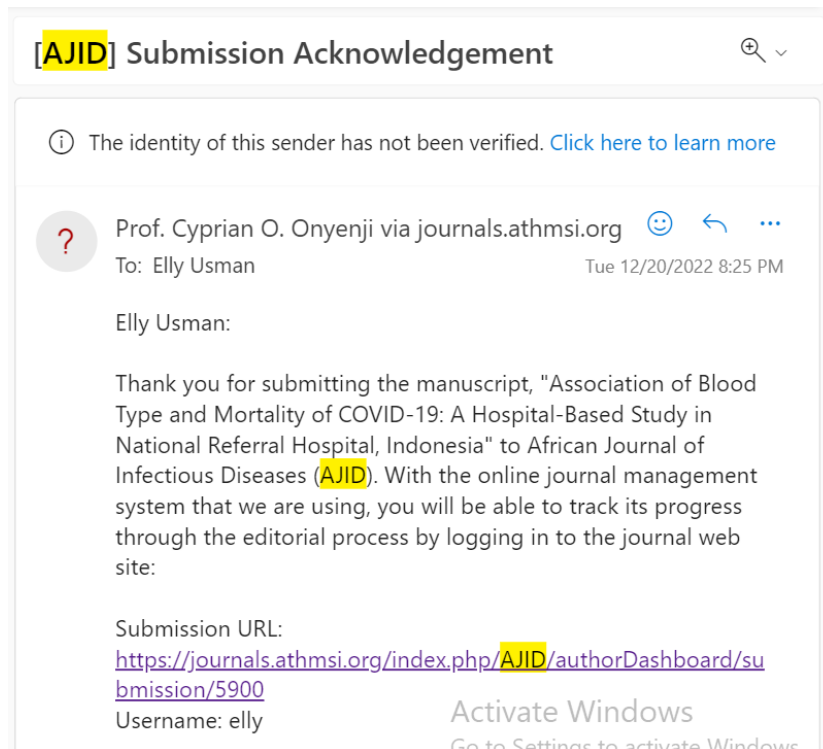


Kronologis Proses Pemasukan (Submission) Artikel hingga Terbit (Published)

Judul artikel	:	Association of Blood Type and Mortality of COVID-19: A Hospital-Based Study in National Referral Hospital, Indonesia
URL	:	https://journals.athmsi.org/index.php/AJID/article/view/5900
Jurnal	:	African Journal of Infectious Diseases
SJR	:	0,26 (Quartil Q4 sejak 2010 bidang medicine hingga sekarang) https://www.scimagojr.com/journalsearch.php?q=19700175226&tip=si&d&clean=0
Submitted	:	20 Desember 2022
Review report	:	15 Januari 2023
Revise version	:	11 Februari 2023
Accepted	:	17 Februari 2023
Article in press	:	28 Maret 2023
Published	:	29 Maret 2023
Similarity index	:	15% (link hasil pemeriksaan turnitin) https://drive.google.com/file/d/1kFa8XHAddv1oT1v58QdZQmSbAIJN7M43/view?usp=share_link

Kronologis sebagai berikut:

1. Manuskrip di submit pada tanggal 20 Desember 2022 dan mendapatkan email pemberitahuan dari editor African Journal of Infectious Diseases bahwa artikel sudah dikirim (submitted) (*Gambar 1*). Original paper terlampir (*Lampiran A*)



Gambar 1. Pemberitahuan editor bahwa manuskrip submitted

2. Email pemberitahuan oleh editor terkait hasil review dari 2 orang reviewer pada tanggal 15 Januari 2023

Notifications ×

[AJID] Editor Decision

2023-01-10 11:16 AM

Elly Usman:

We have reached a decision regarding your submission to African Journal of Infectious Diseases (AJID), "Association of Blood Type and Mortality of COVID-19: A Hospital-Based Study in National Referral Hospital, Indonesia".

Our decision is: Revisions Required.
Kindy revise your manuscript as follows:

1. Consult an English Language Expert to edit the manuscript for grammatical, punctuation and spelling errors;
2. Carefully attend to the reviewers' comments attached hereunder.

Reviewer B:

The general idea and the importance of the subject are completely satisfying. Here are my recommendations to improve this manuscript.

1. Please add more knowledge gaps in the introduction section
2. Please elaborate more on the discussion using the recent related publications.

Thank you.

Recommendation: Revisions Required

Reviewer C:

The authors have presented a very interesting manuscript about the Association of Blood Type and Mortality of COVID-19: A Hospital-Based Study at the National Referral Hospital, Indonesia. This paper is very important because there is currently little definite evidence between COVID-19 with ABO blood types. But here are my comments to improve this manuscript:

1. Please add more novelty in the introduction section
2. Add more suggestions for this result of the study
3. Add further studies and implications for this result of the study
4. Please add the implication of this study in the last section of the discussion

Recommendation: Revisions Required

Gambar 2. Pemberitahuan editor terkait hasil review dari 2 orang reviewer

3. **Author mengirimkan perbaikan manuskrip berdasarkan hasil review dari reviewer dan melakukan resubmission ke jurnal system pada tanggal 11 Februari 2023. Perubahan dan penambahan pada manuskrip penelitian berdasarkan hasil review ditandai dengan tulisan bewarna highlight kuning (*Lampiran B*).**

The screenshot displays two sections of a journal submission system. The top section, titled "Revisions", includes a search bar and an "Upload File" button. Below this, a revision entry is shown for a document named "Manuscript_Dr+Elly+Usman_revised.doc" with ID "20045", dated February 11, 2023, and categorized as "Article Text". The bottom section, titled "Review Discussions", features an "Add discussion" button and a table with the following data:

Name	From	Last Reply	Replies	Closed
Revised manuscript	elly 2023-02-11 07:19 AM	-	0	<input type="checkbox"/>

Gambar 3. Penulis mengirimkan hasil revisi berdasarkan review oleh reviewer

4. **Pemberitahuan editor bahwa manuskrip diterima setelah dilakukan revisi pada tanggal 17 Feburari 2023**

The screenshot shows an email notification from the editor. The subject is "[AJID] Editor Decision" and it is dated "2023-02-17 11:41 AM". The content of the email is as follows:

Elly Usman:

We have reached a decision regarding your submission to African Journal of Infectious Diseases (AJID), "Association of Blood Type and Mortality of COVID-19: A Hospital-Based Study in National Referral Hospital, Indonesia".

