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Re-Infection of COVID-19 at Dr. Moewardi General Hospital, Surakarta, from March 2020 to June 2021

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ABSTRACT

Background: COVID-19 reinfection has been identified and is being studied. Several risk factors, including being a health worker and having A blood type, are linked to reinfection, and comorbidities such as hypertension, obesity, diabetes, and asthma influence the disease's severity. To identify mutational variations associated with viral virulence and spread, genetic studies are required. The purpose of this study is to determine the prevalence of SARS-CoV-2 reinfection, as well as patient characteristics and risk factors related to SARS-CoV-2 reinfection.
Subjects and Method: This is a retrospective cohort study using data from the medical records of patients with COVID-19 reinfection treated at the Dr. Moewardi General Hospital (RSDM) Surakarta from March 2020 to June 2021. A sample was collected from 19 men and 20 women. The degree of COVID-19 infection is the dependent variable. Gender, occupation, comorbidities, and immunization history were the independent variables. The entire sampling method was employed in this investigation (consecutive sampling). Data is handled in Microsoft Excel 2010, and statistical analysis is performed in SPSS version 20.0.
Results: COVID-19 re-infection is equally likely in men and women. The average patient age was 42 years, with patients ranging in age from 25 to 73 years. Patients in the study were classified as either health workers or non-health workers, with 29 (76.3%) and 9 (23.7%) respectively. Due of restricted resources, the average period of COVID-19 re-infection is 197.6 +/- 97 days without genomic sequence investigation. Comorbidities were discovered in 11 of 38 COVID-19 reinfection patients (29%) Only 6 individuals (15.8%) with COVID-19 reinfection had a history of vaccination.
Conclusion: Using convalescent plasma to treat patients with COVID-19 is a rather safe practice. Our analysis demonstrated that the administration of convalescent plasma did not enhance survival or clinical outcomes for COVID-19 patients with moderate to severe disease.

Keywords: COVID-19, COVID-19 reinfection, health workers, comorbidity

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BACKGROUND

COVID-19 reinfection has been identified and is being studied. The prevalence of SARS-CoV-2 re-infection ranges from 7.3 to 21.4% (Azam et al., 2020). The risk of COVID-19 reinfection due to reinfection or reactivation of SARS-CoV-2 is still being studied. Several investigations have indicated that patients with a history of symptom improvement had positive real-timereverse-transcription polymerase chain reaction (RT-PCR) results and negative RT-PCR results (Adrielle dos Santos et al., 2021; Gao et al., 2021; Ozaras et al., 2020).

The mechanism of COVID-19 re-infection is unknown. According to the Gao (2021) study, older people and women are more likely to have re-positive outcomes (Gao et al., 2021). According to Adrielle dos Santos et al. (2021)'s study in Brazil, re-infection causes more severe symptoms than earlier occurrences. Risk factors for reinfection include being a health worker and having A blood type. Comorbid conditions such as hypertension, obesity, diabetes, and asthma are not related with reinfection but do affect the disease severity of moderate or severe COVID-19 reinfection (Adrielle dos Santos et al., 2021).

The gold standard diagnosis of COVID-19 reinfection necessitates genomic sequencing tests, which are not presently available in every healthcare facility. According to Farrukh et al. (2021), positive RT-PCR results after previously being negative could be due to mistake sampling, reinfection with the same viral variation, or a new type of variant that suffered changes. The majority of asymptomatic or minimally symptomatic reinfections are assumed to be the result of past exposure immunity. To identify mutational variations associated with viral virulence and spread, genetic studies are required (Duggan et al., 2021; Falahi and Kenarkoohi, 2020; Farrukh et al., 2021). This study aims to assess the incidence of SARS-CoV-2 reinfection, patient characteristics, and risk factors associated with SARS-CoV-2 reinfection.

SUBJECTS AND METHOD

1. Study Design

This is a retrospective cohort study using data from the medical records of patients with COVID-19 reinfection treated at the Dr. Moewardi General Hospital (RSDM) Surakarta from March 2020 to June 2021.

