Clinical and radiological outcomes of SARS-CoV-2 related organising pneumonia in COVID-19 survivors

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ABSTRACT

Introduction: COVID-19 patients frequently demonstrate radiological organising pneumonia (OP) pattern. The longterm outcome and treatment options for this group of patients remain uncertain. We aim to describe the clinical and radiological outcomes of patients with COVID-19-related OP and identify possible clinical factors associated with inferior radiological outcome.

Materials and Methods: Post-COVID-19 clinic attendees, consisting of post-COVID-19 patients discharged from major hospitals in the state of Selangor during the third pandemic wave of COVID-19 in Malaysia, were enrolled in this retrospective study for 6 months. Physician-scored Modified Medical Research Council (mMRC), patient self-reported quality of life (EQ-VAS) score and follow-up CT scan were evaluated.

Results: Our cohort comprised 131 patients, with a median age of 52 (IQR 39-60) years and median BMI of 29.40 (IQR 25.59–34.72). Majority (72.5%) had co-morbidities, and 97.7% had severe disease requiring supplementary oxygen support during the acute COVID-19 episode. 56.5% required intensive care; among which one-third were invasively ventilated. Median equivalent dose of methylprednisolone prescribed was 2.60 (IQR 1.29-5.18) mg/kg during admission, while the median prednisolone dose upon discharge was 0.64 (IQR 0.51-0.78) mg/kg. It was tapered over a median of 8.0 (IQR 5.8-9.0) weeks. Upon follow-up at 11 (IQR 8-15) weeks, one-third of patients remained symptomatic, with cough, fatigue and dyspnoea being the most reported symptoms. mMRC and EQ-VAS scores improved significantly (p<0.001) during follow-up. Repeat CT scans were done in 59.5% of patients, with 94.8% of them demonstrating improvement. In fact, 51.7% had complete radiological resolution. Intensive care admission and mechanical ventilation are among the factors which were associated with poorer radiological outcomes, p<0.05.

Conclusion: Approximately one-third of patients with SARS-CoV-2-related OP remained symptomatic at 3 months of follow-up. Majority demonstrated favourable radiological outcomes at 5-month reassessment, except those who required intensive care unit admission and mechanical ventilation.

KEYWORDS:

COVID-19, SARS-CoV-2, post-COVID-19, organising pneumonia, Malaysia

INTRODUCTION

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) emerged as a novel coronavirus in 2019. It soon spread globally to cause an unprecedented Coronavirus Disease 19 (COVID-19) pandemic in human history.¹ Malaysia was not spared from this global outbreak. To date, we had experienced four major waves of COVID-19, with 4.6 million reported cases in total, and overall mortality rate of 0.77%.²

A significant number of COVID-19 patients develop severe disease characterised by progressive respiratory failure with features similar to acute respiratory distress syndrome (ARDS).³ ARDS carries high mortality risk and complicates around 33.0-41.8% of COVID-19 patients.^{4,5} Cytokine storm is frequently seen in this group of patients as SARS-CoV-2 could trigger a state of dysregulated and excessive proinflammatory cytokines release, which in turn result in widespread multiorgan failures.⁶ Radiologically, they frequently demonstrate radiographic features that are compatible with organising pneumonia (OP).⁷ OP is a distinct clinicopathological entity characterised by peripherally and basally distributed bronchocentric and perilobular patterns consolidation. Histologically, organisation and of proliferation of granulation tissue buds within distal airspaces of the lungs are frequently described.⁸ Historically, OP demonstrates a dramatic response to prolonged high doses of corticosteroid with favourable outcomes.8 Therefore, high-dose, prolonged corticosteroid therapy was believed to be potentially an important therapeutic player in SARS-CoV-2-related OP during the early phase of the pandemic.Case reports and series had demonstrated promising outcomes with the usage of cortico steroid therapy in this group of patients.⁹ This was also in line with our national guideline recommendations, of which high-dose potent corticosteroid was recommended for patients with severe COVID-19 diseases.10

In this study, we aim to assess the clinical and radiological outcomes of SARS-CoV-2-related OP during their follow-up

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visit after being discharged from acute COVID-19 admission. In addition, we aim to assess differences in clinical parameters between patients with favourable and undesirable radiological outcomes.

