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The effect of convalescent plasma administration on increasing blood IGG and IGM levels as an effort to prevent death due to Covid-19 in ICU Panglima Sebaya hospital, Paser Regency, East Kalimantan

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Abstract

Severe Acute Respiratory Syndrome Corona Virus (SARS CoV2) is the etiology of COVID-19 that can cause severe disease in the young age group. In China, Covid-19's patients with mild-severe signs were 81% (including those without pneumonia and mild pneumonia), 14% with severe disease, and 5% with critical disease. COVID-19 infected people in 31-45 years old was 29, 3%, and the highest death could happen in old age at about 17, 68%. In Paser Regency, East Kalimantan, COVID-19's patients were 2912, cured 2644 people, and died 58 people. Treatment of critical COVID-19's patients was not good enough. It still limited data using antivirus, antibiotic, anti-inflammation, anti thrombotic, and support agents. Another treatment was needed to increase the chance to live. It was convalescent plasma from cured people that would be given to symptomatic patients. This research's goal was to analyze the effect of convalescent plasma to increase IgG and IgM level to prevention of death in COVID-19's ICU. Research's design was quasy experimental. The intervention was convalescent plasma to COVID-19's patients di ICU. The populations were 101 patients in Panglima Sebaya Hospital, Paser Regency. The samples were 50 patients. Independent variable was convalescent plasma. Dependent variables were blood IgG and IgM levels. Data analyzes used pair-*T*-Test if in a normal distribution and Wilcoxon test if not in a normal distribution. The result showed IgG level was 269,18 ± 217,341 before treatment and 1648,1 ± 490.140 after treatment (*p* value = 0.000). IgM level was 78,06 ± 53.757 before treatment and 274,16 ± 160.908 after treatment (*p* value = 0.000). From all of the samples, 75% of them were cured, and the rest were dead. The conclusion was that convalescent plasma increased IgG and IgM levels in the prevention of death from COVID-19 in the ICU.

I. INTRODUCTION

The coronavirus disease pandemic of 2019 (COVID-19) has spread worldwide, resulting in countless deaths and economic suffering. The etiologic factor of the COVID-19 coronavirus disease, which can cause serious sickness in young people, is the SARS CoV2 [1]. According to statistics from

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China, individuals with COVID-19 had 81 percent mild to severe symptoms (including those without pneumonia and those with mild pneumonia), 14 percent severe disease, and 5% critical sickness [2]. COVID-19 patients have an unpredictably poor prognosis, which is influenced by concomitant conditions such as hepatitis, diabetes, cardiovascular disease, obesity, chronic renal disease, and COPD [1]. There were 3,494,671 confirmed cases and 264,475 deaths globally as of May 2, 2020, with 1,153,340 confirmed cases and 67,447 deaths in the United States [3].

According to Joyner 2020's research, the number of deaths from COVID-19 in the United States exceeds that of any other country. In Wuhan, the total case-fatality rate for COVID-19 is roughly 4%, with 14 percent of hospitalized patients and 57 percent of patients on a ventilator admitted to the ICU. The reported US fatality rate ranges from roughly 21% in New York hospitals to 50% in the earliest case series. The United States has a high case fatality rate [4]. As of September 15, 2020, the number of confirmed positive cases in Indonesia had risen to 225,030, with a total of 8,965 deaths [5]. Nearly a third of COVID-19 infections (29.3%) occurred in people aged 31 to 45, although the elderly had the highest fatality rate (17.68 percent). COVID-19 patients showed greater frequencies of hypertension (52.1%), diabetes (33.6%), and other cardiovascular disorders as comorbidities (20.9%) [6]. As of May 15, 2021, 150,901 people had tested positive, 138,310 had recovered, and 10,977 had died in East Java [7]. Meanwhile, the number of COVID-19 positive patients in the Paser Regency area of East Kalimantan has risen to 2912, with 2644 recovering and 58 dying [8].

