

Correlation of SARS-CoV-2 IgG/IgM Levels to COVID-19 Severity in Convalescent Plasma Donor Candidates

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ABSTRACT

Coronavirus Disease-19 (COVID-19) is an infectious disease caused by Sars-CoV-2. The clinical manifestations of COVID-19 vary from asymptomatic, mild symptoms to severe symptoms. Plasma of people recovering from COVID-19 infection will likely contain specific polyclonal antibodies. These antibodies can provide passive immunity to the recipient. This study aimed to analyze the correlation of SARS-CoV-2 IgG/IgM levels to COVID-19 severity and length of negative conversion in COVID-19 patients as convalescent plasma donor candidates. The retrospective research used this study with data collected from May to December 2020. The study sample of 30 patients was taken from the medical record with a population that met the inclusion criteria. IgG/IgM levels were measured using AFIAS-6 Immunoanalyzer. The Shapiro-Wilk and Spearman rho non-parametric correlation tests were used for data analysis. The statistical test results with p-value <0.05 were reported as significant. There was no significant correlation between IgM levels and COVID-19 severity, with a p-value of 0.763 ($p>0.05$) and length of negative conversion with a p-value of 0.998 ($p>0.05$). There was a significant correlation between IgG levels and COVID-19 severity with a p-value of 0.014 ($p<0.05$) and length of negative conversion with a p-value of 0.004 ($p<0.05$). IgM/IgG levels affect the severity of the disease. IgM levels increase at the beginning of infection and decrease as the disease progresses, and IgG levels will increase slowly. IgM levels cannot be used to detect previous SARS CoV-2 infection, whereas IgG levels affect the length of negative conversion. There was a significant correlation between IgG and the severity of COVID-19 with a correlation strength of $R=0.444$ (weak correlation) and with a length of negative conversion with a relationship strength of $R=0.509$ (moderate correlation). SARS CoV-2 IgG levels of convalescent plasma donor candidates correlated to the severity and length of negative conversion.

Keywords: IgM/IgG, COVID-19 severity, convalescent plasma

INTRODUCTION

Coronavirus Disease-19 (COVID-19) is an infectious disease caused by SARS-CoV-2. The clinical manifestations of COVID-19 vary from asymptomatic or asymptomatic mild symptoms to severe symptoms. The most frequently reported symptoms are fever (58.66%), cough (54.52%), shortness of breath (30.82%), malaise (29.75%), weakness all over the body (28.16%), and sputum production (25.33%).¹

In general, viral infections in the body are treated with cellular-based immunity. Antibodies act as intermediaries for cellular cytotoxicity and phagocytosis through innate immune cells such as Natural Killer (NK) cells and macrophages.² Identifying antibody responses based on disease severity can help determine pathogenesis and humoral immunity in cases of SARS-CoV-2 infection.³

Antibodies produced in COVID-19 disease are specific for particular antigens of SARS-CoV-2. There are several SARS-CoV-2 antigens, such as the internal nucleocapsid protein (N) and the external spike protein (S), composed of 2 subunits, S1 and S2. The S1 protein contains a Receptor-Binding Domain (RBD), which plays an essential role in the binding of the virus to the Angiotensin-Converting Enzyme 2 (ACE-2) receptor on host cells during the infection process.

There are different antibody responses to each antigen in patients with different disease severity.^{4,5} Previous studies have stated that antibody responses to SARS-CoV-2 are related to the severity of COVID-19 disease.⁶ Previous research by Wang *et al.* found that IgM levels in patients with mild COVID-19 symptoms were lower than in patients with severe COVID-19.⁷ Imai *et al.* also reported higher antibody levels in patients with severe COVID-19.³

Plasma from people who have recovered from COVID-19 infection, especially after a severe illness, may contain high levels of polyclonal, pathogen-specific antibodies. These antibodies can provide passive immunity to the recipient and are also called convalescent plasma.⁸ The levels of immunoglobulin collected are higher at the time of donation than the expected quantity of natural antibodies. Giving blood plasma from COVID-19 survivors can provide passive immunity to people who are experiencing symptoms of the disease.⁸

Convalescent plasma can be given by donors who must meet several special requirements, namely, aged 18-55 years, do not come from areas that have endemic diseases such as malaria, have no communicable and non-communicable disease as co-morbidities, and should not have recovered more than 3 months from the specified recovery time.⁹

This study aimed to determine the relationship between SARS-CoV-2 IgG and IgM levels with the degree and duration of negative confirmation in COVID-19 patients as potential convalescent plasma donors.