2. Population and Sample

The entire sampling method was employed in this investigation (consecutive sampling). A sample is collected from 19 men and 20 women. All adult patients aged 18 years who had COVID-19 re-infection based on RT-PCR results and were treated in the isolation room at the Dr. Moewardi General Hospital (RSDM) Surakarta from March 2020 to June 2021 were eligible. In this study, the exclusion criteria were missing medical record data.

3. Study Variables

Dependent Variable is the degree of COVID-19 infection. Independent Variable is Gender, Occupation, Comorbidities, and Immunization History.

4. Operational definition of variables

The degree of COVID-19 infection is divided into mild disease, moderate disease, severe disease, and critical ill based on the sign and symptoms.

Gender is divided into men and women.

Occupation is divided into health worker and non-health worker

Comorbidities included asthma, SLE, hypertension, DM, CAD, epilepsy, thymoma, and CKD.

Immunization history devided into a group of vaccinated and un-vaccinated.

5. Study Instruments

The degree of COVID-19 infection was measured by the sign and symptoms.

6. Data analysis

The analysis in this study is presented with the distribution of frequencies and percentages for categorical data.

7. Research Ethics

This clinical study inquiry was permitted by the ethics council of Dr. Moewardi General Hospital Surakarta with a number of 1.037/VIII/HREC/2022.

RESULTS

1. Sample Characteristics

The sample is characterized by sex, age, occupation, infection duration, comorbid, and vaccination status. In this study percentages between men and women are 47.4% and 52.6%, between adults and elderly are 97.4% and 2.6%, and between health workers and non-health worker 76.3% and 3.7%. Average period of COVID-19 re-infection is 197.6 +/- 97 days. The most common comorbid to less common comorbid are hypertension, asthma, coronary artery disease (CAD), thymoma, erythematosus (SLE), diabetic mellitus (DM), epilepsy, and chronic kidney disease (CKD). Comorbid seen in 29% patient. Based on vaccination status, 15.8% have vaccination history (See Table 1).

According to Table 1, both men and women have the same chance of re-infection with COVID-19. The number of infected women was larger than men, with 20 (52.6%) and 18 (47.4%) respectively, although this difference was not statistically significant after statistical analysis with p = 0.917.

The average patient age was 42.133.3 years, with patients ranging in age from 25 to 73 years. According to WHO, researchers separated age into two groups: adults (20-59 years) and the elderly (60 years). The data revealed that the majority of COVID-19 reinfections (97.4%) occurred in adults (37 individuals). The statistical test yielded a value of p = 0.120, indicating that there is no significant link between age and COVID-19 reinfection.

Patients in the study were classified as either health workers or non-health workers, with 29 (76.3%) and 9 (23.7%) respectively. The majority of COVID-19 re-infections were identified in the occupational group of health professionals, with the fisher exact test statistical test results showing a p= 0.025, indicating a significant link between work as a health worker and COVID-19 reinfection.

There is no bivariate analysis of the duration of infection. Comorbidities were discovered in 11 of 38 patients (29%) with COVID-19 reinfection using the Fisher exact test. The statistical test results indicated p= 0.049, indicating that there is a significant link between comorbid history and COVID-19 reinfection.

Vaccination history was detected in just 6 patients (15.8%) with the Fisher exact test statistical test results showing p= 0.373, indicating no significant link between vaccination history and COVID-19 reinfection.

Table 1. Basic Characteristics of Research Subjects

Variable	Disease Degree				Total (n=44)	p
	Mild	Moderate	Severe	Critical		
Sex						0.917
Men	6 (35%)	10 (55.6%)	2 (11.1%)	0 (0%)	18 (47.4%)	
Women	7 (35%)	10 (50%)	3 (15%)	0 (0%)	20 (52.6%)	
Age	(Mean= 31.8; SD= 3.5)	(Mean = 37.9; SD= 7.1)	(Mean= 52.4; SD= 12.5)	-	37.7±9.4	0.120
Adult (20-	13 (35.1%)	20 (54.1%)	4 (10.8%)	0 (0%)	37 (97.4%)	

