ABO / RH-D BLOOD TYPES AND SUSCEPTIBILITY TO SARS-COV-2 INFECTION IN HEALTH CARE WORKERS

Fawad Rahim[1], Said Amin[1], Mohammad Noor[1], Afsheen Mahmood[1], Huma Gul[1], Muhammad Usman[1]

ABSTRACT

Introduction: There are no consistent data regarding the relationship between ABO / Rh-D blood types and susceptibility to SARS-CoV-2 infection from different regions.

Objective: To determine the association between ABO/Rh-D blood types and susceptibility to SARS-CoV-2 infection among health care workers (HCW).

Methods: This was a cross-sectional analytical study carried out at Hayatabad Medical Complex (HMC) & affiliate institutes of Peshawar Medical College Peshawar. A total of 936 HCW were willing to participate. They were screened for IgG/IgM SARS-CoV- 2 antibodies and blood group. Level of IgG/IgM antibodies equal to or more than 1 was taken as positive and was considered as a surrogate marker of past SARS-CoV-2 infection. Values less than 1 were considered as negative. Chi-square test was used to determine the association between ABO/Rh-D blood types and SARS-COV-2 infection. Binary logistic regression analysis was performed to determine the odds of blood types to test positive for SARS-CoV-2 antibodies. P-value of less than 0.05 was taken as significant.

Results: Out of 936 HCWs, 299 tested positive for SARS-CoV-2 antibodies. The proportion of blood type A, B, O and AB were 28.7%, 31.1%, 28.7% and 11.5%, respectively in those HCW who were positive for SARS-CoV-2 antibodies. 25.0 % HCWs with blood type O were positive for SARS-CoV-2 antibodies as compared to 34.4% with blood groups other than O and the difference was statistically significant. The odds of blood type-O for testing positive was 0.63 (95% CI 0.46 – 0.88, p=0.007). 34.4% HCW with blood type-A tested positive as compared to 30.9% with blood type other than A (OR 1.17, 95% CI 0.87 – 1.58, p=0.292). 35.3% HCW with blood type B were positive as compared to 31.9% with Non-B blood types (OR 1.25, 95% CI 0.94 – 1.68, p=0.126). There was no significant difference (p=0.968) between HCWs with blood type-AB and blood types other than AB to test positive (31.8 % and 32.0%, respectively, OR 0.99, 95% CI 0.64 – 1.53). 32.7 % HCWs with Rh-Positive blood types tested positive as compared to 20.7% with Rh-negative status (OR 1.86, 95% CI 0.97 – 3.57, p=0.058).

Conclusion: Health Care Workers with blood type O were less likely to be positive for SARS-CoV-2 antibodies in our study.

Keywords: Health Care Workers, SARS-CoV-2, Blood types

INTRODUCTION

The epidemic of COVID-19 started as an unusual pneumonia in China in December 2019. It quickly spread across the globe & was announced as a pandemic by the World Health Organization.[1] In terms of human lives, it has affected 112,649,371 & the death tally is 2,501,229 as of 26th February 2021.[2] Pakistan reported its first case on 26th February 2020 & till now there are 578,797confirmed cases & its death tally is 12,837.[3]

The infection severity varies from asymptomatic seroconversion, mild/moderate flu-like illness to cytokine storm resulting in multi-organ failure & death.

1Khyber Girls Medical College / MTI – Hayatabad Medical Complex, Peshawar, Pakistan.

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Address for correspondence:
Dr. Said Amin
Department of Medicine, Khyber Girls Medical College / MTI – Hayatabad Medical Complex, Peshawar, Pakistan.
Cell: 0333-9115488,
E-mail: saidamin@live.com

Various risk factors for the diverse outcomes have been identified like gender, advanced age, cardiovascular, respiratory and renal disorders.[4] Molecular abnormalities like distribution of Angiotensin Converting Enzyme (ACE) receptors have been reported to affect susceptibility and outcomes of SARS-CoV-2 infection.[5]has emerged in Chinese people in December 2019 and has currently spread worldwide causing the COVID-19 pandemic with more than 150,000 deaths. In order for a SARS-CoV like virus circulating in wild life for a very long time to infect the index case-patient, a number of conditions must be met, foremost among which is the encounter with humans and the presence in homo sapiens of a cellular receptor allowing the virus to bind. Recently it was shown that the SARS-CoV-2 spike protein, binds to the human angiotensin I converting enzyme 2 (ACE2

