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CORRELATION OF SERUM IMMUNOGLOBULIN G AND IMMUNOGLOBULIN M LEVEL WITH LENGTH OF STAY IN COVID-19 INTENSIVE CARE UNIT AFTER TREATMENT OF CONCALESCENT PLASMA

Efry Sofyan Noor [1]*, Bambang Pujo Semedi [2], Maulydia [3], Elizeus Hanindito [4], Edward Kusuma [5] and Meitria Syahadatina Noor [6]

[1,2,3,4,5] Department of Anesthesiology and Intensive Therapy, Faculty of Medicine, Universitas Airlangga Surabaya.
[6] Master of Public Health Program, Faculty of Medicine, Universitas Lambung Mangkurat.
Email: [1]efry.nor@gmail.com (*Corresponding Author), [2]bpsemedi@gmail.com, [3]maulydia@fk.unair.ac.id, [4]elizeushanindito@gmail.com, [5]edu.surabaya@gmail.com, [6]drmeitria@yahoo.com

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Abstract

The coronavirus disease 2019 (COVID-19) pandemic has had health and economic impacts. Nearly a third of COVID-19 infections were in the 31-45 years age group (29.3%) but the highest mortality rate occurred in the elderly (17.68%). Another therapy needed to improve outcomes for critically ill COVID-19 patients is plasma therapy. This study aims to analyze the correlation of serum IgG and IgM levels with length of stay after convalescent plasma therapy in the COVID-19 ICU, Panglima Sebaya Hospital, East Kalimantan. This type of research is analytic observational with cross-sectional method. Source of data is secondary data from patient registration and medical records. Taking the number of samples using the Slovin formula, obtained 50 samples. The sampling technique used was non-probability sampling. Statistical analysis using the Pearson Correlation test if the data is normally distributed, or the Spearman Correlation Test if the data is not normally distributed. The results showed a correlation between increased serum IgG levels and length of treatment with p values = 0.202 and = -0.184. Correlation results of increasing serum IgM levels with length of treatment with p value = 0.085 and β value = 0.246. There is no correlation between the increase in serum IgG and IgM levels with the length of patient care after convalescent plasma therapy in the ICU COVID-19 Panglima Sebaya Hospital, Kab. Paser, East Kalimantan.

Keywords: IgG Level, IgM level, Length of Stay.

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic has had health and economic impacts. This disease is caused by Severe Acute Respiratory Syndrome Corona Virus (SARS CoV2) which can actually cause severe illness even in young adults.[1] Based on data from China, patients with COVID-19 with mild to severe symptoms reached 81% (including patients without pneumonia and patients with mild pneumonia), 14% with severe disease and 5% with critical illness.[2] As of May 2, 2020, there were 3,494,671 confirmed cases and 264,475 deaths worldwide and in the United States there were 1,153,340 confirmed cases and 67,447 deaths.[3]

Nearly a third of COVID-19 infections were in the 31-45 year age group (29.3%) but the highest mortality rate occurred in the elderly (17.68%). For co-morbidities, patients with COVID-19 had higher rates of hypertension (52.1%), diabetes (33.6%), and other cardiovascular diseases (20.9%).[4] Meanwhile, for the Paser Regency area, East Kalimantan, the number of COVID-19 patients was recorded as positive, the accumulation of positive patients was 2912 people, 2644 people recovered and 58 people died.[5]

The prognosis of COVID-19 patients is unpredictable but is influenced by comorbid factors such as hepatitis, diabetes mellitus, cardiovascular disease, obesity, chronic kidney disease and COPD.[1] According to research conducted by Joyner 2020,[2] The number of deaths from COVID-19 in the US exceeds that of any other country. The overall case fatality rate for COVID-19 is around 4% in Wuhan, of which 14% were from patients admitted to hospital and 57% to patients admitted to the ICU on ventilators. The reported US mortality rate is around 21% in New York hospitals to 50% as reported in the initial case series. US reports case fatality rate.[2] In Indonesia on September 15, 2020, the number of confirmed positive cases in Indonesia reached 225,030 cases with a total of 8,965 cases of death.[6]