Variable	Disease Degree				Total (n=44)	p
	Mild	Moderate	Severe	Critical		
59 year)						
Eldery (≥60 year)	0 (0%)	0 (0%)	1 (100%)	0 (0%)	1 (2.6%)	
Occupation						0.025
Health workers	12 (41.4%)	15 (51.7%)	2 (6.9%)	0 (0%)	29 (76.3%)	
Non-health workers	1 (11.1%)	5 (55.6%)	3 (33.3%)	0 (0%)	9 (23.7%)	
Infection Duration	(Mean= 230.8; SD= 99.3)	(Mean= 197.6; SD = 95.6)	(Mean = 111.0; SD = 32.8)	-	(Mean = 197.6; SD = 97.0)	
Comorbid						0.049
Present	1 (9.1%)	7 (63.6%)	3 (27.3%)	0 (0%)	11 (29%)	
Not present	12 (44.4%)	13 (48.1%)	2 (7.4%)	0 (0%)	27 (71%)	
Vaccination status						0.373
Present	2 (33.3%)	4 (66.7%)	0 (0%)	0 (0%)	6 (15.8%)	
Not present	11 (34.4%)	16 (50%)	5 (15.6%)	5 (13.2%)	32 (84.2%)	

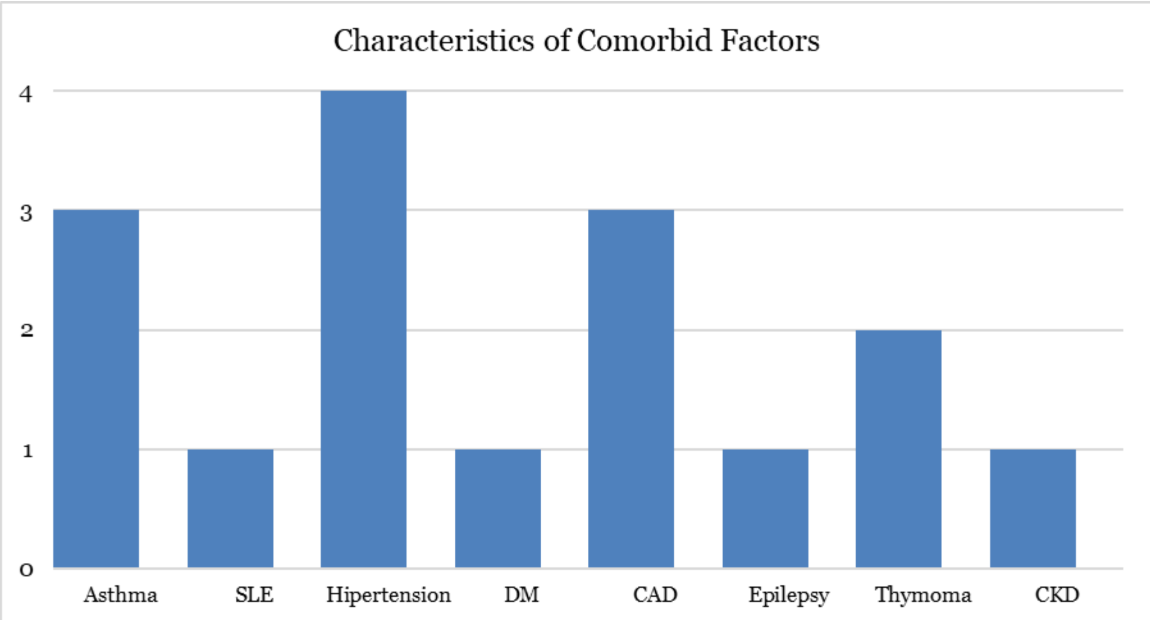

Figure 1. Characteristics of comorbid factors in patients with COVID-19 reinfection

DISCUSSION

According to Table 1, both men and women have the same chance of re-infection with COVID-19. The number of infected women was larger than men, with 20 (52.6%) and 18 (47.4%) respectively, although this difference was not statistically significant after statistical analysis with p = 0.917 (p>0.05).

Ballering AV et al. (2021) conducted a previous study in the Netherlands to investigate gender and gender differences in COVID-19 diagnosis and SARS-CoV-2 testing during the first wave of the COVID-19 pandemic. According to a bivariate analysis, women were more likely than males to have her SARS-CoV-2 PCR and COVID-19 diagnosis.

