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ASSOCIATION BETWEEN BLOOD GROUPS AND COVID-19 OUTCOME CROSS SECTIONAL STUDY

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Abstract

Background: Coronavirus disease 2019 (COVID-19) first started as an epidemic in Wuhan city – China in 2019 then became a pandemic. Certain viral infections showed linkage with certain antigenic determinants of ABO blood groups and Rh factor.

Aim of the study: determine the association between blood groups and Rh factor with COVID-19 infection in a sample of Iraqi patients.

Patients and methods: This cross-sectional retrospective study was conducted among 580 students of a variety of colleges mainly in Baghdad from 6th of December 2021 to 18th of January 2022. An online questionnaire using Google forms was used to collect the data.

Results: A total of 580 samples were collected during the study with 358 (61.7%) females samples and 222 (38.3%) males and there was a significant difference between them (P=0.0001). The mean age of the participants was 20.20± 2.716 years. Of the 580 COVID-19 infected samples collected 289 (49.8%) were blood group O. 133 (22.9%) were blood Group A then 108(18.6%) were blood group B, and 50 (8.6%) blood group AB while with significant difference (P=0.). About 508 (87.5%) of the samples were Rh + who had COVID-19 infection and the remaining 72(12.5%) were Rh – (P=0.0001).

Conclusions: There was an association between Blood group O+ and COVID-19 infection who did not required hospitalization and the blood group AB+ were less susceptible to infection.

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Introduction

Severe acute respiratory syndrome coronavirus - 2 (SARS-CoV-2) virus belongs to the subfamily Coronaviridae the *Coronavirinae* family of enveloped, positive-sense, single-stranded RNA viruses that infect a broad range of vertebrates. The *Coronaviridae* includes alpha, beta, gamma, and delta coronaviruses (1,2). SARS-CoV-2 looks like a crown that provides a bigger binding area and major receptors are ACE2 receptors. It spreads through respiratory droplets through coughing and sneezing, enters the nose through inhalation, and begins multiplying. About 80 % of infected individuals, the symptoms will be mild to moderate and limited to the upper respiratory airways. These individuals can be monitored at home with conservative symptomatic treatment while 20% of infected patients develop lung infiltrates, and some of these patients acquire very serious illness (3,4). There are many comorbidity and risk factors that contribute to severe disease like hypertension, diabetes and obesity (5).

Certain viral infections showed linkage with certain antigenic determinants of ABO blood groups and Cheng et al. 2005 demonstrated the association of coronavirus infection with ABO blood groups in addition to that individual with blood group O was less likely to become infected with COVID-19 compared to non-O blood group persons (6). Furthermore, Zhao et al. 2020 showed that Blood group A patients in Wuhan region hospitals had a higher risk for COVID-19 and higher mortality rate compared with non-A blood groups, whereas blood group O patients was associated with a significantly lower risk for the infection (7). The same observation was showed in United States that SARS-CoV-2 positive patients had a high proportion of blood group A and with a low proportion of blood group O COVID-patients (8). This may be due to presence of extra sugar N-acetyl galactosamine on the surface of blood group A cells that coronaviruses have surface proteins that bind to these sugars (9). Another explanation is the presence of anti-A antibodies that inhibit the binding of S corona virus to ACE2 receptors which is true for blood group B and O and not for AB blood group which had a less susceptibility to COVID-19 infection (10,11). An extra possible explanation for protective of blood group B is that epitopes are exposed to the family of IgM & its highly anti-glycan ABO isoagglutinin activities and these (12). The use of convalescent plasma from recovered patients in treating COVID-19 patients ABO-compatibility must be mandated in any protocol treatment (13).

This study tries to determine the association between blood groups and Rh factor with COVID-19 infection in a sample of Iraqi patients.

Patients and methods

This cross-sectional retrospective study was conducted among 540 students of a variety of colleges in Baghdad from 6th of December 2021 to 26th of December 2021. The study protocol was reviewed by the Scientific and Ethical Committee of Al-Kindy Medical College without funding. Participants' were told about the nature of the study, its voluntary nature, and the right to withdraw at any time they want without negative consequences. Those who wanted to participate in the study were allowed to proceed with filling out the questionnaire.

The Inclusion criteria were all individuals who were previously infected with COVID-19 disease and proved with PCR (polymerase chain reaction) test or CT (Computerized tomography) lung scan while the exclusion criteria were individuals who were suspicious of infection with COVID-19 disease were excluded.

