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ABO Blood Groups and Their Relationship with Coagulation Factor VIII in Healthy Adults

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Abstract

Background: ABO blood group distribution defers with racial and geographic variations. They are related to diseases like cardiovascular diseases, cerebral thromboembolism. ABO blood group system may influence coagulation factor VIII which may increase the future risk of thrombosis. **Aim:** To assess the relation of ABO blood group with coagulation factor VIII in healthy adults. **Material and Methods:** A prospective type of analytical cross-sectional study was conducted in the Department of Physiology, Dhaka Medical College, Dhaka from July 2019 to June 2020. After obtaining ethical clearance, a total of 190 healthy adults were selected from different areas of Dhaka city based on inclusion and exclusion criteria, with ages ranging from 18 - 45 years. The subjects were interviewed and detailed history regarding personal, family, medical and drug were taken. Prior to sample collection, informed written consent was taken from the participants. Individuals of blood group A were selected as group A, blood group B as group B, blood group AB as group AB and blood group O as group O. Coagulation factor VIII was measured in the Department of Hematology and BMT Unit, Dhaka Medical College Hospital, Dhaka. Blood grouping was done in the Department of Physiology, Dhaka Medical College, Dhaka. **Statistical Analysis:** For statistical analysis, ONE

way ANOVA followed by Bonferroni test were considered using SPSS 25.0 version. **Results:** In this study, blood group B was most common (33.2%). Coagulation factor VIII was significantly higher ($p < 0.001$) in blood group A (105.76% ± 11.82%), B (112.00% ± 15.02%), AB (109.80% ± 11.93%) than blood group O (82.00% ± 12.86%). No significant difference was observed among A, B and AB blood groups regarding coagulation factor VIII. **Conclusions:** It can be concluded that blood group A, B, AB individuals may have more chance of thrombosis due to significantly higher coagulation factor VIII than blood group O individuals.

Keywords

ABO Blood Group, Coagulation Factor VIII, Healthy Adults

1. Introduction

ABO blood group was discovered by Karl Landsteiner in 1900. It was the landmark for the modern practice of transfusion medicine [1]. The incidence of ABO and Rh blood groups varies markedly with geographic and racial variations. In Caucasians of America, the predominant blood group is group O (45%) followed by group A (41%), B (10%) and AB (4%). Native American Indians belong almost to blood group O. Among western Europeans, group O occurs in the highest frequency (46%) followed by group A (42%), B (9%) and AB (3%). In Eastern Europe, the predominant blood group is group B (40%) [2]. In Australia and Britain, the commonest blood groups are group O and A followed by group B and AB. In Indo-Pak sub-continent, group B and O occur in the highest frequency [3]. In Bangladesh, the commonest blood group is blood group B (34.4%) followed by group O (30.4%), A (26.7%) and AB (8.6%). The distribution of Rh-positive blood group is 97.4% and Rh-negative blood is 2.6% [4].

Determination of blood group is very essential as it plays an important role in genetics, blood transfusion, forensic medicine and may be related to diseases like duodenal ulcer, diabetes mellitus, urinary tract infection, Rh incompatibility and ABO incompatibility [5]. Blood group O has a strong association with duodenal ulcers [6].

Von Willebrand factor is a large glycoprotein which is synthesized by Weibel-Palade bodies in the endothelial cells and alpha granules of megakaryocytes [7]. It is involved in hemostasis. Von Willebrand factor has two major roles in hemostasis. First, it helps in platelet adhesion and platelet aggregation. Second, Von Willebrand factor is the specific carrier of factor VIII in plasma. It protects factor VIII from proteolytic degradation and prolonging its half-life in circulation. Von Willebrand factor effectively localize factor VIII at the site of vascular injury [8].

ABO blood groups have a relation with plasma von Willebrand factor and factor VIII. Blood group O individuals have 25% lower von Willebrand factor

levels than non-O (A, B, AB) blood group individuals. Among non-O individuals, the AB group has the highest von Willebrand factor level, followed by blood group B and A individuals. Individuals with non-O blood groups show a significantly higher risk of thrombosis than blood group O due to increased von Willebrand factor and factor VIII [9]. Gallinaro *et al.* (2008) observed less von Willebrand factor in blood group O due to faster hepatic clearance of von Willebrand factor leading to shorter plasma half-life of it than non-O blood groups [10].

