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ASSOCIATION OF SUSCEPTIBILITY, SEVERITY IN COVID-19 AND BLOOD GROUP AND RH PHENOTYPES IN WESTERN REGION SAUDI ARABIA

FAWZIAH A. AL-SALMI*
Biology Department, College of Sciences, Taif University, Taif 21944, Saudi Arabia. Corresponding Author Email: f.alsalmi@tu.edu.sa

WALAA SAEED AL-HARTHI
Biology Department, College of Sciences, Taif University, Taif 21944, Saudi Arabia.

SAMAHER AHMAD AL-ZAHRANI
Biology Department, College of Sciences, Taif University, Taif 21944, Saudi Arabia.

WEJDAN ZEED AL-OTAIBI
Biology Department, College of Sciences, Taif University, Taif 21944, Saudi Arabia.

Abstract

Many diseases, including bacterial, viral, and cancerous infections, are linked to blood group. Previous reports display the relationship between the susceptibility of patients to coronavirus disease 2019 and blood group A. In the present study, we investigated the relationship of blood groups and Rh phenotypes with susceptibility to coronavirus disease 2019 infection, severity of disease, recovery period, and mortality of patients in Taif City, west Saudi Arabia. Patients were enrolled from March 2020 to October 2021. A total of 722 real-time PCR (PR-PCR) confirmed coronavirus disease 2019 (COVID-19) in King Faisal Hospital in Taif City. Data was analyzed using the Chi-squared test ($\chi 2$) to evaluate the association of blood groups. The out-finding data indicated that blood types A, B, and Rh+ are more susceptible to infection with SARS-CoV-2 and may develop severe COVID-19 symptoms, while blood types O and Rh are at a lower risk of COVID-19 infection, to an extent. And people with blood type B+ are more likely to die. Finally, out data was confirmed suggesting blood group may play a role in COVID-19 Susceptibility and mortality.

INTRODUCTION

SARS-CoV-2 is a great challenge to public health in the world because it spread rapidly across the world countries which caused over 761,000 deaths [1-3]. COVID-19 has a multi- risks factor for morbidity and mortality such as age, sex, smoking, hypertension, diabetes, and respiratory diseases [4-5]. Coronavirus disease including many symptoms such as sore throat, muscle pain, shortness of breath, dry cough, and fever ageusia. But, the majority of infection patients remain asymptomatic [6-7]. The incubation time of coronavirus disease is 14 days, and sometimes the symptoms take much time to be appears. The COVID-19 symptoms usually appear with 3-7 days [8]. The only way to detected and confirmed the SARS-CoV-2 infection is real -time -PCR and CT -scan [9]. ABO blood group refers polymorphisms within ABO gene which associated with many diseases like red blood cell count, hemoglobin concentration, hematocrit, [10- 12], von Willebrand factor [13-15], myocardial infarction [16-17], coronary artery disease [18], ischemic stroke [19], type 2 diabetes [20], and venous thromboembolism [21]. Also, it link the angiotensin converting enzyme (ACE) activity which play a central role for COVID-

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19 morbidity and mortality [22]. Interestingly, a non-O blood type is considering the main genetic risk factors for venous thromboembolism [23]. Previously, many reports mentioned the relationship between blood grouping and a different infection including P. falciparum [24], H. pylori [25], Norwalk virus [26], hepatitis B virus [27], N. gonorrhoeae [28] and SARS-CoV-1 [29]. Unlike ABO, Rh (D) phenotypes are associated with a few diseases [30]. Importantly, Rh phenotypes are playing a central role in immune response. For instance, Rh (D) is a concern foe neonate as the parents have a different Rh (D) [31]. also, previous reports referred that Rh -positive individuals are protected against the latent toxoplasmosis [32 35].Previous studies displayed the susceptibility of ABO blood groups to viruses such as Middle East Respiratory Syndrome (MERS), hepatitis B, human immunodeficiency virus, norawalk virus, rotavirus [36], dengue virus [37], and SARS coronavirus [38]. Early report from China and Italy mentioned that the relationship between blood group and Rh phenotypes with SARS-CoV-2 infection. The scientists found that individual who have Blood group type A has high odds of getting infected, while the rate of infection and severity seems less among the blood group O. Rh (D) positive blood group is also associated with increased COVID-19 infection and mortality [39-41]. In this work, we investigated the association of ABO and Rh blood group with COVID-19 susceptibility, prognosis, recovery time, and mortality.

