The Relationship between ABO Blood Group and The Severity of COVID-19 at Universitas Airlangga Hospital

Fasqiah Amaliah[a*], Diah Puspita[b], Resti Yudhawati[c]

[*]Correspondence: afasqiah@gmail.com
[a]Medical Program, Faculty of Medicine, Universitas Airlangga, Surabaya
[b]Department of Pathology Clinic, Faculty of Medicine, Universitas Airlangga, Surabaya
[c]Department of Pulmonary and Respiratory, Faculty of Medicine, Universitas Airlangga, Surabaya

Abstract

At the end of 2019, an infectious disease was discovered, has spread rapidly throughout the world, and has become a pandemic called COVID-19. Several risk factors for COVID-19 infection are advanced age and comorbid diseases. However, at the beginning of the pandemic in Wuhan, China there were more patients with blood type A who were confirmed positive than other blood types. The study aimed to analyze the relationship between ABO blood type and the severity and characteristics of COVID-19 patients at Universitas Airlangga Hospital, Surabaya. This study is a retrospective study, using secondary data in the form of medical records of Covid-19 patients at Universitas Airlangga Hospital, Surabaya. From the 104 COVID-19 patients at Universitas Airlangga Hospital, the majority are male (54.8%). Most of the ages are in the range of 45-59 years (37.5%). Most COVID-19 patients at Universitas Airlangga Hospital have blood type O. The most severe degree of infection of COVID-19 patients at Universitas Airlangga Hospital is the severe category (59.6%). There is no significant relationship between ABO blood type and the severity of COVID-19 infection statistically, but blood type O (37.5%) is the most common blood group in all degrees of severity, but blood type B is the most common group in cases of death. (28.1%). There is no significant relationship between ABO blood type and the severity of COVID-19 infection. The characteristics of COVID-19 patients at Universitas Airlangga Hospital are mostly male, aged 45-59 years, and blood type O.

Keywords: COVID-19, ABO Blood Groups, Universitas Airlangga Hospital

1. Introduction

Coronavirus disease 2019 (COVID-19) is an infectious disease that has spread rapidly around the world and is increasing daily. The first case of COVID-19 was discovered in Wuhan, China, on December 31, 2019, caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) virus[1]. SARS-CoV-2 is a betacoronavirus similar to SARS-CoV in that it binds to angiotensin-converting enzyme-related carboxypeptidase (ACE2) to enter host cells[2]. Thus, the virus will attack target organs that express Angiotensin Converting Enzyme 2 (ACE2), such as the lungs, heart, renal system, and gastrointestinal tract[3]. SARS-CoV-2 is transmitted mainly through droplets or splashes of saliva when coughing, sneezing, or talking from a person infected with COVID-19[4]. SARS-CoV-2 begins to replicate actively and causes symptoms in patients such as fever, myalgia, headache, and mild disturbances of the respiratory system to severe infections[5].

Several factors that increase the risk of COVID-19 infection that have been determined by WHO are old age and comorbid diseases such as diabetes mellitus and hypertension[2]. In older people, degenerative anatomy and physiology of the body occur, making them susceptible to disease, and the decreased immune system is the reason age is a risk factor[6]. The second factor that is equally important is the comorbidities of individuals infected with COVID-19, where the most common chronic diseases are type 2 diabetes and hypertension[7]. Infection of SARS-CoV-2 with diabetes might trigger stress condition and increased secretion of hyperglycemic hormones, such as glucocorticoid and catecholamines, which results in elevated blood glucose, abnormal glucose variability and diabetic complications and the impact of uncontrolled diabetes will cause cytokine inflammation, damaging multiple organs[8]. Then on comorbid hypertension, hypertension can worsen the prognosis of COVID-19 due to the consumption of ACE-

inhibitor drugs and Angiotensin II Receptor Blockers (ARBs) as interventions for hypertension drugs that can exacerbate COVID-19[9].