Antiviral medicines, antibiotics, anti-inflammatory, antithrombotic, and vigorous supportive therapy are currently no effective treatment methods for severely ill COVID-19 patients, with relatively limited data. Several clinical trials are underway, including the repurposing of remdesivir, an antiviral drug being studied for Ebola treatment, and hydroxychloroquine, an antimalarial chloroquine derivative used to treat lupus and rheumatoid arthritis. With remdesivir, there is preliminary COVID-19 efficacy data. Although preliminary evidence supports using hydroxychloroquine alone or in combination with azithromycin, bigger controlled trials have indicated that it may be detrimental.

IVIg is another treatment option for Covid-19 patients. This therapy has good benefits, but it is still limited to severe and critical illnesses and is life-saving due to the lack of study on it. Tocilizumab or anti-IL6 antibodies can also be used. This patient is only prescribed in the case of extreme hyper inflammation [9]. Aside from the indications for providing alternative therapies that are particular to the severity of the condition, the therapy is also highly expensive, and it is not available in all hospitals.

Plasma therapy is another treatment option for critically ill COVID-19 patients who need to improve their outcomes. Plasma therapy is a type of treatment in which recovered patients' blood plasma is collected and transfused into symptomatic patients. The treatment was well-tolerated, and there were no transfusion-related adverse effects.

The clinical endpoint evaluation improved in 9 of the 25 patients (36 percent) on day 7 after transfusion. 19 patients (76%) had improved after 14 days of receiving the blood transfusion [10].

Immunoglobulin G (IgG) and Immunoglobulin M (IgM) are protective antibodies seen in convalescent plasma. SARS-CoV infection causes the formation of anti-nucleoprotein (N) IgG antibodies, which can be detected 4 days after the onset of the disease and by seroconversion on day 14. SARS infection resulted in specific IgG and Nabs in 89 percent of individuals who recovered 2 years later. Even though the maximum concentration of IgM was detected 9 days after onset, conversion to IgG took place in the second week [11]. As a result, the researchers hope to see a rise in blood IgG and IgM levels in patients receiving convalescent plasma to avoid mortality from COVID-19 in the ICU by investigating the possible use of convalescent plasma to prevent death from COVID-19. COVID-19 has yet to be treated with a specific medicine or vaccination. Since the spread of the Ebola virus in 2014 and the coronavirus respiratory syndrome in Central Asia in 2015, convalescent plasma therapy has been used. The treatment of COVID-19 patients can include the administration of convalescent plasma.

This is because convalescent plasma can be administered locally and at a reasonable cost [12]. Furthermore, because research on convalescent plasma administration is relatively limited, this study is necessary to assess the efficacy of convalescent plasma therapy in Covid-19 patients.

II. METHOD

This type of research is quasi-experimental by providing convalescent plasma interventions to COVID-19 patients in the ICU. Research variables, namely blood IgG and IgM levels, were examined before and after therapy. 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. The sampling technique used was probability sampling, namely using, purposive sampling. Inclusion criteria for respondents: COVID-19 patients in the ICU unit

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at Panglima Sebaya Hospital in Paser Regency, East Kalimantan, aged 30-70 years, had never undergone convalescent plasma therapy but had indications for it and were continuing treatment until they were discharged from the ICU. Exclusion criteria for respondents: the patient died before or after receiving convalescent plasma treatment. The research instrument is a laboratory examination that uses the Elisa test to evaluate IgG and IgM levels. Data was gathered via primary sources, such as laboratory tests. The Elisa technique is used to acquire data by analyzing blood samples to evaluate blood IgG and IgM levels.

III. RESULTS AND DISCUSSION

This research was conducted at Panglima Sebaya Hospital, Kab. East Kalimantan Paser. Research respondents obtained as many as 50 patients in the ICU Covid-19. After collecting samples and analyzing data, it was discovered that most Covid-19 patients in the ICU who were the majority responses were male (58%) and in the 41-50 year age group (36%), with 84 percent of the population having concomitant hypertension. Patients have comorbidities in general.

TABLE 1
RESPONDENTS AGE AND GENDER-BASED CHARACTERISTICS

Characteristics of Respondents	Gender		Total	Percentage (%)
Age	Male	Female		
21-30	2	2	4	8
31-40	9	6	15	30
41-50	12	6	18	36
51-60	6	7	13	26

According to Table 1, most respondents are between the ages of 41 and 50 years old (36 percent), with 12 male and 6 female respondents.

