Interrelation of Blood Type, Character, and Diseases

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Abstract

Introduction:

Several studies have been done to see if there is a link between infectious diseases and blood groups. However, no studies have been done to see if there is a link between the frequency and severity of leptospirosis and blood types. The goal of this study was to find out if there is a link between blood type and how bad leptospirosis is.

We used a case-control design to examine 2018 leptospirosis cases among hospitalized patients in different hospitals in Punjab ,Pakistan. Patients' loved ones volunteered to be the study's control group. Testing was done to determine the patient's blood type (ABO and Rh) and the extent of the illness. Statistics were evaluated using SPSS 22.

The findings show that 300 participants (150 in the case group and 150 in the control group) joined the study. There were 81.3% males and a mean age of 44.35 15.39 years. O+, A+, and B+ were the most common blood types in both sets of participants. This difference in blood group frequency was statistically significant (P =.037). There was no statistically significant correlation between illness severity and ABO or Rh blood types (P >.05).

Conclusions:

In our analysis, O+ individuals made up the majority of those suffering from leptospirosis. Patients had a much higher frequency of O than controls did, but there was no correlation between leptospirosis and

Rh. People with more advanced disease were more likely to have this blood type. Finally, ABO and Rh blood types do not correlate with illness severity in a statistically significant way.

Keywords: *Interrelation, Blood Type, Character, Diseases*

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Introduction

Blood types A and B are found in different amounts in different groups of people. Mourant et al.2(p1) did a good job of solving the main problems that their findings brought up about where these differences come from. Which came first: natural selection based on differences in fitness between blood groups and traits that depended on the local environment, or random genetic drift and founder effects in small populations that caused the original, lucky frequencies to be multiplied and stabilized over time? Mourant et al. came to the conclusion that "most workers now believe that both processes are working, but it's still not clear which one is more important." 2 We now know how the genes, gene products, and antigens that cause blood type polymorphisms are put together, and in many cases, we know enough about how they work to describe how they interact with outside agents. 3-5 Also, Y-chromosome and mitochondrial DNA haplotype studies in human populations give us new information about how genetic drift and founder effects affect the genetic makeup of different people groups around the world. 6 Now that we have this new information, it seems like a good idea to see if our previous ideas about how natural selection and founder effects affect the distribution of blood types in humans have been true. Human blood-type antigens are found on the surface of red blood cells. These antigens have different phenotypes and genetically determined glycoconjugate structures that affect how these cells work and what goes wrong with them [1, 2]. The structure of the oligosaccharides that bound to the antigens was also used to figure out the blood type. In this case, glycosyltransferase enzymes that help attach sugar molecules to the oligosaccharide chain are primary gene products, while blood group antigens are secondary gene products. Most people's immune systems make antibodies against these carbohydrate parts because they see them as foreign invaders [3]. You can't say enough about how important the blood group system is to medical research on a wide range of diseases [4]. Due to the lack of antigens for some blood groups, the link between blood group and susceptibility to some infectious and non-infectious diseases has been debated. The presence or absence of antigens in certain blood types changes the shape and function of blood membranes. Because blood group activities depend on the structure [1, 5], blood groups can be linked to both illness and health. Blood group antigens are found in leukocytes, certain organs, plasma proteins, platelets, and a wide range of enzymes on the surface of cells [6]. Body fluids that might have blood group antigens are sweat, saliva, breast milk, seminal fluid, urine, gastric secretions, and amniotic fluid [7, 8]. Mutations in a gene's DNA, such as deletions, inversions, insertions, alternative splicing, and single-nucleotide polymorphisms (SNPs), can change the antigens, add new antigens, or even stop the gene from being expressed completely [3]. Most antigens, on the other hand, are made by a single gene. When it comes to antigens, the ones from the good group are some of the most important, have been studied the most, and were found first [9]. The glycoconjugate structures of RBCs act as receptors for exogenous ligands, viruses, bacteria, and parasites, as well as transporters, channels, structural proteins, adhesion molecules, and enzymes [10]. But the exact processes that would explain how blood group antigens and illness are linked in adhesion molecules are not known yet. Surprisingly, though, some of these parts are important for making RBCs. Some work as cell adhesion molecules (CAMs), and others are involved in human illness [11, 12]. Certain blood types have been linked to both infectious [7, 16] and non-infectious [7, 17] diseases. It's possible that both the environment and the genes of the person who gets sick are very important. After Landsteiner found out about the blood group system in 1901, it was looked into as a possible cause of a number of diseases, such as stomach cancer and peptic ulcer.

