ISSN- 2394-5125 VOL 08, ISSUE 02, 2021

PROTHROMBIN TIME (PT) AND ACTIVATED PARTIAL THROMBOPLASTIN TIME (APTT) IN VARIOUS BLOOD GROUP PHENOTYPES

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ABSTRACT

BACKGROUND: Prothrombin time (PT) is used for assessment of extrinsic and common pathway of coagulation; whereas activated partial thromboplastin time (APTT) assesses the intrinsic and common pathway. Variation in blood group phenotypes has been linked to various diseases and their predisposition.

OBJECTIVE: The key objective of this study was to correlate the prothrombin time (PT) and activated partial thromboplastin time (APTT) variations among different ABO blood group types.

METHODOLOGY: This study was cross-sectional, prospective carried out at Department of Pathology and Medicine, Indus Medical College Tando Muhammad Khan for period of 8 months (February 2020 to September 2020). Total of 155 healthy participants were selected in this study. Individuals having bleeding history, medication and co-morbid conditions were excluded from the study. After informed consent, 5mL of whole blood was extracted from every participant to evaluate the coagulation profile and ABO blood group phenotype. SPSS 24.0 was used for analysis of data. A p-value of <0.05 was taken as statistically significant.

RESULTS: Of 155 participants, 59 (38.06%) were having O blood group, 45 (29.03%) were having A blood group, 31 (20%) were having B blood group and 20 (12.9%) were having AB blood groups. While comparing the coagulation parameters among various blood groups, prothrombin time (PT) was shown to be highest in individuals with A blood group in comparison of other blood group phenotypes; while activated partial thromboplastin time (APTT) was highest in individuals with O blood group in comparison of other blood groups, with statistically significant p-value.

CONCLUSION: The study showed that prothrombin time (PT) and activated partial thromboplasltin time (APTT) vary in various blood group phenotypes. Blood group may influence their levels and mechanisms of extrinsic and intrinsic pathways.

Keywords: Prothrombin time, Activated partial thromboplastin time, blood groups, phenotypes, coagulation pathway.

INTRODUCTION

Prior to discovery of ABO blood groups, less knowledge of variations in composition of blood among animals and humans caused high mortality rate. (1) For the medico-legal and clinical use, variations in blood groups are of importance. There are many blood group systems but ABO blood group is very essential. In 1900, Karl Landsteiner discovered systems of ABO blood groups, and it made great impression in transfusion medicine and blood banking. (2) For the ABO blood grouping basis, the antigenic property of red blood cells were labelled as important.

Red blood cell surface membrane consists of antigens as complex oligosaccharides along with various terminal sugars are placed on chromosome. (3) On red blood cell membrane extracellular surface, the A, B and H antigens carbohydrate molecules are complexed. (4) A and B antigens vary in their terminal sugar and their genes are located on chromosome 9 and chromosome 19 respectively. (5) The Mendelian dominance is their pattern of inheritance.

ISSN- 2394-5125 VOL 08, ISSUE 02, 2021

ABO blood grouping has wide extension beside transfusion medicine and immunohaematology. Antigens of ABO blood groups which are present on surface of red blood cells as well as various epithelial cells, have shown correlations between disease and ABO blood groups, [6] out of which cardiovascular diseases and infections represent commonly, and reveal essential involvement in production of various diseases. [7-9] Types of blood group have been predisposed to various diseases. These statements are supported by various researches which proposed correlation with various diseases including duodenal ulcers, diabetes mellitus, gastric carcinoma, peptic ulcers, malignancy, bleeding, urinary tract infection and venous thrombosis. [10-12]

In blood, a dozen of factors of coagulation have been known so far. Such coagulation factors are termed as proteins that are present in inactive form in the blood but their activation occurs when there is damage to blood vessels of tissues. [13] The coagulation status is represented by prothrombin time (PT) and activated partial thromboplastin time (APTT). These tests are commonly utilized for monitoring and screening of deficiencies of coagulation factors. [14-15] Prothrombin time (PT) evaluates disorders of extrinsic pathway and common coagulation pathway. In deficiency of factor I, factor II, factor V, factor VII and factor X, prothrombin time (PT) level becomes abnormal. In deficiency of factor I, factor II, factor V, factor VIII, factor IX, factor X, factor XI and factor XII, the activated partial thromboplastin time (APTT) level becomes abnormal). [17] Gender and ABO blood group are dependant variations in PT and APTT test.