TABLE 2
RESPONDENT CHARACTERISTICS BASED ON COMORBIDITIES AND GENDER

Characteristics of Respondents	Gender		Total	Percentage (%)
Age	Male	Female		
Ada	16	9	25	50
Tidak Ada	13	12	25	50

According to Table 2, the number of respondents with comorbidities is 50%, and the majority of them are male (with a total of 16 respondents), while those without comorbidities are primarily male (with a total of 13 respondents).

TABLE 3
RESPONDENT CHARACTERISTICS BASED ON COMORBID TYPES AND GENDER

Characteristics of Respondents	Gender		Total	Percentage (%)
Age	Male	Female		
Types of comorbid				
Hypertension	11	1	12	48
Diabetes Mellitus	1	3	4	16
Diabetes Mellitus and Hypertension	4	5	9	36

According to Table 3, the number of respondents with comorbid hypertension is primarily male, with 11 respondents, while the number of respondents with comorbid diabetes mellitus is mostly female, with 3 respondents, and the number of responding with comorbid hypertension is mostly female. With 5 respondents, diabetes mellitus was predominantly in the female sex.

The goal of this trial was to give convalescent plasma treatment to 50 Covid-19 ICU patients. IgG and IgM levels were measured before and after treatment.

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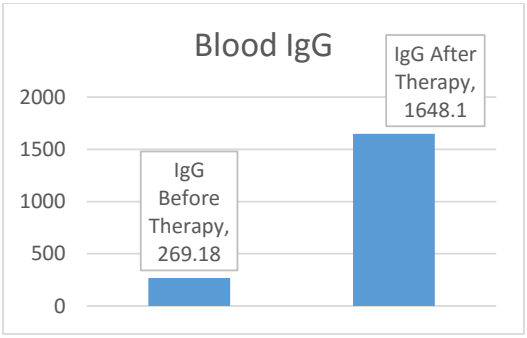

Fig. 1. Levels of IgG in the blood before and after convalescent plasma therapy

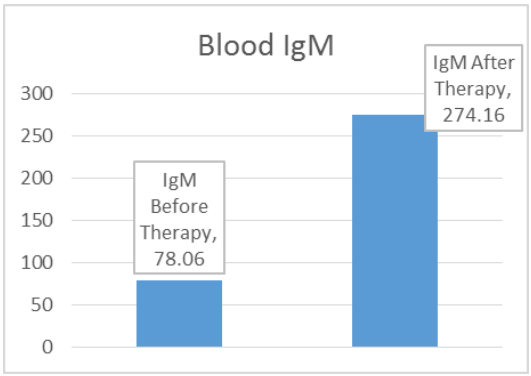

Fig. 2. Pre- and post-convalescent plasma therapy blood IgM levels

There was a rise in blood IgG and IgM levels after convalescent plasma delivery, as seen in Fig 1. This indicates that the patient's immunological response has improved.

TABLE 4
GENDER AND TYPE OF COMORBIDITY OF PATIENTS GETTING CONVALESCENT PLASMA THERAPY

Characteristics of Respondents	Patient Status		Total
	Healed	Died	
Gender			
Male	21	8	29
Female	14	7	21
Type of Comorbid			
Hypertension	8	4	12
Diabetes Mellitus	1	3	4
Diabetes Mellitus and Hypertension	1	8	9

According to Table 4, there were 8 (53.33 percent) male patients with death status and 7 (46.66 percent) female patients with death status. Meanwhile, there were 4 (26.66 percent) patients who died with comorbid hypertension, 3 (20 percent) patients who died with comorbid diabetes mellitus, and 8 (53.33 percent) patients who died with comorbidities.

Meanwhile, based on length of stay data, it is known that patients with death status in the ICU with a length of treatment of 1-14 days. Meanwhile, patients with recovered status continue to be treated in the standard room for 5-7 days of treatment and are clinically improving.