Literature Review

Some infectious diseases have been linked to polymorphism, which has been written about in [24–26]. Because of your A/B antigen status and

whether or not you have anti-A/B antibodies, it's important to know if you have a strong or weak defense against infection. The gene is still there in many different types of vertebrates. Anti-A/B antibodies may be lost over time, so it may not be that important for species to share functional A and B genes. Still, A/B specificity gene conversion that changes amino acids or recombination with non-functional parts of genes may have been a way for organisms to protect themselves from microbial attacks [27]. Glycoconjugates on the outside of red cells work well as places where parasites, bacteria, and viruses can attach [9]. Glycosylation polymorphisms in the blood type may change the links between the host and the pathogen and make people with different glycosylation profiles more or less vulnerable [9]. This is because infectious pathogens often use glycoconjugates on the surface of cells as attachment sites. It's important to remember that some microorganisms can pass on the blood group antigens of their host to other organisms (molecular mimicry). Early etiological studies [9] showed that it was linked to the spread of infectious diseases like cholera. A study published in [28] found that most of the differences in blood types between different parts of the world are due to past epidemics. People think that the "H-like" antigen on the plague bacillus (and cholera) and the "A-like" antigen on the smallpox virus are what make them different from each other. Anti-A (groups B and O) gives resistance to smallpox [1, 29]. Anti-H (groups A1 and B) gives resistance to plague and cholera. People with blood type O were more likely to get a severe infection after getting cholera (Vibrio cholerae strains O1 El Tor and O139), according to reports [26]. People with other blood types were less likely to get a severe infection. In 1996, 87.5% of people with blood type O who got infections like Escherichia coli O157 died in Scotland. People with blood type O are more likely to get cholera, the plague, tuberculosis, and mumps. People with blood type A are more likely to get smallpox and Pseudomonas aeruginosa. People with blood type B are more likely to get gonorrhea, tuberculosis, and Streptococcus pneumoniae, E. coli, and salmonella infections. But because the Norovirus is a strain-dependent pathogen, people with blood type B are less likely to get sick from it and get infected, while people with blood type O are much more likely to get sick [1, 9].

Different strains of *P falciparum* use different blood group proteins as receptors

Red cell receptors exploited by various parasite strains could be identified due to the combination of readily available in vitro culture techniques for studying P falciparum invasion of human red cells and well-characterized unusual blood group characteristics. It was hypothesized, and then proved, that the sialic acid-rich red cell surface glycoproteins known as Glycophorin A (Ena_ cells100) and Glycophorin B (S-s_ cells101) served as parasite receptors. 102-105 Some strains of P falciparum also bind to glycophorins C (GPC) and D (Greed cells). 106-108 Proteins called glycophorins play a significant role on the surface of red blood cells. The most abundant red cell surface proteins are glycophorin A (GPA) and the primary anion transport protein (AE1, Band 3), each with about 106 copies/red cell; glycophorins B, C, and D account for an additional 450 000 copies/red cell. 109,110 Surprisingly however, there is scant experimental evidence that GPA expression has been negatively selected for in response to P falciparum infection. In some parts of Africa, people who carry the hybrid GPA-GPB protein Dantu have red blood cells that are resistant to invasion. Malaria patients in South East Asia often have the GPB-GPA-GPB MiIII protein, and its enhanced expression has been linked to increased patient survival. 112 Sialic acid's role in GPAin receptor formation against P. falciparum malaria Patients with the M1 antigen113 have red cells that produce a glycosylation variation of GPA that has N-acetyl D-glucosamine in portions of the sialic acid-rich O-glycans at the N-terminus. This may be a factor in determining whether or not they are susceptible to malaria.

