ORIGINAL ARTICLE

Lower Risk of Thrombosis in Blood Group O Patients: Are low clotting factor levels the reason?

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ABSTRACT

Background: The ABO Blood group system has been evaluated many a times for increased risk of vascular accidents and heart diseases. This study aims to prove that the reason behind the decreased risk of thrombosis in O blood group population could be the decreased levels of clotting factors in its plasma compared to other blood groups.

Objective: To assess the levels of clotting factors VII, VIII, IX and X in all blood groups to determine whether blood group O has the lowest levels of all clotting factors in its plasma.

Methods: This is a Descriptive Cross sectional study, conducted at Dr. Ziauddin Hospital Karachi and Dow University of Health Sciences over a period of six months. The study involves 16 plasma units divided into four of each blood group. On the day of testing plasma was thawed and assays of factor VII, VIII, IX and X were performed on all blood groups and results noted.

Results: Levels of Factor VIII, IX and X were found to be highest in blood group AB and lowest in blood group O. Factor VII levels varied from others.

Conclusion: Our results showed that factor VII levels vary in different blood groups, may be due to its short half-life. Thus we could not establish a link between ABO blood groups and clotting factor levels.

KEY WORDS: *Fresh Frozen Plasma, Thawed Plasma, Clotting Factors, ABO Blood Groups.*

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INTRODUCTION

ABO blood groups have been the subject of many such research studies to discover the link between genes that control ABO blood groups and various disease processes. For instance, it has been proven that individuals with blood group A have a higher risk of developing gastric cancer and therefore patients with group A are advised to take more precautions and treat early ulcerative disease more aggressively, in order to prevent the condition from progressing.[1]

In the same way, genes that control ABO blood groups may also play a role in controlling blood parameters leading to hematological disorders, such as venous thromboembolism. This group of diseases includes deep vein thrombosis and pulmonary embolism which is notorious for causing sudden death. If a genetic predisposition can be established through the linkage of ABO blood groups, high risk patients' lives may be saved by starting them on medication earlier than their counterparts and monitoring them more stringently for signs and symptoms.

In a study conducted by Sabino et al , the ABO blood system was evaluated for an increased risk of venous thrombosis, heart disease and ischemic stroke. The study showed that non O blood groups had a significant relationship with thrombotic events and the O blood group had a possible protective effect.[2] In another study conducted by Tirado et al, blood group A was found to be an independent risk factor for venous thromboembolism[3], while Larsen et al, showed that blood group AB may also be associated with increased risk estimates for venous thromboembolism in pregnancy and puerperium.[4]

Our study takes these findings one step ahead by further investigating the reason behind the increased risk of thrombosis in non O blood groups. Higher levels of procoagulants like the clotting factors, fibrinogen and prothrombin could be the reason behind the hypercoagulability of non O groups, or it may be due to inactivation of the naturally occurring anticoagulants, like protein C, protein S and antiphospholipid antibodies. Studies have established that blood group O has a significantly lower level of Factor VIII and Von Willebrand Factor but other factor levels have yet to be analyzed.[5]

The main aim behind research is finding new links to establish associations and introduce new treatment modalities based on the findings. The objective is to assess the levels of clotting factors VII, VIII, IX and X in all blood groups in order to find out if blood group O has the lowest levels of all clotting factors in its plasma.

METHODOLOGY

This is a descriptive cross sectional study, conducted at Ziauddin Medical Hospital and Dow University of Health Sciences over a period of six months. Approval from Ziauddin Ethical Review Committee was sought prior to the beginning of the study. A total of 16 blood donors, ten male and six female donors, four of each blood group A, B, O and AB were recruited for this study. After the initial general physical examination, hemoglobin levels were checked and donors were asked to fill out the Universal Donor Health Questionnaire (UDHQ), a prerequisite for donation.

All sixteen units were donated on the same day in order to standardize results. The whole blood was centrifuged to separate red cells and platelets from plasma. This plasma was stored at -30 ^{o} C until testing was performed. On the day of testing, the plasma was thawed for 30 – 45 minutes at a temperature of 35-37^{0} C and then assays of factors VII, VIII, IX and X were performed on each unit of Fresh Frozen Plasma.

