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Original Article

Evaluation of Disease Severity in Relation to Blood Groups in Egyptian Patients with COVID-19

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ABSTRACT

Background: As a new emerging pandemic, COVID-19 is a challenge facing the world. Researches are active to discover factors related to disease severity, as an effort to decrease its impact on health status and mortality.

The Aim of The Work: The current research aimed at exploring if a relationship is present between ABO blood grouping and disease severity and associated mortality associated with COVID-19.

Patients and Methods: This cross-sectional trial was completed at Al-Azhar University Hospital [New Damietta] between January 2021 to June 2021. It included 100 patients with suspicious clinical manifestations of COVID-19, confirmed by positive reverse transcription real-time polymerase chain reaction (rt RT-PCR) test of swabs obtained from their respiratory tract. All patients were subjected to full medical history taking, thorough clinical assessment, laboratory examinations, chest radiography and high-resolution computerized tomography on chest.

Results: The commonest blood group among the study population was group A in (53%), followed by group O in (19%), then group B in (18%) and group AB in (10%). Individuals with blood group A are significantly susceptible to catch COVID-19 infection (p-value= 0.01), whereas those with blood group O are significantly unsusceptible to be infected (p-value= 0.035). Hypertension was frequent among patients with groups A and B compared with groups AB and O (52.8%, 50.0% versus 20% and 5.2% respectively). There was a significant association between group AB and disease severity (p-value= 0.002), while group A was significantly linked to critical disease and mortality (p-value= 0.032). The vast majority of group-O patients (84.2%) had mild disease, whilst mortality was confined to the blood group A.

Conclusion: There is an association between ABO blood groups and either COVID-19 susceptibility, severity and mortality.

Keywords: COVID-19; Blood groups; Severity; Mortality.

INTRODUCTION

Coronavirus disease-19 [COVID-19] is an infectious pandemic caused by a new Coronavirus, known as severe acute respiratory syndrome Coronavirus-2 [SARS-CoV-2] [1]. Clinically, it presents by non-specific manifestations of fever, fatigue and dry cough. However, it could be completely asymptomatic or complicated by severe pneumonia. Computed tomography [CT] is widely used as an initial screening and diagnostic tool of viral pneumonia [including COVID-19] [2].

The real-time, polymerase chain reaction [RT-PCR] is then used to confirm COVID-19 diagnosis by amplification of the nucleic acid particles, detected from respiratory tract or blood specimens. Recent clinical observations suggest that patient's age, male gender and specific chronic medical diseases (e.g., cardiovascular disease, diabetes, obesity, COPD) seem to be risk factors for SARS-Cov-2 infection and severity [3]. With continuation of the pandemic, the global research is working to detect risk factors for COVID-19 and potential therapeutic targets. The probable role of blood groups for prediction of disease and its complications has emerged as a question. New studies continue to add evidence that there is an association between ABO blood groups and vulnerability to development and complications of COVID-19 may be present. However, the situation remains preliminary and controversial [4].

THE AIM OF THE WORK

The current work aimed at exploring if a relationship is present between ABO blood group and the disease severity and mortality related to COVID-19.

PATIENTS AND METHODS

This cross-sectional study was carried out at Al-Azhar University Hospital [New Damietta] during the period from January 2021 to June 2021.

It included 100 adult patients with suspicious clinical manifestations of COVID-19, confirmed by positive reverse transcription real-time polymerase chain reaction (rt RT-PCR) test in their respiratory tract swabs.

Patient was excluded if he/she had any of the following; age under 18 years old, suspicious clinical picture of COVID-19 with negative (rt RT-PCR) test, defective mentality interfering with self-expression and communication, diffuse parenchymatous lung disease, decompensated vital organ disease (e.g., congestive heart failure, end-stage chronic renal disease, liver cell failure or advanced chest disease which greatly affects pulmonary functions), negative Rh-blood group and refusal to participate in the study.

The study was revised and approved by the local and research ethics committee of Damietta Faculty of Medicine [Al-Azhar University].