Circulatory Diseases

Many studies have found that people with blood types other than O have a much higher chance of developing ischemic heart disease and atherosclerosis [36]. In addition, following GWAS (genome-wide association studies) investigated these links between peripheral vascular disease, venous thromboembolism, myocardial, and angina infarction, and a systematic review and meta-analysis published in 2008 validated these associations [1, 37]. Although lifestyle and environmental variables have a larger role in the onset of coronary artery disease (CAD), genetic factors play a larger role in determining an

individual's response to risk factor management. The most important risk factors for cardiovascular disease, including diabetes mellitus, high cholesterol, high blood pressure, and a family history of heart attack, are all inherited in some way. Among these, a history of coronary incidents in the family is the most reliable predictor [1, 38]. DNA at the 9q34 region on c-chromosome is also responsible for transmitting blood types. It was shown that the genes for ATP-binding cassette 2 (ABCA2), which regulates cholesterol levels, are located at the 9q34 locus. Moreover, current research on the 9p21 chromosomal region has revealed that genetic variation significantly impacts the chance of getting CAD. A substantial amount of CAD clustering in families has been attributed to shared genetic vulnerabilities. As a result, blood type inheritance may play a pivotal role in this scenario [9, 38]. Because blood type antigens are linked to the vWF and FVIII protein backbone, they unquestionably alter coagulation. True, people with blood type O are more likely to experience excessive blood loss because of the reduced quantities of vWF and FVIII coagulation components in the plasma; this occurrence is due to the H antigen associated to their backbone [26]. However, those with blood types other than O have been linked to a higher risk of ischemic heart disease and thromboembolic disease due to higher plasma concentrations of coagulation components vWF and FVIII [1, 26]. Pregnant people with blood type AB are more likely to experience intraute preterm labor, preterm birth, or other complications.

Cancer

Recent findings [39–41] demonstrating a correlation between blood type and pancreatic cancer have brought the matter back to the forefront of discussion. Extensive research into the associations between blood type and cancer was conducted in the middle of the 1900s. Blood type antigens are likely involved in cell identification, cell signaling, and cell adhesion, all of which play key roles in carcinogenesis, metastasis, and prognosis [42]. Blood type antigens are also likely involved in the formation of blood clots [43]. The expression of ABH and related antigens shifts throughout carcinogenesis and pathological events, much as it does throughout normal cellular development, aging, and differentiation [9]. This is also the case during aging of cells. ABH antigens are found in the epithelial tissues of the digestive system, the breast, the cervix, the mouth, the lungs, the bladder, and the prostate. On the other hand, glycolipids and glycoproteins derived from these cancerous tissues do not contain any of these antigens [31]. In the case of blood group A, it has been hypothesized that DNA methylation in the promoter region of the gene may inhibit transcription of the associated enzyme, leading to a loss of the A antigen; however, various mechanisms for the reduction of mRNA have been found in A tumors, with each mechanism appearing to be cell line-specific [43]. [Citation needed] Because their transcription is downregulated, the loss of A or B antigens leads to a reduction in the amount of activity produced by A or B transferase. This makes metastasis more likely to occur. This, in turn, leads to an increase in the concentration of additional antigens that function as ligands for selectins, which ultimately makes metastasis easier [31]. The loss of A, B, and H antigens has been shown to have an inverse relationship with the capacity for the tumors to spread [30]. Malignancy occurs, and as normal antigens are lost, tumors begin to acquire new antigens on their own. A model that may account for the described links between the presence or absence of these indicators and the outcome of the disease has been proposed [44]. It is well known that blood type antigens possess features that make them procoagulant and angiogenic, that they act as ligands for selectins, that they promote cellular motility, and that they resist apoptosis. When a person who does not have the A blood type develops a tumor that contains either a true A antigen or a "A-like" antigen that has many of the same characteristics as an A antigen, the antigens on the tumor would be recognized as foreign and attacked by the body's anti-A antibodies [7, 30]. This is because true A antigens and "A-like" antigens share many of the same features as A antigens.

