pagepress

Post-COVID-19 sequelae of the respiratory system. A single-centre experience reporting the compromise of the airway, alveolar and vascular components

Nousheen Iqbal[1,2], Iffat Khanum[1], Muhammad Ali Ibrahim Kazi[1], Syeda Urooj Riaz[2], Uzzam Ahmed Khawaja[2], Safia Awan[1], Muhammad Irfan[1], Ali Bin Sarwar Zubairi[1], Javaid Ahmed Khan[1]

[1]Department of Medicine, Aga Khan University, Karachi; [2]Department of Medicine, Jinnah Medical and Dental College, Bihar Muslim Society BMCHS Sharafabad, Karachi, Sindh, Pakistan

Correspondence: Nousheen Iqbal, Department of Medicine, Jinnah Medical and Dental College, 22-23 Shaheed-e-Millat Rd, Bihar Muslim Society BMCHS Sharafabad, Karachi City, Sindh 74800, Pakistan.
E-mail: naush.akuh@gmail.com

Key words: post COVID-19 complications; infective; non-infective; pulmonary involvement.

Contributions: all the authors made a substantive intellectual contribution. All the authors read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Conflict of interest: the authors declare no conflict of interest.

Ethics approval and consent to participate: the study protocol was approved by the Ethical Review Committee of the Aga Khan University Hospital, Karachi, Pakistan (ERC number assigned 2020-5475-14402).

Informed consent: written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article. The manuscript does not contain any individual person's data in any form.

Availability of data and materials: all data generated or analyzed during this study are included in this published article.

Received: 18 August 2022.
Accepted: 3 October 2022.
Early view: 11 October 2022.

Publisher's note: all claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article or claim that may be made by its manufacturer is not guaranteed or endorsed by the publisher.

Monaldi Archives for Chest Disease 2023; 93:2412
doi: 10.4081/monaldi.2022.2412

Abstract

The long-term sequelae of COVID-19 have now become more common and appreciable. The SARS-CoV-2 virus can cause a variety of infectious and non-infectious pulmonary complications. The purpose of this study is to raise awareness about post-COVID-19 pulmonary sequelae, both infectious and non-infectious, in this geographical area. A retrospective study was conducted from July 1st 2020 to December 20th 2020. A total of 1200 patients were evaluated, with 83 suffering from post-COVID-19 pulmonary complications. The patients' mean age was 62 years (IQR 55-69), with 63 (75.9%) being male. The most common co-morbid illnesses were hypertension (49, 59%) and diabetes (45, 54.2%). The majority of them (37, 44.6%) had severe COVID-19, followed by critical COVID-19 (33, 39.8%). There was no statistically significant difference in recurrence of respiratory symptoms or duration of current illness between non-severe, severe, and critical COVID-19 patients. Non-infectious complications were observed in the majority of patients (n=76, 91.5%), including organizing pneumonia/ground glass opacities in 71 (88%) patients, fibrosis in 44 (55%), pulmonary embolism in 10 (12.5%), pneumomediastinum in 6 (7.4%) and pneumothorax in 7 (8.6%). Infective complications (25, 30.1%) included aspergillus infection in 10 (12.0%) and bacterial infection in 5 (8.47%), with more gram-negative infections and one patient developing *Mycobacterium tuberculosis*. Post-COVID-19 mortality was 11 (13.3%). The long-term pulmonary sequelae of COVID-19 are not rare. Cryptogenic organizing pneumonia, ground glass opacities, and fibrosis were common post-COVID-19 sequelae in our patients. This necessitates frequent close monitoring of these patients in order to initiate early appropriate management and prevent further morbidity and eventual mortality.

Introduction

In December 2019 a deadly respiratory disease originated in Wuhan, China caused by a severe acute respiratory virus (SARS-COV-2) and quickly took shape of a pandemic in March 2020. In Pakistan alone, 1,290,214 cases have been confirmed while over 28,849 people passed away due to COVID-19 [1]. With the virus having been around for more than a year, along the way, the long-term sequelae of SARS-CoV-2 have become more common and identifiable.