An online questionnaire using Google forms was used to collect the data. The participation in it was voluntary and agreed to participate in this study and it was spread over the internet to help achieve the required number of samples and to allocate samples of different age groups. The questionnaire contained many questions divided into 3 sections. The first section consists of 3 questions to acquire the personal data (age, sex). The second section has 2 questions concerned with the blood group of the patient (ABO, Rh factor). The Third final section consisted of Yes or No question to having COVID-19, Check-box for the symptoms of COVID-19 (fever, cough, lose of smell and taste, headache, chest pain, diarrhea), need hospitalization, and admission to respiratory care unit (RCU) or continuous positive airway pressure (CPAP) as Yes/No question Yes/No question to having got the vaccine to COVID.

Statistical analysis method

The data was analyzed using the statistical package for social sciences (SPSS -version 25), Descriptive statistics including frequencies, percentages. Independent-Sample Chi-Square test was used. P-value ≤0.05 was considered statically significant.

Results

A total of 580 samples were collected during the study with 358 (61.7%) samples from females and 222 (38.3%) from males and there was a significant difference between them (P=0.0001)(Table-1-)(Figure-1-). The mean age of the participants was 20.20± 2.716 years (mean± SD) years, ranged from 18 to 27 years (Figure-2-).

Table-1- Sex distribution of participants.

Sex	Numbers(No.)	Percentage(%)	P- value
Male	222	38.3%	0.0001
Female	358	61.7%	
Total	580	100.0%	

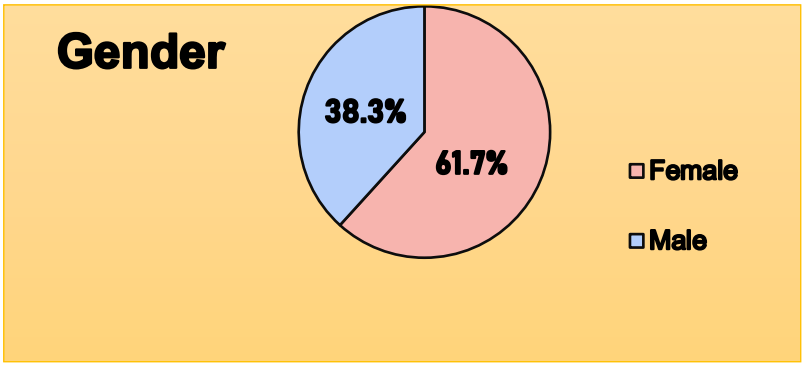

Figure-1- Sex distribution of participants.

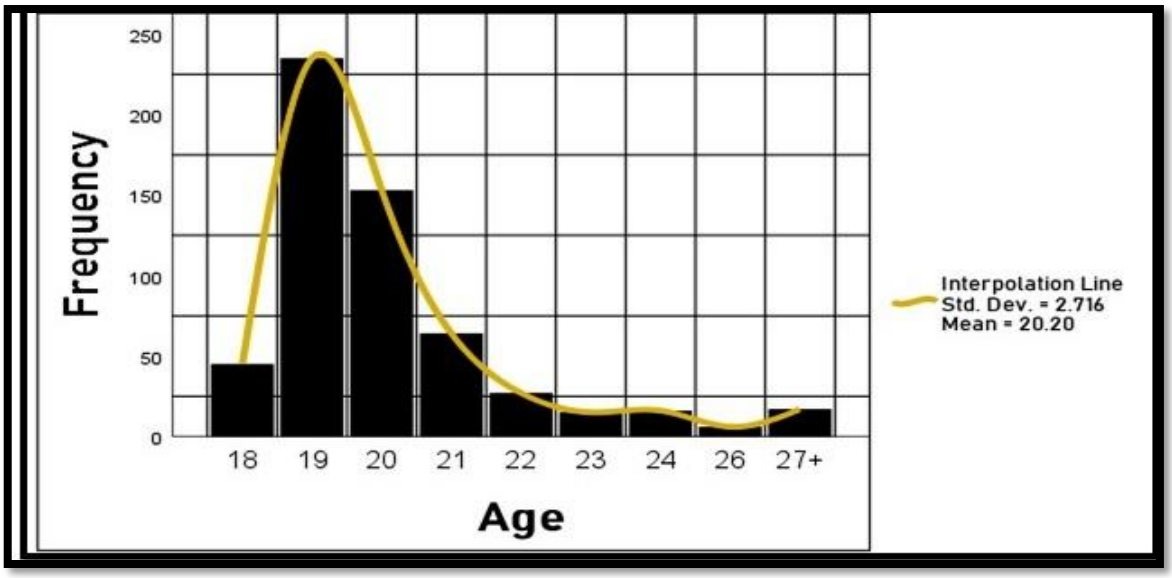

Figure-2- Age distribution of the study group.