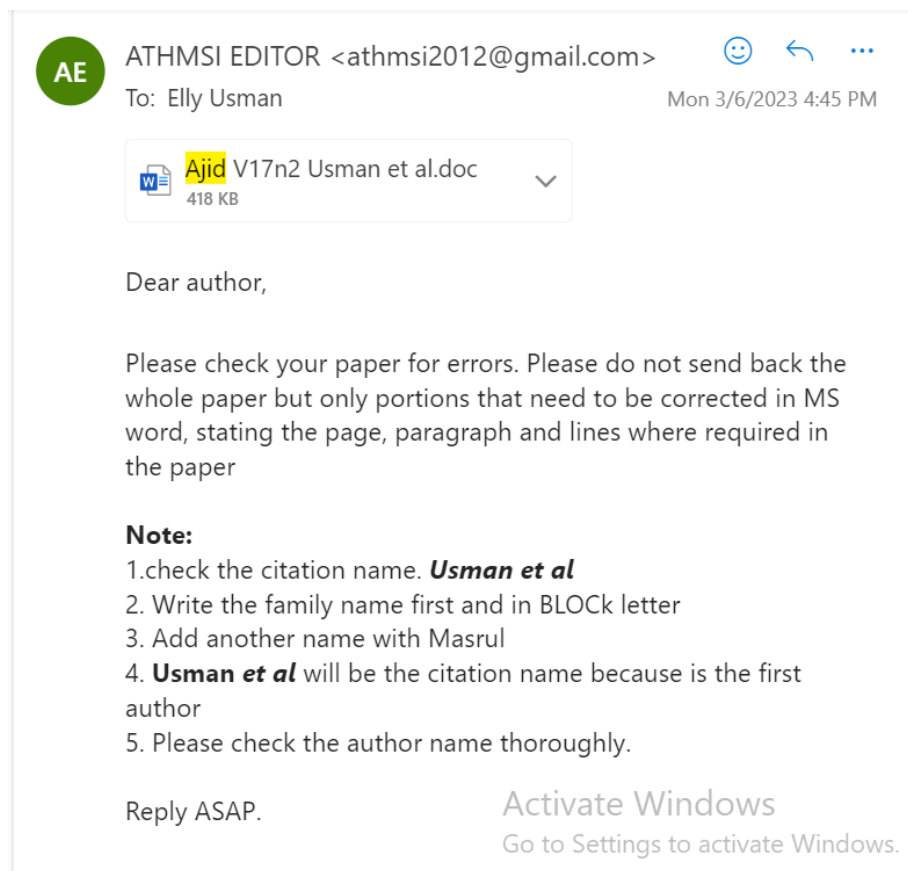
Our decision is to: Accept Submission.

I am pleased to inform you that your revised manuscript has been accepted for publication in AJID. The invoice for the Article Processing Fee (APF) of USD500.00 will be sent to you under a separate cover. Kindly remit the said APF as soon as possible to enable us process your accepted manuscript further.

Congratulations and best wishes.

Gambar 4. Pemberitahuan editor bahwa manuskrip diterima setelah dilakukan revisi

5. Pemberitahuan editor Proofreading Request pada tanggal 6 Maret 2023



Gambar 5. Pemberitahuan editor proofreading request

6. Author langsung mengirimkan proofreading ke journal system pada tanggal 6 Maret 2023

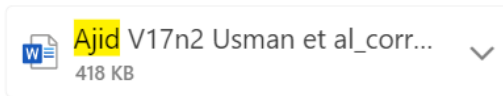


Elly Usman



To: ATHMSI EDITOR <athmsi2012@gmail.com>

Mon 3/6/2023 9:00 PM



Dear Editor,

Thank you very much for your galley proof check. Please find attached the file of my corrected galley proof.

Thank you very much for your kind help and attention.

Best regards,

Dr. Elly Usman



Activate Windows

Go to Settings to activate Windows.

Gambar 6. Author mengirimkan proofreading ke journal system

7. Pemberitahuan editor bahwa artikel sudah diterbitkan pada jurnal African Journal of Infectious Disease. 2023 Mar 29; 17(2):23-27.



ATHMSI EDITOR <athmsi2012@gmail.com>



To: Elly Usman

Tue 4/4/2023 6:56 PM

Dear Author,

You can check your manuscript through this link as it has been published since last week.

<https://journals.athmsi.org/index.php/AJID/issue/view/168>

Okay, thank you!

Great, thank you so much!

Got it, thanks!

Home / Archives / Vol. 17 No. 2 (2023) / Articles

ASSOCIATION OF BLOOD TYPE AND MORTALITY OF COVID-19: A HOSPITAL-BASED STUDY IN NATIONAL REFERRAL HOSPITAL, INDONESIA

Elly USMAN
Department of Pharmacology and Therapeutic, Faculty of Medicine, Universitas Andalas, Padang

Yusticia KATAR
Department of Pharmacology, Faculty of Medicine, Universitas Andalas, Padang, Indonesia.

DOI: <https://doi.org/10.21010/Ajid%20v17i2.4>

Fulltext.Pdf

Published
2023-03-29


How to Cite
USMAN , E., & KATAR, Y. . (2023). ASSOCIATION OF BLOOD TYPE AND MORTALITY OF COVID-19: A HOSPITAL-BASED STUDY IN NATIONAL REFERRAL

Make a Submission

Information

For Readers
For Authors
For Librarians

Keywords



Gambar 7. Pemberitahuan editor bahwa artikel sudah diterbitkan

Research article

Manuscript Title:

Association of Blood Type and Mortality of COVID-19: A Hospital-Based Study in National Referral Hospital, Indonesia

Elly Usman¹, Yusticia Katar¹

Affiliation:

1) Department of Pharmacology, Faculty of Medicine, Universitas Andalas, Padang, Indonesia.

Corresponding author

Elly Usman

Department of Pharmacology, Faculty of Medicine, Universitas Andalas, Padang, Indonesia.

E-mail: ellyusman@med.unand.ac.id

Tel: + 6275131746

Running title

Association of Blood Type and Mortality of COVID-19

Abstract

Background: The ABO blood type is crucial in a number of illnesses, including cancer, cardiovascular disease, and some communicable and non-communicable illnesses. However, there is currently little definite evidence between COVID-19 with ABO blood types.

Aim: The aim of this study was to assess the association between ABO blood type and the mortality of patients infected with COVID-19 in a national referral hospital, Indonesia.

Methods: This study used a retrospective cohort. The research sample was COVID-19 patients who were in Dr. M. Djamil Hospital Padang. The number of samples in this study was 93 subjects. The Chi-square test was used in the data analysis. The data were analyzed using the SPSS version 21.0 program, and $p < 0.05$ was considered significant.

Results: The results of this study found the percentage of mortality of COVID-19 patients was higher for blood group O (46.2%), followed by AB (41.7%), B (26.3%) and A (13.9%). There was a relationship between blood type and mortality in hospitalized COVID-19 patients ($p < 0.05$), where blood type O had the highest risk (OR = 5.31, 95% CI 1.57-17.98) followed by blood type AB (OR = 4.43, 95% CI 1.01-19.58).

