

Post-Acute COVID-19 Syndrome after a Critical COVID-19: A Case Report

Ni Putu Rani Apsari Dewi¹, Anak Agung Gde Upeksha²

¹Intern of Pulmonology and Respiratory Medicine Department, Bali Mandara General Hospital, Denpasar, Bali, Indonesia

²Pulmonologist of Pulmonology and Respiratory Medicine Department, Bali Mandara General Hospital, Denpasar, Bali, Indonesia

Corresponding Author: Ni Putu Rani Apsari Dewi

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ABSTRACT

Introduction: The COVID-19 pandemic has caused many impacts in health, economic and social aspect worldwide. Infection of SARS-CoV-2 affects many organ systems. Post-COVID-19 syndrome is a condition when some of those infected with SARS-CoV-2 are complaining symptoms that persist for weeks to months even the PCR was negative.

Case Illustrations: We present a case of post-acute COVID-19 syndrome in a 59 years old man with persistent respiratory symptoms for 3 months since the onset of a critical COVID-19. He was admitted to the hospital with critical COVID-19 which he received treatment for COVID-19 according to protocol and mechanical ventilation via tracheostomy in intensive care unit (ICU). In the post-acute COVID-19 conditions, he complained of persistent fatigue, shortness of breath, cough, limited walking activity and palpitations.

Discussion: In most cases of asymptomatic, mild and moderate COVID-19 symptoms, patients usually resolve without complications. However, in cases with severe symptoms, systemic hyperinflammation of the immune system occurs due to activation of the SARS-CoV-2 virus which causes various complications in several organs. The management of patients with post-COVID-19 syndrome is determined based on clinical assessment of the patient, radiological examination, and laboratory and pulmonary function tests if possible. Patients with radiological abnormalities without clinical symptoms, evaluation is carried out 8 to 12

weeks after therapy and can be earlier if patients have any complains. Meanwhile patients with clinical symptoms with or without radiological abnormalities, need to evaluate after 4 weeks to see if there is any improvements. In addition to symptomatic treatment, oxygen therapy, rehabilitation, psychotherapy and nutritional therapy can also be given in patients with post-COVID-19 syndrome.

Conclusion: Post-COVID-19 syndrome is a condition that affected almost all of the organ system in the body. The most common symptoms are persistent fatigue, shortness of breath, cough, myalgia, malaise and headache. This condition impact both physical and mental health that persists for weeks or months after being infected with SARS-CoV-2. Patient with post-COVID-19 syndrome should be prioritized due to their impact on the global health burden. Those who diagnosed with post-COVID-19 syndrome also needed psychological and emotional support to deal with persistent symptoms caused by post-COVID-19 condition so the survivors can return to living their lives as before.

Keywords: Post-COVID-19 Syndrome, Long COVID, Post-Acute COVID-19 Syndrome, Critical COVID

INTRODUCTION

Since November 2019, the COVID-19 infection that began in Wuhan, China has resulted in a global pandemic. WHO reported there were more than 400 million people worldwide have been diagnosed of confirmed COVID-19.¹ As 26 January

2022, there are 4,301,193 confirmed COVID-19 cases reported in Indonesia.² The pandemic COVID-19 condition has resulted in a crisis that has an impact on all aspects of human life.¹

Long COVID or post-COVID-19 syndrome, defined as persistence signs and symptoms that continue for more than 12 weeks from the first onset of COVID-19. Those symptoms may persist for couple months after the acute COVID-19 infection.^{3,4} WHO defined post-COVID-19 syndrome as condition occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually 3 months from the onset of COVID-19 with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis.⁵ The Indonesian Society of Respiriology, defined post-COVID-19 syndrome as patient with pulmonary and respiratory or disorders that persists for more than four weeks since the onset of COVID-19 symptoms. Post-COVID-19 syndrome consists of post-acute COVID-19 syndrome (4-12 weeks) and post-COVID-19 chronic (>12 weeks).⁶

