

## Original Research Article

# Susceptibility of blood group ABO and Rh for COVID-19

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### ABSTRACT

**Background:** The ABO and Rh blood group systems are part of the innate immune system and it has been shown that individuals with different ABO and Rh blood groups differ in their susceptibility or resistance to viral and bacterial infections and diseases. With the discovery of blood groups and subsequent great advancement in its study, many workers have tried to find out a possible relationship between the incidence of these blood groups and the incidence of various diseases. Aim of the study was determine the association between COVID-19 virus infection and blood groups.

**Methods:** This retrospective Case- control observational study was performed among subjects reported to hospital situated at central India for RT PCR-COVID-19 sampling during the period between March to September 2020. Total subjects enrolled were 1682.

**Results:** The individuals with blood group Rh factor positive are found to be more susceptible in acquiring COVID-19 disease. Likelihood of getting COVID-19 is more with factor Rh positive in comparison to Rh negative counterparts. The association is observed statistically between Rh factor and status of COVID-19.

**Conclusions:** In conclusion our results implicate that blood group are found to be associated with the status of COVID-19 disease. It is observed that the Rh positive individuals are more susceptible when compared to their Rh negative counterparts in acquiring COVID-19 disease.

**Keywords:** Blood group, COVID-19, Disease association

### INTRODUCTION

On December 31<sup>st</sup> 2019, China notified the outbreak of endemic to the World Health Organization. On 7<sup>th</sup> January the causative virus was identified as a coronavirus. This was merely onset of a new public health crises affected the whole world. On January 30, 2020 the World Health Organization declared the outbreak as a Public Health Emergency of International Concern.

Coronaviruses belong to the subfamily Coronavirinae in the family Coronaviridae, are enveloped non segmented positive sense RNA viruses ranging from 60 nm to 140 nm in diameter with spike like projections on its surface giving

it a crown like appearance under the electron microscope; hence the name coronavirus.<sup>1</sup>

The first fatal case was reported on 11th January 2020. As of Sep 2020, COVID-19 has been confirmed in over 30.6 million individuals worldwide and 5.22 million in India. Total mortality worldwide till now is 972000 and 90000 in India.

Infection is transmitted through large droplets generated during coughing and sneezing by symptomatic patients but can also occurs from asymptomatic people and before onset of symptoms.<sup>2</sup>

Infection is acquired both by inhalation of these droplets directly or touching surfaces contaminated by them and then touching the nose, mouth and eyes. Incubation period is 02 to 14 days (median 05 days). The clinical features of COVID-19 are varied, ranging from asymptomatic state to acute respiratory distress syndrome and multi organ dysfunction. The common clinical features include fever (not in all), cough, sore throat, headache, fatigue, myalgia and breathlessness. The median time from onset of symptoms to dyspnea was 5 days, hospitalization 7 days and acute respiratory distress syndrome (ARDS) 8 days. Complications witnessed included acute lung injury, ARDS, shock and acute kidney injury. Recovery started in the 2<sup>nd</sup> or 3<sup>rd</sup> week. Adverse outcomes and death are more common in the Women who are pregnant, elderly and those with underlying co-morbidities. All ages are susceptible

Multiplex real-time RT-PCR assay has become the method of choice for diagnosis of COVID-19. Blood grouping involves mainly two types of systems, ABO and Rh system. ABO system was introduced by a Karl Landsteiner in 1901. Antigens on RBC decide the phenotype of a person. There is a coat found on RBC. The coat is usually of oligosaccharide

Rh means Rhesus has two genes D and d. Persons with the presence of this gene has positive Rh+ factor while those who lacks this has Rh- factor. The significance of the Rh blood group is related to the fact that the Rh antigens are highly immunogenic.

With the discovery of blood groups and subsequent great advancement in its study, many workers have found out a possible relationship between the incidence of these blood groups and the incidence of various diseases.<sup>3</sup> The present study is intended to determine the association between COVID-19 virus infection and blood groups.

