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Medicine

STUDY ON THE COVID-19 SUSCEPTIBILITY, SEVERITY AND MORTALITY AMONGST THE ABO BLOOD GROUPS

Talib S H*	Professor Emeritus, Department of Medicine, MGM Medical College and Hospital, Aurangabad. *Corresponding Author
Bhattu S R	Associate Professor, Department of Medicine, MGM Medical College and Hospital, Aurangabad.
Pranita B	Resident, Department of Medicine, MGM Medical College and Hospital, Aurangabad.

ABSTRACT **Introduction-** The very well-known CoVID-19 pandemic has been known to present as asymptomatic mild infection to severe life-threatening illness. The spectrum of illness differs among the population depending upon the risk factors, modifiable and/or non-modifiable to a greater extent. With the introduction of a new variant, the spectrum of initial symptoms has widened with increased variability of presenting symptoms. It is observed that few people infected by coronavirus have become seriously ill while others showed little or no signs or symptoms related to CoVID-19. There have been plenty of evidences that suggest the role of ABO blood groups with susceptibility to CoVID-19 pneumonia and its severity. This study was undertaken to investigate the relationship in regards to susceptibility, variabilities between ABO blood groups distribution and clinical characteristics in CoVID-19 patients.

Aims and Objective-

- To analyse the differences in ABO blood group distribution between CoVID-19 patients and the control group
- To find out any relationship between blood type A, B, O and AB with clinical characteristics of CoVID-19 patients admitted in ICU/ non-ICU wings
- To record the outcome of the patient's hospitalization with pneumonic affection/ respiratory failure in relation to blood groups.

Material and Methods- The study was conducted as a retrospective case control study using case records of patients hospitalized as ICU / non-ICU CoVID-19 cases admitted in MGM medical college, Aurangabad during the epidemic for a total duration of 2 years from 2020 to 2022. A total of 325 patients with confirmed diagnosis of CoVID-19 and 325 healthy individuals were selected as controls who all had been to this centre for blood donation, before the onset of outbreak. Demographic characteristics and all clinical details were collected from patients file and reviewed. ABO and Rh Blood determination was conducted in central lab using the gel method. The institutional ethical approval for the study was obtained from the institution.**Conclusion-** The current study showed that patients with blood group A had rapid clinical deterioration and progression of clinical illness with higher mortality. The mortality was observed higher with blood group A than B, O and AB blood groups. The role of ABO blood group in CoVID-19 infectivity requires additional study for accumulating evidences regarding severity and mortality in CoVID-19 disease.

KEYWORDS : CoVID-19, ABO blood groups, Rh blood groups

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Inclusion Criteria-

Records of patients with positive real time polymerase chain reaction (RT-PCR)/ Rapid antigen tests (RAT)test results performed on swabs with synthetic fibres from either nasopharyngeal or oropharyngeal samples with the age of >18yrs. All such patients were considered for the study without any exclusion criteria.

Results-

The patients were studied in two groups according to age <40 years and >40 years. <40 years age cases were 115 (35%) and >40 years were 210 (65%). The distribution of ABO blood groups in both the age groups was statistically insignificant (P= 0.999).

Among cases, male patients were 233 and female were 92. Male predominance was seen among the cases. Male preponderance is observed in control because of higher percentage of male blood donors.

The distribution of A, B, AB and O blood groups in the patients were 105, 101, 90 and 29 respectively whereas in controls these values were 85, 101, 101 and 38 respectively. No preponderance of a particular group was observed. The study was extended to record Rh blood group. Rh positive amongst cases were 303 and Rh negative were 22. Rh positive among controls were 308 and Rh negative were 17. No preponderance was observed in either group.

The distribution of total cases according to blood group and gender revealed male cases 78 (24%) were of blood group A, 71 (22%) of blood group B, 63 (19%) in blood group O and 21(7%) in blood group AB. Among female cases, 27 (8%) were blood group A, 30 (9%) were blood group B, 27 (8%) were O and 8 (3%) were AB. The correlation of gender in different blood group in the studied cases was not significant (P=0.901).

Of 103 (32%) individuals who were admitted to ICU, 79 (24%) were males and 24 (8%) were females. Of 222(68%) individuals were admitted in general wards, among whom 154 (47%) and 68 (21%) were males and females respectively. There was no statistically significant difference in the severity of disease with respect to gender (P=0.1736).

Also, amongst the 103 individuals admitted to the ICU wing, blood group A cases were 39 (12 %), B cases were 27 (8 %), AB cases were 7 (2 %) and O cases were 30 (10 %). No statistically significant difference was found for severity of the disease with respect to ABO blood group (table 1).