The treatment strategy for critically ill COVID-19 patients is still not optimal, namely by administering antiviral, antibiotic, anti-inflammatory, anti-thrombotic and aggressive supportive therapy (Malabadi et al., 2021). Another therapy needed to improve outcomes for critically ill COVID-19 patients is administration of plasma therapy. Plasma therapy is therapy in which blood plasma from recovered patients is collected and transfused to symptomatic patients. The therapy was well tolerated, and no transfusion-related side effects were observed. On day 7 after transfusion, 9 of the 25 patients (36%) had improvement in the clinical endpoint assessment. Within 14 days after transfusion, 19 patients (76%) had improved.[7]

Convalescent plasma contains protective antibodies including immunoglobulin G (IgG) and immunoglobulin M (IgM) (Cao & Shi, 2020). SARS-CoV infection induces the production of IgG antibodies against nucleoprotein (N) which can be detected 4 days after disease onset and by seroconversion on day 14. SARS infection in 89% of patients who recovered, showed specific IgG and Nabs 2 year's post-infection. Even the highest concentration of IgM was detected within 9 days after onset, the conversion to IgG occurred in the second week.[8]

Until now, not many studies have analyzed the effectiveness of convalescent plasma administration by looking at the increase in serum IgG and IgM levels. This study aims to analyze the correlation of serum IgG and IgM levels with length of stay after convalescent plasma therapy in the COVID-19 ICU, Panglima Sebaya Hospital, East Kalimantan.

METHODS

This type of research is analytic observational with cross-sectional method. The independent variable is an increase in serum IgG and IgM levels, and the dependent variable is the length of stay in the ICU COVID-19. Source of data is secondary data from patient registration and medical records. The population is the entire research subject or object under study. The population in this study were COVID-19 patients who were treated in the ICU room at Panglima Sebaya Hospital, Paser Regency, East Kalimantan. The total population during April was 101 patients. Sample inclusion criteria were 30-70 years old, had never received convalescent plasma therapy, had indications for convalescent plasma administration. While the sample exclusion criteria were patients who died before or after convalescent plasma therapy.

Taking the number of samples using the Slovin formula, obtained 50 samples. The sampling technique used was non-probability sampling, namely using purposive sampling according to the inclusion and exclusion criteria. Data analysis used the Pearson correlation test with a 95% confidence level if the data were normally

distributed. If the data is not normally distributed, it will be tested with Spearman's Korean with a 95% confidence level.

RESULT AND DISCUSSION

This study was conducted on 50 ICU COVID-19 patients at Panglima Sebaya Hospital, Paser Regency, East Kalimantan by examining serum IgG and IgM levels before and after convalescent plasma therapy, then calculating the increase in IgG and gM levels. In addition, the length of stay in the ICU is calculated by the difference between the date of discharge and admission to the ICU. Descriptive data of research results as shown in the following table:

Table 1: Descriptive Data on Serum IgG and IgM Levels and Length of Stay in the ICU

NO	Variable	Average ± SD
1	Serum IgG Level	
	Before convalescent plasma therapy	269,18 ± 217,34
	After convalescent plasma therapy	1648,1 ± 490,14
	Increased levels of IgG	1378,92 ± 537,16
2	Serum IgM Level	
	Before convalescent plasma therapy	78,06 ± 53,76
	After convalescent plasma therapy	274,16 ± 160,91
	Increased levels of IgM	196,1 ± 165,89
3	Length of stay in ICU	17.02 ± 14,82

Serum IgG and IgM levels increased after administration of convalescent plasma therapy. Based on the normality test, all data on increased levels of IgG, IgM, and length of treatment had a p value of <0.05, which means the data were not normally distributed. The test carried out is the Spearman Correlation, as follows:

Table 2: Correlation of increased Serum IgG and IgM levels with Length of Stay in the COVID-19 ICU after Convalescent Plasma Therapy