MATERIALS AND METHODS

Study Design

This is a single-center, retrospective study that was carried out at King Faisal Hospital, Taif, Saudi Arabia. The Ethical Committee of King Faisal Hospital, Taif, reviewed and approved the study. It was obtained from the research ethics committee of Taif University and from the Ministry of Health Directorate of Health Affairs in Taif city No. 586-43 (HAQ-02-T-105). We investigated the association of ABO blood groups and Rh phenotypes with susceptibility to COVID-19 infection, severity of disease, length of stay, and mortality of patients. The association was analyzed with the ABO blood group and Rh blood group systems. This study includes real-time PCR (RT-PCR)-confirmed COVID-19 patients who were admitted to the hospital.

Statistical analysis

Data analysis: data were analyzed statistically using (SPSS) version 26. To test the relationship between variables, qualitative data was expressed as numbers and percentages, and the Chi-squared test ($\chi 2$) was used. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The severity of COVID-19 Infection

The severity of severe SARS-CoV-2 is determined by the admission to the intensive care unit (ICU). Figure 1 demonstrates the percentage of respondents and their probability of being infected with COVID-19. Only 27.1% of infected patients had severe SARS-CoV-2

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symptoms. While the rest of the respondents, which represent 72.9% of the total infectious patients, hadn't had severe coronavirus disease in 2019. The association of blood groups and Rh phenotypes with susceptibility to the severity of COVID-19 was analyzed by the blood group distributions of coronavirus infected individuals that required ICU admission and those who did not require ICU admission. Figure2 indicated that the individuals who had blood group O (+ ve) didn't require ICU admission, which represented the majority of all patients with 54.3 %. While the patients who have blood group A (-ve) represent the minority with 2.9%, However, the patients who had blood group A(+ve) suffered from hard symptoms and required ICU admission with 33.3%, while the patients who had AB (-ve) were less susceptible to hard severity with 0.6 percent. Interestingly, the percentage of individuals who have negative Rh phenotypes and suffer from hard COVID-19 symptoms is very small, as the following: 2.9%, 1.2%, 1.4%, and 5.2% for A, B, AB, and O blood groups respectively. In contrast, the percentage of the individuals who have positive Rh phenotypes and suffer from hard COVID-19 symptoms is represented by the major percentage as follows: 21.1%, 3.2%, 10.7, and 54.3% for A, B, AB, and O blood groups, respectively.

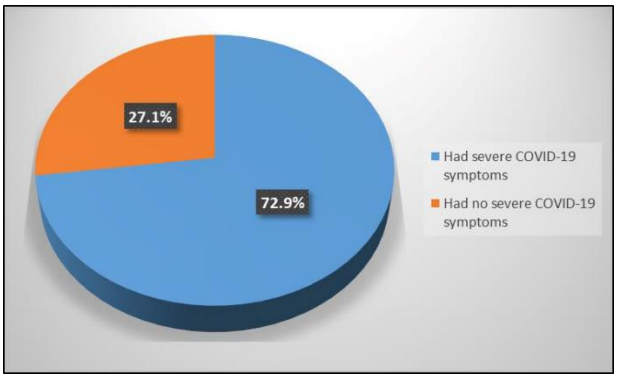

Figure 1: Percentage distribution of studied participants according to the severity of COVID-19 symptoms for all participants

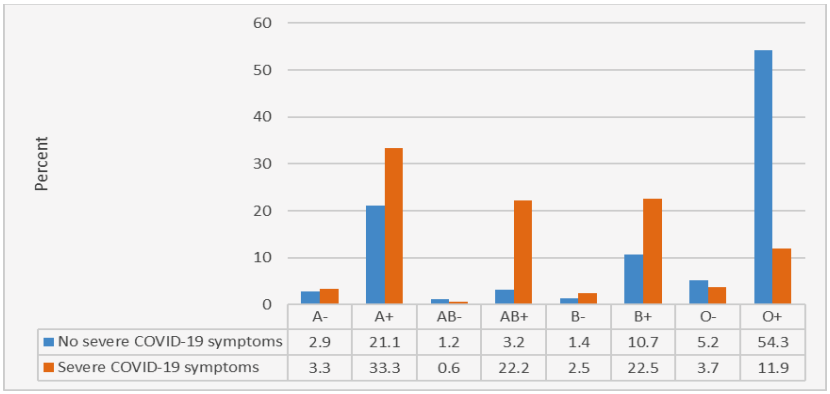

Figure 2: Relationship between severity of COVID-19 symptoms and blood group for all participants