Conclusion: This study confirmed there was a relationship between blood type and mortality in hospitalized COVID-19 patients, where blood type O had the highest risk followed by blood type AB.

Keywords: Blood type, COVID-19, Hospitalized, Mortality

List of Abbreviations

CI: Confidence interval

COVID-19: Coronavirus disease 2019

ICU: Intensive care unit

OR: Odds ratio

SARS-CoV-1: Severe acute respiratory syndrome coronavirus 1

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2

vWF: von Willebrand Factor

Introduction

The COVID-19 epidemic has taken a devastating impact on the world, regardless of age or gender, but especially on older persons who have co-morbid conditions including diabetes and cardiovascular and cerebrovascular disease (Almazeedi *et al.*, 2020; Velavan *et al.*, 2020). Indonesia has also faced a significant increase in COVID-19 patients which has resulted in morbidity and even death (Hikmawati *et al.*, 2021).

ABO blood type has been linked to the presence of COVID-19 infection in earlier studies. The ABO blood type is crucial in a number of illnesses, including cancer, cardiovascular disease, and some communicable and non-communicable illnesses (Fan *et al.*, 2020). Several studies have shown that having blood type O significantly lowers the chance of contracting hepatitis B (Mohammadali *et al.*, 2014; Belali, 2022). In addition, people with blood type A are more likely to develop rotavirus gastroenteritis than patients with blood type B (Mohammadali *et al.*, 2014; Elnady *et al.*, 2017). In addition, it was found that those with blood type AB are 2.5 times more likely than people with other blood types to contract dengue fever (Murugananthan *et al.*, 2018). Previous research on SARS-CoV-1 has found a correlation between blood type and the risk of infection, with people with group O blood having a small chance of SARS-CoV-1 infection (Cheng *et al.*, 2005).

There hasn't been much conclusive evidence to date between SARS-CoV-2 and ABO blood types (Zhao *et al.*, 2021). According to the majority of research, blood type O has a lower probability of developing severe SARS-CoV-2 infection than blood type A, which has a higher risk of infection (Goker *et al.*, 2020). In addition, very little research has been conducted in Indonesia to find a relationship between blood type and mortality of COVID-19 patients (Liu *et al.*, 2021). The purpose of this study was to assess the mortality of COVID-19 infected patients with different ABO blood types.

Materials and Methods

Study design and research sample

This study used a retrospective cohort. The research sample was COVID-19 patients who were in Dr. M. Djamil Hospital Padang, Indonesia. The research was conducted from January to November 2022. There were 93 total samples in this study. Convenience sampling was used as the sampling method in this study. Patients with COVID-19 with moderate to severe clinical severity and thoroughly documented information related to research variables met the inclusion criteria for this study.

Operational definition

Blood type was the study's independent variable (A, B, AB, and O) (Rana *et al.*, 2021). The dependent variable was COVID-19 patient mortality (death, and life) (Sjögren *et al.*, 2021).

Research ethics approval

The Dr. M. Djamil Hospital Padang research ethics commission approved this study after conducting an ethical review (LB.02.02/5.7/192/2022).

Data analysis

Research variables in categorical research are provided as frequency and percentage. While numeric variables are presented in the form of mean \pm SD or median (min-max). The Mann-Whitney test and the Chi-square test were used in the bivariate analysis. The data were analyzed using the SPSS version 21.0 program, and p-value < 0.05 was considered significant.

Results

Subject characteristics (Table 1).

Table 1. Subject characteristics

Characteristics	Mortality		p-value
	Death (n=27)	Life (n=66)	
Sex, f(%)			0.226 ^a
Male	21 (33.9)	41 (66.1)	
Female	6 (19.4)	25 (80.6)	
Age (years), median (min-max)	59 (21-79)	56 (20-83)	0.249 ^b
BMI (kg/m²), median (min-max)	25.15 (15.82-76.10)	24.80 (17.96-55.51)	0.691 ^b
Clinical severity, f(%)			<0.001 ^{a*}
Moderate	1 (2.0)	49 (98.0)	
Severe	22 (61.1)	14 (38.9)	
Critical	4 (57.1)	3 (42.9)	
Laboratory examination, median (min-max)			
Hb (gr/dL)	10.95 (4.4-17.4)	12.00 (4.0-15.7)	0.482 ^b
Ht (%)	28.50 (6-53)	36.00 (15-8,150)	0.114 ^b
Leukocytes (/mm ³)	2,240.50 (66-47,450)	1,400.00 (7-23,160)	0.365 ^b
Platelets	191,000 (229-652,000)	194,000 (44-650,000)	0.722 ^b
D-Dimer (ng/mL)	4,435.00 (1,039-10,000)	777.00 (157-10,000)	<0.001 ^{b*}
Procalcitonin (ng/mL)	0.74 (0.05-171)	0.27 (0.05-171.42)	0.092 ^b
IL-6 (pg/mL)	262.50 (12.20-4,599.00)	34.40 (1.50-600.00)	<0.001 ^{b*}
Ferritin (ng/mL)	1,179.58 (12.40-2,000.00)	710.00 (27.09-2,000.00)	<0.021 ^{b*}
SpO2 (%)	90.00 (48-99)	96.00 (33-99)	<0.001 ^{b*}
Number of comorbid, f(%)			0.009 ^{a*}
None	3 (14.3)	18 (85.7)	
1	2 (10.5)	17 (89.5)	
> 1	22 (41.5)	31 (58.5)	

*p<0.05 considered significant; a, Chi-square test; b, Mann-whitney test

Table 1 shows IL-6 levels, ferritin, SpO2 values, PCT levels, D-Dimer, clinical severity, and the number of comorbidities associated to mortality in COVID-19 patients hospitalized (p<0.05).

Association of blood type and mortality of COVID-19 (Table 2 and Figure 1).

Table 2. Association of blood type and mortality of COVID-19

Obese	Mortality		p-value	OR (95% CI)
	Death (f/%) (n=27)	Life (f/%) (n=66)		
A	5 (13.9)	31 (86.1)	0.543 ^a	0.19 (0.06-0.64)
B	5 (26.3)	14 (73.7)	0.054 ^a	2.21 (0.55-8.89)
AB	5 (41.7)	7 (58.3)	0.021 ^{*a}	4.43 (1.01-19.58)
O	12 (46.2)	14 (53.8)	0.009 ^{*a}	5.31 (1.57-17.98)

*p<0.05 considered significant; a, Chi-square test

Table 2 showed the percentage of deaths of COVID-19 patients was higher for blood group O (46.2%), followed by AB (41.7%), B (26.3%) and A (13.9%). There was a relationship between blood type and mortality in hospitalized COVID-19 patients ($p < 0.05$), where blood type O had the highest risk (OR = 5.31, 95% CI 1.57-17.98) followed by blood type AB (OR = 4.43, 95% CI 1.01-19.58).

