

Clinical Progression of COVID-19 Patient with Extended Incubation Period, Delayed RT-PCR Time-to-positivity, and Potential Role of Chest CT-scan

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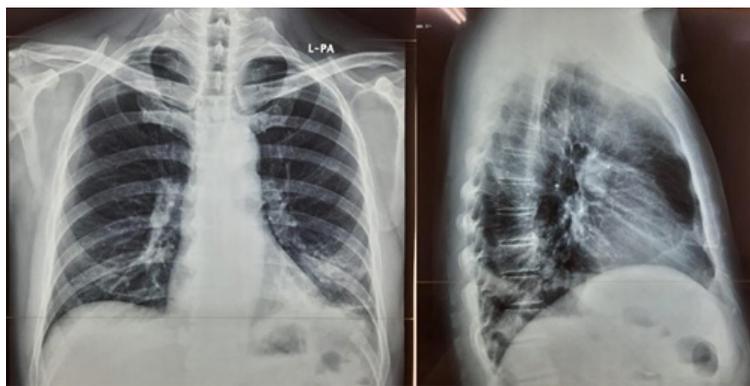


Figure 1. CXR day 7.

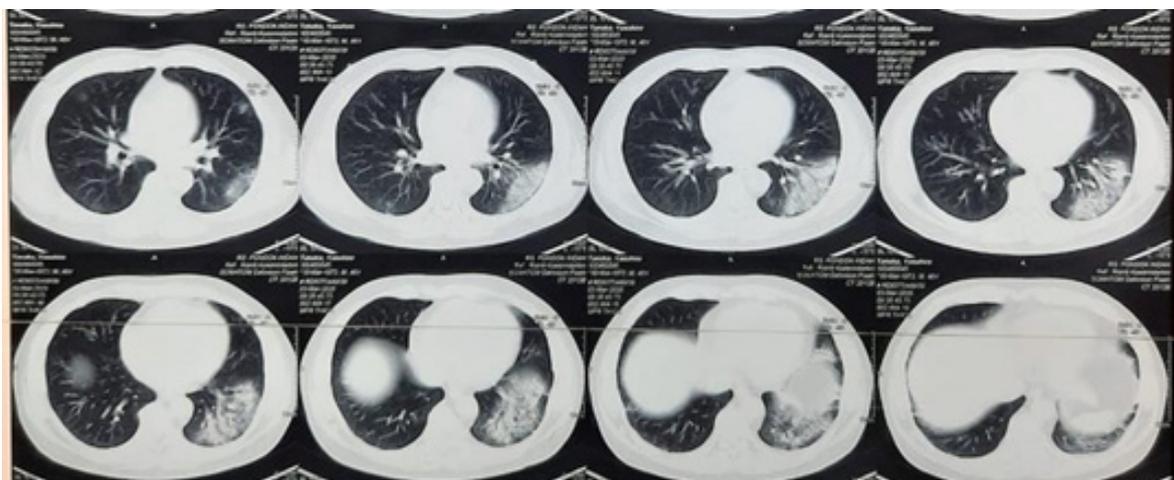


Figure 2. Thorax CT-Scan day 7 of symptoms.