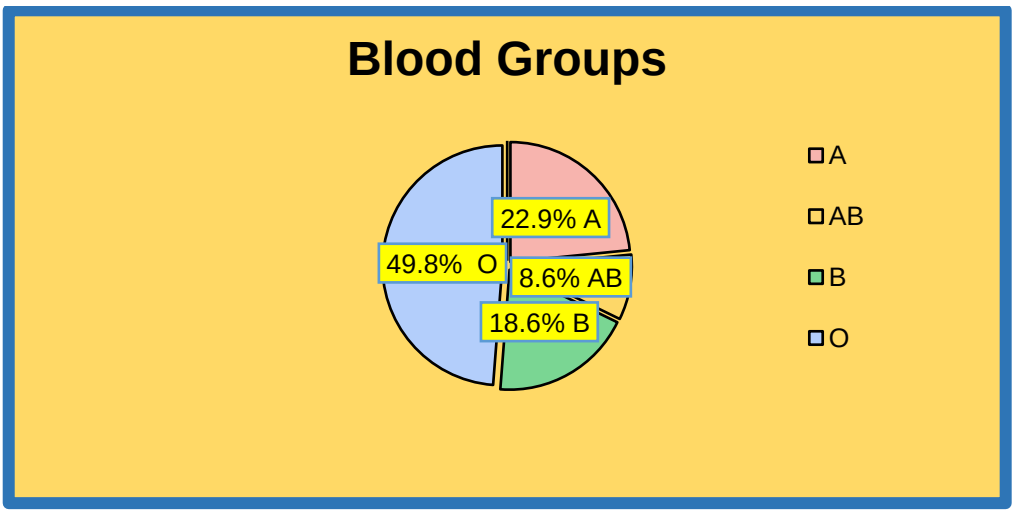

Figure-3- Blood group distribution of study group.

Of the 580 COVID-19 infected samples collected 133 (22.9%) were blood Group A then 108(18.6%) were blood group B and 50 (8.6%) blood group AB while 289 (49.8%) were blood group O with significant difference (P=0.0001)(Figure-3-).

About 508 (87.5%) of the samples were Rh + who had COVID-19 infection and the remaining 72(12.5%) were Rh – (P=0.0001) as shown in Table-2-.

Table-2- Distribution of Rh factor among study group.

Rh	Numbers(No.)	Percentage(%)	P- value
Positive	508	87.5%	0.0001
negative	72	12.5%	
Total	580	100.0%	

Most of COVID-19 patients were complaining from fever, cough, lose of smell or taste, chest pain, headache, and diarrhea and the distribution of these symptoms according to blood group and Rh were demonstrated in table -3-. The most frequent symptom was fever (41.35%) with blood group A,(48.14%) blood group B, (37.37 %) blood group O, (40.35%) Rh +ve, (40.27%) Rh -ve while blood group AB was lose of smell and taste (50%). Most of them were not required hospitalization or RCU treatment. There was a significant association between COVID-19 symptoms (fever, cough, and chest pain) and blood groups (Table-4-). Regarding hospitalization and RCU; there were no significant differences among blood groups shown in table -6-.

Regarding Rh and COVID symptoms; there were no significant difference while there were a significant differences regarding Rh and hospitalization and need RCU admission (table-5-).

Table-3- Distribution of symptoms and hospitalization among study participants' with blood group and Rh.