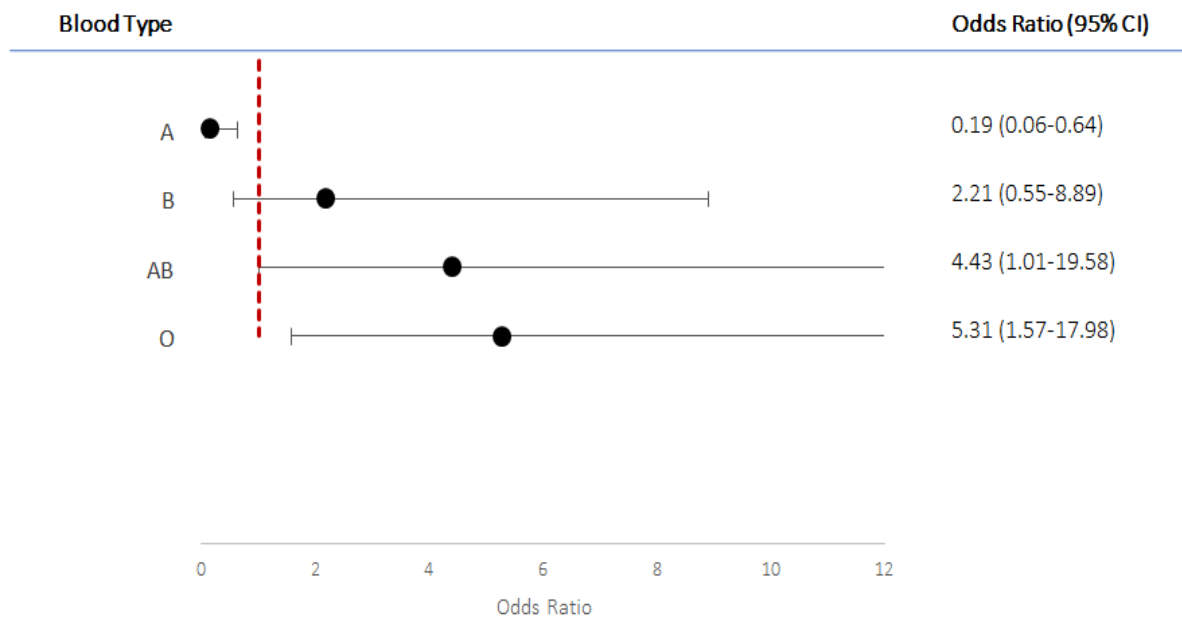


Figure 1. Forest plot blood type and mortality of COVID-19

Discussion

The results of this study found the percentage of mortality of COVID-19 patients was higher for blood group O (46.2%), followed by AB (41.7%), B (26.3%) and A (13.9%). There was a relationship between blood type and mortality in hospitalized COVID-19 patients, where blood type O had the highest risk (OR = 5.31) followed by blood type AB (OR = 4.43).

A previous study has stated that blood type is not associated with the risk of intubation or death in COVID-19 patients. Patients with blood types B and AB are more at risk of experiencing COVID-19 infection (Latz *et al.*, 2020). According to another study, COVID-19 patients had higher prevalences of blood types A and AB. Patients with blood categories A and AB reported delayed seroconversion despite the fact that ABO blood type was not related to presentation or recovery times for COVID-19 (Mahmud *et al.*, 2021).

Apart from anti-A antibodies, the link between group A and severe COVID-19 is increased activity of angiotensin-converting enzyme 1 (ACE-1), with a tendency for cardiovascular complications (Gasso *et al.*, 2014). The severe outcome could also be explained by the higher levels of von Willebrand Factor (vWF) and factor VIII in group A individuals. This increases the risk of thromboembolic disease and the severity of COVID-19 which can lead to death (Dai, 2020).

An individual's blood has a unique characteristic known as a blood type. Because the red blood cell membrane's surface contains a variety of various types of proteins and carbohydrates (Cooling, 2015). Through a variety of processes, blood group antigens can affect the likelihood of developing a disease. These include acting as immune system modifiers in the form of anti-ABO antibodies and acting as immune system receptors or shams for pathogenic pathogens (Leaf *et al.*, 2020).

The strength of this research is that it is the first study conducted to examine the relationship between blood type and death in COVID-19 patients treated in an Indonesian hospital. The limitations of this study were that the use of a retrospective cohort study in this study was not fully able to minimize bias, so a cohort study was needed to explain the causality that occurred. Apart from that, because this study only involved one referral hospital in Indonesia, further research is needed on several referral hospitals in Indonesia, so that the results can be representative of the population. According to another study, COVID-19 patients had higher prevalences of blood types A and AB. Patients with blood categories A and AB reported delayed seroconversion despite the fact that ABO blood type was not related to presentation or recovery times for COVID-19.

According to the study's findings, COVID-19 patients who have blood types O and AB are more likely to die or suffer other complications. Prioritizing patient treatment should be done by healthcare professionals based on the authors' advice to blood type patients with COVID-19 before treating them.

Conclusion

This study identified the relationship between blood type and death in COVID-19 patients who were hospitalized, where blood type O had the highest risk followed by blood type AB. This study can help with the therapeutic management of COVID-19 patients based on blood type so as to reduce the poor prognosis.

Acknowledgements

The authors would like to thank all of the study participants as well as Universitas Andalas for their grant research.

Conflict of interest statement

None.

References

1. Almazeedi, S., Al-Youha, S., Jamal, M. H., Al-Haddad, M., Al-Muhaini, A., Al-Ghimlas, F., and Al-Sabah, S. (2020). Characteristics, risk factors and outcomes among the first consecutive 1096 patients diagnosed with COVID-19 in Kuwait. *EClinicalMedicine*, 24: 100448.
2. Belali T. M. (2022). Distribution of ABO and Rhesus Types in the Northern Asir Region in Saudi Arabia. *Journal of Blood Medicine*, 13: 643–648.
3. Cheng, Y., Cheng, G., Chui, C. H., Lau, F. Y., Chan, P. K., Ng, M. H., Sung, J. J., and Wong, R. S. (2005). ABO blood group and susceptibility to severe acute respiratory syndrome. *JAMA*, 293(12): 1450–1451.