ABO blood group is very important determinant of von Willebrand factor (vWF) and factor VIII levels in plasma; therefore it is known to influence the haemostasis. [18] Studies revealed that individuals with A and B blood groups are more at the risk of developing venous thromboembolism (VTE) and with O blood group and have increased levels of von Willebrand factor and factor VIII, [19-21] making it one of the most important disease correlation for individuals with A and B blood groups. Liu et al. and Wang et al. showed that plasma levels of von Willebrand factor and factor VIII were raised in A and B blood group individuals in comparison to the O blood group individuals. Therefore, A and B blood groups produce a risk factor for high levels of von Willebrand factor and factor VIII in plasma. This study is designed to assess the correlation between haemostatis and blood groups using coagulation screening tests i.e. PT and APTT.

PATIENTS AND METHODS

The study was cross-sectional, prospective conducted at Department of Pathology, Indus Medical College Hospital Tando Muhammad Khan. The study was conducted over a period of 8 months (February 2020 to September 2020). 155 normal participants were selected for the study. After taking ethical approval, informed consent was taken from all included individuals. Only normal individuals aged between 18 years to 40 years were included in the study. Individuals with known bleeding disorders, inflammatory conditions, blood transfusion within last 3 months, individuals on anti-platelet or anticoagulant medication, and individuals with co-morbid risk factors were excluded from the study.

5mL of venous whole blood was extracted by venepuncture using aseptic measures from all participants. 3mL whole blood was transported into 0.5mL of trisodium citrate (3.2%) collection tube, followed by centrifugation at 4000rpm for 10 minutes. The platelet-deficient plasma was obtained to analyze the prothrombin time (PT) and activated partial thromboplastin time (APTT). 2mL whole blood was transported into ethylenediaminetetraacetic acid (EDTA) collection tube for the evaluation of blood group.

The tile method was used for the determination of ABO blood group. On the white-pitted tile, a drop of anti-A, anti-B and anti-AB was placed, followed by placement of drop of blood on each anti-sera and glass rod was used to mix them. Rocking of white tile was continued gently for 4 minutes and was observed for appearance of agglutination.

Manual method was used for the assessment of prothrombin time (PT). The required PT reagent volume was obtained from vial and was incubation was performed at $37^{O}C$ for 10 minutes. 100µL test plasma was transported into tube and incubation was performed for 3 minutes. 200µL of PT reagent (pre-incubated) was immediately mixed and timer was initiated. Time for clot formation was recorded.

Manual method was used to assess activated partial thromboplastin time (APTT). The required calcium chloride ($CaCl_2$) reagent volume was taken for incubation at $37^{O}C$ for 10 minutes. The required APTT reagent volume was obtained from vial and kept at room temperature. 100µL of test sample was transported into tube followed by incubation at $37^{O}C$ for 2 minutes. 100µL of APTT reagent (kept at room temperature) was mixed followed by incubation of mixture at $37^{O}C$ for 3 minutes. 100µL of calcium chloride ($CaCl_2$) reagent was immediately mixed and timer was initiated. Time for clot formation was recorded.

The data was collected and analyzed using SPSS 24.0. Mean and standard deviations were used for the expression of results. The independent t-test was applied to compare between groups. The p-value of <0.05 was considered as significant statistically.

ISSN- 2394-5125 VOL 08, ISSUE 02, 2021

RESULTS

Out of 155 participants, 59 (38.06%) were having O blood group, 45 (29.03%) were having A blood group, 31 (20%) were having B blood group and 20 (12.9%) were having AB blood groups (Figure 1). While comparing the coagulation parameters among various blood groups, prothrombin time (PT) was shown to be highest in individuals with A blood group in comparison of other blood group phenotypes; while activated partial thromboplastin time (APTT) was highest in individuals with O blood group in comparison of other blood groups, with statistically significant p-value (Table 1 and 2).