Despite that, biological markers such as blood type in predicting the risk of COVID-19 infection have not been found[10]. Human blood groups have been used as genetic markers, allowing us to determine the susceptibility of people with different blood types to viruses[11]. The ABO blood group trait reflects polymorphisms in the ABO gene and this gene is suspected of having several relationships with comorbid risk factors for COVID-19[12]. The association between ABO blood group types and viral infections has been reported previously. For example, individuals with blood type O are reported to be more susceptible to Norwalk virus[13]. The same thing was also reported regarding the relationship between ABO blood type and P. falciparum infectivity[14]. Some factors that influenced ABO blood group and susceptibility to certain infectious diseases. Von Willebrand factor and Factor VIII play a vital role in the process of hemostasis. People with the non-O blood group have higher levels of vWf, and factor VIII than people with blood group O[12]. Low levels of vWf and factor VIII will aggravate hemostatic disorders[12]. One of the causative factors is that anti-A antibodies can block the adhesion of SARS-CoV S protein to ACE2 of host cells, where the genome of SARS-CoV-2 is similar to that of SARS-CoV[15].

At the beginning of the COVID-19 pandemic in Wuhan, China, the number of patients with blood group A who were confirmed positive was more than other blood groups and the number of patients with blood type O was the least group who was confirmed positive for COVID-19[10]. However, at the Hacettepe university hospital reported that the most frequently detected blood group was blood group A with 57% amongst the COVID-19 patients. This was followed by blood group O with 24.8%[16]. Heretofore, research on the relationship between blood type and susceptibility to COVID-19 has been done, but the explanation of risk factors for higher severity and the degree of severity in COVID-19 patients based on blood type has not been found clearly. In addition, to supporting data this study aims to determine the relationship between ABO blood type and the severity of COVID-19.

2. Method

This study used a retrospective study aimed to determine the relationship between ABO blood type and the severity of COVID-19. The data is in the form of secondary data obtained from the medical records of COVID-19 patients at Airlangga University Hospital in Surabaya from May to July 2021. This study used a total sampling technique that had been selected from the study population that met the sample criteria during the May - July 2021 period, with a total of 104 patients. The severity of the patient is determined based on WHO the Clinical Management of COVID-19 Patients: Living Guidelines, classified into mild, moderate, severe, and critical disease. However, this study was only divided into three categories of mild, moderate and severe disease, where the critical group was included in the severe group. This research has obtained permission from the Health Research Ethics Committee of Airlangga University Hospital with an Exemption Letter number 210/KEP/2021. Data included age, gender, chronic disease, physical examination, laboratory tests, and patient outcomes. Data was collected using Microsoft Excel 2016 and then statistical evaluation was performed using the IBM SPSS 26 application. Chi-square test was used for the comparison of categorical data $p < 0.05$ was considered statistically significant.

3. Results

A total of 104 patients met the inclusion and exclusion criteria and became study participants. The distribution of the participants based on blood type and degree of severity are shown in Table 1.

Table 1. The Distribution of Severity Degrees COVID-19 Patients Based on Blood Group at Universitas Airlangga Hospital in the May-July 2021.

Severity	A (n=22)		B (n=31)		AB (n=12)		O (n=39)		Total	%
	N	%	N	%	N	%	N	%		
Mild	2	9,1	4	12,9	1	8,3	6	15,4	13	12,5
Moderate	7	31,8	8	25,8	2	16,7	12	30,8	29	27,9
Severe	13	59,1	19	61,3	9	16,7	21	53,8	62	59,6

The majority of Covid-19 patients from May to July 2022 were 39 people with blood type O (15.4%), followed by 31 people with blood type B, 22 people with blood type A, and 12 people with AB blood type. In this study, it was found that most patients were in the degree of severe severity, with a total of 62 people (59.6%). From the data distribution above, a Chi-Square test was carried out on ABO blood type and the degree of severity of COVID-19 based on WHO and obtained a significance value of $p = 0.702$ (> 0.05) so that the decision is on H0 or there is no relationship between blood type and degree severity of COVID-19.

