Investigating the Correlation between the Blood Type and the Rate of Infection by SARS-CoV-2

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BRIEF. Statistical analysis to investigate if certain blood groups are more susceptible to the SARS-CoV-2 virus.

ABSTRACT. From the statistics of patients infected by SARS-CoV-2, it is clear that there is a link between the ABO blood group and the infection rate in individuals. This raised an important question of why certain blood groups are more susceptible to the virus, and whether an expression of the ACE-2 gene correlates to more severe symptoms. I hypothesize that there is a correlation between the ABO blood group and COVID-19 infection rate. I also hypothesize that the ACE-2 expression is enhanced in certain blood types, increasing the risk of infection. I focused on a theoretical approach and statistical analysis to test my hypothesis. Correlating past researches, we concluded that O blood type has a lower infection rate than A blood type. We also came to the same conclusion from the Statistical hypothesis testing with the chi-squared test.

INTRODUCTION.

Research in the field of COVID-19 and SARS-CoV-2 has brought into question the relation between blood type and both the likelihood of infection and the severity of the symptoms of COVID-19. One particular study has identified that those with type-A blood have a 45% greater chance of respiratory failure from COVID-19, whereas those with type-O blood have a 35% lower chance of such [1]. Besides, another study has determined that individuals with type-A blood account for 38% of all ill patients while individuals with type-O blood account for only 26% [2]. From the statistics of patients infected by SARS-CoV-2, it is clear that there is a link between the ABO blood group and both the severity and the infection rate in individuals.

Furthermore, research has also led scientists to believe that a relationship between the amount of ACE-2 genes expressed in a human genome correlates to the severity of the virus's symptoms. The cell surface enzyme, angiotensin-converting enzyme 2, has been proven to bind to the SARS-CoV-2 spike protein and assist the virus with internalizing into human cells. Thus, the binding of the SARS-CoV-S protein to ACE2 is crucial for SARS-CoV infection. One particular study involving single-cell RNA sequencing indicated that Asian males may have higher expressions of ACE2 and experience extreme symptoms because of that. When the study took place, reports of the infection from non-Asian regions for comparison were limited, how-ever, a study from Munich, Germany, reported four cases, all of which show mild symptoms and no severe illness [2]. From the study presented, it is clear that the increase of expressed ACE2 genes in the human genome results in patients experiencing more severe symptoms of the virus. This raised an important question of why certain blood groups are more susceptible to the virus, and whether an expression of the ACE-2 gene correlates to more severe symptoms.

In this research, I want to determine if there is a correlation between the ABO blood group and COVID-19 infection rate.

MATERIALS AND METHODS.

I used statistical hypothesis testing with chi-squared test to determine if there is any correlation between the ABO blood group and the infection rate. For the statistical analysis, patient data was obtained from a research paper published online by Mike Barnkob et al [3]. Original data were extracted from electronic health records capturing all Danish patients, the Danish Microbiology Database, the Danish Civil Registration System, the Danish Authorizations Register for health care workers, the Danish Patient Safety Authorization Register, and the Danish National Patient Register in a pseudo-anonymized form. The data includes all Danish individuals tested for SARS-CoV-2 between 27 February 2020 and 30 July 2020, with a known ABO blood group.

Table 1. Patient data from Danish Microbiology Database

Blood Group	SAR-CoV-2 tested, n				Reference population	
	Positive	%	Negative	%	n	%
O	2851	38.41	193401	41.48	919303	41.70
A	3296	44.41	199211	42.73	934421	42.38
B	897	12.09	52838	11.33	252559	11.46
AB	378	5.09	20782	4.46	98459	4.47
	7422		466232		2204742	

Equality of proportions between blood groups was tested using the likelihood ratio chi-squared test and evaluated at a 5% significance level (95% confidence interval).

First, I verified if the infection rate is proportional to the blood group frequency in the general population. Then I combined one or more blood type in a group and verify if the infection rate is different than the rest. In some cases, I could not reject the NULL hypothesis, so I had alternate hypothesis and checked Type II error (β). In my hypothesis testing I tried to determine the exact difference of infection rate between the groups (e.g., 3% or 4%).

RESULTS.

I was able to reject the first NULL Hypothesis – "The infection rate is proportional to the blood type frequency in the general population" ($\chi^2 = 35.4963 > 12.8381$ (p=0.005, df=3)). This implies the infection rate for at least one of the blood groups is different than the blood group proportion in the general population. To identify which blood group(s) are different from the rest, I designed the second hypothesis test with O & B in one group and A & AB in the other group.