A systematic review and meta-analysis study reported that there are 80% patients complained one or more persistent symptoms after 2 weeks since the onset of COVID-19. Fatigue (58%) was most commonly reported, followed by headache (44%), attention disorder (27%), hair loss (25%), and shortness of breath (24%).⁷ A cohort study of long-term effects of COVID-19 were conducted in Wuhan, China. From 1,655 patients that have been evaluated, 1,038 patients (63%) reported fatigue/muscle weakness, followed by sleep difficulties 437 patients (26%), and then anxiety was reported among 367 patients (23%). Those are the most common symptoms reported by the patients.⁸ Meanwhile in Indonesia, from 419 patients, there were 259 patients (61.8%) experienced post-COVID-19 conditions with fatigue (29.4%) as the most common symptoms, followed by cough (15.5%).⁹

In diagnosing patient with post-COVID-19 syndrome, a complete medical history should be obtained regarding onset and duration of current symptoms, comorbidities, condition of COVID-19 acute infection, and medication history. There is no specific management for patients with post-COVID-19 syndrome. The treatment given is according to the complaints or symptomatic therapy. In addition, oxygen therapy, rehabilitation, psychotherapy and nutritional therapy can also be given in patients with post-COVID-19 syndrome. Routine laboratory assessment, pulmonary imaging, pulmonary function tests (PFTs) and 6MWT should be considered if clinically indicated.⁶

CASE ILLUSTRATION

A 59-years-old male came to emergency room on September 2021 with chief complaint of shortness breath since two days before admitted to the hospital. Shortness of breath felt increasingly worse since morning. He also complained of fever since two days before admitted, diarrhoea since seven days 4 times/day, nausea and vomiting. Patient had no symptoms of cough, flu, loss of taste or smell. History of He has received full dose (twice) of Sinovac vaccine on March 2021. Patient lived in the local transmission area of COVID-19. History of close contact to COVID-19 patients was denied. He had medical history of hypertension without consumed any medicine routinely. A day before admitted, patient went to see Urologist because there was a difficulty of urination and abdominal ultrasound was performed. Patient then diagnosed with benign prostate hyperplasia (BPH) and urine catheter was inserted.

From physical examination, patient's blood pressure was 110/80 mmHg, pulse rate 85 beat per minute, respiration rate 26 times per minute, axillary temperature 36.9°C and SpO₂ 93% room air. From the chest examination, lung auscultation identified crackles in both lung fields, mostly in basal area and no wheezing was found. Complete blood count test showed

Leukocyte $13.27 \times 10^3/\mu\text{L}$; Hemoglobin 14.4 g/dL; Hematocrit 39.4%; Platelets $208 \times 10^3/\mu\text{L}$. Renal function test was within normal limit. D-dimer level was 900 $\mu\text{g}/\text{mL}$ and the blood glucose level were 216 mg/dL. Electrolyte test showed hyponatremia (109 mmol/L) and hypokalaemia (3.1 mmol/L). Chest X-Ray showed infiltrate in both lung fields (Figure 1.) and nasopharyngeal swab RT-PCR result was positive. The initial therapy was oxygen 2 litres per minute using a nasal cannula and the oxygen saturation became 88%. Budesonide, ipratropium bromide and salbutamol were given for inhalation

therapy. He also received therapy for COVID-19 in the form of intravenous remdesivir (200 mg once a day on the first day, continue with 100 mg once on the next day for five days), levofloxacin 750 mg once a day for fourteen days intravenously, n-acetylcysteine 200 mg three times a day intravenously, steroid (dexamethasone 6 mg once a day intravenously), vitamin C 1 g once a day, vitamin D 5000 IU once a day per oral. Patient also received subcutaneous novorapid insulin 10 IU three times a day due to hyperglycemia and KSR (potassium chloride) tablet 600 mg three times a day to correct the hypokalaemia condition.

