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RESEARCH ARTICLE

# A comparative study of the variation in coagulation profile between different blood groups in ischemic heart disease patients and normal subjects

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## ABSTRACT

**Background:** A positive association of coagulation factors has been implicated with the risk of ischemic heart disease (IHD), and so have the associations of the ABO blood groups. **Aims and Objectives:** This study was done in IHD patients and normal individuals to assess the variations of coagulation factors among the different ABO blood groups. **Materials and Methods:** This study included 50 IHD male patients taken as cases and 50 age-matched and sex-matched, apparently healthy males taken as controls. Blood samples were collected from subjects for the analysis of prothrombin time (PT), activated partial thromboplastin time (aPTT), and fibrinogen levels and also for the determining the ABO blood group. **Results:** Majority of the cases belonged to blood group A (36%) while a majority of the controls belonged to blood group O (44%). Among the cases, individuals with blood group A were found to have significantly higher fibrinogen levels, and blood group O individuals had the least fibrinogen levels. Similar pattern was also observed among the controls. The PT and aPTT values were minimum in individuals of blood group A while maximum values were observed in blood group O individuals; both in cases and controls. **Conclusion:** PT and aPTT indirectly assess the coagulant activity of the different factors of the extrinsic and intrinsic pathways, respectively. Shortened levels of PT and aPTT and higher levels of fibrinogen are seen in blood group A individuals. Thus, it can be said that among the various risks associated with the development of IHD, ABO blood group is also one of them wherein blood group A individuals are more likely to the develop the disease while blood group O confers protection against IHD.

**KEY WORDS:** Ischemic Heart Disease; ABO Blood Groups; Prothrombin Time; Activated Partial Thromboplastin Time

## INTRODUCTION

The discovery of the ABO blood groups in 1901 by Landsteiner has its implications not only restricted to transfusion and transplantation medicine but also to other important branches of medicine.[1] There are innumerable reports that have shown associations between this blood group system and diseases such as gastric cancer,[2] periodontal diseases,[3] and cardiometabolic diseases.[4]

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Various studies have demonstrated thrombus formation to be the etiology in the pathogenesis of ischemic heart disease (IHD). Myocardial infarction occurs when a thrombus evolves on a ruptured atherosclerotic plaque followed by vessel occlusion. This exposes tissue factor i.e. factor III to blood which triggers the extrinsic system. Initially believed to measure Prothrombin (Factor II) and hence named so, prothrombin time (PT) was subsequently found to be sensitive to Factors VII, X, V, and

II and fibrinogen abnormalities. Functional activity of Factors VII, X, V, and II determines the extrinsic pathway which is thus measured by evaluating the PT.[5]

According to studies, the intrinsic pathway of coagulation also has contributions to thrombogenicity.[6] This pathway can be analyzed by measuring activated partial thromboplastin time (aPTT)[5] thereby measuring the functional activity of Factors IX, X, XI, and XII.

Time and again there are studies that have shown associations between non-O blood group and various cardiovascular disorders.

The present study was conducted on IHD patients and normal subjects to assess the coagulation tendency in different ABO blood groups by comparing the PT, aPTT, and fibrinogen levels.

## MATERIALS AND METHODS

This study was carried out in the Department of Medicine, Basaveshwar General and Teaching Hospital, Kalaburagi. The study group included 50 newly presenting IHD male individuals aged between 30 and 50 years, diagnosed by the physician on the basis of history, electrocardiographic findings, and other clinical evidence. The control group included 50 healthy age- and sex-matched male individuals.

### Exclusion Criteria

1. Females were excluded from the study as it has been shown that cardiovascular diseases are less likely to occur in premenopausal women due to the female sex hormones.[7]
2. Subjects on anticoagulant drugs.
3. Patients with coexistent valvular diseases, endocrine disorders except for diabetes mellitus for subjects of the study group.
4. In the control group hypertensives, diabetics or those with any kind of systemic diseases and endocrine disorders were excluded.
5. Subjects with active psychiatric disease or central nervous system disorder.

