Original Article

What is in a Blood Group? ABO and Rh Blood Types in COVID–19: Correlation with Clinical Outcomes in A Tertiary Care Centre in India

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Abstract

Background: COVID-19 pandemic has immensely burdened healthcare. Susceptibility and severity of infection though largely determined by an individual's immunity, age and co-morbidities; however, recent literature reported that ABO blood type might be a contributory factor by virtue of its antigenic properties. ***Objective:*** To explore the distribution of ABO & Rh blood types in COVID -19 patients and correlate the same with clinical severity and mortality. ***Methods:*** This retrospective study was conducted from May 2020 to September 2021 at a tertiary care centre. Data of ABO & Rh blood type of COVID-19 patients admitted to our hospital was collected. Details on severity and mortality was obtained from hospital database. Pearson's chi square test was used to compare categorical data. p-value<0.05 was considered statistically significant. ***Results*****:** A total of 548 cases were included, with mean age of 48.8 ±7.1 years and male predominance. O positive (45.1%) and A negative (0.7%) were most and least frequently affected respectively. Majority were Rh positive (96.0%). 143 were severely ill requiring intensive care. Among the fifty-six deceased, most belonged to O blood group. No significant association was observed between blood type with severity/mortality. ***Conclusion:*** ABO blood type cannot be a pivotal biomarker for predicting COVID-19 associated severity and mortality. With limited literature in this field revealing diverse findings, a definitive association between blood type and COVID-19 is challenging. This may indicate unexplored underlying contributing factors, not necessarily blood group or type of antibodies present.

Keywords: Blood group antigens, COVID-19 pandemic, Coronavirus

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Introduction

COVID-19outbreak has infected countries worldwide including developing countries like ours and caused enormous burden on economy and healthcare. Since the declaration of this viral infection as pandemic in 2019, global research has been focussing on identifying methods of diagnosis, treating the infected and preventing its spread.The pathogenesis, progression and clinical presentation of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) have been evolving and intriguing ever since the start

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of this pandemic. Recent research stated that the type of ABO blood type might be a predisposing factor for COVID-19.[1-3] Blood group antigens are recognized to serve as receptors and/or coreceptors for various biological agents, thereby playing a direct role in infection. The same antigens also enhance uptake of virus inside the infected cell, signal transduction and fastening reorganization of membrane microdomains. Differences in antigen expression can alter the first line of defence or innate immune response of the body to infection.[4] Helicobacter pylori,[5] Vibrio cholerae,[6] Hepatitis C virus,[7] Human immunodeficiency virus,[8] and SARS,[9,10] are some of the infectious agents that have been shown to be associated with human blood types.Several reports and studies have cropped up regarding amenability of ABO blood groups to severe COVID-19infection. However, there is paucity of data in Indian scenario and in our geographical area.

Blood grouping being an inexpensive, commonly ordered,quick and basic investigation; Hence, we intended to study the distribution of ABO and Rh blood typesin COVID-19 positive cases and correlate them with severity and mortality.

Methods

This retrospective cross-sectional study was conducted in the Haematology section of central laboratoryof Dr. Chandramma Dayananda Sagar Institute of Medical Education and Research, Harohalli Ramanagara, which is located at a rural geographic region in , Karnataka of South India.

Inclusion criteria: All Reverse transcriptase Polymerase Chain Reaction (RT PCR)/ Rapid Antigen Test (RAT) positive adult patients equal to or more than eighteen years of age admitted to our hospital from May 2020 to September 2021 with blood group reports being available. *Exclusion criteria:*Patients whose blood grouping reports were not available.

Data regarding age, gender, intensive care units (ICU) admission and mortality were obtained from hospital and laboratory database. Blood grouping (ABO and Rh type) was ordered in patients as part of the COVID profile testing. Slide method was used to perform blood grouping, with normal saline being used as control.Antisera used were procured from vendors approved by the hospital vendor management system after vendor feedback evaluation and review. Antisera used was Eryscreen from Tulip Diagnostics (ISO13485 certified company), which is a reagent combi pack under Invitro Diagnostic reagents for routine blood grouping and typing. The reagents comprised ready to use solutions of Anti -A, Anti -B, Anti -D of the immunoglobulin class IgM. Quality checks for affinity and avidity of the anti-sera were run daily as per the laboratory protocols. Doubtful agglutination or groups with weak/late agglutination were confirmed by microscopic examination and gel card method when indicated. The patients were categorized into non severe and severe groups for comparison as per standard national guidelines.[11] Mild and moderate categories were considered as non-severe group. The severe category as per the guidelines was retained as the severe group.