MATERIALS AND METHODS

Design and Participants

A retrospective chart review of post-COVID-19 clinic attendees between February 2021 to August 2021 (6 months duration) in Serdang Hospital, Malaysia, was carried out. A dedicated post-COVID-19 clinic was established in Serdang Hospital during the early phase of COVID-19 pandemic to cater to the need for follow-up for post-COVID-19 patients from the state of Selangor. Our centre received referrals from major hospitals in the state of Selangor as we remained the only hospital equipped with interstitial lung disease services in the state. The study was approved by the Medical Research & Ethics Committee, Ministry of Health Malaysia (*NMRR-ID-22-01910-NSB-IIR, dated 14th September 2022*).

All post-COVID-19 clinic attendees aged 18 years and above during the study period, who were previously admitted for acute COVID-19 episode, were included in this study.Patients who were managed as outpatients during the acute COVID-19 episode, as well as those who defaulted the post-COVID-19 clinic follow-up, were excluded.

Data Collection

Clinical Variables

Baseline demographic characteristics, including age, gender, height, weight, body mass index (BMI), smoking history, and comorbidities were collected. In addition, clinical data regarding COVID-19 admission(oxygen requirement, length of hospital stay, intensive care admission, mechanical ventilation, CT scan findings, and steroid therapy details) were obtained from referral letters and/or electronic medical records.

Physician Scored Dyspnoea Score

Modified Medical Research Council (mMRC) dyspnoea scale was assessed and scored by the managing physician during follow-up. mMRC scale is as follows: 0, dyspnoea only on strenuous exercise; 1, dyspnoea when hurrying or walking up a slight hill; 2, dyspnoea when walking on level ground with people of same age or at own pace on the level; 3, dyspnoea after 100 meters or walking after a few minutes on level ground; 4, dyspnoea to even leave the house or dressing. In addition to current dyspnoea scale during clinic follow-up, patients were asked to recall and assessed by the managing physician for patient's dyspnoea scale upon discharge from COVID-19 admission, and dyspnoea scale pre-COVID-19 admission, i.e., their baseline premorbid status before COVID-19 infection.

Patient Scored Quality of Life Scale

EuroQOL EQ-5D-3L visual analogue scale (EQ-VAS) was used to assess patient's self-reported quality of life (QoL). EQ-VAS is a vertical visual scale ranging from 0 (worst imaginable health) to 100 (best imaginable health). It is used as a quantitative health outcome measurement reflecting patient's own judgement. Patients were instructed to score their current EQ-VAS score during the follow-up, as well as to recall their EQ-VAS score upon discharge from COVID-19 admission and pre-COVID-19 admission, i.e., their premorbid status before COVID-19 infection.

Outcomes of Computed Tomography Thorax

All post-COVID-19 clinic attendees were evaluated by the managing physician. A repeat computed tomography of thorax in high-resolution construction (HRCT) would be scheduled if the initial COVID-19 admission imaging showed features consistent with SARS-CoV-2-related OP. HRCT thorax was obtained in supine position during deep inspiration and breath-holding. Acquired images were assessed and analysed by the in-house general and thoracic radiologists. HRCT reports uploaded into the Picture Archiving and Communication System (PACS) were reviewed and outcomes were recorded.

Statistical Analysis

Data analysis was performed using SPSS version 21 (Chicago, IL, USA).Descriptive statistics of the continuous variables with non-normal distribution were expressed in median and interquartile range (IQR) while continuous variables with normal distribution were expressed in mean and standard deviation. Group comparison was assessed using the Mann–Whitney U-test for continuous non-normally distributed data and t-test for normally distributed data.Chi-square or Fisher's exact test was used for categorical data where appropriate. A *p*-value of <0.05 was considered statistically significant.

RESULTS

A total of 131 patients were included in this study. They were admitted to the major hospitals in Selangor state for COVID pneumonia between November 2020 to April 2021, during which the SARS-CoV-2 variant B.1.524 predominated.¹¹

Baseline Demographic Characteristics

Almost two-thirds of our cohort were male patients (58.8%), and the median age was 52 (IQR 39–60) years. The ethnic distribution followed the multi-racial population of Malaysia, of which Malay ethnicity comprised the majority at 78.6%. Median body mass index was 29.40 (IQR 25.59–34.72) kg/m², and 72.5% had co-morbidities. Half of the cohort were diabetic (51.9%) and hypertensive (50.4%). The detailed baseline demographic characteristics were presented in Table I.