## METHODS

This retrospective Case- control observational study was performed among all consecutive subjects reported to referral COVID-19 Centre military hospital saugor situated at central India for RT PCR- COVID-19 sampling during the period between March to September 2020. Total subjects enrolled were 1682.

### Laboratory analysis

#### Test for COVID-19

An oropharyngeal specimen in swab for RT PCR collected by healthcare provider, placed immediately into 2-3 ml of viral transport medium and sent to central laboratory immediately. Subject positive for RT PCR COVID-19 is considered as COVID-19 positive or COVID-19 virus infection.

### Blood grouping

To do a blood grouping test we use blood lancets to take a blood sample from a finger and we applied three drops of blood on glass slide. Pour one drop of anti A, anti B and monoclonal D on blood drops respectively also label the slide portions as A, B and D. Mix it well. When RBC carrying one of the antigen were exposed to antibodies the agglutination occurs which meant they clump together. This clumping in one of the spot decides the blood group of an individual.

### Statistical analysis

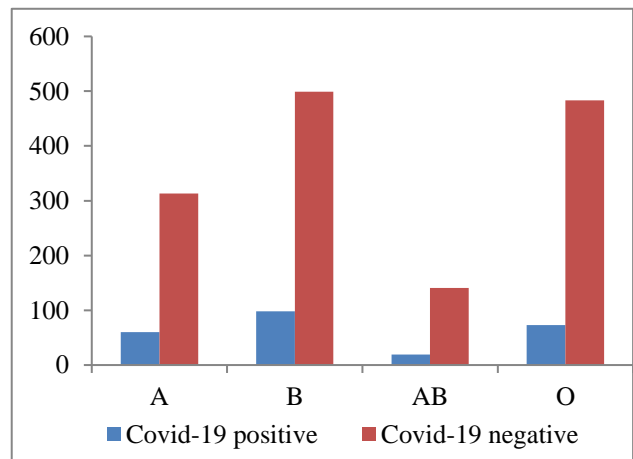
The statistical tool such as, Odds ratio (OR) with 95% confidence interval (C.I) is presented to know the likelihood of acquiring COVID-19 disease with respect to factor Rh status of ABO blood groups of COVID-19 infected individuals.

Chi-square test ( $\chi^2$  test) statistic was also carried out to observe the association between the Rh blood group and COVID-19 infection. A p value <0.05 was considered to be statistically significant.

## RESULTS

There were 1682 subjects enrolled in the study. Among them 250 (14.86%) reported to have COVID-19 infection and 1432 (85.14%) individuals reported absence of COVID-19 infection.

Based on ABO blood group antigens the individuals were kept in four groups A (343), B (593), AB (160), O (536). And furthermore as per Rh factor presence individuals are grouped as factor Rh positive (1589) and Rh negative (93).