Table 2. Characteristics of COVID-19 Patients by Group Blood at Universitas Airlangga Hospital in the May-July 2021.

Characteristics	A (n=22)		B (n=31)		AB (n=12)		O (n=39)		Total	%
	N	%	N	%	N	%	N	%		
Gender										
Female	9	40,9	14	43,7	2	16,7	22	57,9	47	45,2
Male	13	59,1	18	56,3	10	83,3	16	42,1	57	54,8
Age										
≤44	8	36,4	11	34,4	5	41,7	12	31,6	36	34,6
45-59	8	36,4	13	40,6	3	25	15	39,5	39	37,5
≥60	6	27,2	8	25	4	33,3	11	28,9	29	27,9
Chronic Disease										
CHD	1	4,6	1	3,2	1	8,3	0	0	3	2,9
COPD	1	4,6	1	3,2	0	0	1	2,6	3	2,9
CKD	1	4,6	1	3,2	0	0	0	0	2	1,9
Diabetes	5	22,7	3	9,7	0	0	1	2,6	9	8,7
Hypertension	2	9,1	5	16,1	0	0	3	7,7	10	9,6
Mortality										
Death	6	27,3	9	28,1	2	16,7	6	15,8	23	22,1
Survived	16	72,7	23	71,9	10	83,3	32	84,2	81	77,9

Based on Table.2, it was found that COVID-19 patients were dominated by male sex, 57 patients (54.8%), with the widest age range, namely 45-59 years, 39 patients (37.5%), while for mortality, 23 patients were found died and the most common chronic disease was hypertension with 10 people (9.6%).

4. Discussion

In this study, the severity degree of COVID-19 patients is determined based on WHO Clinical guidelines, with mild, moderate, and severe. The study's results showed that the severity of infection of COVID-19 patients at Universitas Airlangga Hospital was mainly in the severe category, with 39 people (37.5%). Data regarding the degree of mild severity was found in 13 people and based on blood types A, B, AB, and O, dominated by blood group O, namely six people (15.8%). Then at moderate severity, there were a total of 29 people, and at moderate severity, were also dominated by blood type O as many as 12 people (31.6%). The degree of severe severity was dominated by blood type O in 14 patients (36.8%). The degree of critical severity was dominated by blood type B in 9 patients (28.1%). The result of the value test where the relationship between blood type and the severity of COVID-19 has a value of 0.702 (p > 0.05), meaning there is no relationship or link between blood type and the severity of COVID-19.

This study has the same result as previous research conducted by Solmaz and Arac stated that blood type did not affect the severity and death from COVID-19. Based on research conducted at Diyarbakir Gazi Yasargil Training and Research Hospital, obtained blood type in patients requiring intensive care or in the highest degree of severity in blood group A as many as 753 patients (45.17%), followed by blood group 0 447 patients (26.81%), B 311 patients (18.65%), and AB 156 patients (88.66%) with a Chi-Square test result of 0.716 (p>0.05)[16].

Several studies that contradict with the result of this study. From the results of research at the Wuhan Jinyintan Hospital, it was found that there was a link between the influence of blood type and the susceptibility to COVID-19 infection in blood groups A and O. The proportion of blood group A among patients with COVID-19 was significantly higher than that among the control group, being 37.8%. Contrarily, the proportion of blood group O in patients with COVID-19 was significantly lower with a percentage of 25.80%, and both blood groups A and O had a p value <0.001[10]. The previous statement is equal to the study of Wu et al which stated that blood type O may be protective, that non-O blood groups may have greater susceptibility to disease, this is because ABO blood type has been associated with previous cardiovascular disease[17]. This is also in line with Chen et al, stating that individuals with blood type O are less likely to be infected with COVID-19[18]. This is because the S/Angiotensin-Converting Enzyme 2 (ACE2) protein depends on the adhesion of these cells to the angiotensin 2 converting enzyme expressing cell line specifically inhibited by human natural anti-A antibodies, possibly blocking the interaction between the virus and its receptor[15].