4. Cooling L. (2015). Blood Groups in Infection and Host Susceptibility. *Clinical Microbiology Reviews*, 28(3): 801–870.
5. Dai X. (2020). ABO blood group predisposes to COVID-19 severity and cardiovascular diseases. *European Journal of Preventive Cardiology*, 27(13): 1436–1437.
6. Elnady, H. G., Abdel Samie, O. M., Saleh, M. T., Sherif, L. S., Abdalmoneam, N., Kholoussi, N. M., Kholoussi, S. M., and El-Taweel, A. N. (2017). ABO blood grouping in Egyptian children with rotavirus gastroenteritis. *Przegląd Gastroenterologiczny*, 12(3): 175–180.
7. Fan, Q., Zhang, W., Li, B., Li, D. J., Zhang, J., and Zhao, F. (2020). Association Between ABO Blood Group System and COVID-19 Susceptibility in Wuhan. *Frontiers in Cellular and Infection Microbiology*, 10: 404.
8. Gassó, P., Ritter, M. A., Mas, S., and Lafuente, A. (2014). Influence of ABO genotype and phenotype on angiotensin-converting enzyme plasma activity. *Journal of the Renin-Angiotensin-Aldosterone System : JRAAS*, 15(4): 580–584.
9. Göker, H., Aladağ Karakulak, E., Demiroğlu, H., Ayaz Ceylan, Ç. M., Büyükaşık, Y., Inkaya, A. Ç., Aksu, S., Sayinalp, N., Haznedaroğlu, I. C., Uzun, Ö., Akova, M., Özcebe, O. I., and Ünal, S. (2020). The effects of blood group types on the risk of COVID-19 infection and its clinical outcome. *Turkish Journal of Medical Sciences*, 50(4): 679–683.
10. Hikmawati, I., and Setiyabudi, R. (2021). Epidemiology of COVID-19 in Indonesia: common source and propagated source as a cause for outbreaks. *Journal of Infection in Developing Countries*, 15(5): 646–652.
11. Latz, C. A., DeCarlo, C., Boitano, L., Png, C. Y. M., Patell, R., Conrad, M. F., Eagleton, M., & Dua, A. (2020). Blood type and outcomes in patients with COVID-19. *Annals of Hematology*, 99(9): 2113–2118.
12. Leaf, R. K., Al-Samkari, H., Brenner, S. K., Gupta, S., and Leaf, D. E. (2020). ABO phenotype and death in critically ill patients with COVID-19. *British Journal of Haematology*, 190(4): e204–e208.
13. Liu, N., Zhang, T., Ma, L., Zhang, H., Wang, H., Wei, W., Pei, H., and Li, H. (2021). The impact of ABO blood group on COVID-19 infection risk and mortality: A systematic review and meta-analysis. *Blood Reviews*, 48: 100785.
14. Mahmud, R., Rassel, M. A., Monayem, F. B., Sayeed, S. K. J. B., Islam, M. S., Islam, M. M., Yusuf, M. A., Rahman, S., Islam, K. M. N., Mahmud, I., Hossain, M. Z., Chowdhury, A. H., Kabir, A. K. M. H., Ahmed, K. G. U., and Rahman, M. M. (2021). Association of ABO blood groups with presentation and outcomes of confirmed SARS CoV-2 infection: A prospective study in the largest COVID-19 dedicated hospital in Bangladesh. *PloS One*, 16(4): e0249252.
15. Mohammadali, F., and Pourfathollah, A. (2014). Association of ABO and Rh Blood Groups to Blood-Borne Infections among Blood Donors in Tehran-Iran. *Iranian Journal of Public Health*, 43(7): 981–989.
16. Murugananthan, K., Subramaniam, S., Kumanan, T., Owens, L., Ketheesan, N., and Noordeen, F. (2018). Blood group AB is associated with severe forms of dengue virus infection. *Virusdisease*, 29(1): 103–105.
17. Rana, R., Ranjan, V., and Kumar, N. (2021). Association of ABO and Rh Blood Group in Susceptibility, Severity, and Mortality of Coronavirus Disease 2019: A Hospital-Based Study From Delhi, India. *Frontiers in Cellular and Infection Microbiology*, 11: 767771.
18. Sjögren, L., Stenberg, E., Thuccani, M., Martikainen, J., Rylander, C., Wallenius, V., Olbers, T., and Kindblom, J. M. (2021). Impact of obesity on intensive care outcomes in patients with COVID-19 in Sweden-A cohort study. *PloS one*, 16(10): e0257891.

19. Velavan, T. P., and Meyer, C. G. (2020). The COVID-19 epidemic. *Tropical Medicine & International Health : TM & IH*, 25(3): 278–280.
20. Zhao, J., Yang, Y., Huang, H., Li, D., Gu, D., Lu, X., Zhang, Z., Liu, L., Liu, T., Liu, Y., He, Y., Sun, B., Wei, M., Yang, G., Wang, X., Zhang, L., Zhou, X., Xing, M., and Wang, P. G. (2021). Relationship Between the ABO Blood Group and the Coronavirus Disease 2019 (COVID-19) Susceptibility. *Clinical Infectious Diseases : an Official Publication of the Infectious Diseases Society of America*, 73(2): 328–331.

LAMPIRAN B

PAPER DENGAN VERSI KEDUA DIKIRIM (REVISED MANUSCRIPT VERSION)

Research article

Manuscript Title:

Association of Blood Type and Mortality of COVID-19: A Hospital-Based Study in National Referral Hospital, Indonesia

Elly Usman¹, Yusticia Katar¹

Affiliation:

2) Department of Pharmacology, Faculty of Medicine, Universitas Andalas, Padang, Indonesia.

Corresponding author

Elly Usman

Department of Pharmacology, Faculty of Medicine, Universitas Andalas, Padang, Indonesia.

E-mail: ellyusman@med.unand.ac.id

Tel: + 6275131746

Running title

Association of Blood Type and Mortality of COVID-19

Abstract

Background: The ABO blood type is crucial in a number of illnesses, including cancer, cardiovascular disease, and some communicable and non-communicable illnesses. However, there is currently little definite evidence between COVID-19 with ABO blood types.

Aim: The aim of this study was to assess the association between ABO blood type and the mortality of patients infected with COVID-19 in a national referral hospital in Indonesia.

Methods: This study used a retrospective cohort. The research sample was COVID-19 patients who were in Dr. M. Djamil Hospital Padang. The number of samples in this study was 93 subjects. The Chi-square test was used in the data analysis. The data were analyzed using the SPSS version 21.0 program, and $p < 0.05$ was considered significant.

Results: The results of this study found the percentage of mortality of COVID-19 patients was higher for blood group O (46.2%), followed by AB (41.7%), B (26.3%), and A (13.9%). There was a relationship between blood type and mortality in hospitalized COVID-19 patients ($p < 0.05$), where blood type O had the highest risk (OR = 5.31, 95% CI 1.57-17.98) followed by blood type AB (OR = 4.43, 95% CI 1.01-19.58).