Quantitative data was expressed as mean±SDand range. Qualitative data was expressed as numbers and percentages. Categorical data was compared using Chi-square test. SPSS software version 26.0 was used for analysis. A p-value<0.05 was considered to be statistically significant.

Results

The study sample comprised of 548 COVID positive patients with an age range of 18 to 92 years, and a mean of 48.82 ± 17.12 years. The group comprised of 318 (58%) males and 230(42%) females with a male-female ratio of 1.4**:**1. Among these, 124 patients (22.63%) belonged to blood group A, 140(25.55%) had group B, 27(4.93%) had group AB and 257(46.89%) had group O. The distribution of ABO and Rh blood groups in the study population is described in Table 1. The most frequently and least frequently encountered blood groups were O positive and A negative respectively. Rh positivity was noted in 526 (96%) of the cases with the rest being negative for the Rh factor. When classified based on severity, in both non severe and severe groups, majority of the patients belonged to O positive blood group (Table 2).Among the 56 patients who succumbed to the disease, O positive group had the most fatalities, followed by A positive and B positive(Figure 1). In the comparative analysis of Rh type regarding severity and mortality, no statistically significant correlation was observed (Table 3).None of the comparative analyses of O, A, B, and AB groups with other blood groups revealed a significant relationship with severity of the disease or mortality (Table 4).

Table 1. Distribution of ABO and Rh blood groups in the study population

Blood Group	Rh Status of cases		Gender		Total number of cases
	Positive	Negative	Male	Female	
A	120	04	66	58	124
B	132	08	89	51	140
AB	27	0	10	17	27
O	247	10	153	104	257

Table 2. Distribution of blood groups in non-severe and severe groups

Blood Group	Rh type	Number of patients	Non-severecases	Severe cases
A	Positive	120	86 (21.2%)	34 (23.8%)
	Negative	4	03 (0.7%)	01 (0.7%)
B	Positive	132	98 (24.2%)	34 (23.8%)
	Negative	8	05 (1.2%)	03 (2.1%)
AB	Positive	27	23 (5.7%)	04 (2.8%)
	Negative	0	0	0
O	Positive	247	185 (45.7%)	62 (43.3%)
	Negative	10	05 (1.2%)	05 (3.5%)
Total		548	405	143

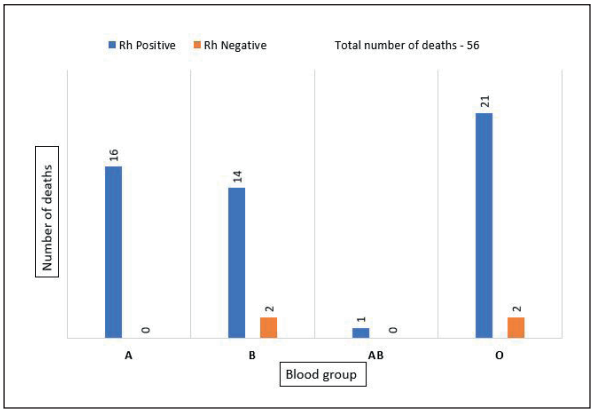

Figure 1. Comparison of mortality between blood groups

Table 3. Analysis of severity and mortality according to Rh-factor

Rh status	Severity of cases			Mortality in cases		
	Severe (n=143)	Non severe (n=405)	p-value	Yes (n=56)	No (n=492)	p-value
Positive	134	392	0.17	52	474	0.36
Negative	9	13		4	18	

Table 4. Analysis of severity and mortality according to ABO blood groups

Blood group in cases	Category of cases			Mortality in cases		
	Severe	Non severe	p-value	Yes	No	p-value
Group A (n=124)	35	89	0.61	16	108	0.34
Other (B,AB,O)	108	316		40	384	
Group B (n=140)	37	103	0.99	16	124	0.69
Other (A,AB,O)	106	302		40	368	
Group AB (n=27)	4	23	1.3	1	26	0.41
Other (B,A,O)	139	382		55	466	
Group O (n=257)	67	190	0.93	23	234	0.43
Other (B,AB,A)	76	215		33	258	

Discussion

The emergence of SARS-CoV-2 virus has led to worldwide public health catastrophe and has affected healthcare systems worldwide. Post emergence of the pandemic in Wuhan province of China,a study reported higher risk of infection for people with blood group A, and lower risk for people with blood group O. [1]Subsequently, association of this infection with ABO blood groups has been described in several studies from China and other countries from Asia, North America, Europe and Middle East.

