

# The Association of ABO Blood Groups and Diseases Including SARS-CoV-2 (COVID-19)

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## ABSTRACT

**Objective:** To review the literature on the association between ABO blood groups and diseases, including Sars-CoV-2 (COVID-19).

**Methods:** Conducted a literature search in google and Pubmed on blood groups and disease associations. Twenty-five reports were analyzed.

**Results:** Significant associations have been reported between specific blood groups and diseases including malaria, cholera, cancer, cognitive impairment, heart disease, hypertension, clotting disorders, longevity, and even intelligence quotient. Recently a number of studies have reported an association between individuals with blood group A and increased risk of infection and severity of disease with COVID-19 infection whereas Group O individuals had significantly less risk.

**Conclusion:** ABO blood groups are associated with the susceptibility and severity of certain diseases. However, they do not necessarily cause diseases as there are likely a number of confounding variables or linked genetic loci. Nevertheless, ABO blood groups may be a contributing factor in specific diseases including COVID-19 infection.

## Keywords

ABO blood group, COVID-19, Infection, Blood groups.

## Key Points

1. ABO blood groups are significantly associated with several diseases including COVID-19.
2. These blood group associations with diseases may or may not be causal.
3. These associations may better predict and aid in the prevention and treatment of disease.

## Introduction

Initial observations in 1901 by Austrian pathologist and Nobel laureate, Karl Landsteiner, led to the discovery of the four main blood groups A, B, AB, and O. Ever since there have been

many reports of associations between blood groups and disease, personality types, and mating compatibility. In the United States, 44% of the general population possess blood group O, 42% blood group A, 10% blood group B, and 4% have blood group AB [1]. Blood groups differ based on an individual's glycosyltransferases or lack of specific glycosyltransferases which confer the presence or absence of A or B antigens. For example, individuals with blood group A have a transferase enzyme that will add an N-acetylgalactosamine to the terminal sugar of the polysaccharide chains found on proteins and lipids. The addition of this specific sugar converts the antigen recognized on the distal portion of the sugar chain from the H antigen to the A antigen. Likewise, individuals with blood group B have a transferase enzyme that will add a galactose to the H antigen conferring the B antigen. Individuals with both transferases will add both A and B antigens,

Group O individuals lack these transferase enzymes and express neither A or B antigens. Since the early 1900s, numerous studies have reported plausible associations between blood groups and certain diseases as well as personality and mating compatibility. There have been a number of systematic reviews of studies which have indicated significant disease associations with ABO blood groups. In this article we will briefly highlight some of the more interesting study findings including the ABO blood group association with COVID-19 infection.

Several studies have found non-O blood groups have a greater likelihood of certain diseases and death from certain medical conditions (Table 1). Compared to blood group O, one review concluded blood group A individuals have a higher incidence of disease, especially cancer. Group A individuals had an elevated rate of cancer of salivary glands (64%), stomach (22%), ovaries (28%), colon (11%) versus group O [2]. One plausible explanation that blood group A has a higher incidence of cancer has to do with the antigens located on the tumor. Tumors with “A-like” antigens may be viewed as foreign in group O individuals and the body responds to attack that tumor whereas group A patients do not recognize the tumor antigen as foreign [3].

Group A	Group B
Colon Cancer (2) COVID-19 (21,22,23) Deep Vein Thrombosis (10) Ovarian Cancer (2) Salivary Gland Cancer (2) Malaria (4) Stomach Cancer (2) Heart Disease (7)	Deep Vein Thrombosis (10) Gonorrhea (2) Salmonella (2) Tuberculosis (2) Malaria (4)
Group AB	Group O
Cognitive Disorders (8) Salmonella (2) Type II Diabetes (2) Deep Vein Thrombosis (10)	Acute Lymphoblastic Leukemia (2) Cholera (6) Hypertension (11) Multiple Endocrine Neoplasia type 1 (2) Peptic Ulcers (2) Tuberculosis (2)

**Table 1:** ABO Groups and Disease Association.

Group A individuals also have a significantly greater risk of severe malaria. Of 293 children with malaria in Ghana, children with complicated malaria were almost two times as likely to be of blood groups A and B versus group O [4]. Roughly 50% of the population of Ghana is group O, 24% group A and 21% group B [5]. As for cholera, blood group is strongly associated with risk of mortality and severity of symptoms. Blood Group O individuals are eight times more likely to be hospitalized for cholera compared to other blood groups [6].

A systematic and meta-analysis of 17 studies of roughly 220,000 participants analyzed if there was an association between ABO groups and coronary artery disease. The combined results of the studies found those who possessed either blood group A or a non-O blood group had a greater risk of coronary artery disease. Blood group A had a 14% greater likelihood of developing heart

disease compared to group O. Moreover, the results indicated that the risk of heart disease in blood group O was significantly lower than that in non-O groups [7].

Interestingly, AB individuals also have an increased likelihood of cognitive impairment, according to a prospective cohort study published in the American Academy of Neurology. Group AB individuals were 82% more likely to develop cognitive and memory issues than any other blood group [8].

Non-O blood types have elevated levels of Von Willebrand factor (VWF) found in the blood plasma. VWF plays a role in platelet aggregation in the blood vessels. Those with non-O blood type have significantly higher levels of VWF compared to group O and appears to put groups A, B and AB individuals at greater risk of blood clotting than group O [9]. A systematic review found the risk of venous thromboembolism among non-O blood group carriers was 1.79 times higher than the O blood group [10]. However, group O individuals generally have higher blood pressure and cholesterol levels. Researchers are still unclear why group O has a lower probability of heart disease, but an increased likelihood of hypertension [11].

