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Persistence Detection of Sars-Cov-2 RNA in Healthcare Workers with COVID-19: A Case Report

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ABSTRACT

Coronavirus Disease 2019 (Covid-19) has now become a concern around the world. Until 6 September 2020, there were 190,665 cases in Indonesia, and it was in the third rank of most cases in the Asian region. It is important to determine the criteria of return to work for healthcare workers with Covid-19 positive in Indonesia. This case report discussed a female patient, 32 years old with chief complaint of fever and itchy throat since 2 days ago. She is a health care worker in the hospital, with a history of treating patients with positive confirmation of Covid-19 for 2 days in the ordinary ward before the case was confirmed with a history of contact approximately 5 days ago. The patient was diagnosed with positive confirmation of Covid-19 and was required for self-isolation. The patient still had positive results of RT-PCR Covid-19 up to the third examination in 30 days after the initial RT-PCR testing, although received specific antiviral treatment with oral oseltamivir and oral supplementation. Based on growing evidence that Sars-Cov-2 may not infectious for more than ten days in the mild-moderate disease, this case report is strengthening the use of symptom-based strategic approach to determine when to return to work in Indonesian healthcare workers with positive COVID-19.

Keywords: COVID-19; health personnel; oseltamivir; return to work; reverse transcriptase-polymerase chain reaction

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Introduction

In December 2019, a new case of pneumonia was found in Wuhan City, China, which was caused by a group of beta coronavirus named 2019-nCov. Recently, it is called Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2). This virus is the seventh member of the coronavirus family that can infect humans. The disease caused by SARS-CoV-2 is called Coronavirus Disease 2019 (Covid-19) which has now become a concern around the world[1–3].

According to WHO, until 6 September 2020, there were 26,763,217 cases of Covid-19 that occurred worldwide. The number of cases in Asia was in the second-highest number of cases based on region, where the number reached 4,689,943 cases. As for Indonesia, there were 190,665 cases, and it was in the third rank of most cases in the Asian region[4].

In a study conducted in London since 23 March 2020, the percentage of asymptomatic covid-19 cases among health care workers was 28 of 396 cases (7.1%) in the first week, 14 of 284 cases (4.9%) in the second week, 4 of 263 cases (1.5%) in the third week, 4 of 267 cases (1.5%) in the fourth week, and 3 of 269 cases (1.1%) in the fifth week[5]. In another study, it was found that 10.1% of Covid-19 cases were health care workers, while the severity and the mortality rate of the disease for them were lower than the patients in general[6]. This case report discussed a 32-years-old female health care worker in a private hospital, who was diagnosed with Covid-19 and had a persistent polymerase chain reaction (PCR) testing positive up to 30 days after initial testing.

Case

A 32-years-old female patient with chief complaint of fever and itchy throat since two days ago. The patient did not have complaints of odynophagia, cough, or shortness of breath. The patient is a health care worker in the hospital, with a history of treating patients with positive confirmation of Covid-19 for two days in the ordinary ward before the case was confirmed with a history of contact approximately five days ago. The patient did not have diabetes mellitus, hypertension, asthma, or obesity. There were none of her family members with a similar illness. The patient did not have any psycho-social problems.

The patient was conscious with a body temperature was 36.5ºC. The other vital signs were normal. There was no abnormality in the head-to-toe physical examination. A Rapid Test was performed with reactive IgM and reactive IgG results five days after the first contact with a covid19 confirmed patient (Figure 1). Then the patient underwent the SARS Cov-2 PCR testing on the 7th and 8th day after the first contact with positive results for both testings. Because this was a mild case and none of the risk factors for developing to severe covid-19 illness, according to recent Indonesia's guideline on Covid-19, we did not perform other examination such as complete blood count and chest radiography[7].

Based on the anamnesis, physical examination, and laboratory testing, particularly the PCR testing result, she was diagnosed with a positive confirmed Covid-19. Because of her mild disease, she was only required to self-isolation for fourteen days.

During self-isolation, the patient only had been receiving the symptomatic drug, such as paracetamol to heal the fever. The patient also had self-treatment with chemical or natural oral supplementations, such as Mega-Zink, Ester-C, and noni juice. The patient still had a subfebrile up to day-7 without any other signs and symptoms. On the 14th day after the first PCR testing, the second PCR testing was carried out with a positive result, so that the self-isolation was continued for fourteen days, even though the patient had a clinical resolution. Fourteen days later, the third PCR testing was still positive. We assessed the possible risk factor for prolonged SARS-Cov-2 viral positivity based on the previous study, namely older age, more severe cases, present of coronary heart disease (CHD), later time of antiviral treatment, lower albumin level, initial lower count of lymphocyte, eosinophils, and CD8+ T cells, and initial higher IL-6 and IL-10 levels[8,9]. Because we did not perform complete blood count examination and cytokine analysis initially, we only found the later time of antiviral treatment as a possible risk factor for persistence Sars-COV-2 RNA positive result in this patient. Five days after the third PCR testing, the patient was given Oseltamivir 75 mg tablets 2 times a day for five days in order to help change the PCR test result.