ABO antigens are expressed on many different cell types including the erythrocytes. They are

structurally carbohydrates which constitute the terminal motifs of either N-linked or O-linked chains of glycoproteins and glycolipids. Literature states that anti-A antibodies specifically hinder the adhesion of SARS-CoV S protein-expressing cells to angiotensin converting enzyme 2 (ACE2) expressing cell lines, thereby playing a defensive role.[12] Activity of ACE2 enzymes in blood group B is comparatively more than those of blood group O, predisposing group B persons to a higher infective risk.[13] Through glycosylation, ABO determinants may influence host–pathogen interactions. The naturally produced Anti-A and Anti-B antibodies may also alter amenability to COVID-19 infection.

It has been shown that A group individuals have a higher and O group individuals,a lower frequency of being infected by COVID-19.[2,14-16] However, a multi-institutional study in Massachusetts observed a higher probability of blood group B individuals to test positive for COVID-19.[17] An Indian study too found a positive correlation between blood group B and COVID-19 infection.[18] Overall, in most research, blood group O was associated with a lesser risk, while non-O blood groups were found to be detrimental.

Our data found O group to be most commonly affected, similar to a cross sectional observational study in Bahrain.[19] Individuals with AB group and Rh negative type showed a lower risk of infection, similar to other studies.[1,3,14] In all the above scenarios including ours, the study groups were defined by a relatively small sample size.

To analyse the association between blood group and severity of COVID-19 infection, distribution of blood groups was compared between infected caseswho required ICU admission (severe) and cases which did not(mild and moderate categories). The blood group distribution was analysed with respect to mortality as well. No significant association was observed between blood group and severity of infection nor blood groups and mortality rates. Our results are in agreement with few other international studies.[17,19] However, researches from China, Bahrain and Turkey found group A to be associated with higher severity and mortality. A cohort study of 383 COVID positive individuals in north India found higher prevalence of moderate to severe infection in A and B positive groups.[20] Another prospective case control study with a large sample size conducted in USA also found no inter relationship between blood of ABO and Rh groups with either disease susceptibility or severity.[21]

Our findings are based on data collected as part of hospital admission through the pandemic. The data is enriched for moderate to severely ill patients. Patients with mild category of disease who treated on outpatient basis and were not included in the study.

To determine susceptibility of a particular blood group in a population to COVID-19, the blood type of affected individuals must be analysed with reference to blood group distribution in that region. The ABO gene is highly polymorphic, and blood types have markedly different distribution across ethnic groups. The population mobility of a region may change the distribution pattern of blood groups over time. Also, a review on relationship between ABO blood types and COVID-19 states that it isthe ABO coefficient of variation, over the frequency of each individual phenotypethat determines impact of the ABO system on virus transmission. This is because frequencies of ABO phenotypes are immensely diverse between populations or geographical areas.[22] A good organization, long duration, serious workload, and high costs are required for determination of blood group distribution in a regional population, which is challenging.

*Strengths and limitations:*The present study was undertaken when the second wave of the pandemic was at its peak in our geographical area. As affordable healthcare is challenging in developing countries like ours, using simple and affordable investigations like blood groups we have tried to correlate the clinical implications. Though not generalizable the study has given insights into creating opportunities for further research regarding blood group antigens and COVID-19. Our study has a few limitations. It included mainly mainly cases admitted to health care facilities and not treated on outpatient basis.This could be one of the contributing factors for varied associations with different blood groups.Varying protocols of

practice and patient management protocols during the pandemic may hinder generalization.

*Future implications:*Results from literature review, and our study, reveal myriad findings making a conclusive association between blood type and COVID-19 challenging. Ancillary studies, with stringent control in terms of topography, genetics, and viral strain, are required to validate association between blood type and COVID-19. Supportive information on blood types would help propose newer treatment strategies, if significant association is proven by large scale studies.

Conclusion

Our study did not observe significant interrelation between ABO and Rh blood type with COVID-19 severity and mortality, though blood group O patients were most affected. This may indicate presence of unexplored underlying factors that may be contributing to association, not necessarily blood group of the individual per se.

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Ethical approval: Ethical approval was obtained fromInstitutional Ethics Committee ofDr. Chandramma Dayananda Sagar Institute of Medical Education and Research, Karnataka, India**(**CDSIMER/MR/0013/IEC/2021).

Contribution of authors: Concept and design of the study: AM, AS; data collection and compilation: AM, AS, NG, BKN and analysis: AM, SS; Manuscript writing, editing and approval of final draft: AM AS, NG, SS, KS, BKN

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