However, when COVID-19 patients required intensive care or were at severe severity, blood type was shown to have a significant impact on intensive care and mortality[16]. The notion that the thrombotic risk is significantly reduced in blood group O compared to non-O blood type[19]. Studies have shown that microthrombosis that develops in COVID-19 infection in the pulmonary vessels contributes significantly to acute respiratory syndrome[20]. Therefore, there was not statistically significant which could determine whether there was a relationship between blood type and the degree of severity of COVID-19.

Conclusion and Suggestion

This study figured out that most of the COVID-19 patients at Universitas Airlangga Hospital had blood type O and the highest number of patients who died were blood group B. However, there was no significant relationship between ABO blood type and the severity of COVID-19 infection in statistical tests. In this study, there are several limitations including the data collection is only done one time and cannot follow research subjects prospectively in analyzing the degree of severity of COVID-19 in longer time and also each region is influenced by heredity or regional race and ethnicity. Researchers suggest further research to collect data in time series (e.g. 1, 3, 6, 12-month) and long duration so that the number of samples is larger and to follow up the efficacy and complications of COVID-19 patients closure in long term and ensure the clinical improvement of patients.

Acknowledgements

References

1. Li, Q., Guan, X., Wu, P., Wang, X., Zhou, L., Tong, Y., Ren, R., Leung, K. S. M., Lau, E. H. Y., Wong, J. Y., Xing, X., Xiang, N., Wu, Y., Li, C., Chen, Q., Li, D., Liu, T., Zhao, J., Liu, M., Tu, W., Feng, Z. (2020). Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. The New England journal of medicine, 382(13), 1199–1207. https://doi.org/10.1056/NEJMoa2001316

2. Zhou, P., Yang, X. L., Wang, X. G., Hu, B., Zhang, L., Zhang, W., Si, H. R., Zhu, Y., Li, B., Huang, C. L., Chen, H. D., Chen, J., Luo, Y., Guo, H., Jiang, R. D., Liu, M. Q., Chen, Y., Shen, X. R., Wang, X., Zheng, X. S., Zhao, K., Chen, Q. J., Deng, F., Liu, L. L., Yan, B., Zhan, F. X., Wang, Y. Y., Xiao, G. F., & Shi, Z. L. (2020). A Pneumonia Outbreak Associated with a New Coronavirus of Probable Bat Origin. Nature, 579, 270-273. https://doi.org/10.1038/s41586-020-2012-7

3. Gennaro, F., Pizzol, D., Marotta, C., Antunes, M., Racalbuto, V., Veronese, N., & Smith, L. (2020). Coronavirus diseases (COVID-19) current status and future perspectives: a narrative review. International journal of environmental research and public health, 17(8), 2690. https://doi.org/10.3390/ijerph17082690

4. World Health Organization (WHO). (2020). WHO Coronavirus Disease (COVID-19) Dashboard. https://covid19.who.int/

5. Cevik, M., Bamford, C., & Ho, A. (2020). COVID-19 pandemic-a focused review for clinicians. Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases, 26(7), 842–847. https://doi.org/10.1016/j.cmi.2020.04.023

6. Hidayani, W. R. (2020). Faktor Faktor Risiko Yang Berhubungan Dengan COVID 19: Literature Review. Jurnal Untuk Mayarakat Sehat (JUKMAS), 4(2), 120–134. http://ejournal.urindo.ac.id/index.php/jukmas%0AArticle

7. Petrie, J. R., Guzik, T. J., & Touyz, R. M. (2018). Diabetes, Hypertension, and Cardiovascular Disease: Clinical Insights and Vascular Mechanisms. The Canadian journal of cardiology, 34(5), 575–584. https://doi.org/10.1016/j.cjca.2017.12.005

8. Wang, A., Zhao, W., Xu, Z., & Gu, J. (2020). Timely blood glucose management for the outbreak of 2019 novel coronavirus disease (COVID-19) is urgently needed. Diabetes research and clinical practice, 162, 108118. https://doi.org/10.1016/j.diabres.2020.