Some studies have shown the influence of ABO blood groups on plasma coagulation factor VIII in different populations. They found that mean factor VIII level was significantly higher in blood group A, B and AB than blood group O individuals [11] [12] [13]. Ohira *et al.* (2007) carried out a study on ABO blood groups and the incidence of Venous Thromboembolism (VTE). They showed factor VIII was significantly higher in patients with VTE than participants free from VTE. They also observed significantly higher level of factor VIII in non-O blood group individuals than blood group O. So, individuals with non-O blood groups may have more chance of thrombosis [14].

The present study was undertaken to assess the relation of ABO blood groups with coagulation factor VIII in healthy adults and to identify those blood groups which may have more chance of thrombotic diseases. This study also aimed to bring awareness to prevent thrombotic diseases related morbidity.

2. Material and Methods

This prospective type of analytical cross sectional study was carried out in the Department of Physiology, Dhaka Medical College, Dhaka from July 2019 to June 2020. A total of 190 Bangladeshi healthy adult male and female, aged 18 - 45 years were selected from different areas of Dhaka city for this study.

1) Study design: Prospective type of observational cross sectional study. It was analytical study and no follow up had done.

2) Study location: Department of Physiology, Dhaka Medical College and Hospital, Dhaka.

3) Study duration: July 2019 to June 2020.

4) Sample size: 190 healthy adults.

5) Sample size calculation: The sample size was estimated on the basis of the difference between two means from previous study. We assumed that the power of the study was 80% and the level of significance was 5%. The sample size actually obtained for this study was 30 healthy adults for each group (Group A, Group B, Group AB and Group O). We planned to include study subjects until fulfillment of minimum 30 subjects in each group.

6) Subjects & selection method: Sample size was divided into four groups on the basis of ABO blood groups.

Group A: 45 healthy adults of blood group A.

Group B: 63 healthy adults of blood group B.

Group AB: 30 healthy adults of blood group AB.

Group O: 52 healthy adults of blood group O.

7) Inclusion criteria

- Age: 18 - 45 years.
- Gender: Male and Female.
- BMI: 18.5 - 24.9.
- Ethnicity: Bengali.

8) Exclusion criteria

- History of blood coagulation disorders.
- Current history of taking anticoagulant, oral contraceptive pill.
- Pregnancy and lactation.
- Presence of any pathological condition such as thromboembolic events, hypertension, diabetes mellitus, anaemia, acute infection, chronic inflammatory disorders, hyperlipidemia, liver disease, renal disease, cerebrovascular disease, psychiatric illness, malignancy.
- Smoker.
- Prolonged immobilization, paralyzed.

9) Procedure methodology

The research work was carried out after obtaining ethical clearance from Research Review Committee of the Department of Physiology and Ethical Review Committee of Dhaka Medical College, Dhaka. Subjects from different areas of Dhaka city were contacted either by phone or in person and details of the study procedure, the nature, purpose and benefit of the study was explained to each subject. They were asked for their voluntary participation. Subjects who were interested to take part in the study were requested to attend the Department of Physiology, Dhaka Medical College, Dhaka, in fasting state. When they came, they were interviewed and detail history regarding personal, family, medical and drug history were taken. Anthropometric measurements of the subjects were done and blood pressure was measured. All the information was recorded in a prefixed data collection form. Prior to blood sample collection, informed written consent was taken from the participants. Coagulation factor VIII was estimated in the Department of Haematology & BMT Unit, Dhaka Medical College Hospital, Dhaka, by using Sysmex fully automated coagulation analyzer machine. Blood grouping was done in the Department of Physiology, Dhaka Medical College, Dhaka, on the basis of presence or the absence of agglutination by slide method. Subjects who were unable to come to Dhaka Medical College, their blood samples were collected from their respective work station or from their home. These blood samples were carried in a cool box to the respective department of Dhaka Medical College Hospital, Dhaka for investigations. Study subjects were grouped into four groups on the basis of blood grouping. Blood sample collection was continued until fulfillment of minimum 30 subjects in each group. To fulfill minimum 30 subjects in each group, equal number of study subjects could not be maintained. Blood samples were collected from total 196 subjects. Among them, two subjects were excluded due to higher SGPT level

above normal range, two subjects were excluded due to higher blood glucose level above normal range, one subject was excluded due to higher serum cholesterol level above normal range and one subject was excluded due to lower haemoglobin concentration level below normal range. At the end, total 190 subjects were included in this study. Out of them, 45 study subjects were included in group A, 63 study subjects were included in group B, 30 study subjects were included in group AB and 52 study subjects were included in group O.