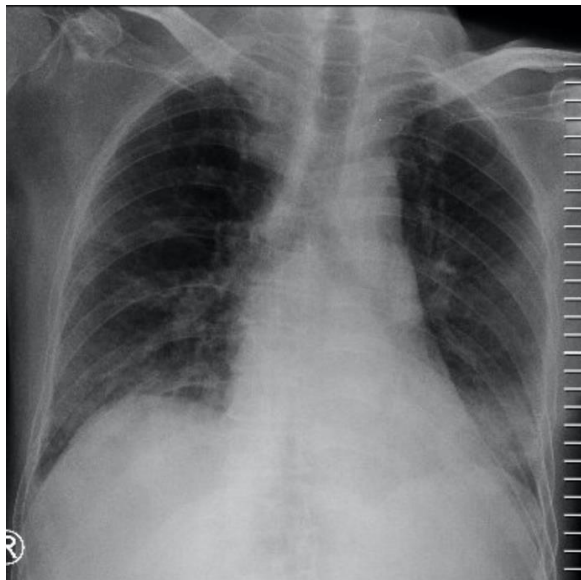


Figure 1. Chest X-Ray (1st Day)

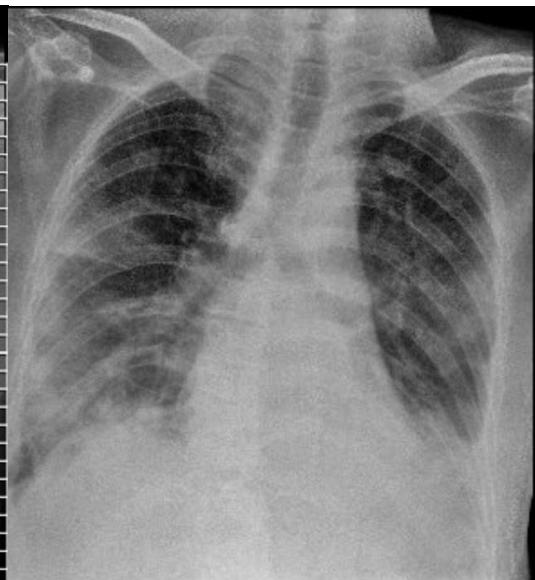


Figure 2. Chest X-Ray (5th Day)

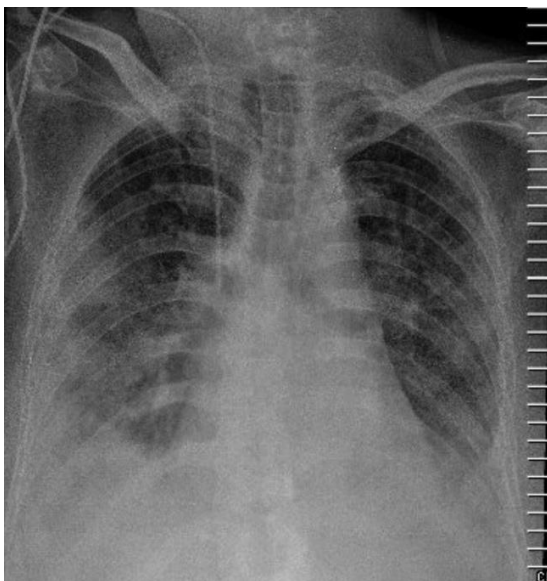


Figure 3. Chest X-Ray (11th Day)



Figure 4. Chest X-Ray (13th Day)

On the fifth day, patient's condition became hypoxic. The respiratory rate was 28 times per minute SpO₂ 96% with 15 litres per minute oxygen flow using non-rebreathing mask. Second chest X-Ray was performed (Figure 2.), showed the infiltrate on both lung fields was increase compared to the first X-Ray. Then he was transferred to the Intensive Care Unit (ICU) where he received additional therapy amikacin 1 gr once a day intravenously and convalescent plasma therapy. On the seventh day, he was tachypneic with SpO₂ became 88% then he received high-flow nasal oxygen at 40 L/minute and drip aminophylline 240 mg on NaCl 0.9% 60 cc per hour. Due to persistent hypoxemia, he was intubated on 11th days after admitted and mechanical ventilatory support with FiO₂ 95% and positive end-expiratory pressure (PEEP) of 8 cm H₂O

was placed. Third chest X-Ray (Figure 3.) showed increasing of the infiltrate in both lung fields. His blood and urine culture were sterile, the endotracheal tube (ETT) culture showed growth of respiratory flora normal. Then he received hydrocortisone 100 mg 4 times a day and cefepime 1 gr three times a day from the pulmonologist. He also received chest physiotherapy from the physiotherapist every day.