Group O individuals seem to have an advantageous blood group. This group has been found to have the lowest probability of developing coronary artery disease and even an enhanced level of fitness [12,13]. People who were blood group O over 75 years of age, group O active athletes over 40, and group O surgeons over age 65 presented an increased level of fitness versus all blood groups. The study suggested that individuals with blood group O have a 60% greater chance of reaching 75 years of age compared to group A individuals [13]. A more recent study examined if ABO groups correlate with life expectancy. The observation was 70% of individuals 100 years or older had group O blood and group B declined the most with age compared to 44% O and 10% B in the general population [14].

Blood Type	Positive Traits	Negative Traits
A	Earnest, Organized	Stubborn, Anxious
O	Easy Going, Leader, Optimistic	Insensitive, Unpunctual
B	Passionate, Creative	Selfish, Uncooperative
AB	Talented, Composed	Eccentric, Two-Faced

**Table 2:** Japanese Blood Type Personality Theory.

In Japanese culture, ABO blood groups are considered important indicators in determining a person's personality and compatibility (Table 2). A 2016 survey found 99% of 3,355 Japanese individuals knew their blood group [15]. In the U.S., 57% of Americans surveyed knew their blood group [16]. Knowing your blood group in Japan is an essential measure of one's work and love life. Japanese dating sites encourage users to upload their blood group to best match the user to a potential spouse. The blood group matches most likely to result in successful marriage are: O Male × A Female, A Male × A Female, O Male × B Female, O Male × O Female [15]. Many corporations in Japan look at an

applicant's ABO group to understand their personality type. Even Japan's softball team that won gold in the 2008 Beijing Olympics separated and trained players according to their blood group [17]. There is no clear scientific consensus that a relationship exists between the ABO blood group and personality traits. However, a recent study hypothesized that the dopamine beta-hydroxylase gene is in linkage with the *ABO* gene [18]. The study detected a significant linkage disequilibrium between different ABO types and differential expression of dopamine beta-hydroxylase that might affect neurotransmitter activity, which in turn is hypothesized to influence behavior and personality [18].

Researchers in 1973 even correlated intelligence quotient (IQ) with ABO blood groups. The study conducted in Oxford, England determined the IQ and ABO blood groups of adults in seven different villages and deemed the differences in IQ to be significant. Mean IQ of blood group O adults was significantly higher than those with blood group A<sub>1</sub> [19]. However, a more recent study also analyzed the association between IQ and blood type. The study consisted of a large sample size of medical professionals and found no association between any blood group and intelligent quotient [20].

Recent studies suggest a significant association between ABO blood groups and an increased risk of contracting SARS-CoV-2 (COVID-19) infection and increased disease severity. One preliminary study in the United States on ABO groups and the coronavirus was conducted in New York City by researchers at Columbia University in April of 2020 and blood typed 1,559 COVID-19 infected patients. The study observed blood group A individuals were 34% more likely to test positive for the virus compared to other blood groups [21]. Another study reported consistent findings with COVID-19 patients at seven different hospitals in the Italian and Spanish epicenters. Those with group A blood had a 45% higher rate of respiratory failure from the virus [22]. Genetic data from that same study also discovered blood group O had a protective effect against the illness and a 35% reduction in risk for coronavirus. At the beginning of the pandemic in March, Chinese researchers at Wuhan Jinyintan Hospital recorded 38% of 1,775 COVID-19 patients were type A and 26% type O compared to 32% A and 34% O in the general population [p-value<0.001] [23]. Out of the four blood groups, group A patients accounted for the greatest proportion of deaths from COVID-19 [p-value=0.008]. Roughly 41% of the 206 coronavirus deaths at Wuhan Jinyintan Hospital were patients with blood group A and group B patients represented the second most deaths with 25% of the deaths [23]. 23andMe released preliminary data of ABO's role in susceptibility to coronavirus. In about 750,000 individuals, blood group O was 9-18% less likely to test positive for coronavirus [24]. Note this study has not been peer-reviewed.

However, a study of 1279 of 1688 crewmembers who became COVID-19 infected on a French navy nuclear aircraft carrier did not find an association between ABO blood groups and increased risk of COVID-19 infection. One plausible reason these results may be inconsistent with the other studies mentioned above is

that the crewmembers were young, healthy adults (median age 28 years old) with no significant co-morbidities and were in extremely close contact for a long period of time which may have lessened the protective effect of O blood group [25].

It is also important to recognize that both studies conducted at Columbia University and China are reported as preprint articles that have yet undergone peer review. ABO blood group association has not been proven to be casual in the severity of the SARS-CoV-2 infection. There are limitations to each study. A Columbia University non-peer reviewed study reported that AB blood groups had a "significant odds decrease" of contracting COVID-19 [21]. However, group AB represented the smallest number of individuals in the study. As for the study conducted in China in March, medical conditions that affect the severity of COVID-19, such as chronic obstructive pulmonary disease, were not accounted for in the research [23]. In addition, it is not clear from these studies what exactly was used as the general population control group in determining ABO group percentage comparisons.

Studies conducted since the early 1900s have demonstrated associations between ABO blood groups and disease. With this knowledge, doctors could use a person's ABO blood group to aid in the prevention or treatment of a disease. Although ABO blood groups can be correlated with the susceptibility and severity of certain diseases, they do not necessarily cause diseases as there are likely a number of confounding variables or linked genetic loci. Theoretically, it is possible the specific ABO blood group antigens or lack thereof could cause biochemical reactions or immune responses that result in greater risk for disease. However, other risk factors such as smoking, low physical activity levels, and poor nutrition are more understood associations and are likely to play a more significant role in the development of an illness than ABO blood group. Nevertheless, ABO blood groups may be a contributing factor in specific diseases including COVID-19 infection.

## Funding

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