10) Statistical analysis

All the parameters were expressed as mean ± SD (standard deviation) and range. One way ANOVA followed by Bonferroni test was performed to compare between groups. p value < 0.05 was accepted as level of significance. Statistical analysis was performed by using a computer based statistical program SPSS (Statistical Package for Social Science) version 25.0.

3. Results and Discussion

Table 1 and Figure 1 show, the number and percent distribution of ABO blood groups of the study subjects. ABO blood groups revealed that group B was predominant with 33.2%, followed by group O with 27.4%, group A with 23.7% and

Table 1. Blood group distribution of the subjects (N = 190).

Blood groups	Number	Frequency
A	45	Percent 23.7
B	63	Percent 33.2
AB	30	Percent 15.8
O	52	Percent 27.4
Total	190	Percent 100

N = Total number of subjects.

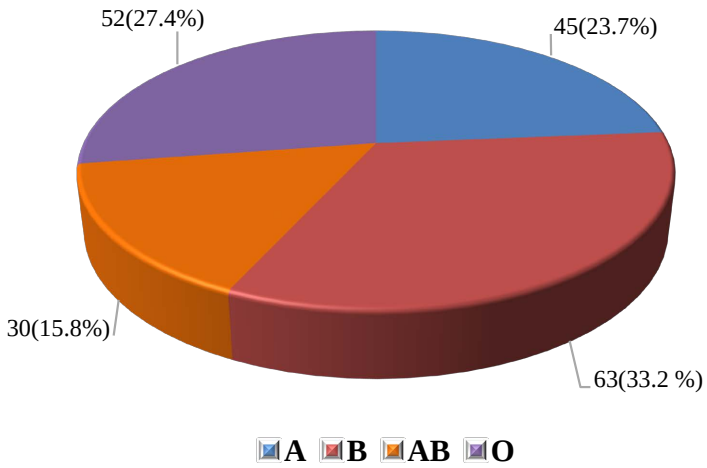

Figure 1. Distribution of study subjects according to blood groups (N = 190). N: Total number of subjects; A: Blood group A; B: Blood group B; AB: Blood group AB; O: Blood group O.

group AB with 15.8%. Almost similar types of results were observed by different researchers [3] [5] [15].

On the other hand, some disagreements observed by various studies which might be due racial and geographic variation. Some researcher found that blood group O was the predominant blood group followed by blood group A, B and AB [11] [14] [16]. Agrawal *et al.* (2014) observed that blood group O was in highest frequency followed by blood group B, A and AB [17]. Choi *et al.* (2014) showed that blood group A was the commonest blood group followed by blood group B, O and AB [13].

Table 2 and Figure 2 show, higher level of mean coagulation factor VIII in blood group B individuals (112.00% ± 15.02%) followed by group AB (109.80% ± 11.93%), A (105.76% ± 11.82%) and O (82.00% ± 12.86%). The mean differences among the groups were statistically significant ($p < 0.001$). The mean difference between group A and O, B and O, AB and O was also statistically significant ($p < 0.001$). No significant difference in coagulation factor VIII level among group A, B and AB. Almost similar types of results were observed by different researchers [14] [18] [19].

Blood group A, B, AB individuals have additional carbohydrate to the terminal carbohydrate of peripheral core of the H substance (precursor antigen). When an additional carbohydrate is added by N-acetyl-galactosamine, blood group A is produced. When an additional carbohydrate is added by the galactose transferase, blood group B is produced. No carbohydrate is added to the H substance due to lack of transferase enzyme, produce blood group O. Von Willebrand factor

Table 2. Coagulation factor VIII of the study subjects in different groups (N = 190).