9. Tignanelli CJ, Ingraham NE, Sparks MA, et al. Antihypertensive drugs and Risk of COVID 19.Lancet Respir Med.2020; 8(5):e30-e31. Doi:10.106/S2213-2600(20)30153-3

10. Zhao, J., Yang, Y., Huang, H., Li, D., Gu, D., Lu, X., Zhang, Z., Liu, L., Liu, T., Liu, Y., He, Y., Wei, M., Yang, G., Wang, X., Zhang, L., Zhou, X., Xing, M., Wang, PG. (2020). Relationship between the ABO blood group and the COVID-19 susceptibility. Clin Infect Dis. https://doi.org/10.1093/cid/ciaa1150

11. Wu, Y., Feng, Z., Li, P., & Yu, Q. (2020). Relationship between ABO blood group distribution and clinical characteristics in patients with COVID-19. Clinica chimica acta; international journal of clinical chemistry, 509, 220–223. https://doi.org/10.1016/j.cca.2020.06.026

12. Souto JC, Almasy L, Muñiz-Diaz E, Soria JM, Borrell M, Bayén L, Mateo J, Madoz P, Stone W, Blangero J, Fontcuberta J .(2000). Functional effects of the ABO locus polymorphism on plasma levels of von Willebrand factor, factor VIII, and activated partial thromboplastin time. Arteriosclerosis, Thrombosis, and Vascular Biology, 20(8), 2024–2028. https://doi.org/10.1161/01.ATV.20.8.2024

13. Hutson, A. M., Atmar, R. L., Graham, D. Y., & Estes, M. K. (2002). Norwalk virus infection and disease is associated with ABO histo-blood group type. The Journal of infectious diseases, 185(9), 1335–1337. https://doi.org/10.1086/339883

14. Cserti, C. M., & Dzik, W. H. (2007). The ABO blood group system and Plasmodium falciparum malaria. Blood, 110(7), 2250–2258. https://doi.org/10.1182/blood2007-03-077602

15. Guillon, P., Clément, M., Sébille, V., Rivain, J. G., Chou, C. F., Ruvoën-Clouet, N., & Le Pendu, J. (2008). Inhibition of the interaction between the SARS-CoV spike protein and its cellular receptor by anti-histo-blood group antibodies. Glycobiology, 18(12), 1085–1093. https://doi.org/10.1093/glycob/cwn093

16. Solmaz, İ., & Araç, S. (2021). ABO blood groups in COVID-19 patients; Cross-sectional study. International journal of clinical practice, 75(4), e13927. https://doi.org/10.1111/ijcp.13927

17. Wu, Y., Feng, Z., Li, P., & Yu, Q. (2020). Relationship between ABO blood group distribution and clinical characteristics in patients with COVID-19. Clinica chimica acta; international journal of clinical chemistry, 509, 220–223. https://doi.org/10.1016/j.cca.2020.06.026

18. Wang, C., Horby, P. W., Hayden, F. G., & Gao, G. F. (2020). A novel coronavirus outbreak of global health concern. Lancet (London, England), 395(10223), 470–473. https://doi.org/10.1016/S0140-6736(20)30185-9

19. Wu, O., Bayoumi, N., Vickers, M. A., & Clark, P. (2008). ABO(H) blood groups and vascular disease: a systematic review and meta-analysis. Journal of thrombosis and haemostasis : JTH, 6(1), 62–69. https://doi.org/10.1111/j.1538-7836.2007.02818.x

20. Tang, N., Li, D., Wang, X., & Sun, Z. (2020). Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. Journal of thrombosis and haemostasis : JTH, 18(4), 844–847. https://doi.org/10.1111/jth.14768