Table 1: Distribution of cases according to ABO blood group & ICU admission

Sr. No.	Blood group	ICU N (%)	Non-ICU N (%)	Total N (%)	Odds Ratio (95 % CI)	P Value
1	A	39 (12 %)	66 (20 %)	105 (32 %)	1.44 (0.88 to 2.35)	0.145 (NS)
2	B	27 (8 %)	74 (23 %)	101 (31 %)	0.71 (0.42 to 1.19)	0.197 (NS)
3	AB	7 (2 %)	22 (7 %)	29 (9 %)	0.66 (0.27 to 1.60)	0.362 (NS)
4	O	30 (10 %)	60 (18 %)	90 (28 %)	1.10 (0.66 to 1.86)	0.694 (NS)
Total		103 (32 %)	222 (68 %)	325 (100 %)	-	-

Similarly, Rh blood group distribution was studied in cases admitted in the ICU. Rh Positive cases were 98 (30 %) and Rh negative were 5 (2%). No statistically significant difference was found for severity of the disease with respect to Rh blood group (table 2).

Table 2: Distribution of cases according to Rh blood group & ICU admission

Sr. No.	Rh blood group	ICU N (%)	Non-ICU N (%)	Total N (%)	Chi square	P value
1	Rh Positive	98 (30 %)	205 (63%)	303 (93 %)	0.876	0.349 (NS)
2	Rh Negative	5 (2 %)	17 (5 %)	22 (7 %)		
Total		103 (32 %)	222 (68 %)	325 (100 %)		-

In our study, of 325 cases admitted, 301 (92.6 %) patients were discharged and mortality found in 24 (7.4%) cases. In the patients who succumbed to death, blood group A were 12 (3.6%), blood group B were 2 (0.6 %), blood group O were 2 (0.6 %) and blood group AB were 8 (2.4 %). Blood group A was associated with poor clinical outcome of the patient and statistically significant outcomes were found for the same (table 3).

Table 3: Distribution of total cases according to blood group & outcome

Sr. No.	Blood groups	Discharge N (%)	Death N (%)	Total N (%)	Odds Ratio (95 % CI)	P Value
1	A	93 (28.6 %)	12 (3.6 %)	105 (33 %)	2.23 0.968 to 5.16	0.05 (S)
2	B	99 (30.4 %)	2 (0.6 %)	101 (31 %)	0.18 0.04 to 0.80	0.2 (NS)
3	AB	27 (8.3 %)	2 (0.6 %)	29 (9 %)	0.922 0.20 to 4.13	0.91 (NS)
4	O	82 (25.2 %)	8 (2.4 %)	90 (27 %)	1.33 0.55 to 3.23	0.52 (NS)
Total		301 (92.6 %)	24 (7.4 %)	325 (100 %)	-	-

Of the 301(92 %) patients discharged, 110 (33.8%) were <40 years of age and 191 (58.7%) were >40 years of age. 24 patients died, with 5(1.5%) in <40 years of age and 19 (5.8%) in >40 years of age. No statistically significant correlation was found between age and outcome of the patients.

Similarly, correlation between gender and outcome of the disease was studied. Of the 71.6% males affected by CoVID-19, 66.1% were discharged and 5.5% died. Of the 28.3% females affected, 26.5% were discharged and 1.9% died. No statistically significant outcome was noted.

Among 109 (33.5%) patients with comorbidities like diabetes mellitus, hypertension, ischemic heart disease, chronic kidney disease etc, 100 (30.8%) were discharged and 9 (2.8%) died. Among patients without any comorbidities ie. 216 (66.5%), 201(61.8%) were discharged and 15 (4.6%) died. No statistically significant correlation was noted.

Discussion-

Biological factors which determine the severity and susceptibility of CoVID-19 infection are still ill understood. The ABO blood grouping are reported to have influences on the susceptibility of the CoVID-19 infection and the severity of the disease [(1)].

Of the known 39 blood group systems and 350 antigens recognized by the ISBT, the ABO blood group system is the most important and the most commonly used system(2). The determination of blood groups depend upon the presence or absence of A or B antigens, both of which are co-dominantly inherited. Depending upon the blood groups, the antibodies present in the circulation of such individuals vary, like presence of antigen A in circulation leads to formation of anti-B antibodies, presence of antigen B in circulation leads to formation of anti-A antibodies, absence of both the antigens, like in blood group O shows the presence of both anti-A and anti-B antibodies in the circulation. In contrast, AB blood group individuals do not show the presence of either anti-A or anti-B antibodies. These antibodies develop within a few months of life produced by our body after exposure with non-self A or B antigens depending upon the individual's blood group, notably during exposure to new food and micro-organisms, commonly the gut microbiota. These antigens are not only present on the RBC surface but also in various body secretions, surface of other human cells, including epithelium, platelets and vascular endothelium[(3)].