NO	Variable	p-value	β-value
1	Increased serum IgG levels with length of treatment	0.202	-0.184
2	Increased serum IgM levels with length of treatment	0.085	0.246

The table above shows that there is no correlation between increased serum IgG levels and length of stay in the COVID-19 ICU at Panglima Sebaya Hospital, Paser Regency, East Kalimantan. This data is strengthened by the value of the correlation coefficient, which is -0.184, which means that the increase in serum IgG has almost no correlation with the length of treatment. In addition, the negative direction means that the higher the increase in serum IgG levels, the shorter the length of treatment, or the lower the increase in serum IgG levels, the longer the treatment in the COVID-19 ICU..

The increase in serum IgM levels with length of treatment also did not show a significant correlation, with a correlation coefficient value of 0.246 which means it has a low correlation. The positive correlation value indicates the higher the increase in serum IgM levels, the longer the treatment in the COVID-19 ICU, or the lower the increase in IgM levels, the longer the treatment in the COVID-19 ICU.

SARS-CoV infection induced the production of detectable IgG antibodies against nucleoprotein (N) 4 days after disease onset and by seroconversion at day 14.[8] Shen,

et al showed that donor recovery from COVID-19 infection already had SARS Co-V specific antibodies with the titer is between 1,800-16,200 and the Nabs titer is between 80-480.

Plasma obtained from the donor and transfused to the recipient within 1 day can help reduce the amount of virus that develops. After convalescent plasma transfusion, the titers of IgG and IgM in the recipient increased over time. The presence of Nabs in the recipient plays an important role in limiting viral infection.[8]

IgG is formed 3 weeks after infection, then increases and can remain in low concentrations for years. IgG serves to neutralize the virus. IgM and IgG levels increase during healing and convalescence. This condition is the basis for giving convalescent plasma from patients who have recovered according to the specified criteria to provide antibodies to Covid-19 patients.[9]

IgM is present on the surface of B cells, it is secreted in the acute phase so that this Ig indicates the presence of an acute phase. IgM and IgG levels increase during healing and convalescence. This condition is the basis for giving convalescent plasma from patients who have recovered according to the specified criteria to provide antibodies to Covid-19 patients.[9]

The increase in serum IgG and IgM levels in this study has not been able to reduce the length of stay in the COVID-19 ICU. However, monitoring of clinical improvement was not evaluated so it is not known how clinical improvement after therapy was. Improvements in the results of investigations were known from the results of examination of elevated serum IgG and IgM levels before and after convalescent plasma therapy. This shows the body's response in increasing the immune response is good.

Although there is no correlation, the average length of treatment for COVID-19 patients in this study is still lower than the previous study, namely the study of Shiddiq et al.,[10] that is 33 days. This shows that although there is no correlation, there is an improvement in the length of the treatment period shown when compared to other hospitals.

In addition, the absence of a correlation between increased levels of IgG and IgM with the length of stay after convalescent plasma therapy can also indicate that there are other therapies besides convalescent plasma therapy that should be given to accelerate the improvement of the patient's condition. Thus, the length of stay in the ICU will be shorter and the patient can avoid death.

The direction of the correlation coefficient of the increase in IgG and the length of treatment is negative, this result is in accordance with the theory that an increase in IgG levels will increase the immune response for patient recovery so that the length of treatment becomes shorter.

Meanwhile, the direction of the correlation coefficient of increasing IgM levels and length of treatment is positive, which means that an increase in IgM levels will increase the length of treatment. These data are not in line with Muljono et al.[9] This is probably caused by IgM is a marker of the acute phase of the immune response that appears early, so it is not appropriate to see the improvement in the condition of patients who are treated for a long period of time. Thus, an increase in serum IgG levels is one indicator that can represent an improvement in the patient's condition.

CONCLUSION

There is no correlation between increased serum IgG and IgM levels with the length of stay for COVID-19 ICU patients after convalescent plasma therapy at Panglima Sebaya Hospital, Kab. Paser, East Kalimantan.

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