Association of blood types has been found with different communicable and non-communicable diseases. It is stated that SARS-CoV-2 is associated with blood type-A.[6-8] As reported recently from China by Zhao et al.[6] that blood group 'A' is associated with a higher risk for COVID-19 as compared to other blood

groups while blood group 'O' offered protection in terms of susceptibility. Zietz et al.[9] from New York reported susceptibility of blood type-B and protective effect of blood type-O to SARS-CoV-2 infection. Moreover, they also found that Rh-D positive blood groups were linked to higher chances of COVID-19. Same findings have been reported from Massachusetts.[10]all adult patients who tested positive for COVID-19 across five hospitals were identified and included from March 6th to April 16th, 2020. Hospitalization, intubation, and death were evaluated for association with blood type. Univariate analysis was conducted using standard techniques and logistic regression was used to determine the independent effect of blood type on intubation and/ or death and positive testing. During the study period, there were 7648 patients who received COVID-19 testing throughout the institutions. Of these, 1289 tested positive with a known blood type. A total of 484 (37.5% Gallian et.al reported that the proportion of seropositive was significantly lower in group O donors (1.32% vs 3.86% in other donors, p = 0.014).[11]

There are contradictory reports regarding the correlation between ABO / Rh-D blood types and vulnerability to COVID-19. To date, there is no published data from Pakistan about the vulnerability of blood types to COVID-19 among HCW. This issue attracted us to determine the association between ABO/Rh-D blood types and COVID-19 among HCW in Peshawar, Pakistan.

MATERIALS AND METHODS

It was a cross sectional study involving 936 health care workers carried out at Hayatabad Medical Complex, Peshawar and affiliate Institutes of Peshawar Medical College, Peshawar.

The study was approved by the institutional review board & the institutional ethical committee. Informed written consent was obtained from every participant. A consecutive sample of 936 HCWs were included in the study. A structured questionnaire was provided to all the participants for recording demographic parameters and other risk factors for contracting the virus. Five-milliliter blood was obtained from each participant, 3 milliliters was transferred to lithium heparin bottle for SARS-CoV-2 antibodies, and 2 milliliter was used for determining the blood types. The sample for SARS-CoV-2 antibodies was immediately centrifuged & was stored at -40 degrees centigrade. It was analyzed using Elecsys® Anti-SARS-CoV-2 Immunoassay for the qualitative detection of IgG antibodies against SARS-CoV-2 (ROCHE) as per manufacturer instructions. The sensitivity & specificity of the immunoassay was 100% & 99.8% respectively as per manufacturer. For validation, positive & negative controlled tests were carried out. The cut off for positive antibodies level was taken as 1 as per manufacturer instruction, and levels less than 1 were considered negative. The participants were informed in person

about the results of the antibodies level. The data were analyzed in SPSS version 21. Descriptive statistics for age, gender, and distribution of blood types for study population were calculated. Proportions of those who tested positive and negative for SARS-CoV-2 antibodies were determined in every blood types. Chi-square test was employed to assess the statistical significance of differences in proportions between those who tested positive in a specific blood group and those who tested positive without that blood group (e.g. positive in blood group A versus positive in non-A blood groups). P-value of less than 0.05 was taken as significant. Binary logistic regression model was applied to find out the odds of individual blood types and Rh-D type to have positive antibodies for SARS-CoV-2.

RESULTS

The demographic parameters of study participants are outlined in Table 1.

Out of 936 HCWs, 299 tested positive for SARS-CoV-2 antibodies. The proportion of blood type A, B, O and AB were 32.1%, 36.1%, 20.4% and 11.4%, respectively in those HCW who were positive for SARS-CoV-2 antibodies.

25.0 % HCWs with blood type O were positive for SARS-CoV-2 antibodies as compared to 34.4% with blood groups other than O and the difference was statistically significant (p=0.007). 34.4% HCW with blood type-A tested positive as compared to 30.9% with blood type other than A (p=0.292). 35.3% HCW with blood type B were positive as compared to 30.3% with Non-B blood types (p=0.126). There was no significant difference (p=0.968) between HCWs with blood type-AB and blood types other than AB to test positive

Table 1: Demographic parameters of study population (n=936)

Age, Mean ± SD (years)	30.78 ± 12.88
Gender, No. (%)	
Male	630 (67.3%)
Female	306 (32.7%)
SARS-CoV-2 antibody, No. (%)	
Positive	299 (31.9%)
Negative	637 (68.1%)
Blood groups, No. (%)	
A	279 (29.8%)
B	306 (32.7%)
O	244 (26.1 %)
AB	107 (11.4%)
Rhesus group, No. (%)	
Positive	878 (93.8%)
Negative	58 (6.2%)