	Symptom	Freq. of positive (No.)	Freq. of negative(No.)	Percentage Of positive (%)
Blood Group No.=133 A	Fever	55	78	41.35%
	Cough	26	107	19.54 %
	Loss of smell/taste	47	86	35.33 %
	Chest pain	22	111	16.54%
	Headache	47	86	35.33%
	Diarrhea	15	118	11.27 %
	Hospitalization	5	128	3.75 %
	Need for RCU	4	129	3.00%
Blood Group B No.=108	Fever	52	56	48.14 %
	Cough	35	73	32.40 %
	Loss of smell/taste	44	64	40.74 %
	Chest pain	29	79	26.85 %
	Headache	42	66	38.88 %
	Diarrhea	13	95	12.03 %
	Hospitalization	7	101	6.48 %
	Need for RCU	5	103	4.62 %
Blood Group AB No.=50	Fever	23	27	46 %
	Cough	17	33	34 %
	Loss of smell/taste	25	25	50 %
	Chest pain	10	40	20 %
	Headache	20	30	40 %
	Diarrhea	6	44	12 %
	Hospitalization	3	47	6 %
	Need for RCU	3	47	6 %

Blood Group **No. 289** **O**	**Fever**	**108**	**181**	**37.37 %**
	Cough	**61**	**228**	**21.10 %**
	Loss of smell/taste	**105**	**184**	**36.33 %**
	Chest pain	**44**	**245**	**15.22 %**
	Headache	**85**	**204**	**29.41 %**
	Diarrhea	**23**	**266**	**7.95 %**
	Hospitalization	**12**	**277**	**4.15%**
	Need for RCU	**10**	**279**	**3.46 %**
Rh No.=508 **+**	**Fever**	**205**	**303**	**40.35 %**
	Cough	**118**	**390**	**23.22%**
	Loss of smell/taste	**195**	**313**	**38.38 %**
	Chest pain	**93**	**415**	**18.30 %**
	Headache	**169**	**339**	**33.26 %**
	Diarrhea	**51**	**457**	**10.03%**
	Hospitalization	**20**	**488**	**3.93 %**
	Need for ECU	**18**	**490**	**3.54%**
Rh No.=72 **-**	**Fever**	**29**	**43**	**40.27 %**
	Cough	**15**	**57**	**20.83 %**
	Loss of smell/taste	**22**	**50**	**30.55 %**
	Chest pain	**9**	**63**	**12.5%**
	Headache	**21**	**51**	**29.16 %**
	Diarrhea	**5**	**67**	**6.94%**
	Hospitalization	**7**	**65**	**9.72 %**
	Need for RCU	**8**	**64**	**11.11 %**

Table-4- Association of Frequency of COVID-19 symptoms with Blood groups.

Symptoms	Blood group A No.=133 No. %	Blood group B No.=108 No. %	Blood group AB No.=50 No. %	Blood group O No.=289 No. %	P -value
Fever	55 41.35	52 48.14	23 46	108 37.37	0.000
Cough	26 19.54	35 32.40	17 34	61 21.10	0.021
Loss of smell/taste	47 35.33	44 40.74	25 50	105 36.33	9.1
Chest pain	22 16.54	29 26.85	10 20	44 15.22	0.05
Headache	47 35.33	42 38.88	20 40	85 29.41	0.19
Diarrhea	15 11.27	13 12.03	6 12	23 7.95	0.50
Hospital Admission	5 3.75	7 6.48	3 6	12 4.15	0.70
Need for RCU CPAP	4 3.00	5 4.62	3 6	10 3.46	0.75

Table-5- Association of Frequency of COVID-19 symptoms with Rh.

Symptoms	Rh+ No.=508 No. %	Rh- No.=72 No. %	P -value
Fever	205 40.35	29 40.27	1.00
Cough	118 23.22	15 20.83	0.65
Loss of smell/taste	195 38.38	22 30.55	0.19
Chest pain	93 18.30	9 12.5	0.22
Headache	169 33.26	21 29.16	0.48
Diarrhea	51 10.03	5 6.94	0.40
Hospital Admission	20 3.93	7 9.72	0.02
Need for RCU	18 3.54	8 11.11	0.00

Participants who had vaccine (94%) had much lower risk of acquiring a COVID infection post vaccination Figure-4-.