After signing an informed written consent, all patients were subjected to the following:

- Full history taking: including age, sex, residence, occupation, socio-economic standard, smoking habit and other special habits of medical importance and associated co-morbidities. Smoking index for smoking patients was calculated using the pack/year method:

  Smoking index= number of smoked packs/day x duration of smoking (years)

- Thorough clinical assessment: including careful general and local examination. Patient's weight and height were estimated and a body mass index (BMI) was calculated from the equation:

  BMI= weight (kg)/squared height (m)

- Laboratory investigation: including ABO blood grouping, complete blood count (CBC), liver function tests, kidney function tests, inflammatory markers (C-reactive protein [CRP], erythrocyte sedimentation rate [ESR] and serum ferritin, lactate dehydrogenase enzyme (LDH), D-dimer test, coagulation profile (prothrombin time [PT], activated partial thromboplastin time [APPT] and international normalization ratio [INR] and arterial blood gases (ABG).

- Radiological investigations: including plain chest x-ray (postero-anterior and lateral views) and high-resolution computerized tomography (HRCT) on chest.

The severity scoring of COVID-19 was based on NIH COVID-19 Treatment Guidelines [5].

It classified COVID-19 severity into five classes (asymptomatic or presymptomatic; mild; moderate; severe; and critical illness).

- Asymptomatic or Presymptomatic Infection: those patients who test positive for SARS-CoV-2 by a virologic test (i.e., a nucleic acid amplification test or an antigen test), with no manifestations consistent with COVID-19.

- Mild Illness: patients with any clinical manifestations of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell). However, at the same time, they did not complaint of shortness of breath, dyspnea, and their chest imaging study revealed normal findings.

- Moderate Illness: patients with clinical evidence of lower respiratory disease (based on clinical or radiological investigations) with an oxygen

saturation (SpO2) ≥94% on room air at the sea level.

- Severe Illness: Patients with one or more of the following: SpO_2 <94% on room air at the sea level, a fractional oxygen arterial partial pressure to fractional inspired oxygen (PaO_2/FiO_2) <300 mm Hg, a respiratory rate >30 breaths/min or lung infiltrates >50%.

- Critical Illness: Patients with respiratory failure, septic shock, and/or multiple organ failure.

Statistical Analysis

Data was anonymized and fed to personal computer with SPSS (Statistical Package of Social sciences) version 21 (SPSS Inc., Chicago, IL, USA). Quantitative variables were expressed as mean ± standard deviation (SD), and tested among the study groups using one-way analysis of variance (ANOVA) test. Categorical variables were expressed as frequency (percentage), and tested using Chi-square test. P-value at the level of significance was <0.05.

RESULTS

In the current study, the most common blood group among the study patients was group-A (53.0%), followed by blood group O (19.0%), then blood group B (18.0%) and finally group AB (10.0%) (Table 1).

Demographic data and associated chronic diseases did not differ significantly among blood groups, with the exception of hypertension which was significantly frequent among patients with blood groups A and B compared with groups AB and O (52.8%, 50.0% versus 20% and 5.2% respectively) (p-value <0.001). The mean age of our patients was (45.70±9.98), with a slight male sex predominance (53.0%). Diabetes was reported in (57.0%), obesity in (55.0%), hypertension in (40.0%), chest diseases in (29.0%), cardiac diseases in (26.0%) and psychological disorders in (13.0%) (Table 2).

The most common clinical presentation was fever (68.0%), followed by malaise (64.0%) then cough, sore throat and headache (62.0%) for each. A significant decrease in the frequency of fever among blood group AB compared with other groups was observed. As well, a significant increase of the frequency of loss of smell among blood group O compared with other groups was recorded. Other clinical manifestations did not show any significant variance among blood groups (Table 3).

When comparing the distribution of blood groups among COVID-19 patients (based on study results), with the distribution of blood groups among the Egyptian people (based on Abdelmonem et al.[6]), to explore the susceptibility for COVID-19 infection among different blood groups, it was found that blood group A showed a significant increased risk to develop COVID-19 infection (p-value= 0.01). On the other hand, blood group O showed a significant decreased risk of having COVID-19 infection (p-value= 0.035). Blood groups B and AB were not associated with a specific risk to catch COVID-19 infection (Table 4).