Baseline COVID-19 Admission Characteristics

Majority (97.7%) of patients required supplementary oxygen during their admission. Median length of hospital stay was 12.50 (IQR 9.00–17.00) days, among which 56.5% required intensive care admission and one-third required invasive positive pressure ventilation for a median of 4.5 (IQR 3.0–9.0) days. All patients had computed tomography evidence of OP, and 42.7% had evidence of concurrent pulmonary embolism. During admission, intravenous methylprednisolone was given at a median equivalent dose of 2.60 (IQR 1.29–5.18) mg/kg/day. Oral prednisolone was prescribed at a median dose of 0.64 (IQR 0.51–0.78) mg/kg/day upon discharge and tapered over 8.00 (IQR 5.85–9.00) weeks (Table I).

Number of patients, n		131
Gender, n (%)	Male	77 (58.8)
	Female	54 (41.2)
Median age, years (IQR)		52 (39-60)
Ethnicity, n (%)	Malay	103 (78.6)
	Chinese	19 (14.5)
	Indian	7 (5.3)
	Indigenous	2 (1.6)
Smoking, n (%)	Current smoker	5 (3.8)
-	Ex-smoker	47 (35.9)
	Never smoker	79 (60.3)
Median body mass index, kg/m2 (IQR)		29.40 (25.59-34.72)
Presence of co-morbidities, n (%)		95 (72.5)
Co-morbidity, n (%)	Diabetes mellitus	68 (51.9)
	Essential hypertension	66 (50.4)
	Dyslipidaemia	33 (25.2)
	Ischemic heart disease	15 (11.5)
	Chronic kidney disease	7 (5.3)
	Asthma and COPD	8 (6.1)
	Malignancy	1 (0.8)
Disease Severity, n (%)	Not requiring oxygen	3 (2.3)
	Requiring supplementary oxygen	128 (97.7)
Admission, n (%)	General ward	57 (43.5)
	Intensive care unit	74 (56.5)
Median admission duration, days (IQR)		12.50 (9.00-17.00)
Highest oxygen requirement, n (%)	Room air	3 (2.3)
	Nasal cannula	28 (21.4)
	Face mask	29 (22.1)
	High-flow nasal cannula	30 (22.9)
	Invasive positive pressure ventilation	41 (31.3)
Median invasive ventilation duration, days (IQR)		4.5 (3.0–9.0)
CT evidence of organising pneumonia, n (%)		131 (100.0)
CT evidence of pulmonary embolism, n (%)		56 (42.7)
Median dose of methylprednisolone given, mg/kg/day (IQR)	2.60 (1.29–5.18)	
Median dose of prednisolone prescribed upon discharge, mg/kg/day (IQR)		0.64 (0.51–0.78)
Median prednisolone tapering duration upon discharge, weeks (IQR)		8.00 (5.85–9.00)

Table I: Baseline demographic and COVID-19 admission characteristics

CT=computed tomography, IQR= interquartile range.

Table II: Clinical and radiological outcomes of post-COVID-19 patients during follow-up

Persistent symptoms during follow-up, n (%)		47 (35.9)
Symptoms, n (%)	Dyspnoea	21 (16.0)
	Fatigue	18 (13.7)
	Cough	13 (9.9)
	Myalgia	10 (7.6)
	Non-specific chest pain	8 (6.1)
	Rhinitis	6 (4.6)
	Headache	6 (4.6)
	Sore throat	3 (2.3)
	Dry mouth	3 (2.3)
Median mMRC, score (IQR)	Baseline (pre-COVID-19)	0 (0-1)
	Upon discharge	2 (1-3)
	During follow-up	1 (0-2)
Median EQ-VAS, score (IQR)	Baseline (pre-COVID-19)	95.0 (80.0–100.0)
	Upon discharge	60.0 (45.0–70.0)
	During follow-up	80.0 (75.0–90.0)
Repeat HRCT thorax available, n (%)		78 (59.5)
HRCT thorax outcome, n (%)	Complete resolution	42 (53.8)
	Residual changes	33 (42.3)
	Fibrotic	3 (3.8)