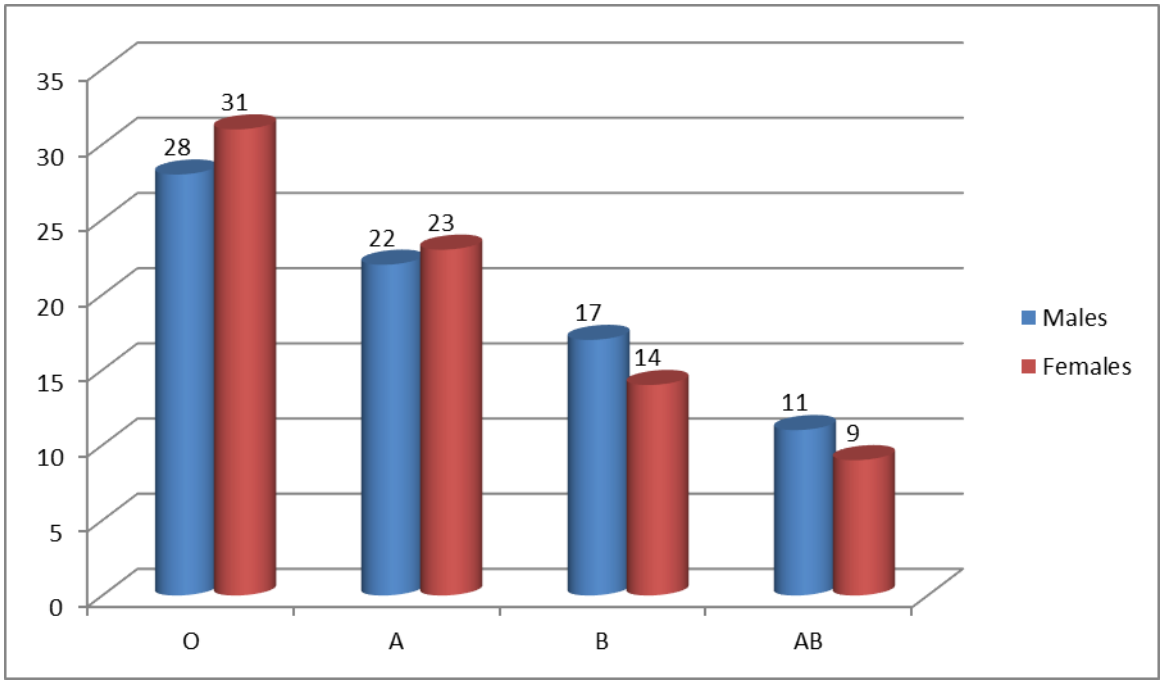

Figure 1: ABO Blood Group Frequencies According to Gender Distribution (n=155)

Table 1: Comparison of Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT) among Various Blood Groups (n=155)

	Blood Group Phenotype				p-value
	O	A	B	AB	
Mean PT (seconds)	14.81 ± 1.98	16.89 ± 2.31	14.01 ± 2.81	15.21 ± 2.45	0.003
Mean APTT (seconds)	40.98 ± 9.53	38.12 ± 11.91	36.57 ± 10.94	40.51 ± 10.88	0.007

Table 2: Levels of Significance among Blood Groups (n=155)

	PT (p-value)	APTT (p-value)
O versus A	0.001	0.031
O versus B	0.31	0.004
O versus AB	0.13	0.011
A versus B	0.004	0.10
A versus AB	0.051	0.49
B versus AB	0.003	0.09

DISCUSSION:

Prothrombin time (PT) and activated partial thrombopalstin time (APTT) are haemostatic investigations that reveal status of coagulation. These investigations are carried out for screening and monitoring of deficiencies of various coagulation factors. [14-15] Limited data is available for correlation of coagulation pathways and ABO blood group system.

Our study revealed significant variation in PT and APTT among various blood groups. Prothrombin time (PT) was higher in blood group A as compared to other blood group phenotypes, while activated partial thromboplastin time (APTT) was increased in O blood group in comparison of other blood group phenotypes. Choi et al. and Fourel et al. showed similar findings. [24-25] In their study, individuals with blood group O were having higher levels of activated partial thromboplastin time (APTT) as compared to other

ISSN- 2394-5125 VOL 08, ISSUE 02, 2021

blood groups; although Choi et al. demonstrated that prothrombin time (PT) did not significantly vary between different groups.

Increased predisposition to bleeding conditions may be seen in patients having higher PT and APTT. Robert et al. postulated in his study that individuals with O blood group have higher bleeding tendency while individuals with A and/or B blood group were more prone to thrombose. Therefore blood group O individuals constitute decreased risk to develop venous thromboembolism (VTE) in comparison of other blood groups. In individuals with A and/or B blood groups, decreased level of APTT may be correlated to higher predisposition to venous thromboembolism (VTE) and cardiovascular diseases. [7, 27]

The findings regarding decreased plasma a von Willebrand factor (vWF) level in individuals having O blood groups is not completely established. Un circulatory von Willebrand factor (vWF), availability of ABH antigenic structures are being considered as basis of molecular phenomenon, which regulate protein activity via various glycosylation degrees. [18, 28] Influence of gender had been shown by Fourel et al. [25] He stated that lower APTT was seen in females. PT varied among gender groups as demonstrated by Abdullah et al. [29] and Aral et al. [30]. Although no significant difference between gender groups was found in our study.

The pattern of distribution of ABO blood group antigens vary among various populations around the globe. As like previous studies, O blood group was most prevalent blood group among all. [31] Further evaluation on larger population areas and wider coverage of geography should be carried out to assess effect of blood group antigenicity on coagulation status of individuals.

CONCLUSION:

Coagulation screening tests i.e. PT and APTT vary among different blood group systems. Individuals with blood group O and A were having higher values of PT and APTT respectively, in comparison of other blood groups. This suggests the effect of presence/absence of blood group antigens on extrinsic and intrinsic pathways of coagulation.

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