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Blood Groups Typing and Their Susceptibility to Pulmonary Complications and Mortality in Patients with COVID-19 Infection

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Abstract— Background*: COVID-19 (coronavirus disease - 2019) is an infectious disease outbreak later on declared as a pandemic by World Health Organization, caused by severe acute respiratory syndrome coronavirus-2. It spread rapidly and can result in severe acute respiratory failure. ABO blood types are determined by cell surface markers that are characterized by a protein or lipid, which has an extension of a particular arrangement of sugars that determines each of the blood types A, B, and O. There are few studies examine the relationship between COVID-19 infection and blood groups distribution among COVID-19 patients.* ***Aim****: The aim of this study is to investigate whether there exists a relationship between the blood groups of the patients and susceptibility to COVID-19 infection and the clinical outcomes defined by clinical improvement, development of pulmonary complication, need for assisted ventilation or death.* ***Subjects and method****: This is a cross sectional study which included 340 adult patients with polymerase chain reaction confirmed diagnosis of COVID-19. Age, sex, blood group and Rh, comorbidities, signs and symptoms, laboratory and imaging finding, need for assisted ventilation and respiratory care unit follow up and mortality of COVID-19 patients were analyzed. Blood groups of 340 adult with COVID-19 were obtained and compared with that blood groups of the general population.* ***Results****: The blood group A was found statistically significantly more frequent among those infected with COVID-19 compared to the general population (37% versus 23.1% , P value = 0.001), whereas the frequency of blood group O was found significantly lower in COVID-19 patients than that in the general population (30% versus 48%, P value = 0.001).Blood groups type does not seen to affect the clinical outcomes of COVID-19 patients in term of clinical improvement, development of respiratory complication, need for assisted ventilation or death (P value >0.05).* ***Conclusion****: The results of this study demonstrate that the blood group A was found significantly more susceptible to COVID-19 infection, while blood group O was found significantly less susceptible to COVID-19. No significant association were found between the blood groups distribution among COVID-19 patients and patients final clinical outcomes in term of clinical improvement, development of respiratory complication, need for assisted ventilation or death.*

Keywords*— Blood groups, COVID-19, Susceptibility, Clinical outcomes.*

I. INTRODUCTION

Several clusters of pneumonia cases of unknown causes were reported in Wuhan city, Hubei province, China, in December 2019. The causative agent of this pneumonia was confirmed as the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), previously named 2019 novel coronavirus (2019-nCoV), and the disease was termed coronavirus disease-2019 (COVID-19)[{1,2}].

The risk of infection is higher for the elderly and for patients suffering from pre-existing illness such as cardiovascular disease, hypertension, diabetes, and chronic respiratory disease [{3}]

The disease begins with flu-like symptoms that include fever, fatigue, dry cough, sore throat, shortness of breath, headache, chest tightness, chest pain, and muscle pain. Some of COVID-19 patients have runny nose, nausea, vomiting, and diarrhea [{4}]. People can be infected without showing symptoms, which allows the virus to spread more effectively from person to person[{1}]. A small number of patients can have headache or hemoptysis[{5,6}].

Reverse transcription polymerase chain reaction–based SARS-CoV-2 RNA detection from respiratory samples (eg., nasopharynx) is the standard for diagnosis. However, the sensitivity of the test varies with timing of testing relative to exposure. One modeling study estimated sensitivity at 33% 4 days after exposure, 62% on the day of symptom onset, and 80% 3 days after symptom onset [{7-9}].

The laboratory abnormalities seen in COVID-19, including elevated serum C-reactive protein (increased in >60% of patients), lactate dehydrogenase (increased in approximately 50%-60%), alanine aminotransferase (elevated in approximately 25%), aspartate aminotransferase (approximately 33%), and low albumin in approximately 75% [{10}].

The most common hematological abnormality is lymphopenia (absolute lymphocyte count<1.0 × 109/L), which is present in up to 83% of hospitalized patients with COVID-19[{1,11}]. In conjunction with coagulopathy, modest prolongation of prothrombin times (prolonged in>5% of patients),mild thrombocytopenia (present in approximately 30% of patients) and elevated D-dimer values (present in 43%-60% of patients) are common[{11-15}].

Pan *et al.*[{16}] found that in early stages (0–4 days after the onset of symptoms), ground glass opacity was the main finding in lower lung lobes; in progressive stages (5–8 days), the progression of lung disease involved three patterns of ground-glass, consolidation, and crazy paving ,while in peak stages (9–13 days), dense consolidation became the prevalent

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feature; in absorption stages (>14 days),ground glass opacity was detected with no crazy paving and resolution of consolidations[16].