HRCT: high resolution computed tomography, IQR: interquartile range, mMRC: modified Medical Research Council, EQ-VAS: EuroQol Visual Analogue Scale

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	Complete Resolution	Residual Changes	<i>p</i> -value
Median age, years (IQR)	50.0	55.0	0.285
	(36.0–60.0)	(42.0–63.5)	
Male gender, n (%)	21	22	0.325
-	(48.8)	(51.2)	
Current or ex-smoker, n (%)	18	14	0.722
	(56.3)	(43.8)	
Median BMI, kg/m2 (IQR)	30.6	27.9	0.025
	(25.8–37.5)	(24.7–30.8)	
Supplementary oxygen during COVID-19 admission, n (%)	40	36	0.185
	(52.6)	(47.4)	
Intensive care unit admission, n (%)	19	27	0.008
	(41.3)	(58.7)	
Invasive ventilation, n (%)	10	19	0.008
	(34.5)	(65.5)	
Median dose of methylprednisolone given, mg/kg/day (IQR)	2.01	4.85	0.003
	(0.78–3.53)	(1.82–6.41)	
Median dose of prednisolone prescribed upon discharge,	0.62	0.70	0.051
mg/kg/day (IQR)	(0.47–0.78)	(0.58–0.81)	
Median prednisolone tapering duration upon discharge, weeks (IQR)	6.00	8.00	0.026
	(5.00-8.00)	(7.00–9.00)	
Interval of HRCT thorax scans, weeks (IQR)	24.0	19.0	0.330
	(13.8–32.0)	(15.0-26.0)	
mMRC during follow-up, score (IQR)	1.00	1.00	0.987
- •	(0.00–1.25)	(0.00–1.75)	
EuroQOL during follow-up, score (IQR)	80.0	82.5	0.771
	(73.7–90.0)	(71.2–90.0)	

Table III: Differences between patients with complete resolution and with residual changes on repeated high resolution computed tomography (HRCT) thorax assessment (n=78)

BMI: Body mass Index, IQR: Interquartile range, HRCT: High-resolution computed tomography, mMRC: Modified Medical Research Council



Fig. 1: Boxplot showing dyspnoea mMRC score (Panel A) and quality of life EQ-VAS score (Panel B) during baseline pre-COVID-19, upon discharge, and follow-up

Clinical Outcomes of Post-COVID-19 Patients During Follow-up Patients were seen at post-COVID-19 follow-up clinic at a median of 11 weeks (IQR 8–15) post-discharge. Almost onethird (35.9%) of patients reported persistent symptoms during follow-up. The commonest symptom reported was dyspnoea (16.0%), followed by fatigue (13.7%) and cough (9.9%). Other symptoms include myalgia, non-specific chest pain, rhinitis, headache, sore throat, and dry mouth (Table II). Median mMRC score during follow-up was 1 (IQR 0–2) while median EQ-VAS score was 80.0 (IQR 75.0–90.0). These were significantly improved compared to patients' scores upon discharge (p<0.001),but did not return to patients' baseline pre-COVID-19 scores (p<0.001), as summarised in Figure 1.

Radiological Outcomes of Post-COVID-19 Patients During Followup

In our cohort, 78 patients (59.5%) had repeat HRCT thorax during follow-up. Repeat HRCT thorax was done at a median of 21.0 (IQR 15.0–30.5) weeks from the first admission CT. Majority (96.1%) of patients had significant radiological