In the next eleven days, the patient performed another Rapid Test with the results of non-reactive IgM and non-reactive IgG. The patient was planned for the fourth PCR testing, but it could not be done due to policy problems. The patient's laboratory testing result is summarized in Table 1.

Figure 1. Rapid test antibody of Sars-Cov-2 result of the patient showed a pink line on IgM and a red line on IgG.

Table 1. The patient's laboratory testing results

Date	Laboratory Testing	Result
7/ 22/ 2020	Rapid Test	IgM reactive/IgG reactive
7/ 22/ 2020	PCR	Positive
7/ 23/ 2020	PCR	Positive
8/ 06/ 2020	PCR	Positive
8/ 20/ 2020	PCR	Positive
8/ 31/ 2020	Rapid Test	IgMnon-reactive/IgG non-reactive
8/ 31/ 2020	PCR	Unprocessed

During self-isolation, the patient had been closely monitoring by the COVID-19 task force team of the hospital with the telemedicine approach. The patient adhered and tolerated the treatment that was given by the hospital internist, without any adverse and unanticipated events. The symptoms resolved in the seven days after initial diagnosis with COVID-19 and seroconversion of the Rapid Test results in fourty days after initial testing. Based on the risk of reinfection of Covid-19 in health care workers, we assessed the clinical criteria of Covid-19 reinfection in this patient. According to Tomassini *et al* (2020), the patients must have an initial SARS-Cov-2 PCR-confirmed illness, followed by clinical recovery and discharge with at least one negative SARS-Cov-2 PCR result, and followed by a confirmed SARS-Cov-2 PCR positive results (with or without symptoms) at least 28 days after the previous SARS-Cov-2 PCR result to fulfill the criteria for possible reinfection of Covid-19 cases[10]. This patient did not meet the second criteria, because the SARS-Cov-2 PCR result still positive until 28 days after initial PCR testing, although there were clinical resolutions of the patient in that period. Finally, the patient had been permitted to return to work according to her health status and last Rapid Test result [11].

Discussion

In this case, the patient is a health care worker at the hospital who is in charge of providing services in an ordinary (non-covid) room. She works 12-hour shifts per day with a system of four days of work and two days off. The patient had married and her husband works as a sailor who had just returned from sailing for about one month before the patient tested positive for Covid-19. The patient was screened for Rapid Test and RT-PCR due to her status as a close contact because she had treated a positive Covid-19 patient. She was then diagnosed as a covid-19 confirmed patient after getting positive results on the RT-PCR testing for two consecutive times with 24 hours interval[7]. The patient was categorized as a symptomatic confirmation case with a fever that was felt for seven days without any other symptoms. Because she only suffered mild illness and none of the risk factors for developing to severe covid-19 illness, according to recent Indonesia's guideline on Covid-19[7], the patient then performed self-isolation at her home.

We did not perform hematology and radiology examination. A recent review suggests that further hematology examination is only performed on hospitalized patient[12]. Also, Ghosh *et al* (2020) suggest that further chest imaging is only performed on a patient with worsening clinical status[13]. In other hand, the RT-PCR testing was carried out periodically four times each fourteen days with a positive result up to the third examination. The 4th RT-PCR testing could not be carried out due to policy constraints from the local health office. The patient was then tested for IgM / IgG with non-reactive results and the patient was allowed to return to work while still adhering to health protocols.

There are two strategies for health care workers to be able to return to work after being confirmed positive for Covid-19, namely based on symptoms and based on the results of the RT-PCR testing. Symptom-based strategies are aimed at health care workers with mild-moderate symptoms who can return to work if they meet three criteria: at least ten days after symptom onset, free of fever for at least twenty-four hours without fever-relieving drugs, and there is an improvement in symptoms (such as cough, shortness of breath, etc.). While the strategy based on the results of the RT-PCR testing for symptomatic health care workers has three criteria: recovery from fever without using fever-relieving drugs, there is an improvement in symptoms (such as cough, shortness of breath, etc.), and two negative results on testing with specimens from the respiratory tract with an interval of at least twenty-four hours. Although the strategy based on the RT-PCR testing is no longer recommended because a positive test does not indicate an infectious condition, this strategy has the advantage that health care workers can return to work more quickly if they meet the existing criteria regardless of time[14]. This is what underlies the repeated RT-PCR testing in this case, even though in Indonesia, generally it follows the guidelines for self-isolation without re-examination[7].

In this patient, the first test to be performed was the combination IgM / IgG test. This examination was chosen as a screening because it has a shorter examination time of fewer than fifteen minutes. The Rapid Test cassette showed a pink line on IgM and a red line on IgM which indicates a reactive result[15]. Reactive IgM can be found on day ten after symptom onset with a peak at day twenty-one or can also be found on day eighteen after exposure to the virus with a peak at day thirty-seven. Meanwhile, reactive IgG can be found on day twelve after symptom onset with a peak on day twenty-nine or can also be found on day twenty after exposure to the virus with a peak on day thirty-seven[16]. When related to this case, on the Rapid Test, IgG had a clearer picture when compared to IgM, so it can be predicted that the patient was exposed to the virus at most thirty-seven days before. In this patient, symptom onset was seen two days before the test. Assuming that the patient was exposed to the virus thirty-seven days previously, this is the case with a long incubation period. The incubation period is the period between the first time an individual is exposed to the virus to the first time the individual shows symptoms, where for the case of Covid-19 it has an incubation period of 0-23 days with a median value of five days (Inter Quartile Range: 2-10 days)[16].