After obtaining ethical clearance from the institution and informed written consent from each subject a prepared questionnaire was given to each subject to answer. The preformed questionnaire included a detailed history of sociodemographic data, history of presenting illness, past and family history including history of hypertension, diabetes mellitus, IHD and thyroid disorders, and personal history including type of diet and any history of addictions such as smoking history and alcohol intake was noted. Thorough general physical and systemic examinations were done.

PT, aPTT, and fibrinogen levels were analyzed on the venous blood samples that were collected from each subject in the Biochemistry laboratory of Basaveshwar Teaching and General Hospital on Sysmex CA-50 (Code- 461-2035-2 Sysmex Corporation Kobe, Japan) Automated Blood Coagulation Analyzer. Determination of the blood group was done using slide agglutination technique.

All data are expressed as a mean± standard deviation. Students unpaired *t*-test and One-way ANOVA were applied to analyze the data. p value <0.01 and p value < 0.05 were taken as highly statistically significant and statistically significant, respectively.

## RESULTS

Table 1 shows the frequency of distribution of different blood groups in cases and controls. Table 2 shows that among the cases, it was observed that the fibrinogen levels were significantly higher in blood group A than compared to the other blood groups. Although not statistically significant it is observed that in blood group A, PT and aPTT levels were the least while blood group O had the greatest PT and aPTT values.

Table 3 shows that among the controls, the difference in various coagulation parameters of the different blood groups is not statistically significant. However, it should be noted that individuals with A blood group have shorter PT and aPTT values and higher fibrinogen levels than the other blood groups.

## DISCUSSION

Our study reveals shorter PT and aPTT values and higher fibrinogen levels in individuals of A blood group than compared to other blood group individuals. This pattern is observed both in the cases as well as the control.

Many studies[8] have shown that in non-O blood group individuals, Factor VIII - von willebrands factor (vWF) complex levels in plasma were in ≈25% more than compared to O blood group individuals. This attributes to higher risks of peripheral vascular disease, thromboembolic disease,

**Table 1:** Incidence of blood groups in cases and in controls

| Blood group | Cases (%) | Control (%) |
|---|---|---|
| A | 18 (36) | 9 (18) |
| B | 14 (28) | 11 (22) |
| AB | 5 (10) | 8 (16) |
| O | 13 (26) | 22 (44) |
| Total | 50 (100) | 50 (100) |

**Table 2:** Coagulation profile among blood groups in cases

| Blood group | Frequency (n) | PT (in seconds) | aPTT (in seconds) | Fibrinogen (in mg/dL) |
|---|---|---|---|---|
| A | 18 | 13.53±1.21 | 33.23±1.71 | 355±11.8 |
| B | 14 | 13.68±1.04 | 33.68±1.56 | 289±9.07 |
| AB | 5 | 13.87±1.21 | 33.75±1.82 | 282.45±17.03 |
| O | 13 | 14.2±1.32 | 33.8±1.93 | 265.8±43.35 |
| *F* value | | 2.38 | 2.52 | 9.51 |
| *P* value | | 0.08 | 0.07 | 0.005** |

**P*<0.05 - statistically significant. *P*<0.01 - highly statistically significant. PT: Prothrombin time, aPTT: Partial thromboplastin time

**Table 3:** Coagulation profile among blood groups in controls

| Blood group | Frequency (n) | PT (in seconds) | aPTT (in seconds) | Fibrinogen (in mg/dL) |
|---|---|---|---|---|
| A | 9 | 14.56±1.78 | 43.09±2.60 | 276.14±22.9 |
| B | 11 | 15.16±2.03 | 43.4±2.57 | 275.8±24.5 |
| AB | 8 | 14.97±2.22 | 43.23±2.4 | 275.2±29.8 |
| O | 22 | 15.58±1.68 | 44±2.44 | 270.7±18.08 |
| *F* value | | 1.74 | 0.86 | 0.27 |
| *P* value | | 0.17 | 0.46 | 0.84 |

**P*<0.05 - statistically significant. *P*<0.01 - highly statistically significant. PT: Prothrombin time, aPTT: Partial thromboplastin time

and arterial diseases including IHD in non-O blood group individuals.