Meanwhile, bivariate analysis revealed that women were more likely than males in the general population to be diagnosed with COVID-19, but these gender differences did not hold true in multiple regression models. This is consistent with earlier research, including a recent meta-analysis of 3,111,714 cases that revealed an equal number of males and women validated her COVID-19 diagnosis (Ballering et al., 2021).

The average patient age was 42.133.3 years, with patients ranging in age from 25 to 73 years. According to WHO, researchers separated age into two groups: adults (20-59 years) and the elderly (60 years). The data revealed that the majority of COVID-19 re-infections (97.4%) occurred in adults (37 individuals). The statistical test yielded a value of p = 0.120 (p> 0.05), indicating that there is no significant link between age and COVID-19 reinfection.

Solomon et al. (2022) discovered that adults who had previously been exposed to a non-SARS-CoV-2 coronavirus were at higher risk than patients with severe COVID-19 disease with other diseases. Young child exposure was not related with lower COVID-19 infection rates, but it was associated with protection from the serious sickness caused by COVID-19 (Solomon et al., 2022).

In the previous study by Azizi et al. (2022) (51.2 men and 68.5 8.88 years old), 29.4% of the 4510 patients tested were positive. Men were 31.6% more likely to be positive than women (p=0.001). Individual gender role characteristics were the most influential predictors in women, whereas cardiometabolic risk factors were relevant in males. Given the gender cluster of characteristics associated with such negative outcomes, her COVID-19-related hospitalization rate among those who tested positive was weakened (Azizi et al., 2022). Previous research by Doerre & Doblhammer (2022) found that sex ratios of infections were less than one in the age range of 10 to 49, indicating a higher risk of infection in women. However, the number of infections and deaths varies only little from models that do not distinguish between sexes or genders (Doerre & Doblhammer, 2022).

The average patient age was 42.133.3 years, with patients ranging in age from 25 to 73 years. According to WHO, researchers separated age into two groups: adults (20-59 years) and the elderly (60 years). The data revealed that the majority of COVID-19 re-infections (97.4%) occurred in adults (37 individuals). The statistical test yielded a value of p = 0.120 (p> 0.05), indicating that there is no significant link between age and COVID-19 reinfection. According to Kang SJ et al. (2020), the overall case fatality rate (CFR) was 2.37% in 11,344 patients with confirmed cases on May 28, 2020, although it was substantially higher in the elderly (10.9% in patients aged 70-79 years and 26.6% in patients 80 years) (Kang & Jung, 2020; Romero Starke et al., 2020).

Older participants with comorbidities had the highest risk of unfavorable outcomes, although older participants without comorbidities had a lower risk than younger participants with comorbidities (Endeshaw & Campbell, 2022).

Another study found that the total CFR for 44,672 cases identified in China as of February 11, 2020 was 2.3%. The CFR, on the other hand, was 8.0% in patients aged 70-79 years and 14.8% in patients aged 80 years. The number of fatalities per 100,000 population, on the other hand, was obvious (New York City Department of Health and Mental Hygiene statistics as of May 11, 2020 and UK Office for National Statistics data as of May 8, 2020). There was an age-dependent exponential increase in mortality. e. In Korea and Italy, around 80% and 90% of deaths occurred in patients aged >70 years and 60 years, respectively (Kang & Jung, 2020).

According to Chen C et al. 2020, each year of life raised the risk of major diseases by 1.9% (HR = 1.019; 95% CI 0.963-1.077), although the findings were not statistically significant. Meng et al. 2020 discovered that elderly patients had a higher risk of dying than those under the age of 60. The combined impacts of both studies revealed a 4% rise (95% CI 2%-5%). The study also discovered a 20% increased risk of death at age 60 compared to age 50, owing to the (nearly) solitary effect of age.

Lior Rennert and Christopher McMahan's retrospective cohort study on the likelihood of COVID-19 reinfection in adults included 44 participants (2.2%) out of 16,101 pupils with a mean age of 20,30. The cohort study conducted by Jose Vitale et al. discovered that the average age for COVID-19 reinfection was 58 years (40-78 years). Leticia Adrielle dos Santos et al. discovered that the average age of COVID-19 reinfection was 39.28.5 years, with a range of 22-58 years, and that there was no significant link between age and COVID-19 reinfection (p= 0.647). In a Danish observational study conducted by Christian Holm Hansen et al., the probability of COVID-19 reinfection in the population aged > 65 years was 8.01%, while the risk groups 0-34 years, 35-49 years, and 50-64 years were 5.92%, 5.16%, and 4.25%, respectively.