Metabolic Diseases

The involvement of blood types in metabolic disease is likely to be nuanced since metabolic disorders are multifactorial and are not controlled by a single gene or antigen. Nonetheless, several interesting connections have been discovered and are described here.

Hypertension

Distinct studies have revealed different connections between blood type antigens and hypertension. Blood type B persons are more likely to have high blood pressure, while A and AB people are less likely [56]. Another study linked blood type A to systolic blood pressure in Caucasians but not Blacks [7, 57]. Rh, Kidd, Duffy, MNS, or P blood types or HLA antigens were not linked to high blood pressure induced by defective sodium and potassium transport in red blood cells [7, 58]. MNS polymorphism is not linked to elevated blood pressure induced by red cell lithium and sodium transport problems [7, 59]. Essential hypertension is diagnosed after other reasons of high blood pressure are ruled out. Atherosclerosis, fibromuscular etiology, renal stenosis (renovascular hypertension), or primary aldosteronism connected to low plasma renin levels were compared to normotensive controls and secondary hypertension patients. Rh, Kidd, Kell, Duffy, P, haptoglobin, PGM-1, and acid phosphatase showed no significant changes [56, 58]. Whites with essential hypertension were considerably different from normotensives [58]. Essential or renovascular hypertension patients had different MNS blood type antigens than healthy ones. Atherosclerotic renovascular hypertension patients displayed three phenotypes [56, 58].

Hyperlipidaemia

Scientists have also looked into how blood type antigens and hyperlipidaemia are connected. It has been shown that people with blood types A and B have higher levels of LDL cholesterol, total cholesterol, and triglycerides and lower levels of HDL cholesterol, but that people with blood type AB are less likely to get hyperlipidaemia [56]. The above research [7, 57] found that blood type A was linked to lower HDL cholesterol and higher total cholesterol, but there was no link with HDL cholesterol. The most interesting thing they found was the link between secretor blood types and serum levels of intestinal alkaline phosphatase (I-ALP) and apo lipoprotein B-48 (apo B-48). I-ALP is needed for chylomicrons to move from the bowels to the bloodstream, so it is a sign of chylomicron absorption. Apo B-48 is a protein that strengthens the chylomicron membrane, so it is a sign of Blood types O and B secretors have much higher serum levels of I-ALP and apo B-48 than blood types A/AB secretors and no secretors of all blood types. As a group, secretors have only about 20% as much I-ALP in their blood as non-secretors, and blood type A secretors have the least activity compared to blood type B and O secretors [7]. I-ALP is thought to be quickly removed from circulation in people who don't have secretors because it is bound to antigens on red blood cells (RBCs) and is accumulated by the A antigens of secretors, while the soluble circulating antigens of O and B secretors link with I-ALP and protect its removal in these people [60]. People with blood type A have less apo B-48 in their blood. This could be because of a genetic change that reduces the activity of I-ALP in the intestines, which leads to less production of chylomicrons [7, 60] and maybe lower cholesterol levels in the blood.

Diabetes Mellitus

No association between Rh blood type and risk of type 2 diabetes mellitus was found in a large prospective study conducted in France (T2DM). Nonetheless, persons with blood type O have the lowest chance of developing type 2 diabetes, followed by those with blood type B, type AB, and type A; however, the risk for people with blood type AB was not statistically significant [7, 61]. When both Rh and blood type were included, those with blood type B+ were found to be at the highest risk, followed by those with blood types AB+, A-, and A+, although the risk was equivalent for the remaining kinds [7, 61]. Blood type AB individuals had the highest risk of T2DM (odds ratio, 1.95) after adjusting for metabolic variables (fasting blood glucose and lipids) [61]. This was followed by those with blood types B and A, who each had a risk of T2DM of 1.26 and 1.21, respectively. One study discovered that people with blood type A had the highest amounts of both blood sugar and insulin, while those with blood type AB had the opposite impact [5]. Blood type O Iraqis were found to have the highest levels of glucose, total cholesterol, and blood pressure, whereas those with blood types A, B, and AB had the lowest risks [7, 61].