The susceptibility of common viral infections such as Norwalk virus and Hepatitis B has been correlated earlier to ABO blood group. Associations have also been frequently observed in infections such as tuberculosis, malaria, cholera, retrovirus, Chikungunya virus, Helicobacter pylori (H. pylori) and Escherichia coli[(4)]. It was also reported that blood group group O individuals were less likely to become infected by SARS-CoV2 virus [(1)].

The mechanisms involved may be –

- Molecular mimicry between pathogen and host
- ABO antigens acting as receptors for the pathogens, natural antibodies and lectins as inhibitors
- ABO acting as receptor for toxins, virulence factors or other pathogenic products[(5)]

Stussi et al in their study suggested the relationship between anti-A and anti-B with virus cell and their interactions. It was observed that the disease was less in patients with circulating anti-A. Also anti-A in group O was more protective than the anti-A in group B, which may be due to increased presence of IgG anti-A, B in plasma of group O individuals.[(6)] Takagi in his study observed a significantly lower mortality in individuals with blood group O.[(7)] Latz et al evaluated relationship between the Rhesus blood group and CoVID-19 and observed a higher incidence of CoVID-19 infection in people with Rh positive status as compared to Rh negative. [(8)]

Li et al suggested a higher risk of hospitalization in blood group A patients with CoVID-19 disease with lower risk in blood group O individuals.[(9)] A nested prospective observational study done by Hoiland et al of critically ill patients with CoVID-19 suggested that patients with blood group A or AB had an increased risk of requiring mechanical ventilation, continuous renal replacement therapy and prolonged intensive care unit admission as compared to blood groups O or B.[(10)]

Another retrospective cohort study done by Barnkob et al suggested ABO blood group as a risk factor for CoVID-19 infection but not for hospitalization or death.[11] Many mechanisms supporting the association of ABO blood groups with susceptibility, severity and mortality due to CoVID-19 infection have been proposed. One such mechanism describes that anti-A and anti-B in the circulation binds to the viral antigens on the surface of the viral envelop, neutralizing them and preventing further infection of the target cells. This could explain the differences in susceptibility of different groups towards the SARS-CoV 2 infection.[12] For example, anti A antibody found in blood group O individuals would bind to the viral envelop produced by an infected group A or AB individual. Controversy exits in this mechanism as the virus in such a group O patient would subsequently lead to viral replication expressing the H antigen on its envelop. The titre of anti A and anti B antibodies found varies from individual to individual, thus, the neutralizing effect of these antibodies is also highly variable. It is also hypothesized that the disease severity is directly related to the amount of infecting viral load and subsequent load of viral replication, neutralizing it with naturally occurring antibodies, e.g. anti A could attenuate the infection, may not prevent it completely but may tone down the severity. The portal of entry, being the respiratory and less commonly digestive tract, these antibodies need to have high concentrations at these sites in order to neutralize the invading virus.

Breiman et al observed identification of SARS-COV-2 S proteins by anti A antibodies, which react and prevent further interaction of the virus with angiotensin converting enzyme 2 receptor (ACE2R), subsequently preventing their entry into the body through the respiratory epithelium. This study supports the concept of dose dependent interaction between the ACE2R and the SARS-COV-2 by the anti A antibodies in a dose dependent fashion. Thus, according to this theory, anti A antibodies block the viral attachment and/or entry. The activity of ACE2 in blood group B was much higher than in blood group O which makes the susceptibility of infection more in blood group B than in O, subsequently explaining the prevalence of more critical patients and higher mortality of patients in blood group B as compared to O.[12]

Wu, Arthur and colleagues argued that the receptor binding domains (RBD) of SARS-COV2 may share sequence similarity to an ancient lectin family known to bind blood group antigens. SARS-COV-2 RBD binds to blood group A expressed on respiratory epithelial cells, which could explain the linkage between blood group A and SARS-COV-2.[13]

The severity of the SARS-COV-2 infection in blood group A individuals with increased angiotensin converting enzyme-1 (ACE1) activity was studied by Goel et al. Blood group A individuals show increased levels of vWF and factor VIII in their circulations, which also predisposes to cardiovascular complications. vWF is an acute phase reactant whose levels are increased in such inflammatory conditions. In individuals of blood group A, the levels of vWF are already on the higher side of the normal, thus, adding to higher severity of infection in individuals with blood group A. The variability in the anti A, anti B titres and affinity of the angiotensin converting enzyme 2 receptor (ACE2R) to bind to the viral envelop may at times confound each other and the factor responsible for the severity of the infection may mask the actual factor responsible for the infection.[5]

Conclusion-

The current study showed that patients with blood group A had rapid clinical deterioration and progression of clinical illness with higher mortality. The mortality was observed higher with blood group A than B, O and AB blood groups.