Another chest X-Ray were performed on 13th day, 17th day, 21st day, and 30th day of admission (Figure 4, Figure 5, Figure 6, and Figure 7) those showed infiltrate continuously increased in both lung fields. Another nasopharyngeal swab RT-PCR also performed on three weeks after admission with positive result. The RT-PCR repeated on five weeks of admission and the result still positive.

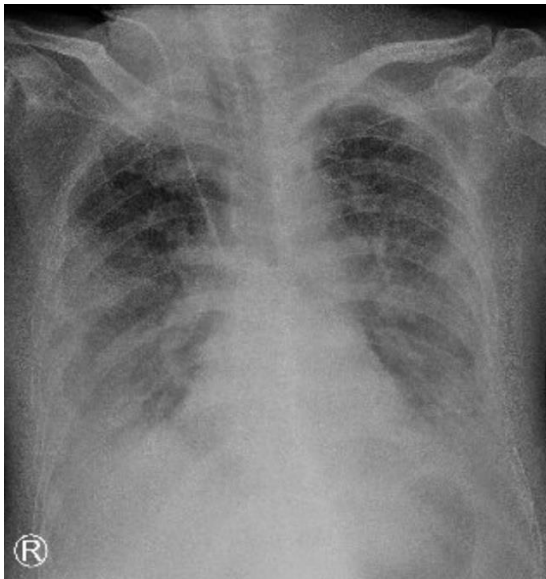


Figure 5. Chest X-Ray (17th Day)



Figure 6. Chest X-Ray (21st Day)

He was tracheostomized on the 28th day of intubation and second the endotracheal tube (ETT) culture showed growth of *Klebsiella Pneumonia* multidrug-resistant organisms (MDRO) sensitive to meropenem, then he received meropenem 1 gr three times a day intravenously. Meanwhile his blood culture was sterile. His nasopharyngeal swab RT-PCR result was negative (repeated twice) after 37 days of admission, then he was transferred to non-isolation intensive care unit (ICU).

The chest X-Ray on 33rd day, 47th day, 71st day of admission (Figure 8, Figure 9 and Figure 10) showed that the infiltrate gradually decreases compared to the last chest X-Ray. Over 62 days after intubation, he was gradually weaned off ventilator support. He was discharged after 74 days, with oxygen therapy at home.

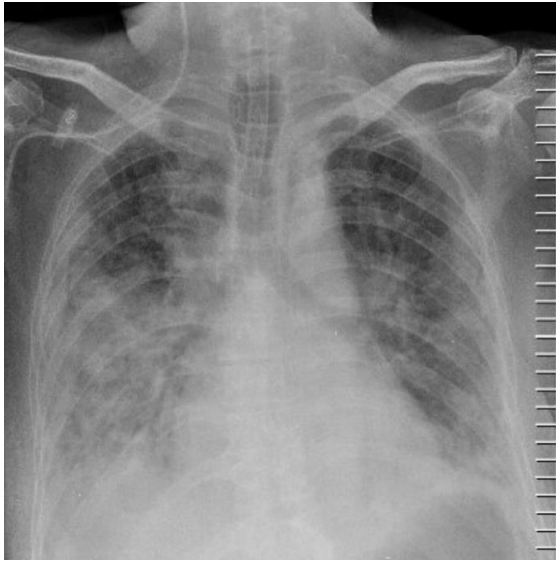


Figure 7. Chest X-Ray (30th Day)



Figure 8. Chest X-Ray (33rd Day)

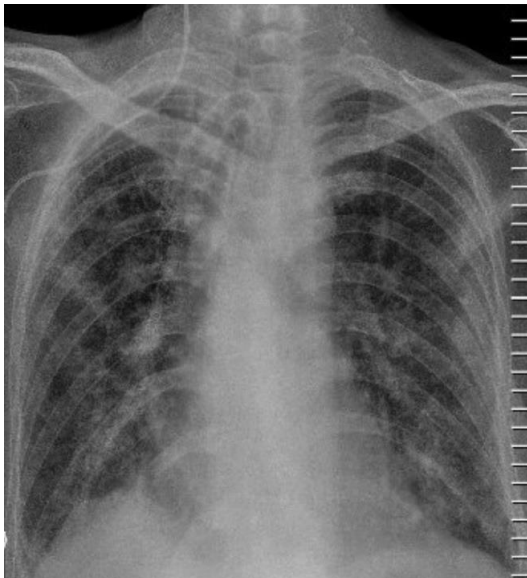


Figure 9. Chest X-Ray (47th Day)