ABO blood types are determined by cell surface markers that are characterized by a protein or lipid, which has an extension of a particular arrangement of sugars that determines each of the blood types A, B, and O[17].

The Aim of Study

The aim of this study is to investigate whether there exists a relationship between the blood groups of the patients and susceptibility to COVID-19 infection and the clinical outcomes defined by clinical improvement, development of pulmonary complication, need for assisted ventilation or death.

II. Patients and Methods

This cross sectional study was conducted in COVID-19 ward at AL- Kindy teaching hospital, from the 1st of May 2020 to 30st of September 2020.The studied sample included total of 340 patients who were positive for the SARS-CoV-2 RNA test through RT-PCR from nasopharyngeal swab. The study include patients with positive COVID-19 RT- PCR test, age > 15,

moderate and severe cases, patients presented with symptoms such as dyspnea, hemoptysis, disturbed level of consciousness associated with chest radiography abnormalities and pulse oximeter saturation < 93% at rest. The study also include patients with shock or other organs failure that require monitoring and treatment in the intensive care unit (ICU). Patients with comorbidities (diabetes mellitus, hypertension, Chronic respiratory disease, cardiovascular disease and history of malignancy) also enrolled for study. Patients with negative COVID-19 PCR test, age < 15 and patients with mild clinical symptoms were excluded from study.

A pretested checklist prepared by researcher was filled. This checklist include detailed history, physical examination and a grouped of selected investigations performed, including complete blood count, random blood sugar, blood urea and Serum creatinine, serum aspartate aminotransferase, serum alanine aminotransferase, serum ferritin, serum lactate dehydrogenase, D.dimer, C. Reactive protein , erythrocyte sedimentation rate, chest computed tomography scan.

The researcher proposal was fully discussed and approved by the ethical and scientific committee in the Iraqi Board of internal medicine.

The permission of health authority at AL-Kindy teaching hospital/Baghdad was taken before data collection.

A written consent was taken from each patients after full explanation of aim of the study and insuring about confidentiality of collected data which will be used for research purpose only and will be anonymous.

The collected data were introduced into Microsoft Excel sheet 2016 and loaded into SPSS V.26 statistical program. Descriptive statistic were presented using tables and graphs.

A Chi-squared test was used to find out significance of association between categorized variables. Independent 2 samples test was used to find out significance of difference between related scale variables.

P value less than 0.05 was considered as discrimination point of significance.

III. Results

A total of 340 adult patients who had positive SARS-CoV-2 PCR completed the study. The mean age of patients was 55.94+ 12.92 years.

We observed a greater number of men than women,63% of patients were male and 37% were female.

Blood groups were obtained for 340 adult patients with PCR confirmed diagnosis of COVID-19, 37% were A ,23% were B, 10% were AB, and 30% were O. Positive Rhesus factor (Rh) accounted for 90%.

Goodness of fit Chi-square test in table 1 shows that 37.1% of patients in this study had blood group A, 22.9% had blood group B, 10% had blood group AB, and 30% had blood group O.

TABLE 1. Goodness of fit Chi square test of blood group in the current study and general population

	Current study	General population	P value
A	126(37.1%)	23.1%	0.001
B	78(22.9%)	21.5%	
AB	34(10%)	7.4%	
O	102(30%)	48%	

In the general population, in our community the distribution of the blood groups reported the blood of 23.1%, 21.5%, 7.4%, and 48% as type A, B, AB, and O respectively [18].

The percentage of patients had blood group A in our study was found to be significantly higher than persons had blood group A in the general population [18], while the percentage of patients had blood group O was found to be significantly lower than persons had blood group O in the general population [18], P value 0.001.

The difference in percentage of Rh-positive patients in current study (90%) was not significant in comparison with that of general population[18](89%), P value 0.556.

Table 2 show that no significant association were noticed between gender and blood group distribution among COVID-19 patients, P value=0.245, or Rh, P value=0.087.

About 40.3% of our patients had hypertension, no significant association was observed between history of hypertension and blood group or Rh distribution among COVID-19 patients in our study (P value 0.263, 0.658 respectively).

About 43.8% of patients had diabetes mellitus, no significant association was found between history of diabetes in COVID-19 patients in our study and blood group distribution, P value=0.095, or Rh, Pvalue =0.412.

About 3.5% of patients were smokers, no significant association was detected between history of smoking in COVID-19 patients in our study and blood group distribution, P value =0.586, or Rh, P value =0.713.