The role of ABO blood group in CoVID-19 infectivity requires additional study for accumulating evidences regarding severity and mortality in CoVID-19 disease.

Table 4: Summary of various studies on the COVID-19 susceptibility, severity and mortality amongst the ABO blood groups [5]

Author	COVID-19 patients	Controls (healthy individuals)	Blood group susceptibility to CoVID-19 infection	Association with severity or mortality from the disease
Zhao J et al	1775	3694	Yes, group A	Group A associated with higher risk of mortality than non-group A
Li J et al	2153	3694	Yes, group A	Group A patients at higher risk of hospitalization. Association with risk of mortality not assessed.
Zietz M et al	14,112	None	Yes, group B & Rh(D)	Severity decreased among blood group A & increased among AB & B. Risk of morality increased for blood group AB & decreased for A & B. Rh-negative blood type protective for mortality.
Wu et al	187	1991	Yes, group A	Group A influenced clinical outcomes but no association with mortality
Latz CA et al	1289	Nil	Yes, positive correlation with group B, AB & Rh(D) Negative with group O	No association with risk of intubation, peak of inflammatory markers and death
Abdollahi A et al	397	500	Yes, group AB	No association of ABO or RHD phenotype with severity or mortality of disease.
Hoiland et al	125 critically ill patients admitted to ICU	Nil	Yes, group A & AB	Higher proportion of COVID-19 patients with blood group A or AB required mechanical ventilation, continuous renal replacement therapy and had longer ICU stay compared with patients with blood group O or B.
Barnkob et al	7422	466 232	Yes, Decreased infection risk in group O	ABO blood group as a risk factor but not for hospitalization or death.
Talib et al	325	325	No	Blood group A associated with higher risk of mortality

REFERENCES-

1. Cheng Y, Cheng G, Chui CH, et al. ABO blood group and susceptibility to severe acute respiratory syndrome. JAMA. 2005;293(12):1450 –1451
2. Piccinni MP, Vultaggio A, Scaletti C, et al. Type 1 T helper cells specific for Candida albicans antigens in peripheral blood and vaginal mucosa of women with recurrent vaginal candidiasis. J Infect Dis. 2002;186:87–93.
3. Pal M, Berhanu G, Desalegn C et al. Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2): an update. Cureus. 2020;12(3)
4. Eder AF, Spitalnik SL: Blood Group Antigens as Receptors for Pathogens; in: Blancher A, Klein J, Socha W (eds): Molecular Biology and Evolution of Blood Group and MHC Antigens in Primates. Berlin, Heidelberg, Springer, Berlin Heidelberg, 1997:268–304
5. Goel R, Bloch EM, Pirenne F et al. ABO blood group and COVID-19: a review on behalf of the ISBT COVID-19 Working Group. Vox Sang. 2021;116(8):849-861
6. Stussi G, Huggel K, Lutz H, et al. Isotype-specific detection of ABO blood group antibodies using a novel flow cytometric method. Br J Haematol. 2005; 130:954–63
7. Takagi H: Down the Rabbit-Hole of blood groups and COVID-19. Br J Haematol. 2020;190:e268–e270
8. Latz CA, DeCarlo C, Boitano L, et al. Blood type and outcomes in patients with COVID-19. Ann Hematol. 2020; 1–6
9. Li J, Wang X, Chen J, et al.: Association between ABO blood groups and risk of SARS-CoV-2 pneumonia. Br J Haematol. 2020;190:24–7.
10. Hoiland RL et al. The association of ABO blood group with indices of disease severity and multiorgan dysfunction in COVID-19. Blood Adv. 2020;4(20):4981–4989
11. Barnkob MB: Reduced prevalence of SARS-CoV-2 infection in ABO blood group O. Blood Adv. 2020;4(20):4990– 4993
12. Breiman A, Ruven-Clouet N, Le Pendu J: Harnessing the natural anti-glycan immune response to limit the transmission of enveloped viruses such as SARS-CoV-2. PLoS Pathog 2020;16:e1008556.
13. Wu S, Arthur CM, Wang J, et al. SARS-CoV-2 Receptor Binding Domain Preferentially Recognizes Blood Group A. Blood Adv.2021;5(5):1305-1309