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Research

THE CORRELATION OF ABO BLOOD TYPES AND COVID-19 SEVERITY IN BETHESDA HOSPITAL YOGYAKARTA

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ABSTRACT
Background COVID-19 is caused by the SARS-CoV-2 virus. The most recent study showed that there was a possible correlation between ABO blood types and COVID-19 risk. However, some studies disproved the correlation. The contradiction indicated that the correlation between the two variables has not been established.
Objective To find the correlation between ABO blood types and the severity of COVID-19.
Methods It applied an observational-analytic method with a retrospective cohort approach. It used secondary data from 2020-2021 in Bethesda Hospital Yogyakarta. Samples were taken using a consecutive sampling technique. The collected data were analyzed using SPSS 26. Univariate analysis was made using descriptive statistics. Sequentially, bivariate and multivariate analyses were made using chi-square, odds-ratio, relative-risk, and ordinal logistic regression analysis.
Results There were 212 data. Blood type O got the biggest percentage (38.2%) with a sample of 81 individuals. There were 88 patients with severe symptoms (41.5%), 86 patients with moderate symptoms (40.6%), and 38 patients with mild symptoms (17.9%). The Chi-square analysis of ABO blood types and the severity of COVID-19 was 0.05 (≤0.05). The blood type B had a 2.8 times higher probability of severe incidence (95% CI 0.618–12.16) than the non-B blood type. Meanwhile, blood type O had a 0.33 times lower probability of severe incidence (95% CI 0.618–12.16) than non-O blood type.
Conclusion The ABO blood types correlated with COVID-19 severity. Blood type O became a protective factor, and blood type B is the risk factor for severe COVID-19.
Keywords: blood types, severity, COVID-19, SARS-CoV2

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INTRODUCTION

COVID-19 is caused by SARS-CoV-2 infection.[1] SARS-CoV-2 is a virus of the family of Coronaviridae and homologous to SARS-CoV.[2] The virus could be transmitted from infected individuals to others through liquid particles of coughing, sneezing, etc. After transmission, it would stick to the angiotensin-converting-enzyme 2 (ACE2) receptor on the surface of the respiratory cell and its membrane would serve as the host cell.[3] It would replicate and produce more RNA. New viruses are released and invade other cells.[4] According to the 3rd edition of COVID-19 management guidelines, the severity of COVID-19 symptoms was classified into 4, including asymptomatic, mild, moderate, and severe.[5] The severity levels were inseparable from various risk factors such as age, sex, hypertension, diabetes, and other comorbidities.[6] Additionally, the most recent study showed that there was a possible correlation between blood types and COVID-19 risk.[7,8] There were a lot of studies indicative of the role of blood types in disease transmission through antigen or antibody and virus interaction.[9,10,11] Studies suggested that natural antibodies could protect the body against infection by certain viruses so that the outcome could be better.[9] However, SARS-COV-2 could relate to antigens on the erythrocyte surface.[11] Some studies showed that individuals of blood type O had a lower

risk than those of non-O blood types.[7,8,11] On the contrary, other studies disproved the correlation between blood types and the severity of COVID-19 infection.[2,12]
The contradiction indicated that the correlation between blood type and COVID-19 has not been established.