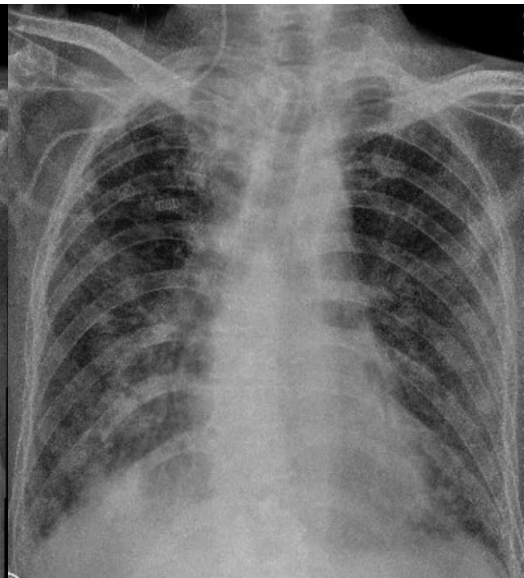


Figure 10. Chest X-Ray (71st Day)

In the post-acute COVID-19 syndrome condition, 3 months after onset of COVID-19, he came to the pulmonology polyclinic complained of persistent fatigue, minimal shortness of breath, limited walking activity and palpitations. He went to see a surgeon for his tracheostomy then it was decannulated. Physical examination was within normal limit. Spirometry test was performed with result: SVC: 10.3%; FEV₁: 16.3%; FVC: 13.1%; FEV₁/FVC:100%. He was later discharged home with mix capsule (consists of theophylline, methylprednisolone, salbutamol, antihistamine, acetylcysteine), mucolytics syrup, budesonide and formoterol inhalation twice a day, once in

the morning, once in the night. His condition was followed-up every week to see the progress of the condition. The next two weeks, he complained of fatigue, shortness of breath that came often and limited walking activity which he was on wheelchair while do his daily activity. There was no cough and palpitations. Patient no longer used oxygen therapy at home with oxygen saturation was at range 92-94% room air. Pulmonary function was evaluated four weeks after the last one with result: SVC: 27.9%; FEV₁: 20.9%; FVC: 16.8%; FEV₁/FVC: 100%. He was prescribed with mix capsule but with lower dose which was once a day and budesonide and formoterol inhalation twice a day.

DISCUSSION

The incidence of post-COVID-19 syndrome or long COVID-19 has been reported since middle 2020. On September 2020, WHO reported there was 35% who had been suffered from COVID-19 claimed that their physical condition was not optimal as before. In the 18-24 year age group without any comorbid conditions, 1 out of 5 patients experienced post-COVID-19 syndrome.¹⁰ There are several risk factors of post-COVID-19 syndrome. The first one is gender, where women tend to experience post-COVID-19 syndrome more often than men. In addition, age also affects the incidence of post-COVID-19 syndrome, where age more than 50 years has a greater risk for the occurrence of post-COVID-19 syndrome. The presence of more than 5 symptoms during acute COVID-19 infection conditions (fatigue, headache, dyspnea, myalgia, loss of taste/smell) and patients with two or more comorbidities prior to COVID-19 infection have a higher risk to experience post-COVID-19 syndrome.^{10,11} The reported case is about 59-years-old man complained of persistent fatigue, shortness of breath, cough, limited walking activity and palpitations. On his acute COVID-19 condition, he complained of fever, fatigue, shortness of breath, nausea and vomiting. He also had history of hypertension and BPH before admitted to the hospital. Due to those history, patient had a high risk to experience post-COVID-19 syndrome.