There exist multiple studies in the literature suggesting that infection with the virus can lead to non-infective pulmonary

complications such as pulmonary fibrosis and impaired quality of life [2,3]. COVID-19 patients developed acute respiratory distress syndrome (ARDS) which often manifests later as pulmonary fibrosis [4]. There have been multiple post-COVID-19 symptoms appeared including but not limited to fatigue, stroke, renal failure, and myocarditis [5]. The incidence of pulmonary embolism (PE) occurrence also increased during COVID-19 due to coagulopathy and endothelial damage. A study showed, 97.4% increase in PE incidence as compared to the pre-pandemic period, 2017–2019 and the proportion of hospitalizations increased from 1.3% to 3.7% [6]. Another late sequela that has been recorded is non-specific respiratory insufficiency, such as dyspnea, both with and without exertion, due to reduced total lung capacity and diffusion lung capacity for carbon monoxide (DLCO) [7].

COVID-19 patients are usually the subject of broad-spectrum antibiotics, immunosuppressant or corticosteroid therapy, and/or supported by invasive or noninvasive ventilation. These all act as risk factors for respiratory fungal infections such as oral candidiasis, pulmonary aspergillosis, or pneumocystis pneumonia [8]. Apart from fungal infections, bacterial superinfections and co-infections with organisms such as *Streptococcus pneumoniae*, *Klebsiella pneumoniae*, *Hemophilus influenzae*, *Escherichia coli*, and *Staphylococcus aureus* are associated with worse outcomes and death despite of anti-microbial therapy [9]. Moreover, the usage of immunosuppressant drugs results in temporary inhibition of immunological function which may lead to the reactivation of latent or inactive tuberculosis (TB) [10].

There have been studies in regard to the long-term sequelae from China [11] and Italy [12]. With the emergence of various post-COVID-19 complications both infective and non-infective, there seems to be a dire need for a local study explaining it in relation to our native population. So the aim and objective of this study are to educate concerning the post-COVID-19 sequelae, both infective and non-infective reported within this geographical area.

Materials and Methods

This was a retrospective study conducted from 1st July 2020 to December 2020. Patients who were admitted or visited the outpatient department of Aga Khan University Hospital (AKUH) with history of confirmed diagnosis of COVID-19 by nasopharyngeal RT-PCR were enrolled. The study protocol was approved by the Ethics Review Committee (ERC) of the AKUH with exemption status.

The disease severity was classified according to the World Health Organization (WHO) classification into non-severe, severe and critically ill patients. Non-severe is defined as absence of signs of severe and critical disease. Severe COVID-19 was defined as patients having respiratory distress with a respiratory rate of 30 breaths per minute or more and oxygen saturations below 90% on room air whereas critical COVID-19 was defined as patients with sepsis, septic shock, ARDS and/or required life-sustaining treatment [13]. Patients who had recovered from COVID-19 infection (first PCR positive) two months back were defined as post-COVID.

The data was collected from AKUH Health Information Management Services (HIMS) department on predesigned proforma. Proforma included basic demographics, disease severity (non-severe, severe and critical), radiology included chest X-ray and high-resolution computed tomography (HRCT) chest, microbiology and pulmonary complications developed during COVID-19 infections (infective and non-infective) and two months after COVID-19 infection recovery.

Inclusion/exclusion criteria

Patients included in the study met the following criteria: i) age 18 years and above; ii) patients with respiratory symptoms such as cough, dyspnea, hypoxia, fever and/or any other respiratory symptoms with negative repeat COVID-19 PCR testing; ii) patients who had COVID-19 infection two months back.

Patients were excluded based on the following criteria: i) age <18 years; ii) active infection; iii) patients presented with extrapulmonary symptoms/ complications; iv) patients with incomplete records and/or left against medical advice; v) underlying known interstitial lung disease (ILD); vi) >2 months of COVID-19 infection.

Although 1200 files were reviewed, only 83 were accepted into the study. Figure 1 depicts the patient enrollment.

Ground-glass opacities (GGO), consolidation, honeycombing/ fibrosis, interlobular septal thickening/reticulation, and emphysematous cysts were among the HRCT findings. Patients with interstitial disease were given 0.5 mg/kg of oral prednisolone, which was gradually tapered down and discontinued after 3-6 months. Oral anticoagulation was continued for 3 months for PE. If the patients' functional status returned to baseline and/or chest imaging revealed complete resolution of lung infiltrates, they were labelled as improved.

Statistical analysis

Descriptive statistics were done and continuous variables with normal and non-normal distributions were reported as mean (SD) and median [inter-quartile range (IQR)], respectively.