METHODS

The study applied an observational-analytic method with a retrospective cohort approach. The observational analytic method is a study that does not provide any intervention to the research subject. A cohort is a research design that studies the relationship between risk factors and their effects. The retrospective cohort itself identifies risk factors and effects in the cohort that occurred in the past. Samples were drawn using a consecutive sampling technique. This technique will include all subjects who met the inclusion criteria in the study until the required number of subjects has been met. The inclusion criteria in this study were patients with confirmed COVID-19 with or without any symptoms. Another inclusion criteria were outpatient or inpatient with confirmed COVID-19. Meanwhile, the exclusion criteria in this study were patients with incomplete medical records. The target population in this study was confirmed COVID-19 patients in the city of Yogyakarta. The accessible population in this study were confirmed COVID-19 patients in the medical record data at Bethesda Hospital Yogyakarta. The sample was taken from secondary data from the 2020 – 2021 period at Bethesda Hospital Yogyakarta.
Data were analyzed using SPSS 26. Univariate analysis was made using descriptive statistics to find out the characteristics of the population of the study. Bivariate analysis was made by calculating the chi-square, odds ratio (OR), and relative risk (RR). Multivariate analysis was made using ordinal logistic regression. Chi-square is a non-parametric statistical test used to test the comparative hypothesis of two samples. Odds ratios (OR) are used to find out whether a particular exposure is a risk factor for a particular outcome. The risk ratio (RR) is a number that describes the risk of certain events occurring in one group to another. Ordinal logistic regression is an analytical method used to analyze the relationship between many independent variables (more than one) with one dependent variable (ordinal).

RESULTS

The population of the study was dominated by males (54.2%). The mean age of the population was 55 years with the youngest age at 9 years and the oldest at 89 years. Similar to the Indonesian population, blood type O patients are the most prevalence percentage with the number of samples of 81 individuals (38.2%), followed by blood types B, A, and AB. The asymptomatic symptoms patient was not found, while the most of the patients had severe symptoms (41.5%). The comorbid patients was 63.7% (Table 1).

Table 1. Population Characteristics

Variable	Total	Percentage
Sex		
Male	115	54.2 %
Female	97	45.8 %
Age		
Lowest	9 y.o.	
Highest	89 y.o	
Mean	54.96 ± 14.750	-
Blood types		
A	49	23.1 %
B	57	26.9 %
AB	25	11.8 %
O	81	38.2 %
Severity		
Asymptomatic	0	-
Mild	38	17.9 %
Moderate	86	40.6 %
Severe	88	41.5 %
Comorbidity		
Yes	135	63.7 %
No	77	36.3 %

Table 2 explain the results of the chi-square analysis, sex was not correlate to the symptoms severity, the p-value was 0.076 ($p > 0.05$). Analysis between comorbidities and severity found a p-value of 0.528 ($p > 0.05$), which means that there is no relationship between comorbidities and severity. Likewise, the analysis of the blood group relationship obtained a chi-square value of 0.05 ($p \leq 0.05$), which means that blood type is related to the severity of COVID-19 symptoms. The chi-square analysis of the

correlation between age and severity showed that the p-value was 0.01 ($p \leq 0.05$), meaning that there was a significant correlation between age and severity.

Table 2. Bivariate Analysis of Sex and Severity

Characteristics	Severity			Total	Chi-square (p)
	Mild	Moderate	Severe		
Sex					0.07
Male	15	46	54	115	
Female	23	40	34	97	
Comorbidity					0.53
Yes	27	52	56	135	
No	11	34	32	77	
Blood types					0.05
A	8	20	21	49	
B	5	27	25	57	
AB	2	9	14	25	
O	23	30	28	81	

Figure 1 showed that most of the patients with mild and moderate severities were <50 years of age, while the patients with moderate and severe symptoms were ≥50 years of age