The disease was of mild intensity among (68.0%) of patients, moderate among (14%), severe among (9%) and critical among (9%). Mortality was reported among 9.0% of the whole study population. There was a significant association between group AB and disease severity (p-value= 0.002), while group A was significantly linked to critical disease and mortality (p-value= 0.032). The vast majority of group-O patients (84.2%) had mild disease and mortality was confined to patients with group A (Table 6).

Table (1): Distribution of the study population regarding ABO blood groups

Blood Group	n	%
A	53	53.0
B	18	18.0
AB	10	10.0
O	19	19.0
Total	100	100.0

Table (2): Demographic data and associated chronic diseases in relation to ABO blood groups among the study population

Blood Group		A	B	AB	O	Total	test	p
Age (years)	**Mean±SD**	47.02±10.86	43.93±10.50	44.17±7.68	44.37±8.30	45.70±9.98	0.65	0.58
Sex	**Male**	28 (52.8%)	8 (44.4%)	6 (60.0%)	11 (57.9%)	53 (53.0%)	0.9	0.82
	Female	25 (47.2%)	10 (55.6%)	4 (40.0%)	8 (42.1%)	47 (47.0%)		
Smoking index (pack/year) (median, IQR)		0.00(20)	0.0(21.25)	14(21.0)	10(19)	0(20.0)	0.08	0.96
Associated chronic diseases	**None**	13(24.5%)	7(50.0%)	1(16.1%)	8(29.6%)	29(29.0%)	3.96	0.27
	DM	37 (62.2%)	9 (50.0%)	5 (50.0%)	10 (52.6%)	57 (57.0%)	1.3	0.72
	HTN	28 (52.8%)	9 (50.0%)	2 (20.0%)	1 (5.2%)	40 (40.0%)	*16.5*	*<0.001**
	Obesity	32 (60.3%)	8 (44.4%)	5 (50.0%)	10 (52.6%)	55 (55.0%)	1.57	0.66
	Chest diseases	15 (28.3%)	4 (22.2%)	3 (30.0%)	7 (36.8%)	29 (29.0%)	0.98	0.8
	Cardiac diseases	13 (24.5%)	5 (27.8%)	2 (20.0%)	6 (31.5%)	26 (26.0%)	0.58	0.9
	Psychological disorders	7 (13.2%)	2 (11.1%)	1 (10.0%)	3 (15.7%)	13 (13.0%)	0.26	0.96

SD: standard deviation, DM: diabetes mellitus, HTN: hypertension, *: statistically significant; IQR: Interquartile range

Table (3): Clinical manifestations in relation to ABO blood groups among the study population

	A		B		AB		O		Total		test	p-value
Blood Group	n	%	n	%	n	%	n	%	n	%		
Fever	38	71.7	14	77.8	2	20.0	14	73.6	68	68.0	*11.99*	*0.007**
Cough	34	64.2	9	50.0	6	60.0	13	68.4	62	62.0	1.55	0.66
Sore throat	29	54.7	13	72.2	5	50.0	15	78.9	62	62.0	4.91	0.17
Malaise	33	62.3	11	61.1	6	60.0	14	73.6	64	64.0	0.97	0.8
Headache	33	62.3	9	50.0	8	80.0	12	63.1	62	62.0	2.48	0.47
Muscle aches	33	62.3	8	44.4	8	80.0	10	52.6	59	59.0	3.95	0.26
Nausea	31	58.5	11	61.1	7	70.0	8	42.1	57	57.0	2.58	0.46
Vomiting	26	49.1	8	44.4	7	70.0	13	68.4	54	54.0	3.8	0.28
Diarrhea	27	50.9	10	55.5	4	40.0	12	63.1	53	53.0	1.6	0.65
Loss of taste	20	37.7	9	50.0	5	50.0	16	84.2	50	50.0	*12.08*	*0.007**
Loss of smell	24	45.3	8	44.4	5	50.0	11	57.8	48	48.0	1.0	0.79

*: statistically significant.