The descriptive data in Fig 1, 2 show both IgG and IgM levels have increased. The statistical analysis examined the differences in immunoglobulin levels before and after convalescent plasma therapy. If the data is regularly distributed, a normality test is performed, followed by a paired t-test. The Wilcoxon test will be used with a 95 percent confidence level if the data is not normally distributed.

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TABLE 5
RESULTS OF STATISTICAL ANALYSIS OF BLOOD IGG AND IGM LEVELS BEFORE AND AFTER CONVALESCENT PLASMA THERAPY

No	Variable	Therapy		Normality	Wilcoxon Test
		Before $\pm$ *SD*	After $\pm$ *SD*		
1	Blood IgG level	269,18 $\pm$ 217,341	1648,1 $\pm$ 490.140	0.000	0.000
2	Blood IgM level	78,06 $\pm$ 53.757	274,16 $\pm$ 160.908	0.000	0.000

The Wilcoxon test assessed the differences before and after therapy since the IgG and IgM data were not normally distributed, as shown in the Table above. The statistical analysis results revealed that blood IgG and IgM levels in Covid-19 ICU patients differed before and after convalescent plasma therapy. This indicates that the offered medication was successful in inducing immunoglobulins to act as the body's immune system's defense against Covid-19 infection.

In comparison to hypertension or diabetes mellitus alone, the results of the study in Table 5 reveal that co-morbid hypertension and diabetes mellitus causes the majority of deaths. Covid-19 can raise the severity and fatality rate of cardiovascular disease and diabetic Mellitus by 2-3 times. An increase in intensional-converting enzyme 2 (ACE2) in people with hypertension and diabetes causes this condition. The ACE2 protein is used by the SARS-Cov-2 virus to enter cells. ACE2 levels will rise as the SARS-Cov-2 virus replicates. This is what makes Covid-19 more severe and increases mortality in people with hypertension and diabetes mellitus [13, 14, 15]. Patients with comorbid hypertension who do not have diabetes have a better chance of recovery. Patients with comorbid diabetes mellitus or a combination of comorbid hypertension and diabetes mellitus have a higher mortality rate. This is related to immunological dysfunction in diabetic Mellitus patients, which exacerbates the cytokine storm seen in Covid-19 patients. The severity of diabetes mellitus in Covid-19 patients would worsen as a result of this uncontrolled cytokine storm [16].

The characteristics of the respondents showed that the infected patients were primarily male, with an average age of 41-50 years. Half of the patients had comorbidities, with hypertension being the most common. Men also make up the majority of respondents in the 41-50 age group. Patients with comorbidities are overwhelmingly male, and comorbid hypertension, the most common comorbid condition, is also overwhelmingly male. Because men have a higher expression of ACE2, they are more likely to contract SARS-Cov-2. Furthermore, as a person's age increases, their immune system weakens, making them more vulnerable to infection [17].

This study's findings also revealed that hypertension was the most common comorbid condition. The rise of hypertension as the most common comorbid condition can be attributed to risk factors associated with the patient's age, which is 41-50 years. Because hypertensive patients have lower lymphocyte counts, they may have a worse prognosis if they become infected with Covid-19 [18].

Diabetes Mellitus was also discovered as a comorbid in this investigation, in addition to hypertension. This condition has the potential to exacerbate inflammation and the immune system [18]. Based on the risk factors identified in this study, the patient's immunity must be triggered in order for it to live and thrive. Convalescent plasma is used as a treatment. Covid-19 individuals with comorbid hypertension and diabetes mellitus might raise IgG levels, as shown in Table 5. A different test showed that there was a substantial difference before and after convalescent plasma delivery, which supported this rise. SARS-CoV infection causes the development of IgG antibodies against nucleoprotein (N), which can be detected four days after the onset of the disease and leads to seroconversion on day fourteen. SARS infection resulted in specific IgG and Nabs in 89 percent of patients who recovered 2 years later [11].