- Fig. 2: Representative Cases.
- Case 1 (Complete Resolution) 49 years old lady with type 2 diabetes mellitus and hypertension presented with severe COVID-19 pneumonia required invasive ventilation (Panel A); patient was treated with intravenous methylprednisolone followed by tapering dose of oral prednisolone over 6 weeks at a dose of 0.54mg/kg/day, repeated CT scan three months later shown complete resolution of initial changes with improvement of mMRC and EQ-VAS score (Panel B).
- Case 2 (Residual Changes) 60 years old lady without chronic medical illness was admitted to intensive care for severe COVID-19 pneumonia requiring high flow nasal cannula oxygen therapy (Panel C); she was treated with intravenous methylprednisolone followed by tapering oral prednisolone at a dose of 0.57mg/kg/day over 4 weeks, repeated CT scan 4 months later shown residual peripheral reticulation (arrow, Panel D) with improvement of mMRC and EQ-VAS score from 3 to 1 and 40 to 90 respectively.
- Case 3 (Fibrotic Complication) 25 years old lady with type 1 diabetes mellitus and Grave's disease presented with severe COVID-19 pneumonia (Panel E) required prolonged ventilation and tracheostomy which was complicated with nosocomial multi-resistant Acinetobacter baumannii pneumonia. She was treated with intravenous methylprednisolone and tocilizumab followed by a tapering dose of oral prednisolone over 8 weeks at a dose of 1mg/kg/day; she improved at 4 months follow up with improvement of mMRC and EQ-VAS score but repeated CT shown focal traction bronchiectasis at the non-dependent area (arrow, Panel F) consistent with post-ARDS and infective changes.

improvement, of which half (53.8%) of them demonstrated complete resolution of COVID-19 changes, while 33 (42.3%) patients had residual radiological changes, and 3 (3.8%) had fibrotic changes on their repeat CT scans (Figure 2, Table II).

Among the 78 patients in whom the HRCT thorax was repeated, there were no significant differences in terms of median age, gender, and smoking status between patients with complete resolution and residual changes (Table III).

Interestingly, we found that patients with residual CT changes had lower median body mass index compared to those with complete resolution (27.9 vs. 30.6 kg/m², p<0.05). Patient who required intensive care admission and those who received invasive ventilation were also associated with residual changes on repeat CT, p<0.01. In contrast, supplementary oxygen requirement during admission was not associated with worse radiological outcomes.

Patients with residual CT changes received significantly higher equivalent dose of methylprednisolone (4.85 vs. 2.01 mg/kg/day, p<0.01) and was discharged with a longer duration of prednisolone tapering period (8.0 vs. 6.0 weeks, p<0.05). There was no statistical difference in prednisolone dose upon discharge, although patients with residual CT changes trend towards higher prednisolone dose. Interestingly, inferior radiological outcome was not associated with worse mMRC or EQ-VAS score in our cohort.

DISCUSSION

The World Health Organization declared COVID-19 as a global pandemic on 11th March 2020. SARS-CoV-2 is one of the deadliest pandemics in human history. Until July 2022, there were more than 569 million confirmed cases, with an overall death rate of around 1.12% worldwide.12 Asian countries generally recorded a lower death rate attributed to younger generation, better adoption of facemask and physical distancing, as well as better preparedness from the previous SARS outbreak.¹³ This lower mortality rate also translates to a huge number of COVID-19 survivors with distinct issues (long COVID-19 syndrome) which need to be addressed.14 Although post-COVID-19 follow-up data on clinical and radiological outcomeshad been published at an immense speed in the global literature, local data from our region is still lacking. In this study, we presented the clinical and radiological outcome of SARS-CoV-2-related OP in Malaysia for the first time, which will aid clinicians in future decision-making.

For clinical outcomes, our study demonstrated that 35.9% of patients remain symptomatic at 11 weeks (*approximate to 3 months*) post-COVID-19. This is in concordance with several studies which have shown that a significant number of patients (16.3–45.9%) remain symptomatic at 3 months.^{15:17} In our cohort, the most reported symptoms were dyspnoea, fatigue and cough, which wereconsistent withthose in other literatures.^{16,17} In addition, our study evaluated specifically the physician-scored dyspnoea scale (mMRC) and patient self-reported quality of life scale (EQ-VAS), and our data indicate that most patients improved but had yet to return to their pre-COVID-19 baseline. For mMRC dyspnoea scale, we

were in line with literature evidence that mMRC score was >0 in most of the patients at 3 months follow-up, however, reassuringly improved with times.^{18,19} Our study is also in agreement with the literature that post-COVID-19 patients had perceived reduced quality of life at 3 months; 79.5% were due to respiratory symptoms.²⁰ Interestingly, we also support the findings from a previous study that dyspnoea and quality of life score were not associated with radiological outcomes.²⁰ This finding further strengthened the fact that long COVID-19 is a multi-factorial condition. Hence, a multidisciplinary approach to address this complex clinical problem is essential.¹⁴