METHODS

The retrospective study was carried out at Dr. Wahidin Sudirohusodo Hospital, Makassar, with a recommendation for Ethical Approval with No. UH22070342.

The research data were collected from May 2020 to December 2020. IgG/IgM levels were measured using the AFIAS-6 Immunoanalyzer and the fluorescence immunoassay (FIA) method.

The research subjects consisted of 30 patients who met the inclusion criteria, namely all convalescent plasma donors who had previously been confirmed positive for COVID-19 according to Polymerase Chain Reaction (PCR) results, at the age of 18-55 years, had IgM/IgG test data, and were negative for COVID -19 from one or more nasopharyngeal and oropharyngeal swabs via PCR results. Patients whose incomplete medical records were excluded from this study.

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 25. The Shapiro-Wilk test was used to assess the normality of the data distribution. The results showed that the data were not normally distributed; therefore, the Spearman rho non-parametric correlation test was used. The statistical test results with p-value <0.05 were reported as significant.

RESULTS AND DISCUSSIONS

Table 1. Characteristics of the potential donor of convalescent plasma

Criteria	Results
Gender (n%)	
Male	26 (86.7)
Female	4 (13.3)
Age (years)	
Mean±SD	39.77±9.29
Median (min-max)	36 (30–61)
IgM levels (AU/mL)	
Mean±SD	0.264±0.65
Median (min-max)	0.035 (0.01–3.16)
IgG levels (AU/mL)	
Mean±SD	16.56±15.6
Median (min-max)	15.34 (0.01 – > 40)
Severity of COVID-19 (n%)	
Mild	12 (40)
Moderate	15 (50)
Severe	3 (10)
Length of negative (days)	
Mean±SD	13.53 ± 2.2
Median (min-max)	12 (12 – 20)

*Saphiro-Wilk test

Based on Table 1, there were 26 (86.7%) males and 4 (13.3%) females convalescent plasma donor candidates, with an average age of 40 years, 12 (40%), 15 (50%), and 3 (10%) subjects with mild, moderate, and severe COVID-19, respectively. The average length of negative conversion was 14 days, the average IgM level was 0.264, and the average IgG level was 13.53.

Table 2. Correlation between SARS-CoV-2 IgM and severity of COVID 19

Severity of COVID-19	IgM Levels	R	P
Mild	0.01 (< 0.01 – 1.59)	0.058	0.763*
Moderate	0.04 (0.01 – 0.30)		
Severe	0.05 (0.01 – 0.28)		

*Spearman correlation test

Table 2 shows that the median IgM level in the mild, moderate, and severe group was 0.01, 0.04, and 0.05, respectively. Spearman correlation test results showed no significant relationship between IgM levels and the severity of COVID-19 with a p-value of 0.763 (p > 0.05).

Table 3. Correlation between SARS-CoV-2 IgG levels and severity of COVID-19

Severity of COVID-19	IgG Levels	R	P
Mild	0.01 (< 0.01 – 32.21)		
Moderate	0.01 (<0.01 – 28.67)	0.444	0.014*
Severe	27.07 (25.19 – 39.25)		

*Spearman correlation test

Based on Table 3, the median IgG level was 0.01, 0.01, and 27.07 in mild, moderate, and severe groups. Spearman correlation test results found that there was a significant correlation between IgG levels and the severity of COVID-19, with a p-value of 0.014 ($p < 0.05$) and a correlation strength of 0.444 (weak correlation).