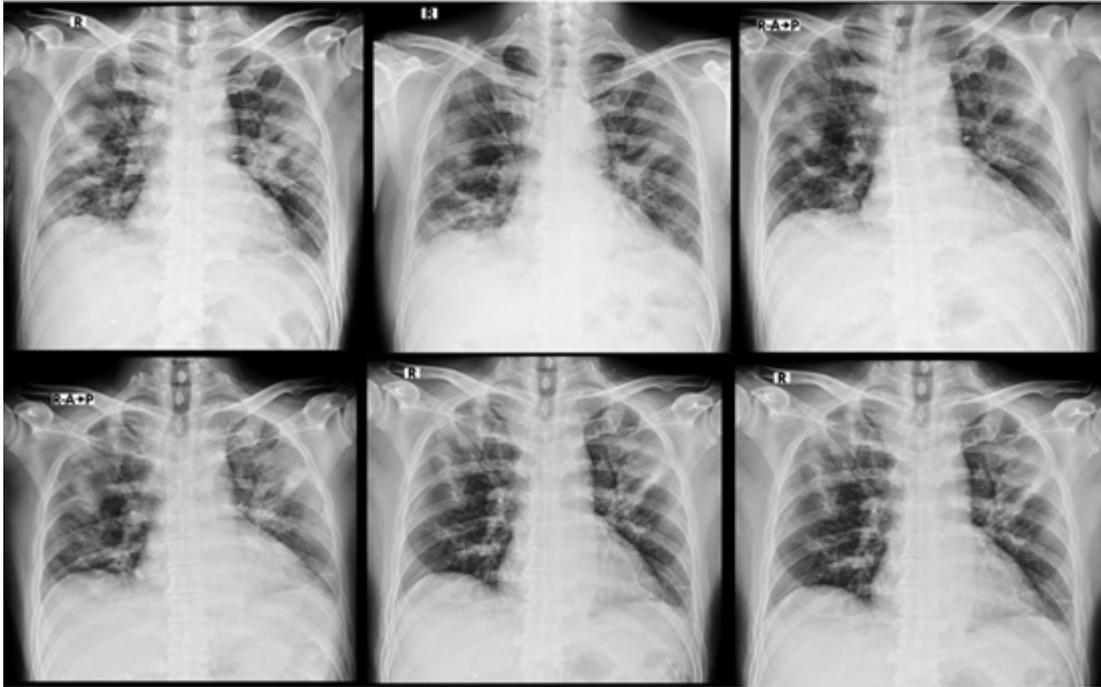


Figure 3. From upper left to bottom right is CXR day 14 to day 19.



Figure 4. CXR day 20 (left), day 21 (middle), day 23 (right).



Figure 5. CXR day 23 (left) and day 25 (right).

Coronavirus Disease 2019 (COVID-19), previously called 2019-nCoV, is a novel disease caused by SARS-CoV-2 which was first identified as outbreak of unknown respiratory illness in Wuhan, China.^{1,2} COVID-19 was declared as global health emergency by WHO on March 11, 2020 and quickly elevated to global pandemic on 11 March 2020.³ COVID-19 symptom is highly various in each patient, with fever, fatigue, shortness of breath, and cough as the main presenting symptoms.⁴ Patient with COVID-19 may show severe symptom with severe pneumonia and ARDS, mild symptom resembling simple upper respiratory tract infection, or even completely asymptomatic.⁵ Approximately 80% of cases is mild. However the number may change as more people are getting tested.⁵ Some experts are estimating that up to 50% of all cases may be asymptomatic carrier.^{6,7}

A 47-year old man, Mr. TY was admitted to emergency room with acute respiratory distress syndrome following 10 days of respiratory symptoms. Patient has no history of travelling overseas. However, he has history of meeting colleague with recent travel history to Japan approximately 2 weeks before onset of symptoms.

The first symptom appeared was mild fever of 37.6°C. No cough or sore throat was reported. On day 3 patient went to local clinic and diagnosed with bronchitis and was given Moxifloxacin as therapy. Chest x-ray (CXR) was done and did not show signs of pneumonia. The attending did not include COVID-19 in the differential since patient has no history of travelling to countries affected by COVID-19.

On day 7, patient reported mild fever of 37.8°C and fatigue. No cough and sore throat were reported. Patient underwent CXR and CT Scan and shows sign of left lobar pneumonia. Patient was treated with Meropenem.

On day 10, patient developed acute respiratory distress syndrome (ARDS). Swab specimen was taken to be tested for COVID-19. The result came out on day 13 and was negative. Swab specimen was taken again for the second time on day 13. On day 14 result came out and was positive. Patient was diagnosed with COVID-19 and was referred to Persahabatan General Hospital Jakarta (PER).

During hospitalization at PER, patient was

treated with Oseltamivir 2x75mg, chloroquine 2x500mg, Levofloxacin 1x750mg, Vitamin C 2 x 1000mg, Vitamin B1 1x100 mg, Vitamin B6 1x100mg, and Vitamin B12 1x200mcg. Clinical condition is gradually improved with total resolution 25 days after onset of symptom.