All Factors VII, VIII, IX and X were determined using STA-Neoplastine CI plus 4 kits (Diagnostica Stago, France) on a STA Compact Analyser. Samples were diluted according to the kit's protocol. A standard curve was run with each assay. Calibration material was a commercial STA calibrator.

The data was analyzed with SPSS 20. All quantitative variables are presented as mean and standard deviation. One-way Analysis of Variance test (ANOVA) was used to compare the quantitative variables. P values < 0.05 were considered statistically significant.

RESULTS

Table 1. Mean values for the Factor VII according to different blood groups

Coagulation Factor VII	Mean	Standard Deviation	P Value
Blood Group A	81.25	13.04799	0.620
Blood Group B	72.75	15.64981	
Blood Group O	73.01	11.78629	
Blood Group AB	65.75	22.32151	

Mean level of Factor VII in blood group A was 81.25%.
Mean level of Factor VII in blood group B was 72.75%.
Mean level of Factor VII in blood group O was 73.01%.
Mean level of Factor VII in blood group AB was 65.75%.

Figure 1: Mean levels of clotting factors in different blood groups

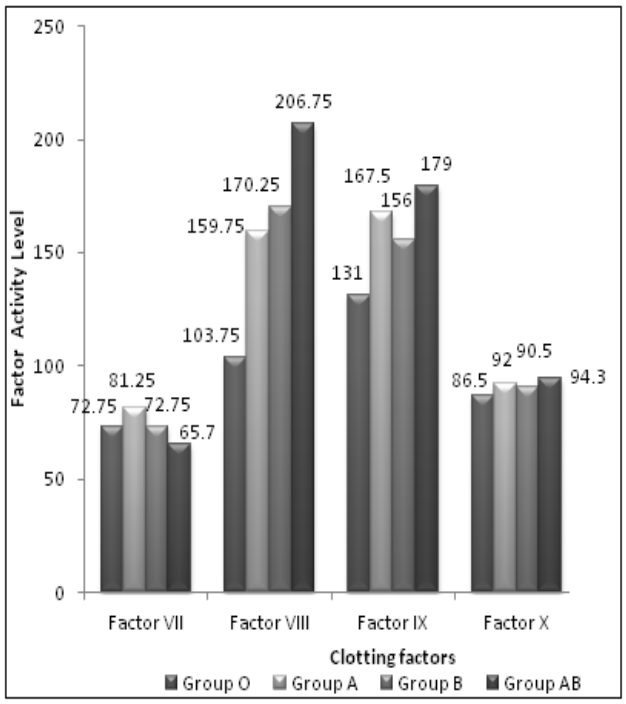

Table 2. Mean values for the Factor VIII according to different blood groups

Coagulation Factor VIII	Mean	Standard Deviation	P Value
Blood Group A	159.75	49.90240	0.030
Blood Group B	170.25	34.61575	
Blood Group O	103.75	32.10789	
Blood Group AB	206.75	72.49080	

Mean level of Factor VIII in blood group A was 159.75%.
Mean level of Factor VIII in blood group B was 170.25%.
Mean level of Factor VIII in blood group O was 103.75%.
Mean level of Factor VIII in blood group AB was 206.75%.

Table 3. Mean values for the Factor IX according to different blood groups

Coagulation Factor IX	Mean	Standard Deviation	P Value
Blood Group A	167.50	13.40398	0.010
Blood Group B	156.00	16.08312	
Blood Group O	131.00	10.51982	
Blood Group AB	179.00	24.23496	

Mean level of Factor IX in blood group A was 167.5%.
Mean level of Factor IX in blood group B was 156.0%
Mean level of Factor IX in blood group O was 131.0%
Mean level of Factor IX in blood group AB was 179.0%.

