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Rismawati Yaswir, Nurhayana Sennang Andi Nanggung, Adi Koesoema Aman, Osman sianipar,  
Purwanto AP, Budi Mulyono, Jusak Nugraha, Rahajuningsih Dharma

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RESEARCH

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## COMPARISON OF FACTOR VIII ACTIVITY IN O AND NON-O BLOOD TYPES

*(Perbandingan Aktivitas Faktor VIII antara Golongan Darah O dan Non-O)*

**Adil Dinata Simangunsong, Yetti Hernaningsih**

### ABSTRAK

Golongan darah ABO telah dinilai untuk terjadinya berbagai proses penyakit. Penelitian terdahulu menyatakan tingginya kejadian trombosis pada golongan darah non O disebabkan tingginya aktivitas faktor VIII dibandingkan golongan darah O. Metode penelitian merupakan analitik observasional secara potong lintang. Sampel darah sitrat dengan nilai APTT dan PTT normal tanpa mempertimbangkan usia, jenis kelamin dan diagnosis. Aktivitas faktor VIII diperiksa menggunakan sysmex CS 2100i. Analisis statistik menggunakan one way Anova untuk golongan darah A, B, O dan uji sampel T independen untuk golongan darah O dan non-O. Dari keseluruhan 30 sampel didapatkan 15 sampel golongan darah non-O dan 15 sampel golongan darah O. Pada golongan darah non-O didapatkan 8 sampel golongan darah A dan 7 sampel golongan darah B. Terdapat perbedaan aktivitas faktor VIII yang tidak bermakna antara golongan darah non-O dan O ( $p=0,277$ ). Pada golongan darah A, B, O, juga didapatkan perbedaan yang tidak bermakna ( $p=0,108$ ). Aktivitas faktor VIII pada golongan darah non-O lebih tinggi dibandingkan golongan darah O, tetapi tidak didapatkan perbedaan bermakna. Pada golongan darah A,B,O juga tidak didapatkan perbedaan bermakna. Mekanisme yang mendasari hubungan antara golongan darah ABO dengan aktivitas faktor VIII sampai sekarang belum diketahui. Tidak didapatkan perbedaan bermakna aktivitas faktor VIII antara golongan darah O dan non-O. Diperlukan penelitian dengan jumlah sampel yang lebih banyak dan mengikut sertakan golongan darah AB.

**Kata kunci:** Aktivitas faktor VIII, golongan darah ABO, PPT dan APT

### ABSTRACT

ABO blood types have been evaluated for the occurrence of a variety of disease processes. Previous studies have claimed that the high incidence of thrombosis in non-O blood types is due to the high activity of factor-VIII compared O blood type. This study was an observational cross-sectional analytical. The samples consisted of citrate blood with normal APTT and PTT values without considering age, sex and diagnosis. Factor VIII activity was examined using Sysmex CS 2100i. Statistical analysis used an one-way ANOVA for A, B, O blood types and independent sample t test for O and non-O blood types. Results from the total 30 samples, 15 samples had non-O blood type and 15 samples of O blood type. In non-O blood type there were eight samples with A blood type and seven samples with B blood type. It was shown that the difference of factor VIII activity was not significant among non-O and O blood types ( $p=0.277$ ). A, B, O blood types also showed no significant difference ( $p=0.108$ ). Conclusion, there were no significant differences between factor VIII activity in O and non-O blood types. Studies with a larger sample size and involving blood type AB are needed.

**Key words:** Factor VIII activity, ABO blood types, PPT and APT

## INTRODUCTION

Factor-VIII (anti-hemophilia factor) is a glycoprotein cofactor which serves as an essential component of the intrinsic pathway. Factor-VIII deficiency results in hemophilia A disease. Factor-VIII is a multidomain glycoprotein with domain structure A1-A2-B-A3-C1-C2, in which the heavy chain consists of A1-A2-B and the light chain A3-C1-C2.<sup>1</sup> Many studies linked ABO blood types with a variety of disease processes.<sup>2,3</sup>

ABO blood types has a functional effect on factor-VIII. Individuals with non-O blood type have higher levels of factor VIII than those with O blood type. Factor VIII is 25–30% lower in O blood type. Factor VIII activity does not differ significantly between A, B and AB, blood types although it is generally higher in AB blood types.<sup>4–9</sup> Several previous studies have demonstrated that factor VIII activity is influenced by age, sex and blood types in healthy people. According to Cooperber & Teitelbaum, factor-VIII is higher in the elderly and in males. Pitney *et al.*<sup>4</sup> stated that factor-VIII is higher in the elderly and not influenced by gender. Preston & Barr<sup>5</sup> stated that the effect of age is not significant, but it is higher in males than females.<sup>4,5</sup>

