The Association of Blood Groups and COVID-19 Infection in Pakistani Population with Respect to Age and Gender in a Case-Control Study

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Abstract

Background: Age may be one of the determinants that increases the probability of COVID-19 infection. Furthermore, gender has been recognized as a major predictor of COVID-19 illness, with males having a larger proportion of severe COVID-19 disease than females. Some biological markers in the host have also been discovered as putative COVID-19 infection indicators. The kind of markers have recently been discovered as a major determinant for COVID-19 infection among these parameters.

Objective: To detect if COVID-19 infection is associated with blood type with respect to age and gender.

Methods: It was a case-control study that took place at COVID ICU of Hussain Lakhni Hospital, Karachi, Pakistan from Jun 2021 to Dec 2021. Cases (n=511) were individuals ranging in age from 15 to 80 years old, of either gender, who had COVID-19 infection confirmed by a real-time PCR test. Healthy people (n=511) served as controls. Data on age, gender, weight, height, BMI, residence, educational status, socio-economic status, comorbid and ABO blood type of patients were collected. The data were analyzed using statistical software SPSS version 23.

Results: The mean age of the subjects was 54.01±11.16 years, 57% were males and 43% were females. COVID-19 infection was 2.84 times higher in people with blood type A (OR=2.84, 95% CI=1.68-4.79) and 2.19 times higher in people with blood group B (OR=2.19, 95% CI=1.29-3.72, p=0.003) than in people with blood group O. In age group≥50 years, the odds of COVID-19 infection were 1.88 times higher in individuals with blood type B as compared to blood group O (aOR=1.88, 95% CI=1.01-3.52). Among females, the odds of COVID-19 infection were 2.51 folds higher in individuals with blood type A as compared to blood group O (aOR=2.51, 95% CI=1.05-6.05). On the multivariable model, no association of blood group with COVID-19 was observed for sub-group of age <50 years and male gender.

Conclusion: Individuals with blood group A have higher liability to acquire COVID-19 than blood group O. In older age, the chances of getting COVID-19 are more in blood type B, and in females, the chances of getting COVID-19 are higher in blood type A.

Keywords: *COVID-19, coronavirus, age, gender, blood groups, ABO blood types.*

INTRODUCTION

COVID-19 is a pandemic virus that originated in Wuhan, China, and is quickly spreading over the world [1]. It is linked to high rates of morbidity and death, which have a considerable impact on public health [2]. On the 17th of January 2022, the World Health Organization recorded 326,279,424 confirmed cases and 5,536,609 fatalities globally [3]. Corresponding statistics for Pakistan on 17th January 2022 show 1,324,147 confirmed cases and 29,012 fatalities. According to these figures, Pakistan is ranked 42nd in the globe [3].

According to an epidemiological review, age may be one of the determinants that increases the probability of COVID-19 infection [4]. COVID-19 can affect people of any age, although older people are more likely to be significantly impacted. Children, on the other hand, have shown mild clinical symptoms, though serious illness has been observed in infants under the age of one year. As a result, COVID-19 may increase the risk of severe respiratory failure in neonates [5, 6]. Furthermore, gender has been recognized as a major predictor of COVID-19 illness, with males having a larger proportion of severe COVID-19 disease than females. Males also have a greater death rate than females [1, 7, 8].

Some biological markers in the host have also been discovered as putative COVID-19 infection indicators. The kind of blood has recently been discovered as a major determinant for COVID-19 infection among these parameters [9-13]. Zhao *et al.* found in their study a larger proportion of blood type A and a lesser proportion of blood type O in the COVID positive patients as compared to the general population of Shenzhen and Wuhan [12]. Another study conducted in Spain and Italy discovered that people with blood type A had a greater risk of COVID-19, but people with blood type O have a lower risk [14]. Ad'hiah *et al.* indicated those with blood group A had higher odds of contracting COVID-19

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infection, especially in males, however, no significant differences were seen in patients of all ages [6].

Since the incidence of COVID-19 in Pakistan is lesser than in our neighboring countries [1], we want to look at the trends in our population to see what the disease's protective factors are. Furthermore, no such analysis has yet been carried out in Pakistan. As a result, the current study aimed to identify the link between blood types and COVID-19 infection in relation to age and gender.

METHODOLOGY

It was a case-control study conducted at the COVID ICU of Hussain Lakhni Hospital, Karachi, Pakistan from Jun 2021 to Dec 2021. The sample size of 1022 (511 cases and 511 controls) was estimated using the Open epi sample size calculator by taking the frequency of O blood type as 25.80% among COVID-19 patients and 33.84% among controls [12], 95% confidence level and 80% power of a test. Cases were patients of age 15 to 80 years, either males or females with COVID-19 positive results confirmed on the real-time PCR test. Controls were healthy individuals *i.e.* family members of COVID-19 infected patients (who were tested negative for COVID-19 infection). Controls were enrolled from the same setting after tested negative. Patients with respiratory illness (COPD and bronchial asthma) were excluded from the study. Non-probability consecutive sampling method was applied for sample selection.

