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Article *in* Virology Journal · February 2017
DOI: 10.4172/2324-8955.1000165

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Journal of Virology & Antiviral Research

Short Communication A SCITECHNOL JOURNAL

Do ABO and Rhesus blood groups affect susceptibility to, and prognosis of Ebola virus infection?

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Abstract

In 2014, the largest Ebola outbreak known to man, thundered through West Africa. It infected close to 30,000 people, and killed over 11,000. Yet, though we have known about Ebola for almost forty years, little data is available on survival and infection patterns of this viral hemorrhagic disease. Examining parallels between blood groups and human disease susceptibility is a valid, and increasingly used method of finding such patterns. This study permitted the observation of the different blood groups in Ebola infected patients and survivors. This was compared against the blood group distribution of the general population as well as those within the study, who succumbed to the disease. Blood group A in particular rose to 36.36% of the survivor population in our study, when it only forms 21.1% of the normal population. It formed 9% of the deceased group. The results show that the disparities in the blood group profiles of the general population, infected patients, survivors and deceased are marked enough to infer that ABO and Rhesus blood groups could be a factor in the infection and survival of Ebola Virus Disease (EVD).

Keywords

Ebola Virus Infection; ABO blood group; Rhesus blood group

Introduction

This study was part of a wider trial to investigate the efficacy of convalescent whole blood for the management of EVD in Sierra Leone. Whole blood from survivors, thought to contain antibodies specific to the disease, was transfused into patients in the active phase of infection. This is believed to supplement or kick start the patient's own immune system production.

Ebola had previously, not been thought native to the West African sub region. Preceding outbreaks were small, confined to rural areas of Sudan, and the Democratic Republic of Congo. However, in 1994, a scientist in the Ivory Coast performing necropsies of diseased chimpanzees, was infected with Ebola. This was thought to have proved the zoonotic nature of the virus. No study has provided definitive data to differentiate infected or survivor traits, from those of the general population. To explain infection patterns, most investigations have focused on viral loads [1]. However ABO and Rhesus blood groups may be a factor that affect how the exposed succumb to the virus. This study seeks to examine whether the distribution of blood groups found in survivors, is consistent with that of the general population, and the infected. The examination leads us to the hypothesis that there is some relationship between ABO and Rhesus blood groups with regards to Ebola infection and survival.

Methodology

The Whole Blood study was conducted under the auspices of the Sierra Leone Ministry of Health and Sanitation clinical Protocol Number MOHS-WBT001, with Professor S.M. Gevao as Principal Investigator. It was granted regulatory authorization by clinical trial authorization number PBSL/CTAN/COBED-001. Implementation was in two parts. The first part of harvesting blood from survivors, was executed by the National Safe Blood Transfusion Services division of the Connaught Hospital in Freetown, Sierra Leone. The other part of the study was conducted by and at the 34 Military Hospital, a recognized Ebola Treatment Unit (ETU) for the Ministry of Health and Sanitation of Sierra Leone. Blood donations were collected from survivors in Kenema and Freetown. These survivors had to have been discharged more than 90 days previously, from a recognized ETU. The study duration was from November 2014 to May 2015. Survivors with valid Government of Sierra Leone discharge certificates were verified, screened, bled, typed and their demographical data was taken. The ABO and Rhesus phenotypes were classified using a haemaglutination standard test. Ebola positive patients by PCR test, undergoing treatment at the 34 Military hospital, were consented into study under the protocol cited and transfused. The control arm of the study was not included in this paper as the patients therein were not typed, and their groups are unknown. All data was collated within a custom database using Microsoft Access to collate primary reports. The results were further analyzed using SPSS version 20 software for further statistical outcomes. The variations within ABO and rhesus blood groups across the different categories of populations were examined. Results were correlated with the blood group distribution of the fatalities in the study.

Results

Survivors who had previously been infected with EVD before the study were recruited through the Sierra Leone Association of Ebola Survivors. Their blood was harvested in three separate bleeding sessions from November 2014 to March 2015. The blood of 77 survivors was stored. 32 of them were Male, 66 were below the age of 40.

