Relationship of Blood Group Type and SARS-CoV-2 Infection: Experience in A Peripheral Military Hospital

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Abstract:

Introduction: *Clinical studies have shown that advanced age and chronic diseases increase the risk of infection. Different studies have found blood groups are also a determining factor of severity. However, in Bangladesh it is yet to have any clinical pattern in this respect. The aim of this study is to find out whether there exists a relationship between the blood groups of the patients and risk of SARS-CoV-2 infection.*

Methods: *The study is a retrospective cohort study. It included all hospitalized RT-PCR confirmed COVID-19 patients in Combined Military Hospital (CMH) Barishal. We included both genders and people who are older than 14 years of age. The study was conducted during the period between 4th June and 3rd August, 2020. In this period total 556 individuals reported and tested for SARS-CoV-2 where COVID +ve patients are served as patient group and COVID –ve patients are served as the controls.*

Results: *Our sample consists of 185 patients; we found a percentage distribution of 34.6%, 39.5%, 5.4%, and 20.54% for blood groups A, B, AB and O,*

respectively. Blood group A was statistically significantly more frequent among those infected with COVID-19 compared to controls (34.6% vs. 21.83%, p-value 0.045 (<0.05); OR: 1.894).On the other hand, the frequency of blood group O was significantly lower in the COVID-19 patients, compared to the control group (20.54% vs 32.88%, p-value0.049 (<0.05); OR: 0.528). Although there was a higher percentage distribution of the B blood group among COVID-19 patients as compared to the control groups, this difference did not reach statistical significance. Also, there was no significant difference in the risk of COVID-19 in blood group AB with a distribution of 6.2% in control group, and5.4% in COVID-19 patients.

Conclusion: *The results of the present study suggest that the blood group A might have a role in increased susceptibility to the COVID-19 infection and the blood group O might be somewhat protective.*

Keywords: *ABO, Rh-D, Blood group system, COVID-19, SARS-CoV-2.*

Introduction

The word "blood group" refers to the antigens present on the red blood cell (RBC) surface. "Blood type"

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refers to a specific pattern of antigen-antibody reaction within a specified setting. Austrian Scientist Karl Landsteiner was the pioneer in describing the ABO blood group system in 1900[1]. O, A, and B types are the major blood groups. Due to the different frequency of different ABO blood types among various populations, the ABO blood groups appear to be important during evolution. The second most crucial antigen in blood transfusions is the rhesus-system[2]. An individual's RBC surface may or may not contains Rh or D-antigen; accordingly, Rh-positive (D-antigen present) or Rh-negative (D-antigen absent) blood group is indicated[3]. ABO antigens are expressed in several human tissues and cells, including epithelium, sensory neurons, platelets, and vascular endothelium. It is also simultaneously expressed as a surface molecule[4,5]. It

is, therefore, no wonder that the clinical relevance of an ABO blood group reaches beyond the conventional frontiers of immune- hematological understanding, where the pathogenesis of a wide variety of human diseases, primarily cancers and infections cardiovascular disorders are involved. Non-O blood group reveals that the risk of venous thrombosis is roughly double[6]. The risk of overall mortality in non-O blood groups is comparatively higher from cardiovascular diseases when compared to individuals with the O blood groups[7,8]. In comparison with blood group O, people with blood group A, AB, or B are vulnerable to develop pancreatic cancer[9]. The ABO phenotype relates to the severity of a number of infectious diseases. The severity of cholera infection (*Vibrio cholerae* strains O1 El Tor and O139) is the most prominent amongst the patients with O blood group[10,11]. It has been found that viral infections are linked to the ABO blood group. ABO blood group antigens may affect the vulnerability to Norwalk virus infection.[12] One study also found that blood group O has lower susceptibility to hepatitis B, C, HIV, syphilis or malaria[13].