Data collection began once the hospital's ethical review committee gave its approval. All of the eligible people gave their informed consent in writing. Data on age, gender, weight, height, residence, educational status, socio-economic status, and comorbidities (hypertension, diabetes, cardiovascular disease, and malignancy) was collected on a pre-designed proforma by the researcher himself. The ABO blood type of patients was identified from the laboratory and blood transfusion section of the institute and noted on the proforma.

SPSS version 23 was used to analyze data. Shapiro-Wilk test was applied to check the distribution of numeric variables like age. Numeric variable like age was presented by mean and SD/mean rank whereas categorical variables like gender, residence, district, education, family monthly income and comorbidities were presented as percentages and frequencies. Univariate logistic regression was applied by considering COVID-19 infection as a dependent variable and socio-demographic factors, comorbidities and blood groups as independent variables. The odds ratio was calculated with a 95% confidence interval. Multiple logistic regression models with respect to age and gender were derived. Models were adjusted for significant factors ($p<0.25$) in univariate analysis. The adjusted odds ratio was calculated with a 95% confidence interval. A statistically significant p-value ≤0.05 was used for final multiple logistic regression models.

RESULTS

Of 1022 subjects, the overall mean age was estimated as 54.01±11.16 years. Of 1022 subjects, 57% were males and 43% were females. The mean weight and height of the subjects were 66.02±11.12 kg and 62.39±5.87 inches respectively. Overall mean BMI was reported as 26.70±5.62 kg/m^2 and the majority of the participants had BMI less than 30 kg/m^2 (74.9%). All of the subjects were urban residents of the Karachi district. Out of 1022 subjects, 43.2% had education till matric and 63.2% had middle socioeconomic status (15,000-30,000 PKR monthly income). Of 1022 subjects, about 48.9% of the subjects had hypertension, 44% had diabetes, 6.6% had cardiovascular disease, and 0.5% had malignancy.

Table **1** depicts the comparison of COVID-19 cases and healthy controls socio-demographic factors, comorbidities and blood groups. Age grouping showed a significant difference between COVID-19 cases and healthy controls (p=0.001). The odds of COVID-19 infection were higher in age <50 years (OR=1.54, 95% CI=1.18-2.01) as compared to age≥50 years. The proportion of males was higher than females in cases and controls but an insignificant difference was observed (p=0.900). The odds of COVID-19 infection were higher in educated classes (matric-graduate level education) as compared to uneducated patients. The individuals with middle-level socioeconomic status had 1.85 times the odds of COVID-19 as compared to other low socioeconomic and high economic status. The odds of COVID-19 infection were 0.67 times lower among patients with diabetes mellitus and 0.34 times lower among patients with cardiovascular disease, whereas the odds of COVID-19 infection were 1.91 times higher among patients with hypertension.

Table **2** shows the comparison of ABO blood type and COVID-19. According to blood group analysis, in patients, blood type A had the highest proportion (50.1 %) followed by blood type B (38%), then AB (5.9%) and lastly O (4.7%). In controls blood type B had the highest proportion (36.6 %) followed by blood type a (36%), then AB (17.8%) and lastly O (9.6%). When compared to healthy controls, COVID-19 subjects had higher frequencies of blood groups A and B. Odds of COVID-19 infection were 2.84 times higher in blood type A (OR=2.84, 95% CI=1.68-4.79, p=0.001) and 2.19 times higher in blood group B (OR=2.19, 95% CI=1.29-3.72, p=0.003) than in blood type O.

Table **3** displays the association of blood types with COVID-19 infection with respect to age and gender, the multiple logistic models were adjusted for factors that were significant in univariate analysis with a p-value<0.25. In the age group≥50 years, the odds of COVID-19 infection were 1.88 times higher in individuals with blood type B as compared to blood group O (aOR=1.88, 95%

Table 1: Comparative analysis of COVID-19 cases and healthy controls with socio-demographic factors, comorbidities.