The patient side of this study was comprised of 40 PCR positive patients infected within the timeframe of the study, that were admitted to the 34 Military Hospital ETU and had all the data necessary on record. Of these 20 were male, 32 were under the age of 40. They were all transfused with 450ml of convalescent blood according to National Safe Blood Transfusion guidelines. The two groups of participants are separate and distinct. Even though the survivors had at one time been patients, to qualify for the study as survivors, they had to have ceased being patients for at least 90 days before the date of harvesting

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Received: December 05, 2016 **Accepted:** December 28, 2016 **Published:** January 04, 2017

their blood. The term "patients" is reserved for those that were admitted in the 34 Military Hospital ETU within the timeframe of the Convalescent Whole Blood Trial.

In the conduct of the study, there was an evident supply/demand imbalance, as O+ convalescent blood always became quickly unavailable. Some of the other blood groups would perish before the 30 day period of use. Throughout the study period, there were no failures in finding veins for transfusions, and no transfusion reactions. No infections of staff occurred, neither were there any accidents. The order of percentage distribution of ABO blood groups among the general population was in decreasing order of magnitude: Group O, Group B, Group A, Group AB (O>B>A>AB) (Figure 1).

Among the patients in decreasing order of magnitude: Group O, Group B, Group A, Group AB (O>B>A>AB) See (Figure 2). Among the survivors, in decreasing order of magnitude: Group O, Group A, Group B, Group AB (O>A>B>AB) (Figure 3). Among the deceased, in decreasing order of magnitude: Group O, Group B, Group AB and A being equal (O>B>AB=A) (Figure 4). The observations in this paper are incidental to the design of the study.

Discussion

An expanding number of publications are drawing parallels between ABO histo groups and human diseases [2,3]. The examinations range from ischemic heart disease [4] to cancer. The literature on the effect of Rhesus groups on diseases is sparse, except for autoimmune diseases and complications in pregnancy. Khode et al, [5] observed that Dengue infections were higher in individuals with O positive blood group (42.8%) when compared with controls (32%). They however could not show any correlation between the blood groups and severity of the disease. Harris et al, [6] showed that once a person is infected with cholera (Vibrio cholerae strains O1 El Tor and O139) the phenotype group O confers a greater likelihood of severe infections than non-O blood group phenotypes. Some research has shown people with blood group O+ are significantly more susceptible to malaria infection [7]. All the mechanisms of susceptibility and prognosis are not totally accounted for. Those that have been studied, seem to arise out of specific interactions between the pathogen and host phenotype. Ebola infections being

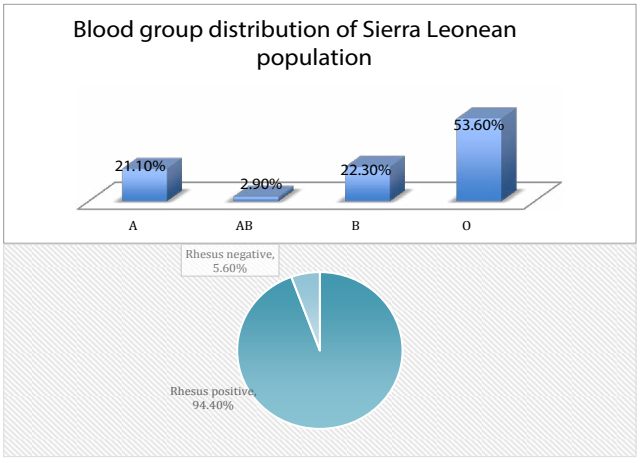

Figure 1: Our observation is based on the 1995 study by Gevao S10. This was cross checked for consistency with blood group distributions in the West-African sub-region and no significant variance was found [11,12]

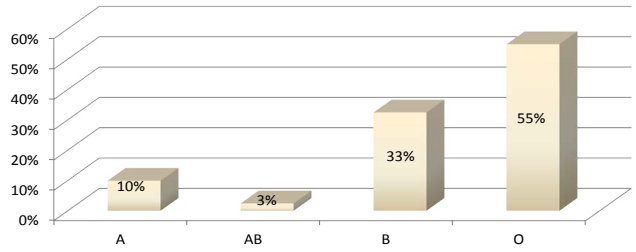

Figure 2: The relative percentages of the different blood groups in infected patients under treatment shows a significant decrease in the percentage of A, (a 52.6% drop) and an increase in the percentage of B of 48%. The increase in O could be considered insignificant. The fact that we have no rhesus negatives in itself may be significant, but could be an artifact from the small numbers. It is worthy of mention that Population distribution with 5.6% Rhesus negative10 should yield a rhesus negative for every 17 patients approximately. In a patient population of 40 we would expect to see at least one negative. **There were no Rhesus negatives in the patient group.**