CXR was done daily for 12 days and shows improvement of infiltrate and consolidation. Patient was discharged on day 27 after onset of symptoms.

Coronavirus Disease 2019 (COVID-19) is caused by SARS-CoV-2 virus, a member of coronaviridae family with crown-like appearance under electron microscope.² Coronavirus (CoV) is a common virus that able to infect various species and causes various disease in multiple organ such as respiratory, enteric, hepatic, and neurological diseases in different animal species, including camels, cattle, cats, and bats. Up until now, seven human CoVs (HcoVs) — have been identified. SARS-CoV-2 belong to the betaCoV category. It is sensitive to ultraviolet rays, heat, and can be effectively inactivated by lipid-solvent.

Transmission of SARS-CoV-2 is mainly through respiratory droplet produced from coughing and sneezing of infected individual. Healthy person can get exposed to these droplet directly or indirectly, for example from contaminated surface.

Based on the available evidence from report of Wuhan COVID-19 early cases, the mean incubation period of COVID-19 is 5.2 days with the 95th percentile of distribution at 12.5 days.⁸ The clinical spectrum of COVID-19 is various. Ranging from asymptomatic forms, mild upper and lower respiratory tract infection, to severe clinical conditions characterized by respiratory failure requiring mechanical ventilation and support in an intensive care unit (ICU), to multiorgan and systemic manifestations in terms of sepsis, septic shock, and multiple organ dysfunction syndromes (MODS).² Mortality and severe manifestations are higher in older individual aged ≥ 80 years (15%) and age 70-79 years (8%). Half of patient with critical conditions had underlying disease such as cardiovascular disease, diabetes, chronic respiratory disease, and oncological disease.

Based on study of clinical progression done in Shanghai, the duration from onset of symptoms to hospitalization was 4 days in symptomatic patients. Most patient are discharged after 16 days. Median duration of fever in all patients is 10 days after onset of symptoms. Radiologic finding was found to be worsening mostly after 7 days after onset of symptoms and show improvement 14 days after onset of symptoms.⁹

Characteristic and clinical progression of COVID-19 in the patient reported in this paper matched with the previous study. The patient was male, 47 year-old with history of contact with person travelling from aboard. The symptoms appear gradually and peaked in the middle of the whole clinical progression. The radiological finding also worsen starting from day 7 of symptom and started to improve starting from day 15 after onset of symptom. However, the clinical progression is overall extended. According to the previous study the mean incubation period of COVID-19 is 5.2 days with the 95th percentile of distribution at 12.5 days. Mr. TY in this paper mostly stayed in the suburban village and did not have travel history within 30 days of onset of symptoms. His last contact with colleague with travel history to affected areas was 14 days before the onset of symptoms. Mr. TY also need to be hospitalized only starting on day 7 after onset of symptom and starting to clinically deteriorate on day 10. This overall extended timeframe of clinical progression resulted in extended duration of hospitalization, which was 27 days, compared to 16 days in previous study.⁹

It is also important to be noted that patient was tested for COVID-19 using RT-PCR on day 10 of symptoms with negative result. Positive result was obtained from swab sample taken on day 13. This delayed time-to-positivity resulted in delayed time-to-diagnosis for this patient. This result consistent with findings from Ai, et al that showed 5.1 days mean interval between initial negative RT-PCR to positive RT-PCR on subsequent testing.

Patient undergone chest CT-Scan on day 7 and found to have left lobar pneumonia, eventhough RT- PCR only showed positive result on day 13. According to study done by

Ai, et al.¹⁰ sensitivity of RT-PCR in detecting COVID-19 is around 59%. On the contrary, 97% of patient with positive RT-PCR have lesion suggestive of COVID-19, even before the RT-PCR showed positive result on initial testing. This result may suggest that in an area with high number of COVID-19 case, CT-Scan might be a better diagnostic tool compared to RT-PCR in diagnosing COVID-19.

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