As shown in table 3 there were no significant differences between mean of age of patients measured in years according

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to blood group, P value=0.728, also there were no significant differences between mean of duration of hospital stay measured in days according to blood group, P value=0.687.

Table 4 shows that means of white blood cells count, lymphocyte count, platelet count, serum ferritin, lactate dehydrogenase and D. dimer were not differ significantly according to blood groups, P value > 0.05 in all conditions.

Mean of hemoglobin level was found to be significantly lower in blood group A patients than other blood groups, P value=0.037.

TABLE 2. Associations between gender, diabetes mellitus, hypertension, smoking and blood group and Rh

			Blood group								Rh			
			A		B		AB		O		POSITIVE		NEG	
			N	%	N	%	N	%	N	%	N	%	N	%
Gender	male	214	73	57.9	49	62.8	26	76.5	66	64.7	205	64.1	9	45
	female	126	53	42.1	29	37.2	8	23.5	36	35.3	115	35.9	11	55
P value			0.245								0.087			
DM	Yes	149	57	45.2	25	32.1	18	52.9	49	48.0	142	44.4	7	35
	No	191	69	54.8	53	67.9	16	47.1	53	52.0	178	55.6	13	65
P value			0.095								0.412			
HTN	Yes	137	58	46.0	25	32.1	13	38.2	41	40.2	128	40	9	45
	No	203	68	54.0	53	67.9	21	61.8	61	59.8	192	60	11	55
P value			0.263								0.658			
Smoking	Yes	12	6	4.8	3	3.8	0	0.0	3	2.9	11	3.4	1	5
	No	328	120	95.2	75	96.2	34	100	99	97.1	309	96.6	19	95
P value			0.586								0.713			

TABLE 3. Differences between means of age and duration of hospital stay according to blood group

	Mean	SD	Bl. gp	N	Mean	SD	P value
Age/ year	55,94	12.92	A	126	55.40	12.837	0.728
			B	78	56.42	14.795	
			AB	34	58.03	11.096	
			O	102	55.54	12.111	
Duration / day	13.42	8.2	A	126	13.88	8.486	0.687
			B	78	12.91	7.917	
			AB	34	14.35	9.695	
			O	102	12.94	7.567	

TABLE 4. Differences between means of laboratory test results according to blood group

	Mean	SD	Bl. group	N	Mean	SD	P value
WBC c/ul	11380	5033	A	126	11553.97	5312.907	0.583
			B	78	11838.46	5284.558	
			AB	34	10623.53	4190.614	
			O	102	11067.65	4752.991	
LM c/ul	855	500	A	126	820.37	482.520	0.560
			B	78	843.19	482.162	
			AB	34	836.65	522.329	
			O	102	913.06	529.243	
Hb% g/dl	12.5	1.8	A	126	12.20	1.768	0.037
			B	78	12.88	1.699	
			AB	34	12.87	1.572	
			O	102	12.61	1.948	
Plt cells /mcL	253891	107105	A	126	259031.75	110215.929	0.830
			B	78	256500.00	106102.958	
			AB	34	242941.18	113971.273	
			O	102	249196.08	102674.632	
RBS mg/dl	247	125	A	126	239.35	121.407	0.544
			B	78	243.45	134.603	
			AB	34	244.76	108.288	
			O	102	262.89	130.144	
S.Ferritinng/ml	626.4	431.9	A	126	623.73	456.855	0.924
			B	78	623.67	409.402	
			AB	34	673.79	372.055	
			O	102	615.87	440.509	
LDH U/L	591.8	274.5	A	126	594.62	324.631	0.390
			B	78	613.41	247.926	
			AB	34	636.44	325.612	
			O	102	557.17	197.170	
D.Dimerng/ml	1285.4	1531.6	A	126	1426.21	1853.477	0.068
			B	78	1524.08	1842.467	
			AB	34	1023.82	946.377	
			O	102	1016.05	759.149	

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Table 5 shows that means of C. reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were not differ significantly according to blood groups, P values =0.410 and 0.672 respectively.

Table 5 shows that the mean CRP=44.8+36.2, no significant difference was noticed between means of CRP according to blood group, P value=0.410.

The mean of ESR=75.3+23.2, no significant difference was noticed between means of ESR according to blood group, P value=0.672.

Table 6 show that ground glass appearance was detected by lung CT scans in all patients, crazy paving, and consolidation were detected in 45% and 45.3% of patient's lung CT scan respectively.

All of COVID-19 patients suffered from bilateral lung involvement in current study, 76.8% have multilobe involvement and opacities in 43% of patients were extended to more than 50% of the lungs area. About 70% of Rh-negative patients showing crazy paving appearance which is significantly higher than that of Rh-positive patients, P value=0.021, otherwise there were no significant association between the type of blood group and lung CT scan findings.