Two-thirds of our patients had repeat HRCT thorax at around 21 weeks (approximate to 5 months) from their first admission scans. In concordance with the literature, majority of patients in our cohort showed significant improvement, among which half of them had complete radiological resolution. From the literature, the reported rates of residual radiological changes at 3-6 months post-COVID-19 were wide (19-82%). In our cohort, 42.3% had residual radiological changes. Reported factors associated with residual changes include advanced age, intensive care admission, and acute respiratory distress syndrome.^{15,19-22} Again, this is consistent with our data. Wu et al. demonstrated good radiological outcomes in their cohort of patients; they were scanned at 3-monthly intervals up to 12 months and they showed patients continued to improveup to 9 months, but remained static thereafter.¹⁸ Reassuringly, all residual changes were non-progressive in nature in their study.¹⁸ Although three patients were reported as having fibrotic features in our cohort, further analysis revealed that two of the patients were having mild non-progressive traction bronchiolectasis with subpleural parenchymal band likely secondary to post-infective changes, while another one was having post ARDS and infective changes after suffering from concurrent multi-drug-resistant Acinetobacter pneumonia during admission. Therefore, the fibrosis sequelae might not be directly related to SARS-CoV-2 infection. Another interesting observation in our study is that patients with residual HRCT changes had lower BMI than patients with complete resolution. A possible explanation is that obese patients were managed more aggressively during COVID-19 admission as it is a known risk factor for deterioration. This may translate to a better outcome due to aggressive management.²³ Nevertheless, we urge to interpret this data cautiously as anthropometric measurement may not always be optimal and accurate in a COVID-19 ward setting.

The survival benefit of steroid therapy was proven in RECOVERY Trial in which patients with SARS-CoV-2 infection mechanical ventilation requiring invasive and supplementary oxygen benefited from a 10-day course of dexamethasone at a dose of 6mg once daily.²⁴ OP is a radiological pattern frequently associated with severe SARS-CoV-2 infection. As OP, often seen in inflammatory interstitial lung disease, is usually corticosteroid-sensitive, the fear of progressive fibrotic OP in severe COVID-19 had led to the prescription of high dose and prolonged steroid during the early phase of the pandemic.25-27 In our study, we demonstrated that favourable radiological resolution was not associated with higher methylprednisolone or prednisolone doses upon discharge. In fact, patients with residual radiological changes were significantly associated with higher methylprednisolone dose and longer prednisolone tapering duration. This is very likely due to the prescription bias of the managing physician, as this group of patients was likely to have more severe diseases requiring higher oxygen supplementation and intensive care admission. A study from the United Kingdom also revealed that only a minority of patients would require rescue steroid therapy after radiological and physiological assessments at 6 weeks after discharge.28 As more data have now emerged, SARS-CoV-2related OP is generally associated with favourable outcomes with good recovery given time.²⁹ We truly believe that the usage of high dose steroid (along with immunomodulator) should only be reserved in severe COVID-19 patients during the acute phase in cytokine storm syndrome, as prolonged high dose steroid may lead to other potential complications, such as sepsis, gastrointestinal bleeding and uncontrolled diabetes mellitus.

LIMITATIONS

Our study is not without limitations. First, the single institution experience with retrospective design may not address the actual clinical and radiological outcomes. However, as patients were recruited from all major hospitals in the state of Selangor, we believe that our data remain useful for the clinicians regionally, as it represents a realworld experience. Second, our study is compounded by survival bias in which we only captured post-COVID-19 clinic attendees; patients who suffered mortality during admission, and those who were re-admitted to respective hospitals, as well as those who defaulted our clinic follow-up were not included. Hence, the high prevalence of patients with favourable radiological outcomes may be biased. Third, as the subjects were required to score their dyspnoea and quality of life score retrospectively for their general conditions upon discharge and pre-COVID-19 status, this practice was subject to recall bias. Forth, we did not describe the exact radiological patterns during follow-up scans, for example, ground glass opacity, traction bronchiectasis, degree of volume loss, but was only based solely on an overall qualitative radiological evaluation. Finally, since we only captured patients during SARS-CoV-2 B.1.524 variant-predominant COVID-19 period, during which the national COVID-19 immunisation program had just started, the clinical and radiological outcomes among vaccinated patients, as well as those infected with other SARS-CoV-2 variants, for example, Delta variant, B.1.617.2 and Omicron variant, B.1.1.529, in the subsequent waves of COVID-19 pandemic could never be ascertained.

