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# A Study to Determine an Association between ABO Blood Groups and Coronavirus Disease 2019

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***Author's contribution***

*The sole author designed, analysed, interpreted and prepared the manuscript.*

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## ABSTRACT

**Introduction:** The Coronavirus pandemic has led millions to succumb to the disease across the world, and overwhelmed the health care system. In this study we aimed at identifying whether the risk of Covid-19 infection is associated with ABO blood groups.
**Methods:** We obtained data of 7056 Covid-19 confirmed cases from Yashwantrao Chavan Memorial Hospital, Pune.
**Results:** The results showed that a significantly higher proportion of individuals with blood group A and AB tested positive for Covid-19, while a significantly lower proportion of individuals with O blood group tested positive for the same disease.
**Conclusion:** Routine ABO testing of Covid-19 patients could guide in decision-making and management of Covid-19.

*Keywords: Histo blood group antigens; pandemic; susceptibility.*

## 1. INTRODUCTION

On March 11, 2020, the World Health Organization declared Covid-19 a global pandemic, which spread to all continents. The virus being extremely contagious led to millions being succumbed to the disease across the world, crippled economies and overwhelmed the

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health care system leaving the entire human population gripping with terror. The ongoing crisis has indeed changed the world fabric with no country being capable enough to tackle this alone. Covid-19 has put not only our healthcare and safety mechanisms, but also nations together to rage war against the common enemy. The Covid-19 pandemic has spurred researchers to find characteristics that render individuals more susceptible to the virus, as well as risk factors that intensify its severity and progression. There is currently no biological marker known to predict the susceptibility to Covid-19 and mounting evidence from across the globe seems to suggest that blood type could play a role in the risk of infection and determining the severity of the symptoms [1].

A study conducted in China compared the ABO blood group distribution of 2,173 patients with Covid-19 confirmed by RT-PCR test from three hospitals (Jinyintan Hospital in Wuhan, Renmin Hospital of Wuhan University, and Shenzhen Third People's Hospital) China with that of normal people from the corresponding regions. The results showed that blood group A was associated with a higher risk for Covid-19 compared to non-A blood groups, whereas blood group O was associated with a lower risk for the infection compared with non-O blood groups [2]. A large retrospective review by Harvard Medical school showed that there appeared to be a greater chance of people with blood types B and AB tested positive for the virus and that symptomatic people with blood type O were less likely to be tested positive. However, no significant association between blood type and worsening of the symptoms of the disease was seen [3,4]. Metanalysis of these data by Franchini and colleagues have found individuals with group O had a lower infection rate compared to individuals of non-O group (OR: 0.81; 95% CI: 0.75, 0.86) [5].

There is a paucity of data regarding the relationship between ABO blood typing and severity of Covid-19 disease. If we can understand how the virus interacts preferentially with the receptors found on respiratory epithelium in people with different blood groups, we may be able to find new drugs or methods of prevention. Also, stringent monitoring of those individuals with susceptible blood groups can be done to prevent them from landing up with serious complications of Covid-19. This study aims at identifying whether the risk of Covid-19 infection is associated with ABO blood groups in a tertiary care hospital.

## 1.1 Aim

To determine an association between ABO blood group and Covid-19 susceptibility in the Indian population.

## 1.2 Objectives

To evaluate the risk of developing Covid-19 in individuals with different blood groups.

## 2. METHODOLOGY

## 2.1 Type of Study

Hospital based study.

## 2.2 Study Population

Individuals coming to the hospital for Covid-19 testing.

## 2.3 Place of Study

Dr. D.Y Patil Medical College, Pimpri, Pune.

## 2.4 Study Duration

6 Months.

## 2.5 Sample Size

7056 individuals.

## 2.6 Data Collection

The data was obtained from Yashwantrao Chavan Memorial Hospital, Sant Tukaram Nagar, Pimpri, Pune and comprised of Blood group wise segregation of Covid positive patients in the year 2020-2021.

## 2.7 Measurements

### 2.7.1 Case definition

A confirmed Covid-19 case was any individual who tested positive for SARS-CoV-2 via a nasopharyngeal (NP) swab. Presence of SARS-CoV-2 virus in the Nasopharyngeal sample was tested by polymerase chain reaction (PCR) analysis.