Malaria

Blood type B gives a selective advantage to malarial illness, as was previously suggested by [1, 63]. It wasn't until 1978 that researchers realized there were much more type A patients known about than B or O. Malaria subtypes were

rarely reported, though [9]. In accordance with their phenotypes, A, B, and AB blood types have different quantities of Lewis antigens than O blood types do because their respective transferases utilise similar precursors [1, 64]. The current theory is that P. falciparum malaria may account for the three-fold higher incidence of the Le (a b_) phenotype in people of African descent [25]. Blood type O has been shown to provide confrontation to severe P. falciparum malaria by lowering resetting processes [1, 65], but the significance of blood types in malaria defense has not received considerable attention. Pathogenesis of severe malaria was associated with resetting and sequestration. In the first, clusters of unhealthy red blood cells and healthy ones coexist. The second pathway suggests that RBCs infected with P. falciparum continue on to adhere to the microvascular endothelium and are subsequently cleared from circulation [9]. Reduced oxygen and substrate availability may result from cytoadherent blockage of the microcirculation [9]. Resetting receptors in red blood cells (RBCs) include the complement receptor type 1 (CR1), which has been shown to transport Knops blood type antigens and result in a reduced number of rosettes in people with the S1 (a) phenotype [66]. The fundamental need for Plasmodium falciparum merozoites to enter human RBCs is the identification of a carbohydrate structure in glycophorin A or B that comprises of sialic acid and galactose [1, 67]. Phenotypes have also been linked to sialic acid, which is shared by certain pathways that employ glycophorins as ligands.

Methodology

The researcher undertook an exhaustive review of this topic, digging up new, sufficient, and up-to-date literature on the same subject. This means that not only was a descriptive summary of the issue obtained, but also contradicting views were fully retrieved, and presented in a clear impression, by excluding critical debates. Related scientific articles from prior years were also incorporated. Blood types/groups were used alongside a set of disease-related phrases to conduct the article search. The article titles and abstracts were used in the selection process.

Results and Analysis

Table 1. *Demographic information of groups, No. (%).*

Variables		Groups		*P* value
		Case	Control	
Age (mean ± SD)		47.04 ± 16.77	47.67 ± 15.91	.424[a]
Sex	Male	122 (82.2)	127 (72)	.128[b]
	Female	232 (14.3)	34 (24)	
Job	Farmer	61 (41)	91 (61)	.611[b]
	Self-employment	53 (33)	36 (23.6)	
	Employee	11 (6.6)	8 (5)	
	Unemployed	25 (16.2)	16 (10.2)	
Underlying diseases		21 (15.66)	7 (5.33)	.352[b]

$P < .05$ was considered significant.

A Mann-Whitney *U* test. B χ^2 test.

Fever and chills in 98% of people, muscle pain in 91.3%, headache in 76.7%, feeling sick in 64%, and throwing up in 42%. Two people died because of the illness, which is a sad thing. Changes in white blood cell count, creatinine, bilirubin, liver enzymes, creatine phosphokinase (CPK), and inflammatory biomarkers were linked to symptoms (P.05) (erythrocyte sedimentation rate [ESR] and C-reactive protein [CRP]).

Table 2. *Comparison of frequency of blood and Rh groups in case and control groups, No. (%).*

Variable		Case	Control	*P* value[a]
Blood groups	A	41 (27.3)	47 (31.3)	.037
	B	28 (18.7)	34 (22.7)	
	AB	3 (2)	11 (7.3)	
	O	78 (52)	58 (38.7)	
Rh	Positive	139 (92.7)	11 (7.3)	.531
	Negative	136 (90.7)	14 (9.3)	

P < .05 was considered significant.

A χ^2 test.

Among all patients (case group), 75.3% had mild-to-moderate leptospirosis, whereas 24.7% had severe leptospirosis. Significantly more people in both groups were O+ than were members of any of the other blood categories (P .05). Blood type (ABO, Rh) and disease severity did not differ significantly (P >.05). (Table 3).