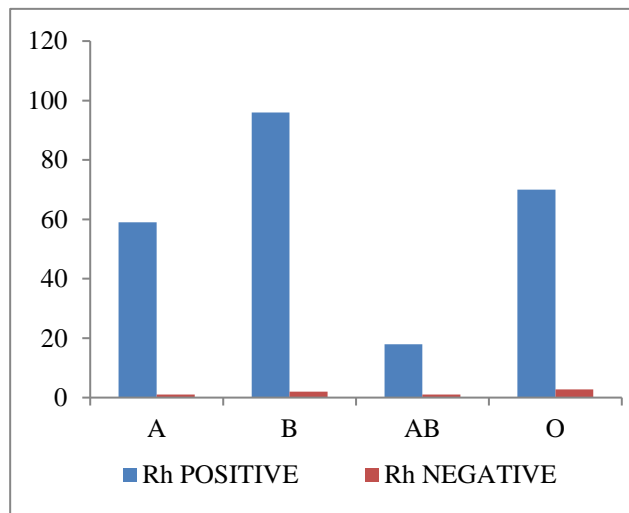


**Figure 1: The representation between various blood groups (ABO) and COVID-19 disease.**

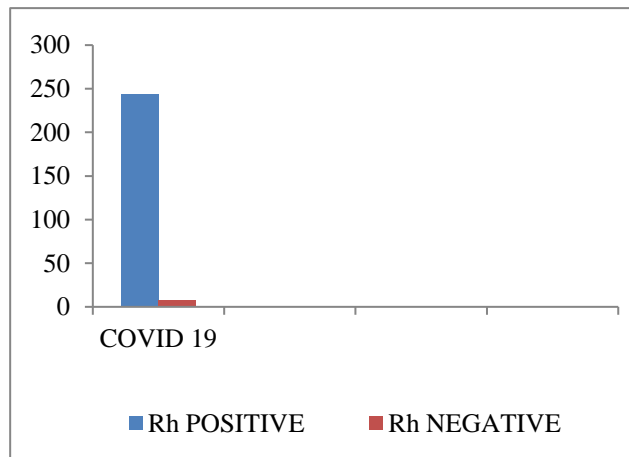
Out of 1682 subjects, 250 were found to be positive for RT PCR COVID-19. Among COVID-19 positive 98 subjects were from blood group B, 73 from O, 60 from A and 19 from blood group AB.

Among COVID-19 positive subject contribution of blood group B is 39.20 and of AB is 7.60%. Out of 98 COVID-19 infected blood group B subject 96 were Rh positive and remaining 2 were Rh negative.

Similarly in blood group O out of 73, 70 were Rh positive, Blood group A out of 60, 59 were Rh positive and in Blood group AB 18 out of 19 were Rh positive. Contribution of factor Rh positive for COVID-19 in Blood group A, B, AB, and O are 98.33, 97.95, 94.73 and 95.89% respectively.



**Figure 2: Representation of various ABO blood groups divided as per Rh factor status and COVID-19.**



**Figure 3: Representation of factor Rh status among COVID-19 disease.**

Overall 243 subjects out of 250 COVID-19 infection were factor Rh positive, Contributing 97.20% of all COVID-19 positive cases.

The odds ratio is one of the familiar statistical measures used to know the likelihood of possessing the risk of acquiring COVID-19 disease. The same measure is used

here to know the likelihood of acquiring COVID 19 disease among various blood groups.

**Table 1: Odd ratio of each ABO blood group for COVID 19 between Rh positive and negative.**

Blood Group	COVID-19 positive	COVID-19 negative	Total	Odd Ratio (95% C.I)
A+ve	59	298	357	2.96
A-ve	01	15	16	
<b>Total</b>	<b>60</b>	<b>313</b>	<b>373</b>	
B+ve	96	471	567	2.44
B-ve	02	24	26	
<b>Total</b>	<b>98</b>	<b>495</b>	<b>593</b>	
AB+ve	18	126	144	2.14
AB-ve	01	15	16	
<b>Total</b>	<b>19</b>	<b>141</b>	<b>160</b>	
O+ve	70	451	521	1.65
O-ve	03	32	35	
<b>Total</b>	<b>73</b>	<b>483</b>	<b>556</b>	

Odd ratio of blood Rh positive A, B, AB and O are 2.96, 2.44, 2.14 and 1.65 in respect of their Rh negative counterparts

**Table 2 Chi square statistic for association of Rh factor and COVID 19.**

Blood group	COVID-19 positive	COVID-19 negative	Total	Chi square
<b>Rh positive</b>	243 (236.18) [0.2]	1346 (1352.82) [0.03]	1589	Chi square statistic=4.1871 p=0.040732
<b>Rh negative</b>	7(13.82) [3.37]	86(79.18) [0.59]	93	
<b>Total</b>	250	1432	1682 (grand total)	

Significant at p<0.05

Chi square statistic is 4.1871. The p value is 0.040732. Significant at p<0.05.