Blood group O individuals have been found to have a higher rate of bleeding complications[9] to the extent that this blood group has the highest incidence of inherited bleeding disorders.[10] This can be explained by a study conducted by Favaloro *et al*. where they observed that levels of Factors VIII, IX, and XII were significantly lower in blood group O individuals in comparison to non-O blood group individuals.[11]

Endothelial cells that line the blood vessels and platelets in the blood synthesize vWF which is a large adhesive glycoprotein that circulates as a series of heterogeneous multimers in the plasma.[12] Being the specific carrier protein of Factor VIII, vWF protects it from proteolytic degradation thereby prolongs its half-life in circulation and hence makes it more localized at the site of injury in the blood vessel.[13] Apart from this vWF and fibrinogen together, play an important role in platelet aggregation. This attributes to the development of atherosclerosis. Moreover, therefore a shortened aPTT can be explained by higher levels of vWF and its accompanying Factor VIII.

The quantity of vWF that circulates in plasma is not only determined by the vWF gene situated on chromosome 12p12 but also determined majorly by other gene loci, of which the most important is the ABO blood group locus situated on chromosome 9q34.[14] vWF binds to platelets by its receptor glycoprotein Ib-V-IX. The expression of ABH gene locus produces N-linked oligosaccharide chains which bind to this vWF receptor protein. These oligosaccharide chains then confer protection to vWF against the enzymatic degradation by a specific metalloprotease called ADAMTS 13.[14,15] Since blood group O individuals lack the expression of the ABH gene, vWF becomes more susceptible to proteolysis by ADAMTS 13, and hence the levels of vWF are lower in them.[16] Consequently, Factor VIII levels are also reduced in these individuals. The higher risks of thromboembolic events in non-O blood group individuals can be thus explained by the higher levels of vWF-FVIII complexes in them.

However, Meade *et al.* found that the association between vWF and the risk of cardiovascular mortality was independent of blood group.[17]

Thromboembolic states have also been attributed to the mutations in various clotting factors with ABO types having associations with these mutations. Activated protein C is a natural anticoagulant, resistance against which has shown to be an important and common causal factor for thromboembolism.[18] This resistance is due to a mutation in one of its cleavage sites on Factor V (Arg506Gln, Factor V Leiden).[19] The incidence of venous thromboembolism (VTE) for those being heterozygous with Factor V Leiden has a relative risk of approximately 3–8 and the relative risk is 80 for those who are homozygous according to case–control studies carried out in the United States.[20]

When age, sex, and race were adjusted in a study by T. Ohira *et al.,*[21] it was found that the odds ratio for having 2 risk factors, i.e. non-O blood group and Factor V Leiden were 6.77 in individuals of VTE. They concluded that the mutation in Factor V modifies the association of non-O blood group with VTE.

### Strength of the Study

In our study, blood group A presented more in cases (36%) than in controls (18%), while blood group O presented more in controls (44%) than in cases (26%). A possible scenario could be that individuals belonging to blood group O who have IHD may survive for shorter periods due to the underlying pathological imbalance between necrosis and revascularization of tissue. These individuals are more prone to bleeding tendencies which could thus hamper the normal physiological healing process.

### Limitation of the Study

Although our study gave us results that are statistically insignificant, it gives us an insight into the possible cause of cardiovascular accidents that are overtly presented in blood group A. Further studies on individual factor assay in relation to ABO blood group are required to be carried out on a larger study group to get significant results.

## CONCLUSION

It can be concluded that by assessing the coagulation tendency through tests such as PT, aPTT, and serum fibrinogen levels, the formation of a thrombus is more likely in blood group A individuals and these individuals have a higher risk of developing peripheral vascular and arterial diseases than compared to the other blood group individuals.

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