We further divided the patients into 3 groups (Non-severe, Severe, Critical) and continuous variables between the groups were compared by using ANOVA or Kruskal-Wallis H test for non-normal distribution variables. Categorical variables were compared by using the chi-square test. All p-values were based on two-sided tests and significance was set at a p-value less than 0.05. The analyses were performed using SPSS (Statistical Package of Social Sciences) version 19.

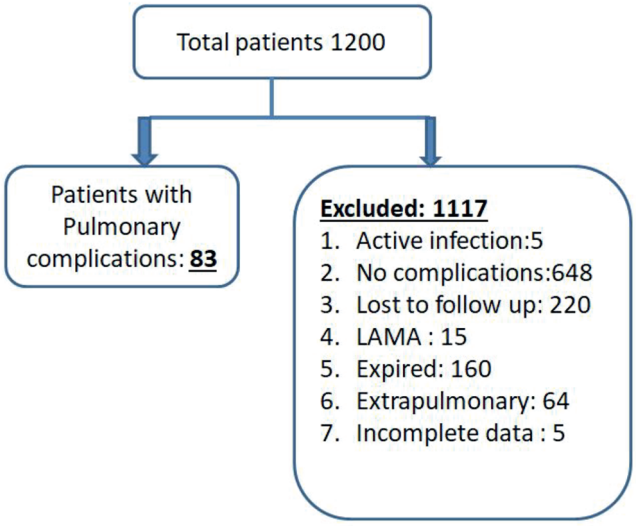

Figure 1. Flow chart of patients' enrolment.

Results

During our study period, out of 1200, 83 patients met the inclusion criteria. The median age was 60.4 ± 10.9 years with male predominance (n=63, 75.9 %). In our study (n=37, 44.6%) patients had severe COVID-19 followed by critical COVID-19 (n=33, 39.8%) and (n=61, 73.5%) required hospitalization. Hypertension (n=49, 59 %) and diabetes (n=45, 54.2%) were the common co-morbid illnesses among patients. Only (n=28, 34.9%) received remdesivir, and anti-IL-6 inhibitor (tocilizumab) was administered to 11(13.3%) patients. Baseline characteristics are shown in Table 1.

There was no significant difference observed for age among the three groups (p=0.07); apart from an upscaling trend in severe COVID-19 cases 21 (56.8%) for 55-65 years of age. During the initial COVID-19 disease, non-infective complications were more common in patients with severe and critical COVID-19 (p=0.001). Cryptogenic organizing pneumonia (COP) (p=0.003) was more frequent in patients with critical COVID-19 as compared to those with severe and non-severe disease. Pneumothorax and pneumomediastinum were also common in patients with critical illness (p=0.04). Only patients with critical COVID-19 developed secondary bacterial pneumonia (p=0.003) during the first phase of the disease. Organisms isolated from respiratory specimens were *Klebsiella* spp, *Pseudomonas aeruginosa* and *Stenotrophomonas maltophilia*. Oral (n=66,79.5%) and parental (n=62, 74.7%) steroids were given to those with severe and critical illness and were continued for a median duration of 14 days (IQR=8-20). A significant number of patients required home oxygen therapy for a minimum of 14 days (Table 2).

Looking at post-COVID-19 presentation, the median duration between clinical improvement and recurrence of respiratory symptoms was 15 days (IQR=10-25). The duration between the onset of symptoms and contact with the healthcare facility was 5 days (IQR=3-8). There were no statistically significant differences among non-severe, severe and critical COVID-19 patients in terms of recurrence of respiratory symptoms and duration of current illness (p=0.35). Shortness of breath was the predominant symptom among all patients, 75 (90.4%) followed by hypoxia 54 (65.1%) and cough 41 (50%). Patients who had critical COVID-19 were more hypoxic compared to non-severe and severe (p=0.002).

The non-infective complications were seen in (n=76,91.5%) of patients, which included organizing pneumonia/ground glass opacities in 71 (88%) patients, followed by fibrosis 44 (55%), pulmonary embolism 10 (12.5%), pneumothorax 7 (8.6%) and pneumomediastinum 6 (7.4%). But there was no statistical

Table 1. Characteristics of the study population (n=83).