Table (4): Association of ABO blood groups with susceptibility for COVID-19 infection

Blood Group	Distribution in COVID-19 patients (based on study results)	Distribution in Egyptian people (based on Abdelmonem et al., 2019)	Chi-square	p-value
A	53.0%	35.12%	*6.48*	*0.01**
B	18.0%	23.12%	0.803	0.37
AB	10.0%	9.47%	0.016	0.89
O	19.0%	31.94%	*4.41*	*0.035**

* Statistically significant.

Table (5): Association of ABO blood groups with COVID-19 severity and mortality

Blood Group		A		B		AB		O		Total		test	p-value
		n	%	n	%	n	%	n	%	n	%		
Severity	**Mild**	33	62.3	13	72.2	6	60.0	16	84.2	68	68.0	3.53	0.31
	Moderate	8	15.1	3	16.7	0	0.0	3	15.8	14	14.0	1.83	0.6
	Severe	3	5.6	2	11.1	4	40.0	0	0.0	9	9.0	*14.43*	*0.002**
	Critical	9	17.0	0	.0.0	0	0.0	0	0.0	9	9.0	*8.77*	*0.032**
Mortality	**Yes**	9	17.0	0	0.0	0	0.0	0	0.0	9	9.0	*8.77*	*0.032**
	No	44	83.0	18	100.0	10	100.0	19	100.0	91	91.0		

*: statistically significant. Used tests in analysis include Chi square or Fisher exact test.

DISCUSSION

The corona virus disease-19 had been detected in Wuhan, China at the end of December 2019. Then, it rapidly spread all over the world [7].

More than 200 countries all over the world reported COVID-19 infection. It threatened human life. World health organization (WHO) declared the infection as an international public health emergency, due to its wide spread and high fatality [8].

In this study, we demonstrated the relationship between ABO blood groups in one hand and COVID-19 severity in the other hand, and investigated whether some blood groups are more or less liable to have the severe or critical forms of the disease in comparison with others. Also, we discussed the relationship between blood groups and disease-related mortality.

In the current work, the mean age of studied patients was 45.7 years, and 53% of them were males. There is no previous explanation for this predilection among COVID-19. However, one explanation could be due to some complications that indirectly increase the infection risk or death among males. For example, cardiovascular diseases and high-risk behaviors (social isolation, smoking, alcoholism and specific occupational exposures) are associated with male gender [9].

In line with us, *Ge et al.*,[10] showed that among their 300 COVID-19 patients, males were more predominant than females, and was more prominent in deceased cases. As well, prior studies revealed that males outnumbered female, and disease was more severe in males. Additionally, mortality was significantly increased in males than females (67.6% vs. 32.4% respectively) [11].

No official data are available about the distribution of ABO blood groups among the Egyptian population. However, international reports marked the O group as the most common in Egypt, these reports depended largely on questionnaires rather than scientific surveys [6]. Most of those questionnaires showed that more than 40% of the Egyptian adults do not know their ABO blood group, rendering the collected data unreliable.

On the other hand, many national studied ranked the ABO blood group A to be the most prevalent among Egyptians, followed by O group, then B group and lastly AB group [12].

The largest Egyptian study investigating the prevalence of ABO blood groups included 40591healthy blood donors, and concluded that 35.12% of Egyptians carry the blood group-A, 31.94% have the blood group O, 23.12% possess the blood group B and the remaining

9.47% are of the blood group AB [6].

Comparing the later distribution as a reference for ABO blood groups distribution in the Egyptian population with our results revealed a significant higher affinity of blood group A to develop COVID-19 infection (p-value= 0.01), whereas blood group O presented a significant lower affinity to develop COVID-19 infection (p-value=0.035). Other blood groups did not show any positive or negative associations.

Recent studies have linked ABO blood groups with susceptibility of COVID-19 infection. Blood groups A, B and AB were proposed to be risk factors for infection. However, group O was linked to a reduced risk [13]. However, a prior study on hospital workers with infection, showed that workers with O-group were less likely to contract SARS-CoV infection than non-O workers [14].

Merging with our results, *Zhao et al.* [15] reported a probable association between blood group-A and an increased risk for COVID-19, while group-O was linked to a lower risk of COVID-19 infection.