Donors recovering from COVID-19 infection had SARS-Co-V specific antibodies with titers ranging from 1,800 to 16,200 and Nabs titers ranging from 80 to 480, according to Shen et al. Plasma from a donor and transfusion to a recipient on the same day can help limit the quantity of virus that develops. The recipient's IgG and IgM titers increased overtime after receiving convalescent plasma transfusion. In fact, the presence of Nabs in the receiver helps to keep viral infection to a minimum. Another study looked at the migration of the SARS-CoV-2 Specific CoV, as well as the formation of Nabs during the course of the disease. Before 10 days after surgery, Nabs titers in individuals infected with SARS-CoV-2 were low. All patients were infected and then only increased, with a peak 10-15 days after disease onset, remaining pretty constant [11].

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Convalescent plasma is obtained from blood donors who have developed antibodies as a result of infection with the coronavirus/Covid 19. Through transfusion or immunoglobulin administration, convalescent plasma will produce passive immunity [19]. Several investigations have found that people infected with COVID-19 develop antibodies to virus particles on their own. Convalescent plasma therapy with anti-SARS CoV 2 antibodies is based on this state [20]. [21] shows that moderate and severe COVID-19 patients receive convalescent plasma therapy with an IgG level indicator [21]. Sun et al also mentioned that convalescent plasma therapy can produce a curative and effective effect for Covid-19 patients, in addition to Maor's research. Previous study found similar results, claiming that convalescent plasma can improve survival for COVID-19 patients with severe degrees. IgG is produced three weeks after infection, then increases and can last for years in low concentrations. IgG acts as a virus neutralizer. During healing and convalescence, IgM and IgG levels rise. This is the basis for providing antibodies to Covid-19 patients with convalescent plasma from patients who have recovered according to the specified criteria. Muldoon and colleagues [21].

Convalescent plasma therapy for patients with Covid-19 improves signs and symptoms, increases oxygen tension, improves radiological features, increases IgM and IgG antibody titers, improves general condition, and improves recovery, according to prior research analysis in his literature review study. As a result, convalescent plasma therapy can be used to treat Covid-19 patients and improve their IgG levels.

Data that is descriptive Table 1, 4 shows that the majority of Covid-19 ICU patients are males between the ages of 41 and 50, with comorbidities accounting for 50% of the respondents. By far, the most common comorbid is hypertension, which accounts for 80% of the cases, and diabetes mellitus accounts for the remaining 20%. Comorbidities increase the risk of clinical severity of Covid-19, necessitating prompt and effective treatment. In hypertension, diabetes mellitus, and non-comorbid groups, convalescent plasma can increase IgM levels. There was a significant difference in IgM levels before and after therapy, as evidenced by this increase. After receiving convalescent plasma, IgM levels rise. Even though the highest concentration of IgM was detected 9 days after onset, conversion to IgG took place in the second week [11].

Through the administration of SARS Cov-2 antibody transfusions, convalescent plasma neutralizes incoming pathogens. Functional antibody refers to an antibody's ability to neutralize pathogens. In addition, IgM, IgA, and IgG are all part of the humoral immune response to SARS Cov-2 [22]. IgM is found on the surface of B cells and is secreted during the acute phase, so this Ig can be used to detect the presence of an acute phase. During healing and convalescence, IgM and IgG levels rise. This is the basis for providing antibodies to Covid-19 patients with convalescent plasma from patients who have recovered according to the specified criteria [22].

The findings of this study are consistent with the findings of the literature review. According to existing literature convalescent plasma therapy improves signs and symptoms, increases oxygen tension, improves radiological features, increases IgM and IgG antibody titers, improves general condition, and improves recovery for patients with Covid-19. As a result, convalescent plasma therapy can be used to treat Covid-19 patients and improve IgM levels. Patients with Covid-19 will have a better chance of recovering if their IgG and IgM levels rise. Table 5 shows that 75 percent of Covid-19 ICU patients who received convalescent plasma therapy recovered. According to these findings, convalescent plasma administration can help prevent Covid-19 deaths.

IV. CONCLUSION

The overall goal of this study was to see how convalescent plasma administration affected IgG and IgM levels in the ICU in order to prevent death from COVID-19. According to the findings of the research and statistical analysis, there is an effect of giving convalescent plasma to an increases in IgG levels in the ICU in order to prevent death from COVID-19, and there is an effect of giving convalescent plasma to an increase in IgM levels in the ICU in order to prevent death from COVID-19.

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