Table 3. *Comparison of the frequency of blood groups based on the severity of leptospirosis, No. (%).*

Variables		Mild to moderate	Severe	*P* value[a]
Blood groups	A	32 (28.3)	9 (24.3)	.915
	B	20 (17.7)	8 (21.6)	
	AB	2 (1.8)	1 (2.7)	
	O	59 (52.2)	19 (51.4)	
Rh	Positive	107 (94.7)	32 (86.5)	.097
	Negative	6 (5.3)	5 (13.5)	

P < .05 was considered significant.

A χ^2 test.

Discussion

Antigens found in blood samples are examples of polygenic features that are commonly found in populations. There are hundreds of different blood group antigens and alleles, and today there are 34 recognized human blood groups. The host's susceptibility to certain infections can be altered by the degree to which blood group antigens are expressed. As coreceptors or receptors, blood groups can have a causal role in the spread of infection caused by bacteria, parasites, and viruses. 16 Leptospirosis, an infection caused by the bacterium Leptospira, is a major health problem for both humans and animals. 17 In our sample, males made up a larger proportion of the population and the majority of the participants were agriculturalists. One of the districts of northern Iran where our research took place is home to a sizable population of people whose primary source of income does not come from farming. Leptospirosis has been linked to both sex and occupational exposure in numerous studies. Human studies into the potential for sex differences in leptospirosis infection have revealed that men are more likely to be infected than women, maybe as a result of occupational exposure. 17,18 Leptospirosis is more prevalent in the tropics and subtropics. 19 Since pathogenic Leptospira can be found in water sources such ponds, rivers, pits, sewers, agricultural fields, and moist soils,20 jobs in the agricultural sector play a key role in occupational

exposure. As a result, farming has been a major occupation for the majority of those infected. 21-23 Middle-aged persons (40-60 years old) have been found to have the highest rates of leptospirosis in various studies17,18,24,25, including our own. Our patients spent fewer days in the hospital on average than those studied by Goris et al.26, which may be because those patients had more advanced cases of the disease. Fever, chills, muscle aches, and headaches are classic manifestations of this condition, and our patients experienced the same symptoms.27 Patients with leptospirosis exhibited the classic features of the disease, including leucocytosis, elevated bilirubin, creatinine, CPK, liver enzymes (alanine transaminase and aspartate transaminase), and inflammatory indicators (CRP and ESR), along with decreased haemoglobin, platelets, serum sodium, and potassium17,22,25.

Conclusion

Our research shows that O+ is the most common blood type among leptospirosis patients. While there was a statistically significant correlation between leptospirosis and the presence of O, there was no such correlation between Rh and the disease. People with more severe cases of the disease had a higher O prevalence. Statistical analysis has shown that ABO and Rh blood types are not associated with illness severity. While many studies have demonstrated a link between ABO blood types and diseases by describing possible mechanisms, other studies have failed to confirm this, and a definitive decision is therefore clouded by inconclusive findings. Nonetheless, data were gathered to prove this hypothesis. The risk of various diseases may be affected by ABO through a variety of known and undiscovered pathways. Now we know that ABO blood types aren't directly responsible for illness, although they can be predisposed to and affected by certain ailments. Diseases tend to be more common in people with blood types other than O. People with high-risk blood types can be screened and trained to make changes to their lifestyles, health behaviors, and environments, among other initiatives that may improve public health, so it's helpful to increase knowledge in this area. Movements of people and the ongoing fight against infectious diseases shed light on the significance of different blood types. There is strong evidence that infectious disease selection has occurred at the level of the ABO and secretor genes, but for other blood group antigens, the distribution of blood group polymorphisms appears to be better explained by founder effects, with the exception of regions with high malaria prevalence. Based on the evidence we have, it appears that resistance to malaria has been the most important selecting force shaping blood types. In addition, further research is needed, particularly at the molecular level, to determine the relationship between ABO blood classes and the diseases they are linked to.

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