TABLE 5. Differences between means of CRP and ESR of patients according to blood group

	Mean	SD	Bl. gp	N	Mean	SD	P value
CRP mg/L	44.9	36.2	A	126	40.83	27.491	0.410
			B	78	48.55	41.876	
			AB	34	49.03	32.304	
			O	102	50.11	74.065	
ESR mm/hr	75.3	23.2	A	126	75.33	25.486	0.672
			B	78	76.64	21.085	
			AB	34	78.35	19.473	
			O	102	73.35	23.366	

TABLE 6. Association between radiological examination results and blood group and Rh

			Blood group								Rh			
			A		B		AB		O		+Ve		-Ve.	
			N	%	N	%	N	%	N	%	N	%	N	%
Crazy paving	Yes	153	55	43.7	38	48.7	12	35.3	48	47.1	139	43	14	70.
	No	187	71	56.3	40	51.3	22	64.7	54	52.9	181	56.6	6	30
P value			0.573								0.021			
Consolidation	Yes	154	57	45.2	37	47.4	13	38.2	47	46.1	147	45.9	7	35
	No	186	69	54.8	41	52.6	21	61.8	55	53.9	173	54.1	13	65
P value			0.837								0.34			
CT site	preferal	79	26	20.6	17	21.8	13	38.2	23	22.5	76	23.8	3	15
	diffuse	261	100	79.4	61	78.2	21	61.8	79	77.5	244	76.3	17	85
P value			0.18								0.369			
Percentage	0.50%	148	62	49.2	31	39.7	12	35.3	43	42.2	140	43.8	8	40
	=<50%	192	64	50.8	47	60.3	22	64.7	59	57.8	180	56.3	12	60
P value			0.373								0.743			

TABLE 7. Association between site of treatment, need for CPAP, final outcome (fate of patient) and blood group and Rh

		N	Blood group								Rh			
			A		B		AB		O		+Ve		-Ve.	
			N	%	N	%	N	%	N	%	N	%	N	%
Site treatment	RCU	138	52	41.3	30	38.5	15	44.1	41	40.2	132	41.2	6	30
	Ward	202	74	58.7	48	61.5	19	55.9	61	59.8	188	58.8	14	70
P value			0.95								0.32			
Outcome	Died	115	38	30.2	28	35.1	14	41.2	35	34.3	111	34.7	4	20
	Cured	225	88	69.8	50	64.9	20	58.8	67	65.7	209	65.3	16	80.
P value			0.65								0.184			
CPAP	Yes	138	52	41.3	30	38.5	15	44.1	41	40.2	132	41.3	6	30
	No	202	74	58.7	48	61.5	19	55.9	61	59.8	188	58.8	14	70
P value			0.950								0.320			

Table 7 shows that 40.6% of patients were admitted to the respiratory care unit (RCU) for assisted ventilation and the case fatality rate was 33.8%.

No significant associations were found between the need for RCU admission, need for assisted ventilation or fatality of the disease and blood group or Rh type of the patients, P value >0.05 in all conditions.

IV. Discussion

In our study, we found that ABO blood groups displayed different association risks for the infection with SARS-CoV-2 resulting in COVID-19.

Specifically, the blood group A was found statistically significantly more frequent among those infected with SARS-CoV-2 compared to the general population, whereas the

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frequency of blood group O was found significantly lower in COVID-19 patients than that in general population.

Around 40.6% of our patients were developed acute respiratory distress syndrome (ARDS) and admitted to the respiratory care unit (RCU) and received continuous positive airway pressure (CPAP).

No significant association was found between the development of ARDS, admission to the RCU, need for assisted ventilation and blood group distribution among COVID-19 patients in this study.

The case fatality rate was 33.8% in our patients, no statistically significant association between blood types and mortality rate in COVID-19 patients was noted.

These results goes in concordance with a Turkish study conducted by Göker *et al*. that demonstrate that the blood group O might be protective while the blood group A might have increased susceptibility to the disease, and it was demonstrated that the blood groups did not have significant predictive effects on the need for ICU hospitalization and mortality. The blood group A was statistically significantly more frequent among those infected with COVID-19 compared to the controls (57% versus 38%, P<0.001;OR:2.1) while the frequency of blood group O was significantly lower in the COVID-19 patients, compared to the control group (24.8% versus 37.2%,P:0.001;OR:1.8).No significant effect of ABO blood groups and Rh systems were demonstrated on the clinical outcomes in term of need for intubation, ICU hospitalization and mortality (P value > 0.05)[19].