CONCLUSION

Approximately one-third of SARS-CoV-2 patients with OP remained symptomatic at 3-month follow-up, with dyspnoea and quality of life scores improving significantly but did not return to baseline. Majority demonstrated favourable radiological outcomes at 5-month reassessment, but patients who required intensive care admission and mechanical ventilation were associated with inferior radiological outcome was not associated with worse dyspnoea and quality of life scores in our cohort.

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DECLARATIONS

This study was approved by the medical research and ethics committee, Ministry of Health Malaysia (NMRR-ID-22-01910-NSB-IIR, dated 14th September 2022).

Availability of data and material The data that support the findings of this study are available from corresponding author (SSK) upon reasonable request.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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AUTHORS CONTRIBUTION

Conceptualisation: SSK, KCL, NAM, MZN, JAAR; data curation and formal analysis: KSS, NAM; Methodology: SSK, NAM, MZS, II; writing original draft: SSK, KCL, NAM; writing review and editing: KCL, NAM, II, UND, JAAR.

REFERENCES

- 1. Cucinotta D, Vanelli M. WHO declares COVID-19 a pandemic. Acta Biomed 2020; 91(1): 157-60.
- 2. Ministry of Health Malaysia. COVIDNOW in Malaysia the official Malaysia government website for data and insights on COVID-19 [Internet]. [cited July 2022] Accessed from:https://www.covidnow.moh.gov.my
- Berlin DA, Gulick RMN, Martinez FJ. Severe COVID-19. N Engl J Med 2020; 383: 2451-60.
- 4. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S,et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med 2020; 180 (7): 934-43.
- 5. Tzotzos SJ, Fischer B, Fischer H, Zeitlinger M. Incidence of ARDS and outcomes in hospitalized patients with COVID-19: a global literature survey. Crit Care 2020; 24: 516.
- 6. Hoyjo S, Uchida M, Tanaka K, Hasebe R, Tanaka Y, Murakami M,et al. How COVID-19 induces cytokine storm with high mortality. Inflamm Regen 2020; 40: 37.
- Carotti M, Salaffi F, Sarzi-Puttini P, Agostini A, Borgheresi A, Minorati D,et al. Chest CT features of coronavirus disease 2019 (COVID-19) pneumonia: key points for radiologists. Radiol Med 2020; 125(7): 636-46.
- Raghu G, Meyer KC. Cryptogenic organizing pneumonia: current understanding of an enigmatic lung disease. Eur Respir Rev 2021; 30(161): 210094.
- 9. Vadász I, Husain-Syed F, Dorfmüller P, Roller FC, Tello K, Hecker M,et al. Severe organizing pneumonia following COVID-19. Thorax 2021; 76: 201-4.
- Ministry of Health Malaysia. Clinical management of confirmed COVID-19 cases in adult and paediatric [Internet]. [cited July 2022] Accessed from: https://covid-19.moh.gov.my/garispanduan/garis-panduan-kkm/ANNEX-2E-CLINICAL-MANAGEMENT-OF-CONFIRMED-COVID-19-31052022.pdf