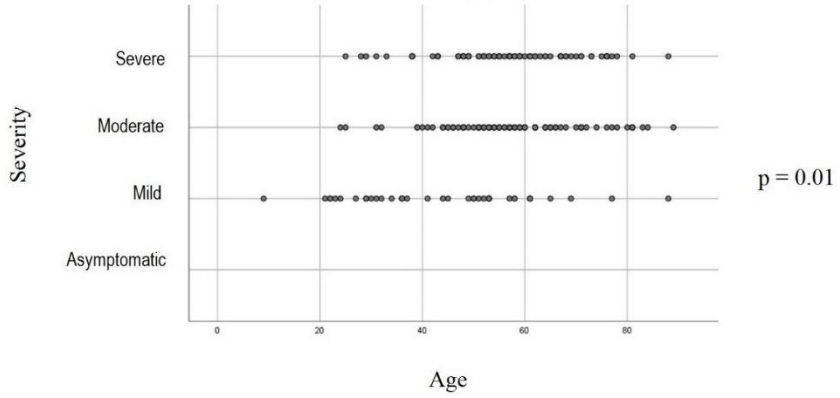

Figure 1. The Scatter Diagram of the Correlation between Age and Severity

The OR value of 3.07 means that the patients with the blood type O tended to have a 3 times higher probability of having asymptomatic-mild symptoms as compared to those of the non-O blood types. The RR value of 2.48 means that the mild symptoms of the patients with blood type O had a 2.5 times higher probability as compared to those of the non-O blood types. The RR of the moderate-severe symptoms indicated that the patients of blood type O had a 0.8 times lower probability of having severe symptoms as compared to those of the non-O blood types (Table 3).

Table 3. Estimated Risks of Blood Type O/Non-O and Symptoms Severity

95% Confidence Interval	Value	Lower	Upper

The OR of blood types (O/Non-O)	3.07	1.49	6.32
The relative risk of mild symptoms	2.48	1.38	4.47
The relative risk of severe symptoms	0.81	0.69	0.94

The blood types A and AB did not have any correlation with the incidence of severe symptoms. A significant correlation was found between the blood types B and O and the severe symptoms. Blood type B had a 2.8 times higher probability of the incidence of severe symptoms as compared to the non-B blood types. Meanwhile, the blood type O had a 0.33 times lower probability of the incidence of severe symptoms as compared to the non-O blood types (Table 4).

Table 4. The OR of the ABO Blood Types and Severe Symptoms

Blood Types	p-Value	OR	95% Confidence Interval
A vs Non-A	0.739	1.15	0.49 – 2.72
B vs Non-B	0.035*	2.81	1.04 – 7.61
AB vs Non-AB	0.168	2.74	0.62 – 12.16
O vs Non-O	0.002*	0.33	0.16 – 0.67

**Significant at p<0.05*

Table 5 showed that the comorbidity did not have any correlation with the symptom severity. However, it was observed that blood type and sex had a correlation with the symptom severity, and it was also the case of age. The OR value <1 of the blood types indicated that blood type O had a protective nature. The OR value of the sex indicated that males had 1.7 times higher severity than females.

Table 5. Multivariate Analysis of Ordinal Regression

Variable	p-Value	OR	95% Confidence Interval
Sex	0.042*	1.71	1.02 - 2.88
Comorbidity	0.403	0.79	0.38 - 0.99
Age	0.002*	1.03	0.46 - 1.36
Blood types	0.047*	0.58	1.01 - 1.05

**Significant at p<0.05*

DISCUSSION

Most of the patients in the study were males (54.2%). It showed that males were more susceptible to COVID-19 than females. It might be because the males had higher mobility outside the house, while the females in Indonesia spent more time doing domestic jobs.[13] The mean age of the population was 55 years with the age range of 9-89 years. The findings were similar to those of prior studies showing that COVID-19 could affect all age groups of both young and old individuals.[14] The data showed that blood type O represented the biggest number and was followed by blood types B, A, and AB. Consistent with the findings, the demographical characteristics of the Special District of Yogyakarta were the same.[15] The findings of the severity of the population of the study showed that the majority of the hospitalized patients had severe symptoms (41.5%), while there was not any asymptomatic patient found in the population. A similar study found that most COVID-19 patients looking for medical help had severe symptoms (41.1%).[16] The data showed that most of the patients in the study had comorbidities. It might be because there were comorbidities or immunocompromising conditions that could increase the probability of infection as a result of decreasing immunity. In such a situation, individuals were at high risk of infection though the individuals have got complete vaccination.[6]