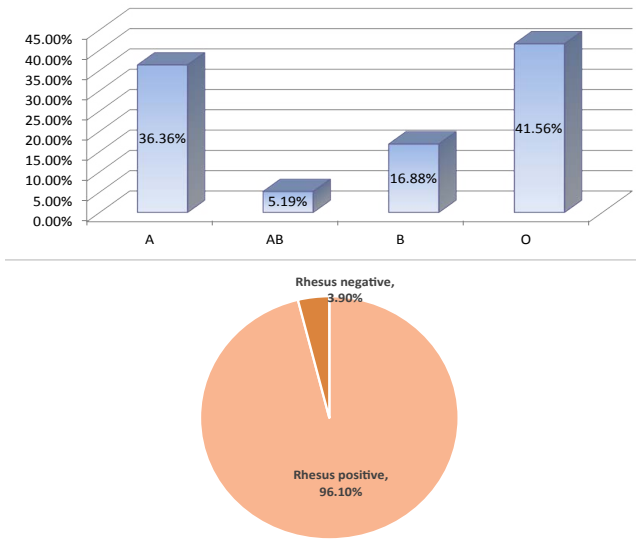

Figure 3: The blood group distribution of Survivors shows that the A blood group is very close behind O in dominance, pointing to the high survival of this blood group. Blood group B generally, has been reduced from 22.3% in the general population to just 16.88%. The Rhesus negative is some 30% below the expected of 5.6%.

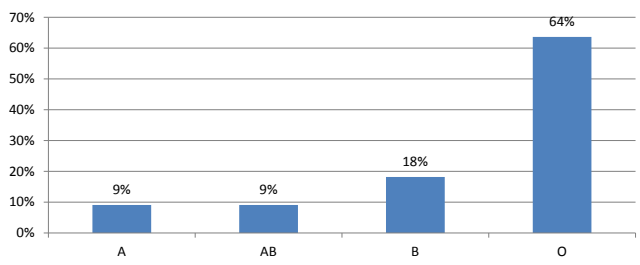

Figure 4: The small number of 11 in the deceased group could explain why we have no negative rhesus. There is some degree of artifact introduced by the population size but the very high percentage of O deaths, coupled with low percentage of A deaths are consistent with the results for infected and survivors. **There were no Rhesus negatives in the deceased group.**

Table 1: ABO blood groups among the normal population, patients and transfused.

	A	AB	B	O
Population blood group	469(21.20%)	64(2.90%)	494 (22.30%)	1186(53.60%)
Patients	4(10%)	1(3%)	13(33%)	22(55%)
Survivors	28(36.36%)	4(5.19%)	13(16.88%)	32(41.56%)
Mean	22.52	3.69667	24.06	50.0533
Std. Deviation	13.2295	1.29423	8.20285	7.38867
Std. Error of Mean	7.63805	0.747225	4.73592	4.26585
Mortality	1(9%)	1(9%)	2(18%)	7(64%)

Table 2: Blood groups of Population, Trans and Patients (TWO- WAY ANOVA).

	Blood groups of Population, Trans and Patients				
Two-way ANOVA	Ordinary				
Alpha	0.05				
Source of Variation	% of total variation	P value	P value summary	Significant?	
Blood groups	84.54	0.0076	**	Yes	
Subjects	0.004358	0.9992	ns	No	
ANOVA table	SS	DF	MS	F (DFn, DFd)	P value
Blood groups	3266	3	1089	F (3, 6) = 10.94	P = 0.0076
Subjects	0.1684	2	0.08418	F (2, 6) = 0.0008460	P = 0.9992
Residual	597.0	6	99.50		
Number of missing values	0				

relatively new, further investigations will be needed to pinpoint these exact interactions. In the case of Denge, individuals who lack an antigen have natural antibodies with the ability to agglutinate cells carrying that antigen. The antigens are carbohydrate in nature; the immundominant sugar in the case of the A determinant is N-Acetyl-D-galactosamine, and that in the case of the B determinant is d-galactose. Galactosyltransferases are involved in the synthesis of these carbohydrates. The antibody that recognizes these carbohydrates is primarily natural IgM. Interestingly, several dengue viral proteins have been shown to be glycosylated, and antibodies, particularly IgM, produced in patients with dengue-virus infection have been shown to cross-react with host cells [5].