Furthermore, RT-PCR testing was carried out twice with an interval of 24 hours with positive results for both. To confirm a case of Covid-19, it is necessary to detect SARS-CoV-2 virus RNA by examining the Nucleic Acid Amplification Test (NAAT) such as real-time reverse-transcription polymerase chain reaction (rRT-PCR) with swab samples from the upper airway, namely nasopharyngeal and oropharyngeal and/or sputum from the lower airway[17]. In this patient, the positive result was obtained from the nasopharyngeal and oropharyngeal specimen, so that this patient was declared a positive confirmation patient for Covid-19[7]. On the 14th and 28th days after initial testing positive, the patient retesting for the RT-PCR with a positive result. As a comparison, in one study conducted in China, some cases recurrent positive after being discharged from the hospital[18]. It was found that the period for a symptomatic Covid-19 patient to become negative based on RT-PCR testing with a nasopharyngeal swab sample was up to 45.6 days from symptom onset[19].

In another study, it was found that patients who were positive for covid-19 would become negative on the RT-PCR testing on the 33rd day after symptom onset, especially for health care workers, the RT-PCR testing would be negative on twenty-three days from the first positive examination. In this study, it was also stated that a persistent positive condition among health care workers occurred at a mean age of 35 years with 67.2% being women[20]. A condition in which the PCR examination is persistently positive only shows the presence of the virus but does not indicate that the patient is still infectious. One of the causes of this condition is the insufficiency of the immune system of the sufferer and the insufficiency of neutralization antibodies (NAbs)[18]. This explains why the criteria for health care workers who are confirmed positive Covid-19 are preferred using criteria based on symptoms for return to work[14].

During self-isolation, the patient had a specific treatment with antiviral, namely oseltamivir to help change the PCR test results. In a clinical study of four patients with confirmed mild or no symptoms of COVID-19, administration of oseltamivir 2 times 75 mg daily was able to improve symptoms and CT scan image abnormalities and was able to quickly change the RT-PCR test results to negative[21]. This effect may appear when early treatment is given, rather than late treatment[22]. Although other clinical studies have shown that administering oseltamivir is ineffective in improving outcome in symptomatic COVID-19 patients[23]. Further studies are needed to confirm the effectiveness of oseltamivir in the treatment of COVID-19.

During treatment, the patient felt that she was been receiving therapy according to her needs. The patient also felt pleasant because she was closely monitored by the COVID-19 task force team of the hospital and got great social support from their fellow healthcare workers and family. However, the patient was still worried whether she still had the virus in her body or not, because the last RT-PCR examination was not done. At least, according to simple algorithm for return to workplace employer algorithm by Shrank *et al* (2020), rapid antibody testing and clinical status had been performed on this patient to guide how will she return to work [11].

Finally, the patient underwent a Rapid Test eleven days apart from the last PCR with non-reactive results for IgM and non-reactive results for IgG. Based on the description of this case, it can be concluded that the positive Sars Cov-2 RT-PCR testing can be persistent up to 30 days after the initial RT-PCR testing. Some possible risk factors for prolonged SARS-Cov-2 viral positivity are older age, more severe cases, present of coronary heart disease (CHD), later time of antiviral treatment, lower albumin level, initial lower count of lymphocyte, eosinophils, and CD8+ T cells, and initial higher IL-6 and IL-10 levels[8,9]. Later time of antiviral treatment may be the risk factor for prolonged Sars-Cov-2 detection in this patient.

Especially for health care workers in Indonesia who are confirmed positive for Covid-19, it is recommended to use a symptom-based strategic approach to determine when to return to work. Use adequate personal protective equipment and perform strict general precautions procedures is essential after the health care worker returns to work. In our knowledge, this is the first scientific case report in Indonesia regarding a health care worker who has persistent Sars-Cov-2 RNA detection up to thirty days after the initial positive result. There was a limitation of this report due to the absence of supporting laboratories, such as complete blood counts and albumin level measurements to analyze the risk factor for prolonged viral shedding on this patient.

In conclusion, the persistence of Sars-Cov-2 RNA detection may be revealed up to 30 days after initial positive PCR testing and may be associated with later antiviral treatment. Based on growing evidence that Sars-Cov-2 may not infectious for more than ten days in the mild-moderate disease, this case report is strengthening the use of symptom-based strategic approach along with simple algorithm antibody testing to determine when to return to work in Indonesian healthcare workers COVID-19 confirmed case.

Conflict of Interest
Nothing to declare.

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