The resulting chi-square value indicated that there was not any correlation between the comorbidities and the severity. Though the results of some prior studies were in contradiction to those of the recent study, there were some other studies suggesting that comorbidities of some diseases such as hypertension did not have any significant

impact.[17,18] It might be because the COVID-19 patients with the comorbidity of hypertension were usually given angiotensin-converting enzyme inhibitors (ACE inhibitors) and angiotensin receptor blockers (ARB) therapies. The two medicines could increase ACE which theoretically could in turn increase SARS-CoV-2 in tissues. However, the fact was that ACE2 on the contrary protected the lungs against injury risk. It took place because the increase in the ACE2 dissolved in blood circulation would help lessen the viral load, bind the circulating SARS-CoV-2, and reduce their attachment to tissue ACE2.[19] Analysis results showed that there was a correlation between age and severity. Figure 1 corroborated the results of the analysis showing that symptom severity was more likely to increase with age. The finding was consistent with prior studies suggesting that old patients (>60 years) were more likely to have severe symptoms and to be at high risk of respiratory failure.[20] It was because adults' innate immunity response tended to be overactive and ineffective. It was indicated by uncontrolled production of proinflammatory cytokine (i.e., cytokine storm) that resulted in tissue injury.[21,22]

The results of the chi-square test showed that there was a correlation between the ABO blood types and the COVID-19 severity. The results of the OR and RR analyses showed that blood type O tended to be protective, while blood type B became the risk factor for severe symptoms. The findings were consistent with prior studies suggesting that there was a correlation between the ABO blood types and the susceptibility to COVID-19.[7,8,11] Generally, prior studies suggested that the blood types A and B correlated to the increase in the risk of COVID-19, while the blood type O was more likely to have protective nature. It could be explained by some mechanisms, including: (1) The anti-A antibody of the individuals of the blood type O was more likely to have a protective nature because the blood types A and B produced anti-A/anti-B antibodies, respectively, especially IgM, while the individuals of the blood type O produced IgG.[10] (2) SARS-CoV-2 would produce glycan antigen similar to host antigen (i.e., antigen A or B). When the SARS-CoV-2 produced certain glycan antigens and infected other individuals of different blood types, an adversative antibody would block the interaction between virus spike protein and the ACE2 of host cells. In this case, the anti-A antibody of the individuals of the blood types O and B prevented infection by binding A-like antigen extant in envelope SARS-CoV-2.[9] (3) The SARS-COV-2 could bind N-acetyl galactosamine (antigen A) group on the erythrocyte surface of the blood type A. Therefore, blood type A had more potential to have a high viral load.[11] (4) The ACE2 activity in blood type B was more intense than that in blood type O. It resulted in a high viral bond of blood type B.

Multivariate analysis was made to measure the impact of independent variables. Sex, age, and blood type were variables related to COVID-19 clinical outcomes. The results of the chi-square analysis showed that sex did not have any correlation with COVID-19 severity. However, they showed that the variable correlated with severity. It was because the multivariate analysis examined each of the variables simultaneously so that the variable of the sex correlated because of the presence of other variables.[22]

CONCLUSION

It was concluded that blood type correlated with COVID-19 severity. The results of the study showed that blood type O became the protective factor against severe COVID-19, while blood type B became the risk factor for severe COVID-19.

RECOMMENDATION

It would be better for future researchers to specifically analyze the comorbidity of individual diseases and equalize the samples of each blood type.

It was expected that health institutions could better anticipate any outcome of the patients of the non-O blood types, while at the same time paying good attention to those of the blood type O. Though the study confirmed the correlation between the ABO blood types and the COVID-19 severity, it was expected that the individuals of the blood type O did not underestimate the COVID-19.

For individuals of non-O blood types, the researchers emphasized that prevention is the most important thing in warding off COVID-19 regardless of the risk factors. The prevention included taking safe social distancing, washing, wearing masks, and

vaccination.

CONFLICT OF INTEREST AND FUNDING RESOURCES

All authors have no conflict of interest. The authors covered all of the necessary costs for the study.

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