N.B.: ($\chi 2$ =281.25, p-value = < 0.001)

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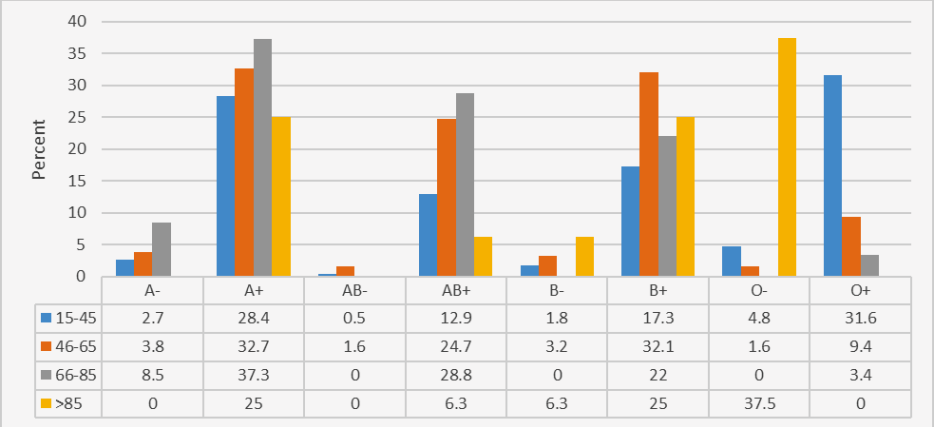
Association Analysis by Age

Chi-square test was used to compare the blood groups and age groups of the COVID-19 patients. As shown in figure 3, COVID-19-infected patients were divided into four groups as ≤45, ≤65, ≤85 and >85 years old. Blood group O (+) was observed to be more susceptible to infection in patients with age group ≤45 years with 31.6%. Furthermore, blood group A (+) was found to be more susceptible to infection in patients aged ≤65 to < 85 years, with 32.7 and 37.3%, respectively. However, blood group Ab (-) was observed to be less susceptible to infection in patients with all age group ≤45, ≤65, ≤85 and >85years years of age with 0.5, 1.6, 0 and 0 % respectively.



	A-	A+	AB-	AB+	B-	B+	O-	O+
15-45	2.7	28.4	0.5	12.9	1.8	17.3	4.8	31.6
46-65	3.8	32.7	1.6	24.7	3.2	32.1	1.6	9.4
66-85	8.5	37.3	0	28.8	0	22	0	3.4
>85	0	25	0	6.3	6.3	25	37.5	0

Figure 3: Relationship between participants' age and blood group for all participant

N.B.: ($\chi 2$ =173.15, p-value = < 0.001).

Association Analysis by Gender

The COVID-19-infected patients were divided into two groups by gender as shown in figure 4. ABO blood group distribution among the two groups showed no difference except for the blood group B. Male patients of blood group AB (+) and B (+) are more prone to COVID-19 than the female patients with the same blood group. While, female patients of blood group O (+) are more prone to COVID-19 than the male patients with the blood group O (+). The association is compared in one-vs.-all blood group manner.

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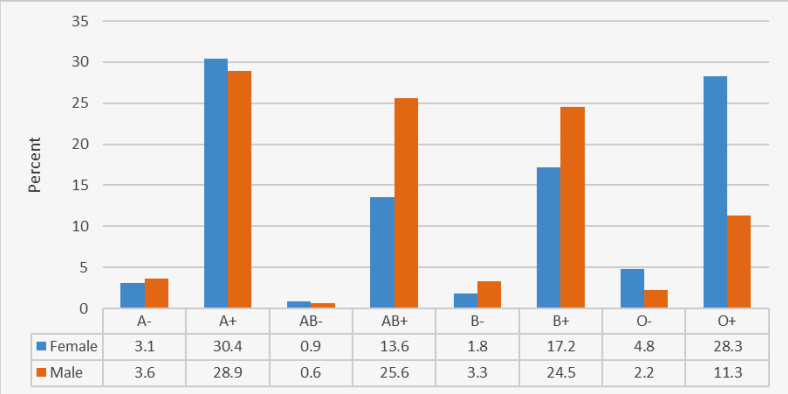

Figure 4: Relationship between participants' gender and blood group for all participants

N.B.: ($\chi 2$ =69.23, p-value = < 0.001)

Association Analysis by Comorbidity

The comorbidities of the patients were considered to have affected the progression of the disease. Also, it limited treatment of the patient. The common comorbidities in our study were hypertensive (HTN), Diabetes Mellitus (DM) Heart diseases Kidney diseases Obesity Respiratory diseases as table 1 displayed, 640 of the total patients who had comorbidity suffered from severe symptoms of COVID-19. The patients who suffered from HTN and DM represent the major number (127 patients) of the COIVD-19 severity, while kidney diseases represent the minor number of patients (19 patients).