I could not reject the second NULL Hypothesis – "O and B combined has a 3% lower infection rate compared to the reference population. A and AB combined have a 3% higher infection rate" ($\chi 2 = 0.36 < 3.84146$ (p=0.05, df=1); $\beta = 0.1$ at 2%). To identify which one is more dominating in the second group (A or AB), I separated out A from the rest in the third test.

I could not reject my third NULL Hypothesis – "A has a 3% higher infection rate than the reference population. All other groups (O, B, AB) combined have a 3% lower infection rate" ($\chi 2 = 2.84 < 3.84146$ (p=0.05, df=1); $\beta = 0.005$ at 2%). To identify which one is more dominating in the first group (O or B), I separated out O from the rest. Also, I tested with higher threshold (4%) to compare against the A group.

I could not reject my fourth NULL Hypothesis – "O has a 4% lower infection rate than the reference population. All other groups (A, B, AB) combined have a 4% lower infection rate" ($\chi 2 = 1.62 < 3.84146$ (p=0.05, df=1); $\beta = 0.1$ at 3%).

Table 2. Summary of test results

Blood Group	**Infection Rate (Compared to reference population)**
O + B	3% Lower
A + AB	3% Higher
Blood Group	**Infection Rate (Compared to reference population)**
A	3% Higher
O+ B + AB	3% Lower
Blood Group	**Infection Rate (Compared to reference population)**
O	4% Lower
A + AB + B	4% Higher

DISCUSSION.

At 95% confidence level, hypothesis tests suggest that O & B combined has a 3% lower infection rate, this indicates that certain commonalities between O &B (***presence of Anti-A antibody***) may be responsible for the lower infection rate. Type O alone has a 4% lower infection rate compared to all other types combined indicates that there is something unique about the blood type O (***absence of antigen in red blood cell***) which is not present in B, which is responsible for lowering the infection rate further. My result agrees with other research published regarding the correlation between blood type and COVID-19 infection rate.

Limitations: Our data considered Denmark, which is around 87% Danish. The results of our study, while suggesting a potential correlation, cannot be conclusive for other ethnic groups. Also, the Gender and Rh (+, -) factor is not considered. In the future, I would like to analyze data from different ethnic groups to understand how COVID-19 infection varies by blood-type in their ethnicity.

CONCLUSION.

Statistical hypothesis tests support initial theoretical deductions and suggest that ABO gene could impact the COVID-19 infection rate. Knowledge and further verification of these could pave the way for new suppressants to decrease the expression of these genes and minimize the infection efficacy of SARS-CoV-2 in individuals, especially those with type-A or AB blood. Considering that the correlation between the infection rate by blood type, individuals with type-A blood can be prioritized in vaccination queues.

Other research led scientists to believe that a relationship between the amount of ACE-2 genes expressed in a human genome correlates to the severity of the virus's symptoms. Is it possible that B & O blood type may have reduced ACE-2 expression or Anti-A antibodies of B & O blood type inhibits the interaction between SARS-CoV spike protein and its cellular receptor? These need to be further researched.

SUPPORTING INFORMATION.

1. Figure S1. Theoretical deduction to establish the hypothesis.
2. Figure S2. SARS-CoV-2 utilizes the ACE-2 receptor as an entryway.
3. Figure S3. Reduced levels of cardiac ACE-2 in hypertension.
4. Method M1. SARS-CoV-2 binds with ACE-2 as their main receptor. Higher ACE-2 expression could suggest a higher rate of SARS-CoV-2 infection.
5. Method M2. Reduced levels of cardiac ACE2 have been reported in hypertension (HT).
6. Method M3. B and O blood group more susceptible to hypertension than blood groups A & AB.
7. Method M4. Reduced ACE2 expression for blood type B & O.
8. Method M5. Anti-A antibodies present in blood type B & O.
9. Method M6. Natural antibodies of the ABO blood system could inhibit the interaction between SARS-CoV spike protein and its cellular receptor by anti-histo blood group antibodies.
10. Method M7. M5 & M6 suggest Anti-A antibodies of B & O blood type could inhibit the interaction between SARS-CoV spike protein and its cellular receptor.
11. Method M8. M1, M4 & M7 suggests B & O blood type has a lower infection rate than A and AB blood type.

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