Parameter	**Groups**			
	Group A ($n_1 = 45$)	**Group B ($n_2 = 63$)**	**Group AB ($n_3 = 30$)**	**Group O ($n_4 = 52$)**
Coagulation factor VIII (%)	105.76 ± 11.82	112.00 ± 15.02	109.80 ± 11.93	82.00 ± 12.86
Statistical analysis	***p*-value**			
Groups	**Coagulation factor VIII**			
A vs B vs AB vs O	<0.001*			
A vs B	0.101^{NS}			
A vs AB	1.000^{NS}			
A vs O	<0.001*			
B vs AB	1.000^{NS}			
B vs O	<0.001*			
AB vs O	<0.001*			

Results were expressed as Mean ± SD. One way ANOVA followed by Bonferroni test was performed to compare between groups. N: Total number of subjects; n_1: number of subjects in group A; n_2: number of subjects in group B; n_3: number of subjects in group AB; n_4: number of subjects in group O. The test of significance was calculated for all comparisons and p value < 0.05 was accepted as level of significance. ^{NS}not significant, *significant. Group A: blood group A; Group B: blood group B; Group AB: blood group AB; Group O: blood group O.

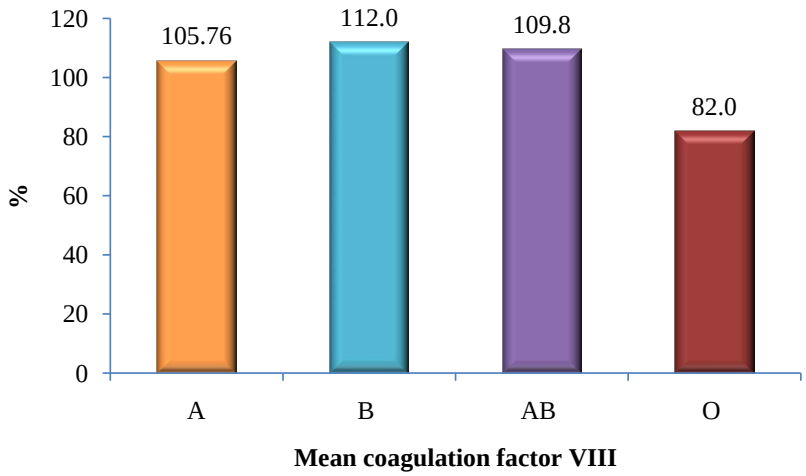

Figure 2. Mean coagulation factor VIII of the study subjects in different groups (N = 190). N: Total number of subjects; A: Blood group A; B: Blood group B; AB: Blood group AB; O: Blood group O.

is a large glycoprotein which is synthesized by Weibel-Palade bodies in the endothelial cells and alpha granules of megakaryocytes. Lowest plasma Von Willebrand factor level is present in genotype OO individuals (Blood group O) due to lack of additional terminal sugar. Plasma Von Willebrand factor is proteolized by metalloprotease enzyme ADAMTS13. Proteolysis is faster for group O Von Willebrand factor than group A, B, AB Von Willebrand factor. So blood group A, B and AB have more von Willebrand factor than blood group O. Von Willebrand factor is the specific carrier of factor VIII in plasma. It protects factor VIII from proteolytic degradation and prolonging its half-life in circulation. Thus von Willebrand factor protects factor VIII from proteolytic degradation and prolonging its plasma half-life in A, B, AB blood groups. This might be the cause of increased coagulation factor VIII level in blood group A, B and AB [7] [8] [11].

On the other hand, Albanez *et al.* (2016) found no significant difference in coagulation factor VIII level among ABO blood groups. They selected study subjects aged 1 - 17 years. They suggested that, the effect of ABO blood group on von Willebrand factor was limited in young age. Young age group might be the reason of contrary of the findings from present study [20]. Another research showed that factor VIII level was significantly higher in blood group A than blood group B, AB and O. Factor VIII level was significantly higher in blood group B than blood group AB and O. No significant difference was found between blood group AB and O in case of factor VIII level. This disagreement in findings might have occurred due to variation of von Willebrand factor in different races [21]. Loganathan *et al.* (2019) found no significant difference in factor VIII among blood group A, B, AB and O. They estimated factor VIII from fresh frozen plasma. That might be the cause of disagreement in findings [22]. Rejto *et al.* (2020) observed no significant difference among ABO blood groups in case of coagulation factor VIII. They include non severe haemophilia patients

as study subjects. This might be the reason of contrary in findings from present study [23].

4. Conclusion

After analyzing the results of the study, it can be concluded that blood group B is the most common (33.2%) among the study subjects. Blood group A, B, AB individuals may have more chance of thrombosis due to significantly higher coagulation factor VIII than blood group O in this study.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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