Table 4. Mean values for the Factor X according to different blood groups

Coagulation Factor X	Mean	Standard Deviation	P Value
Blood Group A	92.00	16.63330	0.865
Blood Group B	90.50	7.23418	
Blood Group O	86.50	11.95826	
Blood Group AB	94.25	15.12999	

Mean level of Factor X in blood group A was 92.0%.
Mean level of Factor X in blood group B was 90.5%.
Mean level of Factor X in blood group O was 86.5%.
Mean level of Factor X in blood group AB was 94.25%.

DISCUSSION

Genetic predisposition to disease has always been an important means of predicting disease before its occurrence and it gives the patient more time and options to tackle the problem. ABO blood groups have been a popular target for many such studies, with researchers showing significant results in diseases like gastric ulcers , acute lymphoblastic leukemia and discoid lupus erythrematosis amongst other.[1,6,7] In a study by Akgul et al a connection of ABO blood groups with neonatal hyperbilirubinemia was checked, whereas in a study by Flavarjani et al tried to link ABO blood groups with breast cancer, but

both studies concluded that no such link existed.[8,9]

Multiple studies have established that blood group O has a cardioprotective effect. O'Donnell et al. postulated that this may be due to the effect of ABO groups on von Willebrand factor synthesis or clearance, whereas Clark et al. suggests Factor V Leiden mutations may also play a role.[5,11]

Establishing a link between ABO blood groups and clotting factor levels will not only help determine which patients are at a higher risk for thromboembolism, but may also help in transfusing the most beneficial FFP unit to patients who have coagulation factor deficiencies.

An additional advantage would be that the right product can be chosen in situations where group specific products are not necessary. For example, if FFPs need to be transfused to an AB negative patient, the blood group with the highest level of clotting factors can be given, be it of any group.

Our study aimed to assess Factor VII, Factor VIII, Factor IX and Factor X to see if any pattern can be identified within the four blood groups. According to our results, Factor VII levels showed a narrow range of activity from 65% to 81%, with group AB having the lowest and group A having the highest levels. A possible explanation is that Factor VII is known to have a short half life which may rapidly affect the activity levels among individuals.

Factor VIII results showed a wide range of activity ranging from 103.75% in group O plasma and 206.75% in group AB plasma. Similar results have been obtained in previous studies which further validate our findings that blood group O plasma have the lowest levels of clotting factor VIII in it and reconfirm the link between Factor VIII and ABO blood groups.[5,3]

Factor IX levels also varied significantly with 131.0% seen in group O donors and 179.0% found in group AB donors, again the levels being lowest in blood group O just like seen in the study conducted by O'Donnell et al.[5] Factor X results showed group O to have the lowest activity of 86.5 % and group AB having the highest activity level of 94.25%. The results were statistically non significant but showed the same trend seen with Factors VIII and IX.

Careful analysis of the data shows that three out of four factors showed the same trend of being highest in group AB and lowest in group O, with the exception of Factor VII which can be explained by its short half life and narrow range of values. Our results do not support our hypothesis that there are increased levels of clotting factors in non O blood groups and lowest in blood group O, leading to increased risk of thrombosis in non O blood group population and having a possible protective effect in O blood group population, due to the variation seen in factor VII levels compared to other clotting factors.

These initial results are valid but the study has a few limitations which can be overcome by measuring the remaining clotting factors, by increasing the sample size and further standardizing the donor population, to remove any bias of gender, diet, body mass, ethnicity, etc.[12,13]

CONCLUSION

A link could not be established between the different blood groups and clotting factors as levels of factor VII vary from the trend observed for other clotting factors. Levels of factor VIII, IX and X were found to be highest in blood group AB and lowest in blood group O, on the other hand, levels of factor VII vary from the trend seen for other clotting factors. This may be due to its short half life or other reasons which need to be further investigated. Thus we could not establish a link between ABO blood groups and clotting factor levels so the decreased risk of thrombosis in non O blood groups cannot be attributed to clotting factor levels.

In the human genetic code, we can find answers to all our questions. By diving deeper into established entities, we may stumble onto new links and connections which may give us new information about old problems, helping us pinpoint individuals at high risk and opt for early management and better patient care.

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