### 2.7.2 Statistical analysis

Chi-squared ($X^2$) Test of goodness of fit was used to compare the distributions of blood

groups between samples. Statistical values were considered significant at $p<0.05$. Statistical analysis was performed using Epi-info statistical software (version 7) and Microsoft Excel.

## 2.8 Selection Criteria

### 2.8.1 Inclusion criteria

All individual who tested positive for Covid-19 by RT-PCR.

### 2.8.2 Exclusion criteria

All individuals who tested negative for Covid-19.

## 3. RESULTS

**Table 1. Blood group pattern and Covid-19 susceptibility**

| Blood Group | Covid-19 susceptibility [(n%)] |
|---|---|
| A | 1970(27.91) |
| B | 2251(31.90) |
| AB | 709(10.04) |
| O | 2126(30.13) |
| **Total** | **7056** |

**Table 2. Blood group pattern distribution in the Indian Population**

| Blood Group | Percentage (%) |
|---|---|
| A | 23 |
| B | 33 |
| AB | 7 |
| O | 37 |

**Table 3. Extrapolation of Covid-19 susceptibility to the entire population of India**

| Blood Group | Observed [(n %)] | Expected [(n %)] |
|---|---|---|
| A | 1970(27.91) | 1623(23) |
| B | 2251(31.90) | 2328(33) |
| AB | 709(10.04) | 494(7) |
| O | 2126(30.13) | 2611(37) |
| **Total** | **7056** | **7056** |

## 4. DISCUSSION

As of October 13, 2021 approximately 34 million people succumbed to the coronavirus in India. Table 2 shows the blood group distribution pattern across India; O being the most common blood group (37%) closely followed by B (33%), followed by A (23%) while AB is the least prevalent at 7% [6]. A study conducted in Pune found a similar pattern of blood group distribution indicating no significant geographical variation in distribution [7]. The results of our study show a positive association between Blood group and susceptibility to Covid-19. A significantly higher proportion of individuals with blood group A and AB tested positive for Covid-19, while a significantly lower proportion of individuals with O blood group tested positive for the same disease. These findings are consistent with literature findings of the past cases.

## 4.1 Analysis of Susceptibility to Covid-19 infection

Out of the 7056 Covid positive sample we obtained, 27.91% patients belonged to a blood group, while 31.90% belonged to B, 10.04% to AB and 30.13% to O blood group. As shown in Table 3, we extrapolated the data obtained to that of the general population of India and using Chi-square of goodness of fit; a chi-square value of 122.889 was obtained and a p value of 0.000 indicated a significant statistical association between Covid-19 and Blood group.

We observed that a significantly higher proportion of individuals with A and AB blood group tested Covid positive [Observed=27.91%; Expected=23%; $p<0.05$] and AB [Observed=10.04%; Expected=7%; $p<0.05$], while a significantly lower proportion of individuals with O blood group tested positive for Covid-19 [Observed=30.13%; Expected=37%; $p<0.05$]. Our results are similar to findings of past literature as most studies identified a higher proportion of blood group A, and a lower proportion of blood group O being susceptible to the Corona virus. However, through our study we additionally found that blood group AB was also more susceptible to Covid-19. The possible mechanisms to explain the differences in SARS-CoV-2 infection by ABO type are as follows: -

## 4.2 The Anti-ABO Antibodies

Each RBC expresses about 2 million copies of genetically encoded Histo-blood group antigens (HBGA) on its surface which are synthesized by many epithelial cell types, such as the respiratory and digestive tracts that are known to emit large amounts of viral particles [8]. In addition to serving as antigenic barriers during transfusion, transplantation and pregnancy, HBGA oligosaccharides physiologically influence hemostasis and, therefore, confer disease risks

in infectious and non -infectious diseases. Multiple mechanisms have been proposed by which HBGAs can interact with pathogens at the portal of entry, or alter disease progression/severity, as well as affect clinical presentation. Individuals who express a specific HBGA are more susceptible to infection, whereas individuals without it are completely resistant or, at least, protected from severe diseases [9].