Table 1: Relationship between severity of COVID-19 symptoms and participants' comorbidity for all participants

Variable	COVID-19 severity		$\chi 2$	p-value
	Not severe	Severe		
Comorbidity				
No	29	290	69.92	**< 0.001**
Yes	317	640		
If yes, what disease? (No.:319)				
HTN and DM	3	127		
DM	8	13	90.35	**< 0.001**
Heart diseases	0	34		
Kidney diseases	1	19		
Obesity	13	39		
Respiratory diseases	4	58		

blood group A, AB, and B were associated with significantly increased risk of mortality when compared to O blood group, simaliarly, positive Rh (D)+ was associated with significantly increased risk of mortality as figure 5 showed.

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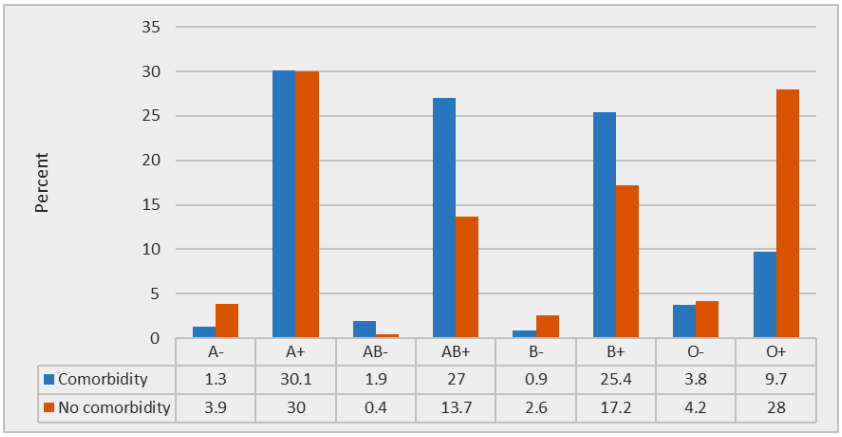

Figure 5: Relationship between participants' comorbidity and blood group for all participants

N.B.: ($\chi 2$ =81.92, p-value = < 0.001)

Association Analysis by death rate

As figure 6 revealed, the death rate among hospitalized patients who have positive Rh phenotypes due to the COVID-19 severity represents the major rate with the following percentage: 29.4%, 30.3%, and 33.6 for A, AB, and B, respectively. The death rate of patients who have negative Rh phenotypes is very low, with the following percentages: 0, 0, 1, and 3.4 % for A, AB, B, and O respectively.

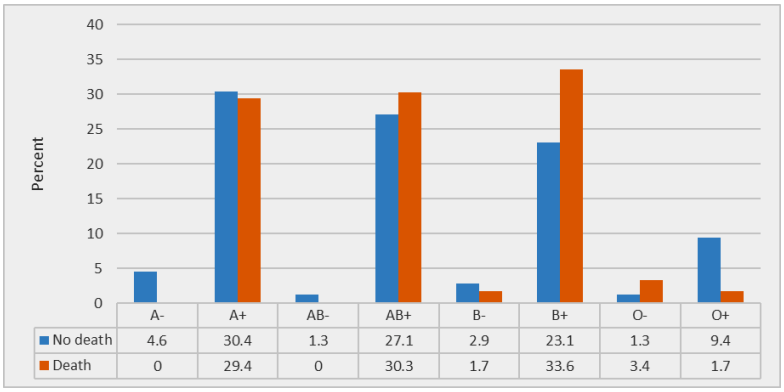

Figure 6: Relationship between death among hospitalized patients and blood group for all participants

N.B.: ($\chi 2$ =250.66, p-value = < 0.001).