Variables	n (%)
Age, years	60.4±10.9
Median (IQR); range	62 (55-69); 27-84
Severity of disease	
Non-severe	3 (15.7)
Severe	137 (44.6)
Critical	33 (39.8)
Sex	
Male	63 (75.9)
Female	20 (24.1)
Comorbidity	
Diabetes mellitus	45 (54.2)
Hypertension	49 (59)
Ischemic heart disease	11 (13.3)
Asthma	4 (4.8)
COPD	1 (1.2)
Chronic lung disease	2 (2.4)
Chronic kidney disease	2 (2.4)
Inpatient	61 (73.5)
Outpatient	22 (26.5)
Treatment	
Oral steroids	66 (79.5)
IV steroids	62 (74.7)
Antivirals	29 (34.9)
TOCI	11 (13.3)
Remedsivir	28 (33.7)
Plasma therapy	4 (4.8)
Mechanical ventilation	4 (4.8)
Non-invasive ventilation	26 (31.3)
Duration of steroids; median (IQR) in days	14 (8-20)

Table 2. During COVID-19 infection.

Variables	Total, n (%)	Non-severe, n (%)	Severe, n (%)	Critical, n (%)	p-value
Age					
<55	19 (22.9)	6 (46.2)	5 (13.5)	8 (24.2)	0.07
55-65	36 (43.4)	4 (30.8)	21 (56.8)	11 (33.3)	
>65	28 (33.7)	3 (23.1)	11 (29.7)	14 (42.4)	
Complications	47 (56.6)	0	19 (51.4)	28 (84.8)	<0.001
Infective	6 (7.2)	0	1 (2.7)	5 (15.2)	0.07
Bacterial resp	7 (8.4)	0	0	7 (21.2)	0.003
Blood	56 (67.5)	8 (61.5)	23 (62.2)	25 (75.8)	0.42
Non-infective	50 (60.2)	0	23 (62.2)	27 (81.8)	<0.001
Pulmonary embolism	1 (1.2)	0	1 (2.7)	0	0.53
Organizing pneumonia	12 (14.5)	0	2 (5.4)	10 (30.3)	0.003
Pneumothorax	4 (4.8)	0	0	4 (12.1)	0.04
Pneumomediastinum	6 (7.2)	0	1 (2.7)	5 (15.2)	0.07
Oxygen dependency	45 (54.2)	0	17 (45.9)	28 (84.8)	<0.001
Non-invasive ventilation long term	6 (7.2)	0	1 (2.7)	5 (15.2)	0.07

difference among non-severe, severe and critical COVID-19. It is interesting to note that 6 (46.2%) of non-severe COVID-19 patients also developed fibrosis as shown in (Table 3).

Infective complications were noted in 25 (30.1%) of post-COVID-19 patients but were statistically not significant among three groups, (p=0.24). Fungal pneumonia, diagnosed on the basis of positive culture of respiratory secretions and/or serum fungal markers (galactomannan, and beta d-glucan) was found in 10 patients and organisms isolated were PCP, *Aspergillus* spp and *Syncephalustrum*. Gram-negative organisms were predominantly responsible for secondary bacterial pneumonia. One patient also developed smear-positive pulmonary tuberculosis.

Patients with lung parenchymal involvements like GGO, fibrosis were treated with intravenous followed by oral steroids for a mean duration of 12 weeks. The overall mortality was 13.3%. Although patients with critical COVID-19 had higher mortality as compared to non-severe and severe disease (24.2 *vs* 7.7 *vs* 5.4%), but this difference did not reach statistical significance (p=0.1) as demonstrated in Table 3.

Discussion

Long-term pulmonary complications in survivors of COVID-19 are challenging yet less understood issues of the current pandemic that carries significant consequence. In our study, patients with COVID-19 developed pulmonary complications, mostly non-infective in etiology like organizing pneumonia/ground glass opacities (GGO), followed by fibrosis, pulmonary embolism, pneumothorax and pneumomediastinum irrespective of the disease severity, overall mortality was found to be 13.3%.

In our study, patients were old and predominately male. There are certain factors that can increase the risk of development of pulmonary sequelae after COVID-19 such as old age, prior co-morbid illnesses, acute respiratory distress syndrome (ARDS), severe and critical disease, prolonged ICU stay and invasive ventilation [14,15]. In a case series by Ahmed *et al*., all patients who developed pulmonary sequelae after COVID-19 had severe and critical diseases [16]. This is in contrast to the findings of our study as patients with non-severe COVID-19 also developed post-infection complications after recovery from the initial illness. This could be probably due to ongoing inflammation in the lung parenchyma. This finding lays emphasis on the importance of continuous and close monitoring of symptoms even for those patients with non-severe COVID-19.