Conclusion: This study confirmed there was a relationship between blood type and mortality in hospitalized COVID-19 patients, where blood type O had the highest risk followed by blood type AB.

Keywords: Blood type, COVID-19, Hospitalized, Mortality

List of Abbreviations

CI: Confidence interval

COVID-19: Coronavirus disease 2019

ICU: Intensive care unit

OR: Odds ratio

SARS-CoV-1: Severe acute respiratory syndrome coronavirus 1

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2

vWF: von Willebrand Factor

Introduction

The COVID-19 pandemic has taken a devastating impact on the world, regardless of age or gender, but especially on older persons who have co-morbid conditions including diabetes and cardiovascular and cerebrovascular disease (Almazeedi *et al.*, 2020; Velavan *et al.*, 2020). Indonesia has also faced a significant increase in COVID-19 patients which has resulted in morbidity and even death (Hikmawati *et al.*, 2021).

ABO blood type has been linked to the presence of COVID-19 infection in earlier studies. The ABO blood type is crucial in a number of illnesses, including cancer, cardiovascular disease, and some communicable and non-communicable illnesses (Fan *et al.*, 2020). Several studies have shown that having blood type O significantly lowers the chance of contracting hepatitis B (Mohammadali *et al.*, 2014; Belali, 2022). In addition, people with blood type A are more likely to develop rotavirus gastroenteritis than patients with blood type B (Mohammadali *et al.*, 2014; Elnady *et al.*, 2017). In addition, it was found that those with blood type AB are 2.5 times more likely than people with other blood types to contract dengue fever (Murugananthan *et al.*, 2018). Previous research on SARS-CoV-1 has found a correlation between blood type and the risk of infection, with people with group O blood having a small chance of SARS-CoV-1 infection (Cheng *et al.*, 2005).

There has not been much conclusive evidence to date between SARS-CoV-2 and ABO blood types (Zhao *et al.*, 2021). According to the majority of research, blood type O has a lower probability of developing severe SARS-CoV-2 infection than blood type A, which has a higher risk of infection (Goker *et al.*, 2020). In addition, very little research has been conducted in Indonesia to find a relationship between blood type and mortality of COVID-19 patients (Liu *et al.*, 2021). However, there is increased interest in the relationship between blood type, and the risk of infection. Everyone agrees that individuals differ from one another, but it is rare for people to be able to predict whether a person's blood type makeup makes them more or less likely to contract an infection when exposed to viruses (Kim *et al.*, 2021). The purpose of this study was to assess the mortality of COVID-19 infected patients with different ABO blood types.

Materials and Methods

Study design and research sample

This study used a retrospective cohort. The research sample was COVID-19 patients who were in Dr. M. Djamil Hospital Padang, Indonesia. The research was conducted from January to November 2022. There were 93 total samples in this study. Convenience sampling was used as the sampling method in this study. Patients with COVID-19 with moderate to severe clinical severity and thoroughly documented information related to research variables met the inclusion criteria for this study.

Operational definition

Blood type was the study's independent variable (A, B, AB, and O) (Rana *et al.*, 2021). The dependent variable was COVID-19 patient mortality (death, and life) (Sjögren *et al.*, 2021).

Research ethics approval

The Dr. M. Djamil Hospital Padang research ethics committee approved this study after conducting an ethical review (LB.02.02/5.7/192/2022).

Data analysis

Research variables in categorical research are provided as frequency and percentage. While numeric variables are presented in the form of mean \pm SD or median (min-max). The Mann-Whitney test and the Chi-square test were used in the bivariate analysis. The data were analyzed using the SPSS version 21.0 program, and a p-value < 0.05 was considered significant.

Results

Subject characteristics (Table 1).

Table 1. Subject characteristics

Characteristics	Mortality		p-value
	Death (n=27)	Life (n=66)	
Sex, f(%)			0.226 ^a
Male	21 (33.9)	41 (66.1)	
Female	6 (19.4)	25 (80.6)	
Age (years), median (min-max)	59 (21-79)	56 (20-83)	0.249 ^b
BMI (kg/m²), median (min-max)	25.15 (15.82-76.10)	24.80 (17.96-55.51)	0.691 ^b
Clinical severity, f(%)			<0.001 ^{a*}
Moderate	1 (2.0)	49 (98.0)	
Severe	22 (61.1)	14 (38.9)	
Critical	4 (57.1)	3 (42.9)	
Laboratory examination, median (min-max)			
Hb (gr/dL)	10.95 (4.4-17.4)	12.00 (4.0-15.7)	0.482 ^b
Ht (%)	28.50 (6-53)	36.00 (15-8,150)	0.114 ^b
Leukocytes (/mm ³)	2,240.50 (66-47,450)	1,400.00 (7-23,160)	0.365 ^b
Platelets	191,000 (229-652,000)	194,000 (44-650,000)	0.722 ^b
D-Dimer (ng/mL)	4,435.00 (1,039-10,000)	777.00 (157-10,000)	<0.001 ^{b*}
Procalcitonin (ng/mL)	0.74 (0.05-171)	0.27 (0.05-171.42)	0.092 ^b
IL-6 (pg/mL)	262.50 (12.20-4,599.00)	34.40 (1.50-600.00)	<0.001 ^{b*}
Ferritin (ng/mL)	1,179.58 (12.40-2,000.00)	710.00 (27.09-2,000.00)	<0.021 ^{b*}
SpO2 (%)	90.00 (48-99)	96.00 (33-99)	<0.001 ^{b*}
Number of comorbid, f(%)			0.009 ^{a*}
None	3 (14.3)	18 (85.7)	

1	2 (10.5)	17 (89.5)
> 1	22 (41.5)	31 (58.5)

*p<0.05 considered significant; a, Chi-square test; b, Mann-whitney test

Table 1 showed IL-6 levels, ferritin, SpO2 values, PCT levels, D-Dimer, clinical severity, and the number of comorbidities associated with mortality in COVID-19 patients hospitalized (p<0.05).

Association of blood type and mortality of COVID-19 (Table 2 and Figure 1).