Characteristics	Cases (n=511) n (%)	Controls (n=511) n (%)	OR (95% CI)	p-value
Age groups				
<50 years	145 (28.4)	194 (38)	1.54 (1.18-2.01)	0.001*
≥50 years	366 (71.6)	317 (62)	Reference category	
Gender				
Male	290 (56.8)	288 (56.4)	Reference category	
Female	221 (43.2)	223 (43.6)	0.98 (0.76-1.26)	0.900
BMI category				
<30 kg/m^2	376 (73.9)	390 (76.8)	Reference category	
≥30 kg/m^2	133 (26.1)	118 (23.2)	0.85 (0.64-1.13)	0.283
Education level				
Illiterate	49 (9.6)	100 (19.6)	Reference category	
Matric	200 (39.1)	241 (47.2)	1.69(1.14-2.50)	0.008*
Intermediate	227 (44.4)	135 (26.4)	3.43(2.29-5.13)	0.001*
Graduate	35 (6.8)	35 (6.8)	2.04(1.14-3.64)	0.016*
Socioeconomic status				
Low	107 (20.9)	159 (31.1)	Reference category	
Middle	359 (70.3)	287 (56.2)	1.85 (1.39-2.48)	0.001*
High	45 (8.8)	65 (12.7)	1.02 (0.65-1.62)	0.902
Diabetes mellitus				
No	311 (60.9)	261 (51.1)	Reference category	
Yes	200 (39.1)	250 (48.9)	0.67 (0.52-0.86)	0.002*
Hypertension				
No	220 (43.1)	302 (59.1)	Reference category	
Yes	291 (56.9)	209 (40.9)	1.91 (1.49-2.45)	0.001*
Malignancy				
No	509 (99.6)	508 (99.4)	Reference category	
Yes	2 (0.4)	3 (0.6)	0.66 (0.11-3.99)	0.656
Cardiovascular disease				
No	493 (96.5)	462 (90.4)	Reference category	
Yes	18 (3.5)	49 (9.6)	0.34 (0.19-0.60)	0.001*

Data expressed as n (%)
Binary logistic regression was applied, OR= Odds ratio, CI: Confidence interval
*Significant at 0.05 level of significance

Table 2: Comparison of ABO blood type and COVID-19 (n=1022).

Characteristics.	Cases (n=511) n (%)	Controls (n=511) n (%)	OR (95% CI)	p-value
Blood groups				
O	24 (4.7)	49 (9.6)	Reference category	
A	256 (50.1)	184 (36)	2.84 (1.68-4.79)	0.001*
B	201 (39.3)	187 (36.6)	2.19 (1.29-3.71)	0.003*
AB	30 (5.9)	91 (17.8)	0.67 (0.35-1.27)	0.225*

Data expressed as n (%)
Binary logistic regression was applied, OR= Odds ratio, CI: Confidence interval
*Significant at 0.25 level of significance

Table 3: Association of blood types with COVID-19 stratified by age and gender.

Age groups	<50 years	p-value	≥50 years	p-value
Blood groups	**Adjusted OR (95% CI)[a]**		**Adjusted OR (95% CI)[a]**	
O	Reference category		Reference category	
A	2.55 (0.72-9.077)	0.146	1.85 (0.98-3.47)	0.06
B	1.68 (0.45-5.86)	0.456	1.88 (1.01-3.52)	0.047*
AB	0.81 (0.19-3.39)	0.773	0.74 (0.34-1.62)	0.462
Gender	**Male**	**p-value**	**Female**	**p-value**
Blood groups	**Adjusted OR (95% CI)[b]**		**Adjusted OR (95% CI)[b]**	
O	Reference category		Reference category	
A	1.74 (0.82-3.66)	0.144	2.51 (1.05-6.05)	0.039*
B	1.82 (0.86-3.83)	0.116	1.78 (0.74-4.26)	0.195
AB	0.53 (0.21-1.33)	0.181	1.19 (0.43-3.31)	0.729

Binary logistic regression was applied, OR= Odds ratio, CI: Confidence interva
[a]Model adjusted for education status (Matric, intermediate, graduate), middle socioeconomic status, diabetes, hypertension and cardiovascular disease
[b]Model adjusted for age group<50 years, education status (Matric, intermediate, graduate), middle socioeconomic status, diabetes, hypertension and cardiovascular disease.
*significant p<0.05

CI=1.01-3.52). Among females, the odds of COVID-19 infection were 2.51 folds higher in individuals with blood type A as compared to blood group O (aOR=2.51, 95% CI=1.05-6.05).

DISCUSSION

Blood group antigen distribution varies by population and has been connected to several infections and hereditary disorders [15, 16]. Specific antigens have an advantage over others due to the prevalence of certain infections and genetic abnormalities [17]. Blood types have been linked to a variety of diseases and infections, according to literature. The SARS-CoV1 infection has been linked to blood type A, H-pylori infection has been linked to blood group O, malaria has been related to blood types A and B, hepatitis B has been linked to blood types B and O, Norwalk virus has been linked to blood type O, and so on [16-20]. The current study was conducted to evaluate the interaction of COVID-19 infection with blood type. We compared the blood type of healthy individuals with infected COVID-19 patients with respect to age and gender.