Respiratory symptoms are not the only sign and symptoms included in post-COVID-19 syndrome. It affected almost all of the organ system in the body. The most common symptoms are persistent fatigue, shortness of breath, cough, myalgia, malaise and headache.^{9,12} Those symptoms may last and persistent for weeks or months, even more than 6 months after the acute condition. Patient with post-COVID-19 syndrome may also experience anxiety, depression and also sleep disorder.^{8,12} There are several hypothesis of post-COVID-19 syndrome mechanism. The acute SARS-CoV-2 infection may cause damage to the

endothelial tissue that activate immune system and inflammation of the lung. Due to chronic inflammation, the damage of endothelial tissue may activate fibroblast and cause fibrotic changes. Elderly patient with history of acute respiratory distress syndrome (ARDS) had risk of developing fibrotic changes of lung.^{12,13} In the reported case, in the post-COVID-19 condition patient complained of persistent fatigue, minimal shortness of breath, limited walking activity and palpitations three months from the onset of COVID-19. Patient also had history of ARDS before that increased the risk of post-COVID-19 syndrome.

The diagnostic criteria for post-COVID-19 syndrome are a) patient has been confirmed COVID-19; b) there are pulmonary and respiratory symptoms or disorders that persists for more than 4 weeks since the onset of COVID-19; c) one or more of the following symptoms and/or signs: dry cough or phlegm, shortness of breath/heavy breathing/ breathlessness, limited activity, chest discomfort/pain, sore throat. Post-COVID-19 syndrome categorized into two, post-acute COVID-19 syndrome and post-COVID-19 chronic syndrome. The difference between those category is the duration of the symptoms. For the post-acute COVID-19 syndrome, the symptoms persists for more than 4 weeks until 12 weeks, and the post-COVID-19 chronic syndrome more than 12 weeks.^{5,6,14} From the case description above, it is known that the complaints felt by the patient when he went to the pulmonology polyclinic were in accordance with the diagnostic criteria for post-acute-COVID syndrome.

Treatment for the post-COVID-19 syndrome divided into three groups based on symptoms and radiological findings. Treatment given for the first group, patient with no clinical symptoms but there are abnormalities from radiological examination were multivitamins, symptomatic therapy according to the complaints and the pulmonary function test result. Evaluation needed after 8-12 weeks or maybe earlier if

there is any complains. For the other two groups, those are patient with clinical symptoms with or without abnormalities from radiological examination were given 1) symptomatic therapy; 2) multivitamins; 3) bronchodilator if there are any symptoms of respiratory obstruction or the result of the pulmonary function test shows an obstruction; 4) mucolytics and antioxidant; 5) antibiotics if there is any bacterial infection. In patient with clinical symptoms and abnormalities of radiological examination, anti-inflammatory therapy may be considered, one of these or combination: a) macrolide (azithromycin 250 – 500 mg or clarithromycin 250 – 500 mg or erythromycin 250 mg) for minimal one month and need to re-evaluated; b) steroid (oral or inhalation). For the last two groups, progress of the treatment needs to evaluate after 4 weeks. Treatment can be continued and need to re-evaluate after 3 months and 6 months if there are any improvements. Other possible cause and etiology need to find out if the complaints or radiological finding get worse.^{6,15} The treatment of post-COVID-19 syndrome on the reported patient were according to the patient's complaints. Patient given steroid inhalation due to the spirometry test result showed there was an obstruction. From the treatment evaluation after 4 weeks, there was an improvement both from the clinical symptoms and pulmonary functions.

CONCLUSION

Post-COVID-19 syndrome is a condition that affected almost all of the organ system in the body. The most common symptoms are persistent fatigue, shortness of breath, cough, myalgia, malaise and headache. This condition impact both physical and mental health that persists for weeks or months after being infected with SARS-CoV-2. Patient with post-COVID-19 syndrome should be prioritized due to their impact on the global health burden. There is no specific management for patients with post-COVID-19 syndrome. The treatment given is according to the complaints or

symptomatic therapy. In addition, oxygen therapy, rehabilitation, psychotherapy and nutritional therapy can also be. Those who diagnosed with post-COVID-19 syndrome also needed psychological and emotional support to deal with persistent symptoms caused by post-COVID-19 condition so the survivors can return to living their lives as before.

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Disclosure of Interest

The authors declare that they have no conflicts of interest concerning this article.

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