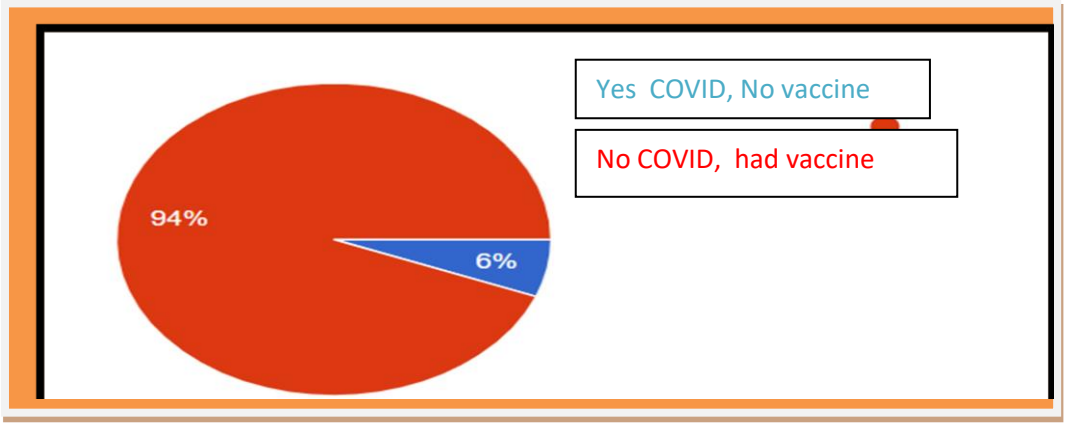

Figure-4- Distribution of vaccinated study group.

Discussion

Coronavirus pandemic disease is rapidly spreading worldwide causing high numbers of infections and death among infected patients (14). COVID-19 has variable clinical manifestations like fever, cough and dyspnea. This disease may progress to respiratory failure and need CPAP or RCU while others end with death (15). There is no specific biological marker can forecast the progress of the disease and in this study several risk factors for COVID-19 infection have been described like age, sex, and laboratory findings like blood groups and Rh (16).

This study illustrated that there was an association between Blood group O+ and COVID-19 infection while the blood group AB+ were less susceptible to infection. This study were in conflict with other studies in China, Hong Kong, Turkey that found blood group A was associated with an increased risk of COVID-19 infection, while group O was associated with a decreased risk (17,18,19). It is in disagreement with other study in Iraq showed also increased incidence with blood group A and decrease infection with blood group O(20,21).

This may be due to the average young age of this study group that is lower than in other studies. In addition to that; a lower sample size than mentioned studies. Other possible cause was type of sample collection because study samples were treated in home while the type of sample collection in other studies were all of them were hospitalized and our sample were blood group O which less susceptible to infection when they were infected they had a mild disease that not required hospitalization as shown in this study.

Blood group O was resists to infection and this may be due to presence of sugar N-acetyl galactosamine on their surface of Blood group A that COVID virus had surface proteins bind to this sugar and this sugar is missing on O blood group cells(22).In addition to that; patients with blood group O had lower lower ACE levels that S spike of the virus attached to it which confer a high protection rate against coronavirus infection (23). Another probable explanation is that during the evolutionary phenotype formation of blood groups, epitopes which is anti glycan blood group are exposed to IgM that down regulated by glycosylation in the non-O groups. These immune characteristics may not be present in the O blood group(24). Patients with A blood group had an increased risk of cardiovascular diseases. The A antigen might protect P-selectin and intercellular cell adhesion molecule from enzymatic cleavage thus promoting stronger and longer binding of leukocytes to the vascular wall. Adhesion molecules attached to the endothelium would increase adhesion, inflammation, and decreased circulation. These effects may prompt A blood group individuals to a higher risk for atherothrombotic disease than blood groupO (25,26).

This study attempted to evaluate the possible association between the COVID-19 infected patients and symptoms, need RCU and CPAP and the ABO blood group and Rh. There were no significant differences among them except fever, cough and chest pain showed significant difference among blood group only and not Rh (table-4-,-5-). Most of participants'

cases suffered a mild to a moderate case of COVID due to a lower average age of sample group (younger age group) as seen from low percentages of symptoms in Table-4-5-.

In Iraq COVID registered a number of 2.3 million cases in the period from early 2020 up to May of 2022, with most of the cases during March of 2020 to September of 2021 with 25 thousand deaths mainly among elderly and immune compromised patients(27). In a study done in Al-Najaf city- Iraq; they concluded that the COVID-19 infection may occur in all blood groups with the same degree of severity(28).

Ellinghans *et al.* 2020 (29) done a genome wide association study involving 1980 patients with COVID-19 with severe disease (respiratory failure) in Europe; they confirmed involvement of ABO blood group with a 3p21.31 gene cluster as a genetic susceptibility locus in patients with COVID-19 with respiratory failure.

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