In the current investigation, age, and blood type were discovered to be potential determinants for COVID-19 infection in Pakistani patients. The majority of people infected with COVID-19 were between the ages of more than and equal to 50 years in our study. In a previous study, Ad'hiah *et al.* discovered that older persons (over 50) are more at risk of COVID-19 than younger adults [6]. Jamal *et al.* also found that majority of the Pakistanis of age 51-60 years were highly affected by COVID-19 infection [21]. Furthermore, the severity and prognosis of the disease are strongly dependent on the patient's age. The majority of COVID-19-positive hospitalized patients (80%) were over 65 years old and had a 23-fold higher risk of death than those under 65 [22-24]. This finding might be related to the fact that older persons are more likely to suffer from severe illness as a result of physiological changes that occur with age and underlying health conditions [6].

Gender is also a significant determinant in COVID-19 infection, with males having a larger risk of infection than females [25]. In the current study, males outnumbered females (56.8% *vs.* 43.2%) among COVID-19 patients. This is comparable to Pakistani research by Jamal *et al.* which found that men were more common than females (51.2 percent *vs.* 48.8%) among 1160 individuals with COVID-19 infection [21]. Another Pakistani research by Rahim *et al.* also discovered that the majority of COVID-19 patients were males (68.6%) [25]. On contrary, various reviews and meta-analysis researches reported similar frequency of males and females among COVID-19 cases, but males had higher rates of morbidity and death than females [7, 8, 26]. This disparity might be attributed to variations in immunology between males and females, making males more susceptible to COVID-19-related complications than females [6]. Another reason for a high proportion of males than females among COVID-19 cases in Pakistan is greater exposure of males than females in our setting, as females are usually confined to their homes and mostly unemployed [27].

The main findings of the current investigation revealed a significant disparity in blood group proportions in both patients and controls (p=0.001). The proportion of people with blood type O was lower in cases (4.7% vs 9.6%), whereas the number of those with blood type A was higher (50.1% vs 36%) than in controls. These findings suggest that individuals with blood type O are less likely to get COVID-19 virus infection, but people with blood type A are more likely. In research by Ad'hiah *et al.* blood type A was shown to be the most prevalent among COVID-19 patients, while blood type O was found to be the least common [6]. A Pakistani study by Noor *et al.* also found that in individuals with COVID-19 infection, blood type A was considerably greater and blood type O was much lower [17]. Noreen *et al.* found blood type B was the most frequent blood in both cases and controls (33.1% and 41.88%), whereas blood AB was the least frequent in both cases and controls (16.72% vs 9.04%). Furthermore, they discovered that the proportion of COVID-19 patients with blood type A was higher than the proportion of controls (25.2% vs 21.1%), whereas the number of cases with blood type O was lower in cases than controls (25% vs 28%) [27]. Zhao *et al.* also concluded that those with blood type A had a higher chance of contracting COVID-19 [12]. A genome-wide association study carried out in Europe showed individuals with blood type A had a higher risk of getting COVID-19 infection, but blood type O exhibited a protective link when compared to other blood types [14].

In the current study, the results of multiple logistic regression revealed that at age≥50 years, the chances of COVID-19 infection were significantly associated with blood group type B with a p-value=0.047. Dissimilar findings were observed in the study conducted in China, the proportion of blood type A was higher in older patients [28]. With respect to gender in our study, among females, the odds of COVID-19 were significantly higher among individuals with blood A. While in a Chinese study, blood group A was most common in male COVID-19 patients than in female COVID-19 patients [29].

The non-random sampling approach, the lower sample size, and data collection from a single facility were some of the study's drawbacks. To confirm the findings of the current study and enhance the generalizability of the results, future multi-center studies with bigger sample sizes are needed.

CONCLUSION

Individuals with blood group A are more liable to acquire COVID-19 infection, whereas having blood type O is a protective factor. At an older age, the chances of getting COVID-19 are more in blood type B, and in females, the chances of getting COVID-19 are higher in blood type A.

ETHICS APPROVAL

The study was approved by the ethical review committee of Hussain Lakhani Hospital, Karachi Pakistan (Ref#ERC-

HLT-2021-001). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the Helsinki declaration.

CONSENT FOR PUBLICATION

Written informed consent was obtained from all the eligible participants.

AVAILABILITY OF DATA

Data is available from the corresponding author on a reasonable request.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHOR'S CONTRIBUTION

Amani Amir and Syed Tajammul Ali: Conception or design of the work, Final approval of the version to be published, Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Maleeha Sadaf: Drafting the work or revising it critically for important intellectual content, Final approval of the version to be published

Khadijah Abid: The acquisition, analysis, or interpretation of data for the work, Final approval of the version to be published

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