Corona virus disease 2019 (COVID-19) surfaced in the city of Wuhan located in China, at the end of 2019. This virus rapidly spread and caused the current global pandemic[14]. In Bangladesh up to August 4, 2020 there are 242102 COVID-19 patients with 3184 deaths[15]. Numerous risk factors for COVID-19 have been reported. An increase in the patient's age has become synonymous with a rise in the risk of developing complications and has demonstrated higher death rates. Various studies have concluded that the male gender is more at risk and show more severe complications[16,17]. Various comorbidities such as, inflammatory bowel disease (IBD)[18], pre-existing kidney disease[19], and diabetes mellitus[20] are documented risk factors. A new school of thought and finding is indicative that certain blood groups are more susceptible to the COVID-19 infection in comparison to others. A study conducted by Zietz et al., in the New York-Presbyterian (NYP) group of facilities discovered that Blood group A was associated with increased odds of testing positive for COVID-19 (OR 1.338, 95% CI [1.072-1.672], p=0.009), while O blood groups were associated with decreased odds of testing positive (OR 0.804, 95% CI [0.654-0.987], p=0.036)[21]. This study also follows previous research study on SARS-CoV-2 by

Ellinghaus et al. where they found that patients with blood type A have a higher risk than other blood groups (OR, 1.45;

95% CI [1.20-1.75], P=0.000148) and for blood group O when compared with the other blood groups (OR, 0.65; 95% CI [0.53-0.79], P=0.0000106)[22]. Göker et al. reported that blood group A was (57%) higher amongst the COVID-19 patients followed by the blood group O (24.8 %)[23].

The linkage and effects of blood groups have been hypothesized using different facts:

For example, blood groups are dictated by sugars, and coronaviruses in the cattle have surface proteins that bind to sugars. It might be of value to consider the extra sugar N-acetyl galactosamine, on the surface of blood group A cells [24], possibly suggesting more pathogen contact. This sugar is missing on blood group O cells[24].

SARS-CoV-2 replicates in respiratory and gastrointestinal epithelium[25], that can synthesize A or B glycan antigens, depending on the phenotype. If the S protein of an A, B, or AB group induvial carries respective glycan antigens, it is possible that binding of the respective antibodies can block the interaction between S protein and ACE2, thereby offering complete or incomplete protection[26]. Thus, infectivity between ABO groups can presumably be predicted e.g. the virus produced in an individual with blood group B will be carrying antigen B and has a higher chance of infecting a person with blood group B or AB, as compared to blood group A or O. This can explain the least number of cases in blood group O that contains both antibody-A and antibody-B. It is also believed that once the infection is fully established, it then replicates in the individual's epithelial cells and thus exhibits that individual's antigen, rendering the individual's antibodies ineffective[26].

Here, we investigated the relationship between the ABO blood group type and the susceptibility to COVID-19 in patients who reported to CMH Barishal.

Methods:

Study Design and Participants
This retrospective cohort study included confirmed COVID-19 patents of 14 years or older, irrespective of gender, who were admitted in CMH Barishal from June 4, 2020 to August 3, 2020.

Data Collection

A confirmed case of Covid-19 was identified as a positive result for nasal and pharyngeal swab specimens in real-time reverse transcriptase—polymerase-chain-reaction (RT-PCR) assay.[27] Hospitalized, clinically suspected, total 556 cases were enrolled. RT-PCR confirmed patients (185) were the study cohort, and negative ones were comparator.**Statistical Analysis**

Statistical analysis was performed by using IBM, SPSS version 25. Standard descriptive and analytical statistics were used to analyze the data. Chi-square test was used to test for significant difference and P-value ≤ 0.05 was considered significant.

Results:

The blood group distribution of 185 patients diagnosed with PCR positivity as A, B, O, AB were 34.6%, 39.5%, 20.54% and 5.4% respectively. Rh (+) was 98.9% and Rh (–) 1.1%. The blood group distribution of remaining 371 individuals the comparison group as A, B, O, AB were 21.83%, 39.08%, 32.88% and 6.2%, respectively. Rh (+) was 95.7% and Rh (–) was 4.3% (Table 1). When the test negative comparison group was compared to the COVID-19 patient group, it was observed that the COVID-19 infection rate was statistically significantly higher in those with blood group A (34.6% vs. 21.83%, p-value 0.045; OR: 1.894). In terms of Rh blood group system, it was determined that Rh positivity was also associated with COVID-19 diagnosis but not at significant level (p= 0.163, OR: 4.040) (Table 1). It was observed that the blood group O was significantly lower in the COVID-19 patient group in comparison to the controls (20.54% vs 32.88%, p-value 0.049; OR: 0.528). Although there was a higher percentage distribution of the B blood group among COVID-19 patients as compared to the control groups, this

Table 1: Summary of COV+ vs COV- comparison of individual blood types.