- 11. Sam IC, Chong YM, Abdullah A, Fu JYL, Hasan MS, Jamaluddin FH,et al. Changing predominant SARS-CoV-2 lineages drives successive COVID-19 waves in Malaysia, February 2020 to March 2021. J Med Virol 2020; 94(3): 1146-53.
- Ritchie H, Mathieu E, Rodés-Guirao L, Appel C, Giattino C, Ortiz-Ospina E et al. Coronavirus Pandemic (COVID-19) [Internet]. [cited July 2022] Accessed from:https://ourworldindata.org/ coronavirus
- Landoni G, Maimeri N, Fedrizzi M, Fresilli S, Kuzovlev A, Likhvantsev V, et al. Why are Asian countries outperforming the Western world in controlling COVID-19 pandemic? Pathog Glob Health 2021; 115(1): 70-2.
- 14. Lopez-Leon S, Wegman-Ostrosky T, Perelman C, Sepulveda R, Rebolledo PA, Cuapio A, et al. More than 50 long-term effects of COVID-19: a systematic review and meta-analysis. Sci Rep 2021; 11: 16144.
- 15. Jutant EM, Meyrignac O, Neurnier A, Jaïs X, Pham T, Morin L, et al. Respiratory symptoms and radiological findings in post-acute COVID-19 syndrome. ERJ Open Res 2022; 8: 00479-2021.
- Lorenzo RD, Conte C, Lanzani C, Benedetti F, Roveri L, Mazza MG, et al. Residual clinical damage after COVID-19: a retrospective and prospective observational cohort study. PLoS ONE 2020; 15(10): e0239570.
- Fernández-de-las-Peñas C, Palacios-Ceña D, Gómez-Mayordomo V, Florencio LL, Cuardrado ML, Plaza-Manzano G,et al. Prevalence of post-COVID-19 symptoms in hospitalized and nonhospitalized COVID-19 survivors: a systematic review and metaanalysis. Eur J Intern Med 2021; 95: 55-70.
- Wu X, Liu X, Zhou Y, Yu H, Li R, Zhan Q, et al. 3-month, 6month, 9-month, and 12-month respiratory outcomes in patients following COVID-19-related hospitalisation: a prospective study. Lancet Respir Med 2021; 9: 747-54.
- 19. Lerum TV, Aaløkken TM, Brønstad E, Aarli B, Ikdahl E, Kund KMA,et al. Dyspnoea, lung function and CT findings 3 months after hospital admission for COVID-19. Eur Respir J2021; 57: 2003448.
- 20. Gianella P, Rigamonti E, Marando M, Tamburello A, Gauthier LG, Argentieri G,et al. Clinical, radiological and functional outcomes in patients SARS-CoV-2 pneumonia: a prospective observational study. BMC Pulm Med 2021; 21: 136.

- 21. Guler SA, Ebner L, Aubry-Beigelman C, Bridevaux PO, Brutsche M, Clarenback C, et al. Pulmonary function and radiological features 4 months after COVID-19: first result from the national prospective observational Swiss COVID-19 lung study. Eur Respir J 2021; 57: 2003690.
- 22. Han X, Fan Y, Alwalid O, Li N, Jia X, Yuan M,et al. Six-month follow up chest CT findings after severe COVID-19 pneumonia. Radiology 2021; 299(1): e177-186.
- 23. Popkin BM, Du S, Green WD, Beck MA, Algaith T, Herbst CH,et al. Individuals with obesity and COVID-19: a global perspective on the epidemiology and biological relationships. Obes Rev 2020.
- 24. RECOVERY Collaborative Group, Horby P, Lim WS, Emberson JR, Mafham M, Bell JL, et al. Dexamethasone in hospitalized patients with Covid-19.N Engl J Med 2021; 384(8): 693-704.
- 25. Arabi YM, Chrousos GP, Meduri GU. The ten reasons why corticosteroid therapy reduces mortality in severe COVID-19. Intens Care Med 2020; 46(11): 2067-70.
- 26. Okamori S, Lee H, Kondo Y, Akiyama Y, Kabata H, Kaneko Y, et al. Coronavirus disease 2019-associated rapidly progressive organizing pneumonia with fibrotic feature: two case reports. Medicine (Baltimore)2020; 99(35): e21804.
- Ministry of Health Malaysia. Organizing pneumonia in COVID-19. In: Post COVID-19 management protocol 1st edition. Medical Development Division Ministry of Health Malaysia; 2021: 54-61.
- Myall KJ, Mukerjee B, Castahnheira AM, Lam JL, Benedetti G, Mak SM,et al. Persistent post-COVID-19 interstitial lung disease. An observational study of corticosteroid treatment. Ann Am Thorac Soc 2021; 18(5): 799-806.
- 29. Wang Y, Jin C, Wu CC, Zhai H, Liang T, Liu Z,et al. Organizing pneumonia of COVID-19: time-dependent evolution and outcome in CT findings. PLOS One 2020: 15(11): e0240347.