GGOs and pulmonary fibrosis were the common non-infective complications present among our patients, which were also reported in prior studies [17-19]. There are several mechanisms responsible for inflicting GGOs and pulmonary fibrosis (PF) in patients with SARS-CoV-2 infections such as viral-mediated activation of fibrotic pathways, host inflammatory response and mechanical trauma [20-21]. Although no definite data is available, few studies have reported that around one third of hospitalized patients with COVID-19 develop pulmonary fibrosis due to certain risk factors such as advanced age, ICU stay, mechanical ventilation, and smoking [22-23]. GGOs and pulmonary fibrosis were noted in all three groups irrespective of the disease severity. This is an important finding, and we suggest for long-term follow-up of these patients even with non-severe COVID-19.

PE was responsible for 12.5 % of post-COVID-19 non-infective complications in our study. It was found that SARS-CoV-2 infection is associated with an increased risk of thrombosis and thromboembolism in the acute phase of the disease, especially in patients with severe and critical COVID-19 [24,25]. However, thromboembolic events can also happen after recovery from infection even in the absence of prothrombotic risk factors [26-28]. Even though associated with severe and critical disease in the majority, patients with asymptomatic and mild COVID-19 also developed PE after disappearance of the acute symptomatic stage of infection and complete improvement [26-28]. Current guidelines

Table 3. Post-COVID-19 symptoms.

Variables	Total, n (%)	Non-severe, n (%)	Severe, n (%)	Critical, n (%)	p-value
Symptoms					
Cough	41 (50)	9 (69.2)	20 (54.1)	12 (37.5)	0.12
Shortness of breath	75 (90.4)	12 (92.3)	34 (91.9)	29 (87.9)	0.82
Hypoxia	54 (65.1)	4 (30.8)	22 (59.5)	28 (84.8)	0.002
Fever	19 (22.9)	1 (7.7)	11 (29.7)	7 (21.2)	0.25
Chest pain	11 (13.4)	2 (15.4)	5 (13.9)	4 (12.1)	0.95
Symptoms duration	5 (3-8)	7 (4.5-12)	5 (3-7)	4 (3-7.5)	0.35*
Interval between post-COVID presentation days	15 (10-25)	20 (14.5-30)	15 (12.5-23)	14 (9-23)	0.20*
Pneumothorax	7 (8.6)	2 (15.4)	0	5 (15.2)	0.054
Pneumo-mediastinum	6 (7.4)	0	1 (2.9)	5 (15.2)	0.08
Pulmonary embolism	10 (12.5)	0	5 (13.5)	5 (16.7)	0.30
Fibrosis	44 (55)	6 (46.2)	21 (56.8)	17 (56.7)	0.78
GGOs/OP	71 (88.8)	13 (100)	30 (81.1)	28 (93.3)	0.10
Consolidation	28 (35)	3 (23.1)	11 (29.7)	14 (46.7)	0.21
Cavitation/cyst formation	8 (10)	2 (15.4)	3 (8.1)	3 (10)	0.75
Infective complications	25 (30.1)	2 (15.4)	10 (27)	13 (39.4)	0.24
Outcome					
Improved	56 (67.5)	11 (84.6)	24 (64.9)	21 (63.6)	0.11
Lost to follow-up	14 (16.9)	1 (7.7)	10 (27)	3 (9.1)	
Died	11 (13.3)	1 (7.7)	2 (5.4)	8 (24.2)	
Left against medical advice	2 (2.4)	0	1 (2.7)	1 (3.0)	

GGO/OP, ground glass opacity/organizing pneumonia; *Kruskal-Wallis H test.

do not recommend prolonged thromboprophylaxis after clinical improvement in patients with COVID-19. However, further studies need to be conducted for confirmation [29]. Pneumothorax and pneumomediastinum were observed predominantly in our patients who had history of critical COVID-19. It was found that pneumothorax can occur in any phase of the disease and even as a late sequela after recovery from initial infection in the absence of prior pulmonary disease or barotrauma [30,31].