**DISCUSSION**

The ABO and Rh blood group systems are part of the innate immune system and it has been shown that individuals with different ABO and Rh blood groups differ in their susceptibility or resistance to viral and bacterial infections and diseases.<sup>4,5</sup> A relationship between blood groups and disease was first hypothesized by Kaipainen and Vuorinen during 1960, and the gene involved in ABO blood groups was discovered in 1990.<sup>4,6</sup> A strong association has been described between peptic ulcer disease and blood group O; between stomach cancer, pernicious anemia, diabetes mellitus and blood group A; and between hepatocellular carcinoma and blood group A.<sup>7,8</sup> A study in Nigeria in 2015 also proved the existence

of a link between asthma and blood group A.<sup>9</sup> In the field of dermatology and venereology, potential associations have also been shown between lichen planus and blood group A, pemphigus and seborrheic dermatitis and blood group B, and vitiligo and blood group AB.<sup>3</sup> The relationship of blood groups of population and their susceptibility to diseases like plague, small pox, malaria, cholera etc. suggest the possible role of blood group antigen in the occurrence of diseases. During the past twenty years there are many reports documenting the role of blood group antigens as receptors for parasites, bacteria and viruses.<sup>10</sup> Association of blood groups with HBV infection and fibrosis severity in HCV infection has been reported earlier.<sup>11</sup>

Furthermore, in the study of Sayal in 1996 about subjects of the armed forces, a relatively increased incidence of HIV infection was observed in persons with blood group O and relatively lower incidence in blood group B.<sup>3</sup> Incidence of HIV infection was also low in Rh-negative subjects. Antigen responsible for blood grouping is not restricted to RBC surface only. It is present on other type of cells surface also. Therefore addressing these antigens as blood group only would be under estimation. There is a possible relationship between the incidence of blood group and the natural defense mechanism against infection. The level of natural antibodies in humans may be different in different ABO blood groups.

Contemporary, a study published in Annals of Hematology, conducted at Massachusetts General Hospital (MGH) found that people with blood group O has least risk of contracting the novel corona virus infection. In Denmark study done on 473654 people who were tested for corona virus between February and July 2020 revealed least number of people was from blood group O for COVID-19 infection.

In this present study also a significant association has been found out between COVID-19 infection and blood groups.

Maximum number of COVID-19 case is from blood group B, followed by Blood group O. Minimum number of case is from blood group AB. For each group of ABO blood groups, contribution of factor Rh positive is more than 95% as compared with Rh negative counterparts. Overall 97.20% of COVID-19 positive case is from Rh positive blood groups only.

The likelihood of acquiring COVID-19 disease by B positive subjects is 2.44 times more than B negative subjects i.e.  $OR_B = 2.44$  (95% C.I.). In the same manner the likelihood of acquiring COVID-19 disease by AB positive and O positive subjects is 2.14 and 1.67 times more than AB negative and O negative subjects  $OR_{AB} = 2.14$  (95% C.I.) and  $OR_O = 1.65$  (95% C.I.) respectively.

$\chi^2$  test results showed the statistical significance at  $p < 0.05$ , which suggests that there exists an association between the Rh blood group and the risk of acquiring COVID-19. The

individuals with blood group Rh factor positive are found to be more susceptible in acquiring COVID-19 disease. Likelihood of getting COVID-19 is more with factor Rh positive in comparison to Rh negative counterparts. The association is observed statistically between Rh factor and status of COVID-19.

A relation of blood group and COVID-19 susceptibility cannot be denied. But being a novel disease it is subject of debate, more data and more research required before making firm conclusion.

## CONCLUSION

In conclusion our results implicate that blood group are found to be associated with the status of COVID-19 disease. It is observed that the Rh positive individuals are more susceptible when compared to their Rh negative counterparts in acquiring COVID-19 disease. Using odds ratio (OR), the differences can be observed in between the Rh positive individuals and Rh negative individuals of ABO blood groups, where the Rh positive individuals are likely to have more chance of acquiring COVID-19 disease than that of Rh negative individuals. The interpretation on risk of acquiring COVID-19 disease is given based on the OR value of each blood group with respect to their Rh positive and Rh negative blood groups. The role of blood group antigens as important key factors in disease development is evident from earlier studies and hence their possible role on COVID-19 susceptibility cannot be ruled out and needs further investigation.

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