycopyrronium, formoterol, and budesonide on coronavirus HCoV-229E replication and cytokine production by primary cultures of human nasal and tracheal epithelial cells. Respir Investig 58(3):155–168
14. Zhu L, She ZG, Cheng X, Qin JJ, Zhang XJ, Cai J, Lei F, Wang H, Xie J, Wang W, Li H (2020) Association of blood glucose control and outcomes in patients with COVID-19 and pre-existing type 2 diabetes. Cell Metab 31(6):1068–1077
15. Zhao Q, Meng M, Kumar R, Wu Y, Huang J, Lian N, Deng Y, Lin S (2020) The impact of COPD and smoking history on the severity of COVID-19: A systemic review and meta-analysis. J Med Virol 92(10):1915–1921
16. W-Jie G, Liang W-H, He J-X, Zhong N-S (2020) Cardiovascular comorbidity and its impact on patients with COVID-19. Eur Respir J 55:2001227
17. Guan WJ, Liang WH, Zhao Y, Liang HR, Chen ZS, Li YM, Liu XQ, Chen RC, Tang CL, Wang T, Ou CQ (2020) Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. Euro Respiratory J 55(5):2000547
18. Djaharuddin I, Munawwarah S, Nurulita A, Ilyas M, Tabri NA, Lihawa N (2021) Comorbidities and mortality in COVID-19 patients. Gac Sanit 1(35):S530–S532
19. Girardin JL, Seixas A, Ramos Cejudo J, Osorio RS, Avirappattu G, Reid M, Parthasarathy S (2021) Contribution of pulmonary diseases to COVID-19 mortality in a diverse urban community of New York. Chron Respir Dis 28(18):1479973120986806
20. Wan Y, Shang J, Graham R, Baric RS, Li F (2020) Receptor recognition by the novel coronavirus from Wuhan: an analysis based on decade-long structural studies of SARS coronavirus. J Virol 94(7):e00127-e220
21. Singh D, Mathioudakis AG, Higham A (2022) Chronic obstructive pulmonary disease and COVID-19: interrelationships. Curr Opin Pulm Med 28(2):76
22. Lippi G, Henry BM (2020) Chronic obstructive pulmonary disease is associated with severe coronavirus disease 2019 (COVID-19). Respir Med 167:105941

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