Patients in the study were classified as either health workers or non-health workers, with 29 (76.3%) and 9 (23.7%) respectively. The majority of COVID-19 reinfections were identified in the occupational group of health professionals, with the fisher exact test statistical test results showing a p value of 0.025 (p 0.05), indicating a significant link between work as a health worker and COVID-19 reinfection. Respiratory pandemics are especially dangerous when disseminated by droplets and human touch. Health care workers (HCWs) play an important role in combatting the coronavirus disease 2019 (COVID-19) pandemic, but they are also dealing with severe acute respiratory syndrome coronavirus 2 (SARS-CoV) (SARS-CoV-2). It is believed that they account for 10-20% of global infection. The World Health Organization (WHO) has produced guidelines for personal protective equipment (PPE), hand hygiene practices, and universal mask rules in healthcare institutions to safeguard healthcare workers from the danger of occupational exposure to the virus (Dzinamarira et al., 2021).

HCPs working at VHA facilities with more than 5% positive COVID-19 test rates among inpatients had a greater risk of contracting COVID-19 infection compared to HCPs working at facilities with 5% steady-state positive rates, according to Oda G et al., (2021). (table 1). Infection risk was 1.73 (95% CI = 1.62 to 1.84) (P 0.001), 2.32 (95% CI = 2.13 to 2.51) (P 0.001), and 3.32 (95% CI = 3.04-3.62) (P0.001) times higher in facilities with moderate, high, and very high inpatient prevalence, respectively, than in facilities with lower inpatient prevalence.16 However, a research by Dzinamarira et al., (2022) found that health care workers (HCWs), who are on the front lines of the pandemic, are most at risk of becoming infected through direct or indirect contact with infectious pathogens. In Africa, the number of infected frontline workers climbed from 2,217 on May 26 to 4,830 on June 7, 2020, in 36 countries. As of August 15, statistics from 37 nations revealed that approximately 300,000 healthcare workers have contracted COVID-19, with over 2,500 of them dying (Dzinamarira et al., 2021).

Due of restricted resources, the average period of COVID-19 re-infection is 197.6 +/- 97 days without genomic sequence investigation. COVID-19 re-infection is validated by PCR using a different genomic strain than the prior infection or within 90 days following the resolution of the first infection, which was also confirmed by PCR. This investigation also discovered 16 patients who were not included in the study sample and were infected for an average of 25 days following the first infection. However, Jingzhou Wang et al. found 11 COVID-19 reinfection cases with various genomic strains with durations ranging from 31 to 89 days and 1 reinfection case with a length of less than 30 days. The study published in The Lancet Infectious Disease by Richard L Tillett et al. first described a case of COVID-19 reinfection in the United States within 48 days and discovered distinct genomic sequences despite the patient's rigorous self-isolation (Oda et al., 2021).

Comorbidities were discovered in 11 of 38 patients (29%) with COVID-19 reinfection using the Fisher exact test. The statistical test results indicated p= 0.049, indicating that there is a significant link between comorbid history and COVID-19 reinfection. In our analysis, the most common comorbid comorbidities were hypertension in four individuals, asthma in three, and coronary artery disease (CAD) in three. Figure one depicts one patient each with systemic lupus erythematosus (SLE), diabetic mellitus (DM), epilepsy, and chronic kidney disease (CKD).

Previous research by Sanyaolu A et al. (2020) found that comorbidities increase the likelihood of infection. A meta-analysis study on COVID-19 comorbidity included 1,786 patients, 1,044 of whom were men and 742 of whom were women, with a mean age of 41 years. Hypertension (15.8%), cardiovascular and cerebrovascular disease (11.7%), and diabetes (9.4%) were the most frequently reported comorbidities in these patients. Co-infection with HIV and heaptitis B (1.5%), malignancy (1.5%), respiratory disease (1.4%), renal disease (0.8%), and immunodeficiency (0.01%) were the less prevalent consequences (Sanyaolu et al., 2020).