Table 2: Association of blood groups with SARS-CoV-2 antibody status

Blood Groups		SARS-CoV-2 anti-bodies positive No. (%)	SARS-CoV-2 anti-bodies Negative No. (%)	P value	Odds to be SARS-CoV-2 anti-bodies positive with 95% CI
A	Blood type-A	96 (34.4%)	183 (65.6%)	0.292	1.17 (95% CI 0.87 – 1.58)
	Non-A Blood types	203 (30.9%)	454 (69.1%)		
B	Blood type-B	108 (35.3%)	198 (64.7%)	0.126	1.25 (95% CI 0.94 – 1.680)
	Non-B blood types	191 (30.3%)	439 (69.7%)		
O	Blood type-O	61 (25.0%)	183 (75.0%)	0.007	0.63 (95% CI 0.46 – 0.88)
	Non-O blood types	238 (34.4%)	454 (65.6%)		
AB	Blood type-AB	34 (31.8%)	73 (68.2%)	0.968	0.99 (95% CI 0.64 – 1.53)
	Non- AB blood types	265 (32%)	564 (68%)		
Rh	Rh-Positive	287 (32.7%)	591 (67.3%)	0.058	1.86 (95% CI 0.97 – 3.57)
	Rh- Negative	12 (20.7%)	46 (79.3%)		

(31.8 % and 32.0%, respectively). 32.7 % HCWs with Rh-Positive blood types tested positive as compared to 20.7% with Rh-negative status (p=0.058) (Table 2).

On binary logistic regression analysis, the odds of blood type-O for testing positive for SARS-CoV-2 antibodies was 0.63 (95% CI 0.46 – 0.88), while those for blood type-A, B and AB were 1.17 (95% CI 0.87 – 1.58), 1.25 (95% CI 0.94 – 1.680) and 0.99 (95% CI 0.64 – 1.53). Rh-positive status had odds of 1.86 (95% CI 0.97 – 3.57) to test positive.

DISCUSSION

There has been increasing interest to identify patient-specific risk factors that would determine vulnerability to SARS-CoV-2 infection. Apart from demographic and epidemiological risk factors, the role played by biological markers has been studied. Of late, ABO blood type and Rhesus status have been suggested as a cause for variable predisposition to COVID-19. Studies on the relationship of ABO/Rh-D blood types with SARS-CoV-2 infection are not consistent in their findings, and researchers have not arrived at a plausible explanation for their results.

In this study, HCW with blood type-O were less likely (OR 0.63, 95% CI 0.46 – 0.88) to be positive for SARS-CoV-2 antibodies as compared to those with blood type other than type-O (25.0% vs 34.4%, p=0.007). Similar protective effect of blood type-O has been reported in other studies [6,7,9,10,12,13] This protection has been attributed to Anti-A antibodies in those with blood type-O.[14] Since people with blood type-B also have Anti-A antibodies like blood type-O, differences in immunoglobulin subclass (IgM in former and IgG in latter) in Anti-A antibodies have been postulated for the consistently documented protective behavior of blood type-O.[12,15]

34.4% HCW with blood type-A tested positive as compared to 30.9% with blood type other than A (OR 1.17, 95% CI 0.87 – 1.58, p=0.292). Though result of this study did not reach statistical significance, higher susceptibility to COVID-19 in those with blood type-A has been reported by Zhao et al., Li et al. and Fan et al.[6–8] Moreover, Latz et al. and Abdollahi et al. have not found any correlation between blood type-A and susceptibility to COVID-19.[10,13]

35.3% HCW with blood type B were positive as compared to 30.3% with Non-B blood types but the difference was not statistically significant (OR 1.25, 95% CI 0.94 – 1.680, p=0.126). This is consistent with results of Zhao et al.[6] Li et al.[7], Fan et al.[8], from Wuhan, China, and Abdollahi et al.[13] from Tehran but in contrast to studies carried out by Latz et al.[10] in Boston, and Zeitz et al.[9] in New York. Since people with blood type-B also have Anti-A antibodies like blood type-O, differences in immunoglobulin subclass (IgM in former and IgG in latter) in Anti-A antibodies have been postulated for the consistently documented protective behavior of blood type-O, and not blood type-B [12,15].

There was no significant difference (p=0.968) between HCWs with blood type-AB and blood types other than AB to test positive (31.8 % and 32.0%, respectively, OR 0.99, 95% CI 0.64 – 1.53). This is in contrast to findings of Zhao et al.[6], Latz et al.[10] and Abdollahi et al.[13]

Significantly higher proportion of Rh-Positive blood types tested positive (32.7 % vs 20.7%, p=0.058) as compared to Rh-negative blood types. Rh-positive

blood types were more likely to test positive as compared to Rh-negative blood types (OR 1.86, 95% CI 0.97 − 3.57). This is in contrast to findings of Latz et al.[10] and Zietz et al.[9] However, Abdollahi et al.[13] have observed no correlation between Rh(D) blood type and susceptibility to SARS-CoV-2.