With regard to Covid-19; Firstly, HBGA glycans on SARS-COV-2 S protein enhance the affinity of the Coronavirus to ACE-2 receptor, its cellular receptor. Secondly, anti-A and/or anti-B antibodies present in blood group O individuals could bind to corresponding antigens on the viral envelope and contribute to viral neutralization, thereby preventing target cell infection [10]. Thus, as blood group O individuals possess both types of antibodies, they might benefit from a better protection than blood group A or B individuals who possess either of them and even more so than blood group AB people who have none of them. However, this kind of protection requires sufficient amounts of the anti-A and anti-B antibodies and it is seen that individuals who possess low titers of anti-A or of anti-B antibodies are expected to be at a higher risk of infection than people with high titers [11]. The involvement of natural anti-ABO antibodies in COVID19 infection is thus a possibility. It is fascinating to note that they act by preventing infection or by decreasing the viral load but as soon as virus replication has taken place in the new host, newly formed virions will carry autologous glycans that can no longer be recognized by the allogeneic anti-ABO antibodies. Also, a recent study has shown that protection exclusively takes place in situations of ABO incompatibility as the SARS-coV-2 viral particles transmitted in ABO incompatible situations would be neutralised by anti- A and anti-B antibodies [11]. This can have an impact on the pandemic by significantly enhancing its progression because many ABO compatible encounters will take place as the pandemic progresses. These observations reiterate the efficacy of social distancing [12]. Thirdly, HBA glycans on target cells can serve as receptors for SARS-COV-2 and emerging evidence from study conducted by Wu *et al* showed that the spike protein RBD binds to the A type 1 antigen suggesting that receptor-binding domain (RBD) of SARS-CoV-2 may share sequence similarity to an ancient lectin family known to bind blood group antigens. SARS-CoV-2 RBD binds the blood group A expressed on respiratory epithelial cells, which could explain the linkage between blood group A and SARS-CoV-2 infection [13].

### 4.3 ABO Blood Groups and the Furin Cleavage Site

The SARS-Cov-2 S-(spike) protein is heavily glycosylated with N-glycan and O-glycans. Entry of SARS-CoV-2 virus into the cell involves pre-activation of the S protein by a proprotein convertase called furin [14]. The furin cleavage site is surrounded by O-glycosylation sites, which may impact the ability of furin to cleave the S protein. In a recent study by Abdelmassih et al it was proposed that a negative relationship between blood type O and furin-related proprotein convertases [15]. In addition, furin levels modulated by the ABO phenotypes could play a role in the endothelial pathogenicity of SARS-CoV-2. In these conditions, the impact of ABO phenotypes on furin could take place both at the infection level and at the late stage of severe disease [15].

### 4.4 ABO Blood Groups and the Gut Microbes

It is known that gut microbes contribute a major role in controlling innate immunity and inflammation since they trigger the synthesis of anti-A and anti-B antibodies. Recent studies showed that the gut microbiota of COVID-19 patients appears distinct from that of healthy controls. A study by Mäkivuokko and colleagues showed increased levels of Actinobacteria in blood group B individuals when compared to other blood groups [16]. Since these bacteria are associated with the development of Inflammatory Bowel disease, they may also facilitate the development of cytokine storm seen in Covid-19. Another study reported lower levels of in the gut of blood group A secretors than in non-A secretors [17]. B. obeum is an anaerobic gut bacterium that plays an important role in recovery process from diarrhea. A decreased level of these bacteria is associated with several inflammatory, autoimmune conditions, and aging [18], it may also be responsible for a higher risk of uncontrolled inflammation among blood group A COVID-19 patients than among other ABO blood types.

## 5. CONCLUSION

Routine ABO testing of Covid-19 patients could guide in decision-making. For instance, higher

care is to be provided to individuals with higher risk blood groups. If verified by future studies, the findings of our study would have several potential clinical implications. Firstly, people with blood group A and AB might need stronger and stringent personal protection to reduce the chance of infection; Secondly, SARS-CoV-2-infected patients with blood group A and AB might need to receive more vigilant surveillance and aggressive treatment. However, the role of ABO blood group in Covid-19 disease requires additional study; likewise, people with any blood group would need to exercise the wisdom of careful practice to avoid SARS-CoV-2 infection.

## 6. LIMITATIONS

We lack data regarding the outcomes of Covid-19 infection and hence cannot comment upon the possible association between Covid-19 severity and Blood group. Additionally, we lack demographic data of individuals (e.g. Age and other comorbidities) which could be confounding factors.

## CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

## ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

## COMPETING INTERESTS

Author has declared that no competing interests exist.

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