Table 2. Association of blood type and mortality of COVID-19

Obese	Mortality		p-value	OR (95% CI)
	Death (f/%) (n=27)	Life (f/%) (n=66)		
A	5 (13.9)	31 (86.1)	0.543 ^a	0.19 (0.06-0.64)
B	5 (26.3)	14 (73.7)	0.054 ^a	2.21 (0.55-8.89)
AB	5 (41.7)	7 (58.3)	0.021* ^a	4.43 (1.01-19.58)
O	12 (46.2)	14 (53.8)	0.009* ^a	5.31 (1.57-17.98)

*p<0.05 considered significant; a, Chi-square test

Table 2 showed the percentage of deaths of COVID-19 patients was higher for blood group O (46.2%), followed by AB (41.7%), B (26.3%), and A (13.9%). There was a relationship between blood type and mortality in hospitalized COVID-19 patients (p <0.05), where blood type O had the highest risk (OR = 5.31, 95% CI 1.57-17.98) followed by blood type AB (OR = 4.43, 95% CI 1.01-19.58).

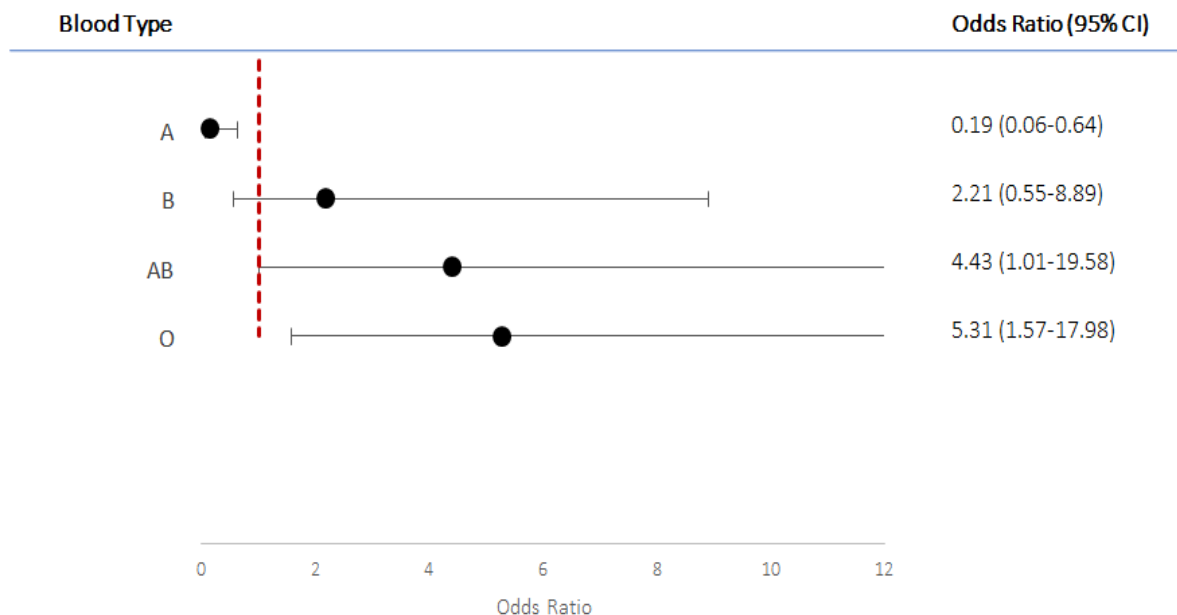


Figure 1. Forest plot blood type and mortality of COVID-19

Discussion

The results of this study found the percentage of mortality of COVID-19 patients was higher for blood group O (46.2%), followed by AB (41.7%), B (26.3%) and A (13.9%).

There was a relationship between blood type and mortality in hospitalized COVID-19 patients, where blood type O had the highest risk (OR = 5.31) followed by blood type AB (OR = 4.43).

A previous study has stated that blood type is not associated with the risk of intubation or death in COVID-19 patients. Patients with blood types B and AB are more at risk of experiencing COVID-19 infection (Latz *et al.*, 2020). According to another study, COVID-19 patients had higher prevalences of blood types A and AB. Patients with blood categories A and AB reported delayed seroconversion despite the fact that ABO blood type was not related to presentation or recovery times for COVID-19 (Mahmud *et al.*, 2021).

Apart from anti-A antibodies, the link between group A and severe COVID-19 is increased activity of angiotensin-converting enzyme 1 (ACE-1), with a tendency for cardiovascular complications (Gasso *et al.*, 2014). The severe outcome could also be explained by the higher levels of von Willebrand Factor (vWF) and factor VIII in group A individuals. This increases the risk of thromboembolic disease and the severity of COVID-19 which can lead to death (Dai, 2020).

An individual's blood has a unique characteristic known as a blood type. Because the red blood cell membrane's surface contains a variety of various types of proteins and carbohydrates (Cooling, 2015). Through a variety of processes, blood group antigens can affect the likelihood of developing a disease. These include acting as immune system modifiers in the form of anti-ABO antibodies and acting as immune system receptors or shams for pathogenic pathogens (Leaf *et al.*, 2020).

Previous studies identified inconsistent results, but it did discover certain tendencies that might point to a blood type-related greater vulnerability to COVID-19 infection or to a blood type-related protective effect for certain Rh-negative blood types (Rana *et al.*, 2021; Miotto *et al.*, 2021). COVID-19 is not only at risk by blood type but many other factors, including age or pre-existing medical disorders, are likely to have a larger, dominant role in defining personal risk from COVID-19, regardless of whether a particular blood type is linked to a higher risk of catching COVID-19 and developing severe disease (Pendur *et al.*, 2021).

The strength of this research is that it is the first study conducted to examine the relationship between blood type and death in COVID-19 patients treated in an Indonesian hospital. The limitations of this study were that the use of a retrospective cohort study in this study was not fully able to minimize bias, so a cohort study was needed to explain the causality that occurred. Apart from that, because this study only involved one referral hospital in Indonesia, further research is needed on several referral hospitals in Indonesia, so that the results can be representative of the population. According to another study, COVID-19 patients had higher prevalences of blood types A and AB. Patients with blood categories A and AB reported delayed seroconversion despite the fact that ABO blood type was not related to presentation or recovery times for COVID-19.

The implication of this study according to the study's findings, COVID-19 patients who have blood types O and AB are more likely to die or suffer other complications. Furthermore, more research is required to comprehend the molecular pathways through which blood groups may influence vulnerability to COVID-19 infection and, ultimately, to create treatments for viral infections and illnesses. Prioritizing patient treatment should be done by healthcare professionals based on the authors' advice to blood type patients with COVID-19 before treating them.

Conclusion

This study identified the relationship between blood type and death in COVID-19 patients who were hospitalized, where blood type O had the highest risk followed by blood

type AB. This study can help with the therapeutic management of COVID-19 patients based on blood type so as to reduce the poor prognosis.

Acknowledgements

The authors would like to thank all of the study participants as well as Universitas Andalas for their grant research.

Conflict of interest statement

None.