Except for the protective behavior of blood type-O which has been constantly documented in studies from different regions of world, researchers have found inconsistent results about susceptibility of blood types A, B and AB to SARS-CoV-2. This suggests that presence of Anti-A antibodies alone does not offer protection against infection with SARS-CoV-2. Since studies on the topic have enrolled population from different ethnicities which might have accounted for the differences in outcomes, genetic make-up may be an additional factor in determining susceptibility to COVID-19. Because this study was focused on HCWs who have higher exposure and infection rates as compared to general population, its findings may not represent the trends in general population. Studies involving larger samples from general population are needed to ascertain the role of ABO/Rh blood types in pathogenesis of COVID-19.

CONCLUSIONS

Having blood type-O is likely to offer protection against infection by SARS-CoV-2 to HCWs. Since HCWs have higher exposure to SARS-CoV-2, general population may not show similar susceptibility to SARS-CoV-2 infection based on their blood groups. This can be established by research on large, representative samples from general population.

REFERENCES

1. W.H.O. Virtual press conference on COVID-19 − 11 March 2020 [Internet]. Available from: https://www.who.int/docs/default-source/coronaviruse/transcripts/who-audio-emergencies-coronavirus-press-conference-full-and-final-11mar2020.pdf?sfvrsn=cb432bb3_2: (accessed 09/06/2020)

2. W.H.O. WHO Coronavirus Disease (COVID-19) Dashboard [Internet]. Available from: https://covid19.who.int/?gclid=CjwKCAjw1K75BRAEEiwAd41h1OSTbAOdEK4-U4n0tVe2nMkkHxqRC6zkC9JS0YUa8s5mvPTG2sXQhxoCFsgQAvD_BwE: (accessed 09/12/2020)

3. COVID Portal Pakistan [Internet]. Available from: http://covid.gov.pk/: (accessed 09/12/2020)

4. Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020;382(18):1708−20.

5. Devaux CA, Rolain JM, Raoult D. ACE2 receptor polymorphism: Susceptibility to SARS-CoV-2, hypertension, multi-organ failure, and COVID-19 disease outcome. J Microbiol Immunol Infect. 2020;53(3):425−35. Available from: https://doi.org/10.1016/j.jmii.2020.04.015

6. Zhao J, Yang Y, Huang H, Li D, Gu D, Lu X et. al. Relationship between the ABO Blood Group and the COVID-19 Susceptibility [Internet]. 2020. Available from: https://www.medrxiv.org/content/10.1101/2020.03.11.20031096v2: (accessed 03/28/2020)

7. Li J, Wang X, Chen J, Cai Y, Deng A, Yang M. Association between ABO blood groups and risk of SARS-CoV-2 pneumonia. Br J Haematol. 2020;190(1):24−7.

8. Fan Q, Zhang W, Li B, Li D-J, Zhang J, Zhao F. Association Between ABO Blood Group System and COVID-19 Susceptibility in Wuhan. Front Cell Infect Microbiol. 2020;10(July):1−7.

9. Zietz M, Tatonetti N. Testing the association between blood type and COVID-19 infection, intubation, and death [Internet]. medRxiv : the preprint server for health sciences. 2020. Available from: https://www.medrxiv.org/content/10.1101/2020.04.08.20058073v2: (accessed 04/02/2020)

10. Latz CA, DeCarlo C, Boitano L, Png CYM, Patell R, Conrad MF, et al. Blood type and outcomes in patients with COVID-19. Ann Hematol. 2020;99(9):2113−8.

11. Gallian P, Pastorino B, Morel P, Chiaroni J, Ninove L, de Lamballerie X. Lower prevalence of antibodies neutralizing SARS-CoV-2 in group O French blood donors. Antiviral Res. 2020;181:104880. Available from: https://www.sciencedirect.com/science/article/pii/S0166354220302941

12. Gérard C, Maggipinto G, Minon JM. COVID-19 and ABO blood group: another viewpoint. British Journal of Haematology. 2020.

13. Abdollahi A, Mahmoudi-Aliabadi M, Mehrtash V, Jafarzadeh B, Salehi M. The novel coronavirus sars-cov-2 vulnerability association with abo/rh blood types. Iran J Pathol. 2020;15(3):156−60.

14. Guillon P, Clément M, Sébille V, Rivain JG, Chou CF, Ruvoën-Clouet N, et al. Inhibition of the interaction between the SARS-CoV Spike protein and its cellular receptor by anti-histo-blood group antibodies. Glycobiology. 2008;18(12):1085−1093.

15. Stussi G, Huggel K, Lutz HU, Schanz U, Rieben R, Seebach JD. Isotype-specific detection of ABO blood group antibodies using a novel flow cytometric method. Br J Haematol. 2005;130:954−63.