Blood Group	COV+ counts N=185	COV- counts N=371	OR	95% CI	P-value
A	A: 64 (34.60%), Other than A: 121 (65.4%)	A: 81 (21.83%), Other than A: 290 (78.17%)	1.894	(1.011–3.551)	.045
B	B: 73 (39.5%), Other than B: 112 (60.5%)	B: 145 (39.08%), Other than B: 226 (60.92%)	1.018	(.577–1.795)	0.952
O	O: 38 (20.54%), Other than O: 147 (79.46%)	O: 122 (32.88%), Other than O: 249 (67.12%)	0.528	(.278–1.001)	0.049
AB	AB: 10 (5.4%), Other than AB: 175 (94.6%)	AB: 23 (6.2%), Other than AB: 348 (93.8%)	0.864	(.263–2.834)	0.809
Rh	Rh D + : 183(98.9%) Rh D – : 2(1.1%)	Rh D + : 355(95.7%) Rh D – : 16(4.3%)	4.040	(.488–33.420)	0.163

N = Number of individuals having the given blood type who have a recorded test (positive or negative) for SARS-CoV-2, and reports percentages relative to all blood groups.

OR = Odds ratio (COV+ vs COV-).

95% CI = Confidence interval on the OR.

difference was not significant. Also, there was no significant difference in the risk of COVID-19 in blood group AB with a distribution of 6.2% in control group, and 5.4% in COVID-19 patients.

Discussion:

Numerous studies have been published to date on the relationship between blood groups and diseases. [29-32] These studies include hepatitis B, hepatitis C, HIV, West Nile Virus, SARS-CoV and SARS-CoV-2 viruses.[28,30,33] In all these studies raised an issue that some blood groups may be susceptible to viral infections and some groups may be protective. Although many models of this predisposition or protectionism have been established, the mechanism has not been fully elucidated and has been suggested as possible causes. Natural anti-blood group antibodies, particularly anti-A antibody, of the ABO system to block the interaction of SARS-CoV spike protein and angiotensin converting enzyme 2 may be considered as one of the reasons suggested.[34] Several studies investigated the relationship between the ABO blood groups and COVID-19 infection. The first study was conducted in China and it was published on March, 2020.[34] The second study was conducted in New York, USA, and published on April, 2020.[35] In our control group, we found that blood groups B (39.08%) and O (32.88%) were the two most frequent blood groups which also follow the previous study about the general distribution of ABO and Rh blood group among the general population of Bangladesh where most frequent blood groups were B (39.8%) and O (27.6%).[36] In this study, we found that ABO blood groups displayed different association risks for the infection with SARS-CoV-2 resulting in COVID-19. Specifically, blood group A was associated with an increased risk whereas blood group O was associated with a decreased risk, thus demonstrating that the ABO blood type is a biomarker for differential susceptibility of COVID-19. These findings are consistent with similar risk patterns of ABO blood groups for other corona virus infection found in previous studies. For example, Cheng *et al.* reported that the SARS-CoV infection susceptibility in Hong Kong was differentiated by the ABO blood group systems.[30] The authors found that compared with non-O blood group hospital staff, blood group O hospital staff had a lower chance of getting infected.

Our study has few limitations:

First, sample size was small in case of both patient group (185) and control group (371). Second, severe or critical cases were not included in this study due to less availability.

Conclusion:

Considering all data we found that blood group A was statistically significantly more frequent among those infected with COVID-19 compared to controls On the other hand, the frequency of blood group O was significantly lower in the COVID-19 patients, compared to the control group. The findings in the present study would have several potential clinical implications. 1) People with blood group A might need particularly strengthened personal protection to reduce the chance of infection; 2) It might be helpful to introduce ABO blood typing in the evaluation of SARS-CoV-2 infection; 3) blood group A may get priority in SARS COV-2 vaccine. However, the SARS-CoV-2 situation is evolving rapidly, and discoveries and anomalies are being reported daily. Therefore, it is advised to have more researches in this field before the blood groups added to the list is added as a risk factor for SARS-CoV-2 infection.

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