References

1. Almazeedi, S., Al-Youha, S., Jamal, M. H., Al-Haddad, M., Al-Muhaini, A., Al-Ghimlas, F., and Al-Sabah, S. (2020). Characteristics, risk factors and outcomes among the first consecutive 1096 patients diagnosed with COVID-19 in Kuwait. *EClinicalMedicine*, 24: 100448.
2. Belali T. M. (2022). Distribution of ABO and Rhesus Types in the Northern Asir Region in Saudi Arabia. *Journal of Blood Medicine*, 13: 643–648.
3. Cheng, Y., Cheng, G., Chui, C. H., Lau, F. Y., Chan, P. K., Ng, M. H., Sung, J. J., and Wong, R. S. (2005). ABO blood group and susceptibility to severe acute respiratory syndrome. *JAMA*, 293(12): 1450–1451.
4. Cooling L. (2015). Blood Groups in Infection and Host Susceptibility. *Clinical Microbiology Reviews*, 28(3): 801–870.
5. Dai X. (2020). ABO blood group predisposes to COVID-19 severity and cardiovascular diseases. *European Journal of Preventive Cardiology*, 27(13): 1436–1437.
6. Elnady, H. G., Abdel Samie, O. M., Saleh, M. T., Sherif, L. S., Abdalmoneam, N., Kholoussi, N. M., Kholoussi, S. M., and El-Taweel, A. N. (2017). ABO blood grouping in Egyptian children with rotavirus gastroenteritis. *Przegląd Gastroenterologiczny*, 12(3): 175–180.
7. Fan, Q., Zhang, W., Li, B., Li, D. J., Zhang, J., and Zhao, F. (2020). Association Between ABO Blood Group System and COVID-19 Susceptibility in Wuhan. *Frontiers in Cellular and Infection Microbiology*, 10: 404.
8. Gassó, P., Ritter, M. A., Mas, S., and Lafuente, A. (2014). Influence of ABO genotype and phenotype on angiotensin-converting enzyme plasma activity. *Journal of the Renin-Angiotensin-Aldosterone System : JRAAS*, 15(4): 580–584.
9. Göker, H., Aladağ Karakulak, E., Demiroğlu, H., Ayaz Ceylan, Ç. M., Büyükaşık, Y., Inkaya, A. Ç., Aksu, S., Sayinalp, N., Haznedaroğlu, I. C., Uzun, Ö., Akova, M., Özcebe, O. I., and Ünal, S. (2020). The effects of blood group types on the risk of COVID-19 infection and its clinical outcome. *Turkish Journal of Medical Sciences*, 50(4): 679–683.
10. Hikmawati, I., and Setiyabudi, R. (2021). Epidemiology of COVID-19 in Indonesia: common source and propagated source as a cause for outbreaks. *Journal of Infection in Developing Countries*, 15(5): 646–652.
11. Kim, Y., Latz, C. A., DeCarlo, C. S., Lee, S., Png, C. Y. M., Kibrik, P., Sung, E., Alabi, O., and Dua, A. (2021). Relationship between blood type and outcomes following COVID-19 infection. *Seminars in Vascular Surgery*, 34(3): 125–131.
12. Latz, C. A., DeCarlo, C., Boitano, L., Png, C. Y. M., Patell, R., Conrad, M. F., Eagleton, M., & Dua, A. (2020). Blood type and outcomes in patients with COVID-19. *Annals of Hematology*, 99(9): 2113–2118.
13. Leaf, R. K., Al-Samkari, H., Brenner, S. K., Gupta, S., and Leaf, D. E. (2020). ABO phenotype and death in critically ill patients with COVID-19. *British Journal of Haematology*, 190(4): e204–e208.

14. Liu, N., Zhang, T., Ma, L., Zhang, H., Wang, H., Wei, W., Pei, H., and Li, H. (2021). The impact of ABO blood group on COVID-19 infection risk and mortality: A systematic review and meta-analysis. *Blood Reviews*, 48: 100785.
15. Mahmud, R., Rassel, M. A., Monayem, F. B., Sayeed, S. K. J. B., Islam, M. S., Islam, M. M., Yusuf, M. A., Rahman, S., Islam, K. M. N., Mahmud, I., Hossain, M. Z., Chowdhury, A. H., Kabir, A. K. M. H., Ahmed, K. G. U., and Rahman, M. M. (2021). Association of ABO blood groups with presentation and outcomes of confirmed SARS CoV-2 infection: A prospective study in the largest COVID-19 dedicated hospital in Bangladesh. *PloS One*, 16(4): e0249252.
16. Miotto, M., Di Rienzo, L., Gosti, G., Milanetti, E., & Ruocco, G. (2021). Does blood type affect the COVID-19 infection pattern?. *PloS one*, 16(5): e0251535.
17. Mohammadali, F., and Pourfathollah, A. (2014). Association of ABO and Rh Blood Groups to Blood-Borne Infections among Blood Donors in Tehran-Iran. *Iranian Journal of Public Health*, 43(7): 981–989.
18. Murugananthan, K., Subramaniyam, S., Kumanan, T., Owens, L., Ketheesan, N., and Noordeen, F. (2018). Blood group AB is associated with severe forms of dengue virus infection. *Virusdisease*, 29(1): 103–105.
19. Pendu, J. L., Breiman, A., Rocher, J., Dion, M., & Ruvoën-Clouet, N. (2021). ABO Blood Types and COVID-19: Spurious, Anecdotal, or Truly Important Relationships? A Reasoned Review of Available Data. *Viruses*, 13(2), 160: 1-20.
20. Rana, R., Ranjan, V., and Kumar, N. (2021). Association of ABO and Rh Blood Group in Susceptibility, Severity, and Mortality of Coronavirus Disease 2019: A Hospital-Based Study From Delhi, India. *Frontiers in Cellular and Infection Microbiology*, 11: 767771.
21. Sjögren, L., Stenberg, E., Thuccani, M., Martikainen, J., Rylander, C., Wallenius, V., Olbers, T., and Kindblom, J. M. (2021). Impact of obesity on intensive care outcomes in patients with COVID-19 in Sweden-A cohort study. *PloS one*, 16(10): e0257891.
22. Velavan, T. P., and Meyer, C. G. (2020). The COVID-19 epidemic. *Tropical Medicine & International Health : TM & IH*, 25(3): 278–280.
23. Zhao, J., Yang, Y., Huang, H., Li, D., Gu, D., Lu, X., Zhang, Z., Liu, L., Liu, T., Liu, Y., He, Y., Sun, B., Wei, M., Yang, G., Wang, X., Zhang, L., Zhou, X., Xing, M., and Wang, P. G. (2021). Relationship Between the ABO Blood Group and the Coronavirus Disease 2019 (COVID-19) Susceptibility. *Clinical Infectious Diseases : an Official Publication of the Infectious Diseases Society of America*, 73(2): 328–331.