Meta-analysis from Wuhan and Shenzhen, China have demonstrated that the frequency of blood group A in patients with COVID-19 was significantly higher than that in normal people, being 37.75% in the former versus 32.16% in the later (P value < 0.001) and the proportion of blood group O in the patients with COVID-19 was significantly lower than that in normal people, being 25.80% in the former versus 33.84% in the later (P value <0.001). This study also observed a similar distribution pattern of high risk blood group A and low risk blood group O in dead patients. Blood group A was associated with a higher risk of death compared with non-A groups, with an OR of 1.482 (95% CI 1.113-1.972, P=0.008), while blood group O was associated with a lower risk of death compared with non-O groups, with an OR of 0.660 (95% CI 0.479-0.911, P=0.014)[20].

In addition, a study conducted by Solhpour *et al.* who reviewed three hospitals of corona virus care centers in Tehran, Iran and select 93 hospitalized patients (they were all younger than 45 years old, with no underlying disease and no history of getting immunosuppressive medications such as corticosteroids and chemotherapy agents during the last 12 months) with hypoxia who were diagnosed infected by COVID-19 found that the blood group type A was significantly more frequent in COVID-19 compared to the general population (65% in former versus 32.09% in the later; P value <0.05), on the other hand the proportion of blood type O in COVID-19 patients was significantly lower than blood group O in the general population (2% in the former versus 36.49% in the later; P value <0.05).This study also demonstrate high association between blood group A and severe hypoxia which needs invasive ventilation in young patients without underlying disease and no history of drug consumption and they hypothesize that the protein that define type A and B blood group might affect the immune system's production of antibodies , perhaps these blood types have slower immunity as a result [21].

Ellinghans *et al.* a genomewide association study, involving 1980 patients with COVID-19 and severe disease (defined as respiratory failure) at seven hospitals in Italian and Spanish epicenters of COVID-19 pandemic in Europe, this study identified a 3p21.31 gene cluster as a genetic susceptibility locus in patients with COVID-19 with respiratory failure and confirmed a potential involvement of the ABO blood system[22].

The association signal at locus 9q34.2 coincided with the ABO blood group locus; in this cohort, a blood group specific analysis showed a higher risk in blood group A than in other blood groups and a protective effect in blood group O as compared with other blood groups [22].

The mean age of patients in our study was 55.94+12.92 year and males accounted for majority of patients in our population (63% male versus 37% female). No significant association were found between age and gender of the patients and distribution of blood groups among COVID-19 patients (P value > 0.05).

A bout 40.3% of our patients had hypertension and 43.8% of patients had diabetes mellitus, no significant association were found between history of diabetes or hypertension and distribution of blood types or Rh among COVID-19 patients, P value > 0.05 in both conditions.

These results are in agreement with Göker *et al*. study [19], that found statistically no significant association between age, sex, history of diabetes mellitus, hypertension and blood group and Rh distribution among COVID-19 patients (P value > 0.05).

No significant association were found between smoking history and blood type distribution in our patient (P value > 0.05) and statistically no significant associations between any of the peak inflammatory markers and distribution of blood groups and Rh among COVID-19 patients were found. An identical results were revealed by Christopher A. Latz *et al*. in the state of Massachusetts who shown no significant association between ABO blood groups distribution among COVID-19 patients and history of chronic illness, smoking history and elevation of the inflammatory markers (P value > 0.05) [23].

V. CONCLUSIONS

1-The present study conclude that the blood group O might be protective while the blood group A might have increased susceptibility to the COVID-19.

2-There was no significant effect of blood type on patients final clinical outcomes in term of clinical improvement, development of pulmonary complication, need for assisted ventilation or death.

3- No significant association were found between smoking history and blood type distribution in our patient and statistically no significant associations between any of the

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peak inflammatory markers and distribution of blood groups and Rh among COVID-19 patients were found.

4- No significant association were found between history of diabetes or hypertension and distribution of blood types or Rh among COVID-19 patients.

Recommendations

1-The limitation of this study is the somewhat small number of patients with the clinical outcomes may have caused the failure in demonstrating the effect of blood groups on clinical outcomes in statistical terms.

2-There is a need for further molecular studies to elucidate the relationship between the blood groups and the disease. Prospective larger multicenter studies may be needed in order to further elucidate the role of possible somewhat protective role of the blood group O.

3- Large replication studies with complete information should be encouraged to pursue and are needed to verify the present findings

4-Obviously, people with any blood type all need to exercise the wisdom of careful practice to avoid COVID-19.

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