DISCUSSION

The relationship between blood groups and diseases has been explored for several diseases, including viral diseases. Interestingly, HBGAs are complex molecules that exist on the surface of the red blood cell membranes. The present study was conducted to observe the relationship between ABO and Rh phenotypes on susceptibility to

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coronavirus disease 2019 infection, disease severity, and mortality. The study also compares the susceptibility of infection with gender, age, and blood group types. We seek to analyze the association of ABO and Rh blood groups for the risk of coronavirus disease infection in 2019 among the population in Taif, Saudi Arabia. The data indicated that those individuals with blood groups A or B were more disposed to COVID-19, whereas those with blood groups O or AB had a significantly lower risk of infection. On comparing the distribution of ABO and Rh blood groups of COVID-19-infected patients with the general population of Taif, there was a significant increase in infected individuals with blood groups A or B. A significant decrease in the number of COVID-19 patients with blood groups O and AB was also observed. Also, the patients have ABO blood group A with positive RH have more severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) while the patients have AB with negative Rh have less severe acute respiratory syndrome coronavirus 19 (COVID-19), as figure 2 displays. As a result, Fan et al. reported that it was observed that blood group A was significantly higher in infected individuals than in the healthy control group population, while blood group O in COVID-19-infected patients was significantly lower [43]. Basically, the anti-A antibodies exist in the plasma of blood groups O and B but are absent in blood group A. It inhibits SARS-COV2 adhesion on host cells, preventing the virus's S protein from interacting with ACE 2 on the cell surface [44]. When comparing Rh (D)+ and Rh (D) COVID-19-infected individuals to the healthy group, Rh (D)+ individuals are significantly more likely to become infected than Rh (D) negative individuals [45]. In our work, comparing the Rh (D)-positive and Rh (D)-negative COVID-19-infected individuals, a strong association was observed in Rh (D)-positive individuals having a significantly higher susceptibility to COVID-19 infection than the Rh (D)-negative individuals. The majority of the data in this context agrees that infection and death are more common in the elderly [47]. The current study compared ABO and Rh blood group distribution and found an association of age groups with the susceptibility of COVID-19 infection. In the present study, ABO blood group-old individuals (more than 45 years old) with blood groups O and A were more susceptible to infection with COVID-19 as shown in figure 3. While the elderly with the AB blood group were less. Interestingly, male patients of blood groups AB and B are more susceptible to COVID-19 than female patients of the same blood group. However, female patients of blood group O are more prone to COVID-19 than male patients. Liu et al. reported that blood group A was associated with a significantly increased risk of mortality when compared to the non-A blood group [46]. Our study was agreement with other articles which found that ABO and Rh blood groups are associated with mortality in COVID-19 patients. This finding makes sense because older adults are more likely to have comorbidities including diabetes, heart disease, hypertension, and chronic lung disease, as well as a weakened immune system. According to the findings, age is one of the risk factors for death from COVID-19. The majority of the data in this context agrees that infection and death are more common in the elderly.

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CONCLUSION

The data presented above show that ABO blood groups and Rh phenotypes influence the risk of SARS-CoV-2 infection, and several studies also show that ABO phenotypes influence disease severity. Our study has found that blood groups A, B, and Rh+ are more disposed to COVID-19 infection, whereas blood groups O, AB, and Rh are significantly lower risk of COVID-19 infection. The risk of death in patients with COVID-19 in blood group B+ was significantly higher than in patients with other blood types. Elderly male patients with underlying conditions, especially those with cardiovascular disease (particularly hypertension), need to be quarantined and protected from COVID-19 infection or receive special medical care to prevent clinical worsening and severe disease progression. We also recommend conducting studies linking COVID-19 to blood groups and elevated regions. Based on study results, we recommend that to help determine treatment options and measure exposure levels in people, the ABO blood group may be included as a routine part of the management of SARS-CoV-2 and other coronavirus infections in both patients and medical personnel.

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Data Availability Statement

The original contributions presented in the study are included in the article/Supplementary Material; further inquiries can be directed to the corresponding author.

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Conflicts of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Ethics Statement

The studies involving human participants were reviewed and approved by Institute ethics committee, King Faisal Hospital, Taif city. The ethics committee waived the requirement of written informed consent for participation. It was obtained from the research ethics committee of Taif University and from the Ministry of Health Directorate of Health Affairs in Taif city No. 586-43 (HAQ-02-T-105).

Author Contributions

FA-S wrote the manuscript and performed data analysis. FA-S had full access to data in the study and take responsibility of the data integrity. FA-S take responsibility of the accuracy of data analysis. FA-S edited the manuscript, and FA-S is responsible for data collection.

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