Similarly, *Wu et al.* [16] noted increased risk of COVID-19 infection in individuals with blood group-A (OR: 1.249, $P < 0.001$) and reduced odds of infection among individuals with group-O (OR: 0.699, $P < 0.001$) in the 31000 patients included in their study.

In agreement with us a huge meta-analysis of 225556 subjects, mean age of 54 years showed that the absolute risk reduction (aRR) of SARS-CoV-2 infection for blood group-O versus (A, AB and B blood groups together) was 0.88, reflecting that patient with "O" blood group is less liable to catch infection than other blood groups. In addition, the same study concluded that Rhesus-negative blood group was protective against infection especially with those of group O (O^-) [17].

On the same line, *Bryan et al.* [18] found an increased risk of infection in A- and a reduced risk in O-blood groups. Also, *Diaz et al.* [19] reported that blood group-A was the commonest in COVID-19 infection. Compared to the healthy individuals (without COVID-19 infection), blood group A was more common in the COVID-19 than non-COVID-19 groups and the O-blood group was less common among COVID-19 than the non-COVID patients. As well, Li *et al.*,[20] reported that COVID-19 infection was seen more in group A and less in group-O than in normal population.

Many theories explained the protective nature of blood group O to Coronavirus infection (including COVID-19). One of them is that the anti-A and anti-B antibodies produced in subjects with group O could potentially block viral adhesion to cells, that could explain the lower risk of infection associated with blood group-O [3]. In addition, subjects with blood group-O had a lower value of angiotensin-converting enzyme (ACE), while group A had positive link within ACE activity. ACE activates angiotensin, and thus lower ACE levels can reduce the hypertension risk, a risk for COVID-19 infection [21].

In this study, we reported that severe form of disease was significantly higher in AB group when compared with A, B and O groups (40% vs. 5.6%, 11.1% and 0% respectively) (p-value= 0.002), while the critical form was significantly higher in the A group in comparison with B, AB and O groups (17% vs. 0%, 0% and 0% respectively) (p-value= 0.032). The mild and moderate forms showed non-significant associations with blood groups.

These results are corresponding to those obtained by an American study included 125 patients, which demonstrated that critically ill patients with COVID-19 infection who had blood group A or AB had a higher risk for mechanical ventilation (MV), continuous renal replacement therapy (CRRT) and prolonged stay in intensive care unit (ICU) than those with blood groups O or B [18].

Similarly, *Wu et al.* [16] recorded that individual with blood group AB had an increased risk to have sever COVID-19 infection (OR: 2.424, CI: 0.934-6.294).

In the current study, we observed a significant positive association between COVID-19-related mortalities and blood group A (17%), and all recorded mortalities were confined to the blood group A. This association was not found in other blood groups (0%), with a p-value= 0.032.

These findings are coinciding with *Diaz et al.*,[19] who found that patients with blood group A had a longer stay in ICU and a higher mortality rate. Likewise, *Zhao et al.*,[15] reported a possible association between blood group A and a higher risk for COVID-19 mortality.

Meeting us in many points, an Egyptian study included 507 patients reported that non-O blood groups were associated with increased risk of severe disease; (7.1%) in group A+, (26.7%) in group A−, (11%) in group B+ and (9%) in group AB respectively, compared with only (3.1%) of the O group patients. As well the non-O patients were of higher risk of mechanical ventilation; (5.9%) in group A+, (13.4%) in group A−, (11.1%) in group B+, (9%) in AB group, whereas it was only (1%) in group O. Moreover, mortality was high in blood groups A and B, (4.37%) and (5.5%), respectively, while in blood group O it was only (1%) [22].

In contrary to our results, Lehrer and Rheinstein [23] concluded that ABO blood groups had no relation to COVID-19 susceptibility nor mortality. Furthermore, Ishaq *et al.*,[24] observed no association between blood groups and either COVID-19-related severity or mortality.

Conclusion: There is an association between ABO blood groups and either COVID-19 susceptibility, severity and mortality.

Financial and Non-Financial Relationships and Activities, and Conflicts of Interest

None

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