Other chronic comorbidities in viral diseases include: B. Prolonged pro-inflammatory conditions and congenital and adaptive immunological dysfunction, which may be the primary reasons for poor clinical outcomes in SARS-CoV-2 patients. Obesity and an increase in her BMI were similarly associated with an increased risk of aggravation in COVID-19-infected patients, according to Fathi et al. (2020) (Hadi & Pramana, 2021).

According to Ejaz et al. (2020), the risk of ICU admission in COVID-19 patients with diabetic comorbidity is 14.2% greater than in patients without diabetes. Obesity is one among the less-publicized comorbidities associated with COVID-19 infections. COVID-19 patients with cardiovascular comorbidities require early therapy to decrease morbidity and mortality (Ejaz et al., 2020). According to data from the United States Administrative Claims Database, 14% of adults infected with Covid-19 experienced new clinical symptoms within six months. After other viral infections, the incidence is 1.65% greater. Interstitial lung illness, respiratory failure, congestive heart failure, cardiac arrhythmias, and type 2 diabetes were among the clinical outcomes (Adab et al., 2022).

Vaccination history was detected in just 6 patients (15.8%) with the fisher exact test statistical test results showing p value = 0.373 ($p>0.05$), indicating no significant link between vaccination history and COVID-19 reinfection.

According to Lin DY et al., (2022), initial immunization lowered SARS-CoV-2 infection rates as well as the probability of hospitalization or death. Furthermore, compared to no previous infection, the efficacy of previous SARS-CoV-2 infection reduces future infection rate and danger of hospitalization or death from reinfection (due to previous infection itself). (With the same vaccines as provided). In comparison to primary immunization alone, the relative efficacy of six popular combinations of primary and booster vaccines in reducing SARS-CoV-2 infection rate was higher. After around 2-4 weeks, the estimated relative efficacy peaked and subsequently declined over time (Lin et al., 2022). Vaccines also reduce the risk and duration of long-term symptoms of Covid, but their effectiveness is less than reducing mortality and severe illness (Adab et al., 2022).

B cells become more active at the start of an infection, secreting IgM and IgA on days 5-7 and IgG on days 7-10. IgM and IgA levels begin to fall on day 28, while IgG levels peak on day 49. T cell activity will be stimulated by concurrent COVID-19 infection, with a peak in 2 weeks. Grifoni et al. discovered that SARS-CoV-2-specific memory CD4 and memory CD8 cells were present in 100% and 70% of patients who recovered from COVID-19, respectively.

The strength of the antibody and T cell response is highly dependent on the severity of COVID-19 infection, whereas the activity of immunity related to protection is dependent on neutralizing antibodies that can recognize the viral receptor binding domain (RBD) on viral spike proteins, preventing viral binding to the angiotensin receptor-converting enzyme II. Neutralizing antibodies from helper1 T cells, IgG1 and IgG3, can bind to RBD. Human immunezation is thought to encourage the formation of neutralizing antibodies capable of recognizing spike proteins.

During the healing period, a decrease in the activity of neutralizing IgG antibodies against SARS-CoV-2 may increase vulnerability to reinfection. This is due to a drop in antibody levels caused by the short lifespan of plasma blasts and effector B cells generated during the first week of infection. The key to preventing reinfection is to maintain high antibody levels following infection or immunization.

Antibodies with anti-RBD titers and limited neutralizing activity were detected in one-third of recovered COVID-19 cases, particularly in mild or asymptomatic patients. The strength of neutralizing antibodies is greatly reliant on antigen exposure, with neutralizing antibodies being most prevalent in severe infection. In mild situations, low neutralization activity is assumed to indicate limited virus sterilizing activity.

Leticia Adrielle dos Santos et al. compared antibody levels in reinfected individuals to controls in their study. In reinfected patients, SARS-CoV-2-specific IgG levels were found to be extremely low. This study also discovered that 10% of reinfected health professionals had very low neutralizing antibody levels in the fourth month following the first COVID-19 infection.

AUTHOR CONTRIBUTION

JA wrote the main manuscript text, prepared figures, and reviewed the manuscript.

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CONFLICT OF INTEREST

There is no conflict of Interest in this study.

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