Based on Table 4, the median IgM level was 0.035. Spearman correlation test results found no significant correlation between IgM levels and the length of negative conversion in COVID-19 patients with a p-value of 0.998 ($p > 0.05$).

Based on Table 5, the median IgG level was 15.34. Spearman correlation test results found that there was a significant relationship between IgG levels and the length of negative conversion in COVID-19 patients with a p-value of 0.004 ($p < 0.05$) with a correlation strength of 0.509 (medium correlation).

Research conducted at Dr. Wahidin Sudirohusodo Hospital from May to December 2020 found that the research subjects comprised 86.7% males and 13.3% females with an average age of 40 years. This result was in line with a study by Chen *et al.*, which states that COVID-19 cases often occur, especially in men, and age is one factor affecting the severity of the disease. The study's results found 40% mild, 50% moderate, and 10% severe COVID-19 with an average conversion length of 14 days. The

average IgM and IgG level was 0.264 and 13.53, respectively.¹⁰

The median IgM level in this study's mild, moderate, and severe groups was 0.01, 0.04, and 0.05, respectively. Spearman correlation test results found no significant correlation between IgM levels and the severity of COVID-19 with a p-value of 0.763 ($p > 0.05$). In addition, this study's median IgG level in mild, moderate, and severe groups was 0.01, 0.01, and 27.07, respectively. Spearman correlation test results found that there was a significant relationship between IgG levels and the severity of COVID-19, with a p-value of 0.014 ($p < 0.05$) and a correlation strength of 0.444 (weak correlation). These results were in line with a study by Fenty and Putra, which demonstrated a different response of antibodies characterized by IgM and IgG levels from both COVID-19 patient groups. The IgM and IgG levels in the non-severe group were relatively lower than the severe group, with $p < 0.05$.¹¹

Studies by Ozturk *et al.* suggested that IgM and IgG levels affect the severity of the disease. IgM levels increase at the onset of infection and decrease as the disease progresses. Contrastingly, IgG levels will slowly increase until the 7th week after SARS-CoV-2 infection. Zhenjiang *et al.*, in their study, suggested that high IgG levels were detected in patients with severe COVID-19. This study found the average IgM and IgG levels of 0.264 and 16.56, respectively.^{12,13}

The median IgM level in this study was 0.035. Spearman correlation test results found no significant correlation between IgM levels and the length of negative conversion in COVID-19 patients with a p-value of 0.998 ($p > 0.05$). This study can be attributed to Orner *et al.* stating that IgM levels do not indicate previous SARS-CoV-2 infections. The median IgG level in this study was 15.34. Spearman

Table 4. Correlation between SARS-CoV-2 IgM levels with the length of negative conversion of COVID-19 patients

Length of Negative Conversion (days) (Median (min-max))	IgM Levels (AU/mL) (Median (min-max))	R	P
12 (12 – 20)	0.035 (0.01 – 3.16)	0.001	0.998*

*Spearman correlation test

Table 5. Correlation between SARS-CoV-2 IgG levels with the length of negative conversion of COVID-19 patients

Length of Negative Conversion (days) (Median (min-max))	IgG Levels (AU/mL) (Median (min-max))	R	P
12 (12 – 20)	15.34 (0.01 – 40)	0.509	0.004*

*Spearman correlation test

correlation test results found that there was a significant relationship between IgG levels and the length of negative conversion in COVID-19 patients with a p-value of 0.004 ($p < 0.05$) and a correlation strength of 0.509 (moderate correlation), indicating that more extended negative conversion led to higher IgG levels. This result was in line with a study by Jin *et al.*, which reported that positive IgG levels (88.9%) increased before conversion to negative by molecular detection.¹⁴

CONCLUSIONS AND SUGGESTIONS

There was a correlation between SARS CoV-2 IgG levels in potential convalescent plasma donors and the severity of disease and duration of negative conversion in COVID-19 patients. However, there was no correlation between SARS CoV-2 IgM levels in potential convalescent plasma donors and the disease severity and length of negative conversion in COVID-19 patients.

Further research investigating the antibody with more characteristics and population is still needed.

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