Secondary bacterial pneumonia and fungal pneumonia were present in 30% of the study participants. The immunosuppressive therapy used to treat severe SRAS-CoV-2 can be considered as a risk factor for bacterial and fungal infections. Among fungal infections, COVID-19-associated pulmonary aspergillosis (CAPA) was common in our present study, also reported in published studies from different parts of the world. The overall incidence of CAPA was reported between 2.5-35.0% in the literature [32,33]. Limited evidence, mostly case reports, is available about PCP infections complicating the course of SARS-CoV-2 infections making it difficult to understand the true incidence, risk factors and prognosis of PCP co-infection. All three patients in this study had critical COVID-19, were given tocilizumab during the acute stage, had received steroids for a prolonged duration and showed complete recovery after treatment with trimethoprim-sulphamethoxazole. As PCP is associated with high mortality in patients with COVID-19, it should be considered a differential diagnosis in COVID-19 patients with a lack of clinical improvement in respiratory symptoms [34]. The mortality was 13.3 % in patients with late sequelae after recovery from COVID-19 acute infections. This is higher as compared to that reported by Romero-Duarte et al. [35].

Limitations

There were several limitations that applied to our study. It is a single centre study with a small sample size. We did not have long-term follow-ups of all the patients beyond 3 months. All investigations, especially PFT's were not available in every patient which can provide detailed information about the functional status of lung parenchyma. Repeat CT chest could not be done to assess radiological improvement in all patients due to financial limitations as this is a non-funded study.

Conclusions

In conclusion, patients may develop airway, vascular and alveolar complications after the resolution of the COVID-19 infection that are not uncommon with the incidence escalating as the pandemic persists. These pulmonary complications can detrimentally impact the quality of life, lead to increased ICU admissions and eventual mortality. Cryptogenic organizing pneumonia/ground glass opacities and fibrosis were frequently seen as post-COVID-19 sequelae in our patients which merits frequent close monitoring to start early appropriate management. Further long-term clinical follow-up, referral to a chest physician promptly and timely intervention on the onset of pulmonary complications post-COVID-19 can help curtail both morbidity and mortality.

References

1. Pakistan Government. COVID-19 Health advisory platform by Ministry of National Health Services Regulations & Coordination 2021. Available from: https://covid.gov.pk/stats/pakistan
2. Ojo AS, Balogun SA, Williams OT, Ojo O. Pulmonary fibrosis in COVID-19 survivors: Predictive factors and risk reduction strategies. Pulm Med 2020;2020:6175964.
3. Wang F, Kream RM, Stefano GB. Long-term respiratory and neurological sequelae of COVID-19. Med Sci Monit 2020;26: e928996.
4. Leask A. COVID-19: is fibrosis the killer? J Cell Commun Signal 2020;14:255.
5. Kamal M, Abo Omirah M, Hussein A, Saeed H. Assessment and characterisation of post-COVID-19 manifestations. Int J Clin Pract 2021;75:e13746.
6. Hauguel-Moreau M, Hajjam ME, De Baynast Q, et al. Occurrence of pulmonary embolism related to COVID-19. J Thromb Thrombolysis 2021;52:69-75.
7. George PM, Barratt SL, Condliffe R, et al. Respiratory follow-up of patients with COVID-19 pneumonia. Thorax 2020;75: 1009–16.
8. Salehi M, Ahmadikia K, Badali H, Khodavaisy S. Opportunistic fungal infections in the epidemic area of COVID-19: A clinical and diagnostic perspective from Iran. Mycopathologia 2020;185:607–11.
9. Vaillancourt M, Jorth P. The unrecognized threat of secondary bacterial infections with COVID-19. mBio 2020;11:e01806-20.
10. Yang H, Lu S. COVID-19 and tuberculosis. J Transl Intern Med 2020;8:59–65.
11. Xiong Q, Xu M, Li J, Liu Y, Zhang J, Xu Y, et al. Clinical sequelae of COVID-19 survivors in Wuhan, China: a single-centre longitudinal study. Clin Microbiol Infect 2021;27: 89–95.
12. Carfì A, Bernabei R, Landi F Gemelli Against COVID-19 Post-Acute Care Study Group. Persistent symptoms in patients after acute COVID-19. JAMA 2020;324:603–5.
13. No authors listed. Update to living WHO guideline on drugs for covid-19. BMJ 2022;376:o80.
14. Esendağli D, Yilmaz A, Akçay MŞ, Özlü T. Post-COVID syndrome: pulmonary complications. Turk J Med Sci 2021;51: S3359-71.
15. Ali RMM, Ghonimy MBI. Post-COVID-19 pneumonia lung fibrosis: a worrisome sequelae in surviving patients. Egypt J Radiol Nucl Med 2021;52:101.
16. Ahmed OF, Amin BJH, Abdullah BA, et al. Post COVID-19 pulmonary complications; a single center experience. Ann Med Surg 2021;72:103052.
17. Mandal S, Barnett J, Brill SE, et al. 'Long-COVID': a cross-sectional study of persisting symptoms, biomarker and imaging abnormalities following hospitalisation for COVID-19. Thorax 2021;76:396-8.
18. Nabahati M, Ebrahimpour S, Khaleghnejad Tabari R, Mehraeen R. Post-COVID-19 pulmonary fibrosis and its predictive factors: a prospective study. Egypt J Radiol Nucl Med 2021;52:248.
19. Kamal M, Abo Omirah M, Hussein A, Saeed H. Assessment and characterisation of post-COVID-19 manifestations. Int J Clin Pract 2021;75:e13746.
20. McDonald LT. Healing after COVID-19: are survivors at risk for pulmonary fibrosis? Am J Physiol Lung Cell Mol Physiol 2021;320:L257-L65.
21. Ghose M, Islam T. Facing the challenge of post COVID-19 pulmonary fibrosis: What is so unique about it? Bangladesh Crit Care J 2020;8:102-7.
22. Rai DK, Sharma P, Kumar R. Post covid 19 pulmonary fibrosis. Is it real threat? Indian J Tuberc 2021;68:330-3.
23. Li Y, Wu J, Wang S, et al. Progression to fibrosing diffuse alveolar