ABO antigens are not just expressed on red blood cells, but are also highly expressed on the surface of a variety of human cells and tissues, including the epithelium, sensory neurons, platelets, and the vascular endothelium [7,8]. With higher rosette rates among non-group O compared to group O erythrocytes incidence of malaria may not be entirely correlated to ABO histo-blood group per se, but rather to co-receptors in parasite and vascular cytoadherence [9].

Our study however, suggests that in Ebola it is not so much a higher infection rate of Blood Group O, but rather a greater resistance of blood group A especially, and possibly negative rhesus generally. Also, from the data available to us, there seems to be a greater infection of Blood Group B with reduced survival. Blood Group O may not be affected to greater or lesser degree. The low numbers prevent us from conclusively drawing firm determinations. They suggest that further investigations are needed in these areas. Our observation is based on the 1995 study by Gevao S [10]. This was cross checked for consistency with blood group distributions in the West-African sub-region and no significant variance was found [11,12].

The relative percentages of the different blood groups in infected patients under treatment shows a significant decrease in the percentage of A, (a 52.6% drop) and an increase in the percentage of B of 48%. The increase in O could be considered insignificant. The fact that we have no rhesus negatives in itself may be significant, but could be an artifact from the small numbers. It is worthy of mention that Population distribution with 5.6% Rhesus negative [10] should yield a rhesus negative for every 17 patients approximately. In a patient population of 40 we would expect to see at least one negative. There were no Rhesus negatives in the patient group. The blood group distribution of Survivors shows that the A blood group is very close behind O in dominance, pointing to the high survival of this blood group. Blood group B generally, has been reduced from 22.3% in the general population to just 16.88%. The Rhesus negative is some 30% below the expected of 5.6%. The small number of 11 in the deceased group could explain why we have no negative rhesus. There is some degree of artifact introduced by the population size but the very high percentage of O deaths, coupled with low percentage of A deaths are consistent with the results for infected and survivors. There were no Rhesus negatives in the deceased group.

Statistical analysis

A Two-Way Anova test (Table 1) was conducted to compare the ABO blood groups among the general population, patients and survivors at α=0.05. There's no significant difference between the subjects (i.e. general population, patients and survivors) as the p value=0.9992 (p>0.05) which is acceptable since all the subjects are expressed in percentage but a Post-hoc analysis showed a very significant difference within the groups (among the various blood groups). There was a very significant difference in ABO blood groups (Table 2) with blood groups A (Mean=22.52, SD=13.23), AB (Mean=3.70, SD=1.30), B (Mean= 24.06, SD=8.20) and O (Mean= 7.39, SD=4.27) at a P value of 0.0076 (P<0.001).

The order of percentage distribution of ABO blood groups among the general population was O>B>A>AB, among the patients O>B>A>AB, among the survivors O>A>B>AB and among the deceased is O>B>AB=A. Since p=0.0076 (p<0.001), it implies that the order of the differences among the blood groups is significant.

From the results above, we can see a positive correlation with regards the distribution of ABO blood groups among the patients infected and the ABO blood group distribution among the general population except that people with blood groups A were infected less.

Conclusions

The results indicate that persons with blood group A get infected less and survive more in the event of Ebola exposure. It appears that persons with blood group B get infected more and survive less in the event of Ebola exposure. The seemingly high death rate of infected with blood Group O is an artifact produced by the apparent lower susceptibility to, and better prognosis of blood group A of Ebola infection. It also appears though difficult to conclude due to the low numbers that persons with negative Rhesus group generally are infected less and survive more than those with a positive Rhesus group in the event of Ebola exposure, particularly if they are of blood group A.

Acknowledgements

The Whole blood study was carried out with funds graciously provided by the WHO. Many thanks must go to the Pharmacy Board of Sierra Leone, unnamed workers of the 34 Military Hospital for their courage in the face of adversity, the National Safe Blood Services of Sierra Leone for their perseverance to bring us "safe Blood" even in dangerous times, and the Sierra Leone Association of Ebola Survivors for filling the need.

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