damage in a series of 30 minimally invasive autopsies with COVID-19 pneumonia in Wuhan, China. Histopathology 2021;78: 542-55.
24. Klok F, Kruip M, Van der Meer N, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thromb Res 2020;191:145-7.
25. Jandial A, Gupta A, Malviya A, Agastam S, Kumar D. Coagulation abnormalities & thromboprophylaxis in COVID-19. Indian J Med Res 2021;153:606-18.
26. Vechi HT, Maia LR, Alves MdM. Late acute pulmonary embolism after mild Coronavirus Disease 2019 (COVID-19): a case series. Rev Inst Med Trop Sao Paulo 2020;62:e63.
27. Nauka PC, Oran E, Chekuri S. Deep venous thrombosis in a non-critically ill patient with novel COVID-19 infection. Thromb Res 2020;192:27.
28. Brem FL, Rasras H, El Ouafi N, Bazid Z. Bilateral pulmonary embolism in patients recovered from asymptomatic COVID-19 infection. Cureus 2021;13:e13848.
29. Cuker A, Tseng EK, Nieuwlaat R, et al. American Society of Hematology living guidelines on the use of anticoagulation for thromboprophylaxis in patients with COVID-19: May 2021 update on the use of intermediate-intensity anticoagulation in critically ill patients. Blood Adv 2021;5:3951-9.
30. Sahagun J, Chopra A, David AG, et al. Secondary spontaneous pneumothorax in a COVID-19 recovered patient. Cureus 2021;13:e16415.
31. Nunna K, Braun AB. Development of a large spontaneous pneumothorax after recovery from mild COVID-19 infection. BMJ Case Rep 2021;14:e238863.
32. Nasir N, Farooqi J, Mahmood SF, Jabeen K. COVID-19-associated pulmonary aspergillosis (CAPA) in patients admitted with severe COVID-19 pneumonia: An observational study from Pakistan. Mycoses 2020;63:766-70.
33. Chong WH, Neu KP. The incidence, diagnosis, and outcomes of COVID-19-associated pulmonary aspergillosis (CAPA): a systematic review. J Hosp Infect 2021;113:115-29.
34. Chong WH, Saha BK, Chopra A. Narrative review of the relationship between COVID-19 and PJP: does it represent coinfection or colonization? Infection 2021;491079-90.
35. Romero-Duarte Á, Rivera-Izquierdo M, de Alba IG-F, et al. Sequelae, persistent symptomatology and outcomes after COVID-19 hospitalization: the ANCOHVID multicentre 6-month follow-up study. BMC Med 2021;19:129.