In normal subjects, the activity of factor-VIII ranges from 50–150%.<sup>7</sup> High factor-VIII can be caused by stress, pregnancy, atherosclerosis, obesity, high triglyceride levels and acute phase response (malignancy and chronic inflammation). Some previous studies have claimed that non-O blood types have the risk of thrombosis and O blood type with the risk of hemorrhage.<sup>4,6,8,10–12</sup> Factor-VIII is an acute phase protein and is increased temporarily during an inflammatory process. Kamphuisen's study showed no relationship between factor VIII activity and CRP (C-Reactive Protein) in venous thrombosis patients. They also revealed that high activity of factor-VIII settles until several months after the occurrence of venous thrombosis. These results are consistent with a study by O'Donnell.<sup>13–15</sup>

Several studies have demonstrated that a high activity of factor VIII is persistent and serves as a risk factor for thrombosis, but it has not been known how much the cut-off value is of factor-VIII that leads to thrombosis.<sup>4</sup> The Genetic Analysis of Idiopathic Thrombophilia (GAIT) study found a relationship between factor VIII activity with a Activated Protein C resistance in the pathogenesis of thrombosis. Activated Protein C resistance increases the risk of venous thrombotic events.<sup>13,14</sup> High factor-VIII with

the possibility of thrombosis is associated with a genetic disorder, that is the presence of the locus on chromosome <sup>18,4,13,14</sup>

This study was conducted to determine whether factor VIII activity in non-O blood type was higher than that in O blood type and factor VIII activity in the A, B and O blood types using Sysmex CS-2100i. In addition, the authors also wanted to find out the cause of high-factor VIII activity in O blood type compared to that of non-O, which is still controversial. This study aimed to determine whether there were differences in factor-VIII activity in O and non-O blood type.

## METHODS

This study was an observational analytic cross-sectional study. The study was conducted November 2014 at the Clinical Pathology Laboratory, Dr. Soetomo Hospital. The inclusion criteria were blood samples in citrate tubes with normal results of APTT and PPT, regardless of age, sex and diagnosis of disease. Sample size in this study was 30 samples. The samples were venous blood in tubes containing 3.2% sodium citrate and citrate blood with a ratio of 9: 1. A total of 30 samples with normal APTT and PPT were selected and blood type examination was done, yielding in 15 non-O blood type (8 A blood type and 7 B blood type) and 15 O blood type.

Examination of factor VIII activity was carried out on each blood type. The samples were divided into 2 groups. Group 1 comprised samples of A, B, O blood types and group 2 O and non-O blood type. APTT, PPT and-factor VIII activity examination was done by the method of photo optical using Sysmex CS-2100i. Statistical analysis used SPSS 13.

Data were analyzed using one way Anova comparative test for A, B, O blood types and independent sample t test for O and non-O blood types, with a significance level of  $p < 0.005$  was considered statistically significant and the confidence level was 95%.

## RESULTS AND DISCUSSION

Data normality test of factor VIII in blood types A, B and O shows that all data had a normal distribution, so to test the difference of factor VIII in A, B and O blood types one way ANOVA as used (Table 1).

**Table 1.** Results analysis of comparative test of factor VIII activity in A, B and O blood types

Blood types	Factor VIII activity				P value
	Min	Max	Mean	SD	
A	128.8	175.1	149.8	17.6	0.108
B	68.2	178.5	127.6	37.7	
O	105.8	151.4	128.2	13.3	

**Table 2.** Results analysis of comparative test on factor VIII activity in O and non-O blood types

Blood types	Faktor VIII Activity				P values
	Min	Max	Mean	SD	
Non O	68.2	178.5	138.0	31.2	0.277
O	105.8	151.4	128.2	13.3	

One Way ANOVA test results on the data of factor VIII activity in A, B and O blood types revealed  $p=0.108$ . This result indicated that there was no difference in factor VIII activity between A, B and O blood types.

Normality test of factor VIII activity in O and non-O blood types showed that both had a normal distribution, so to examine differences in the factor-VIII activity in O and non-O blood types used independent sample t test (Table 2).

The result of independent sample t test on factor VIII activity in O and non-O blood types revealed  $p=0.277$ . This result indicated that there was no difference in factor-VIII activity in O and non-O blood types.

Factor-VIII activities in A, B, O blood types showed no difference ( $p=0.108$ ). The highest factor VIII activities were found in A blood type (mean=149.8;  $\pm$ SD=17.6), followed by O blood type (mean=128.2%;  $\pm$ SD=13.3) and B blood type (mean=127.6;  $\pm$ SD=13.3). A study by Preston & Barr<sup>7</sup> stated that there were significant differences in factor VIII activity, in which the A blood type and B is higher than O. While non-O and O blood type also showed no significant difference ( $p=0.277$ ) in factor VIII activity in non-O (mean=138.0%;  $\pm$ SD=31.2) and O (mean=128.2%;  $\pm$ SD=13.3) blood types. Some previous studies also revealed no significant difference between non-O and O blood types.<sup>7</sup>

Differences in blood type phenotypes are partially dependent on the race. In Caucasians A1=33%, A2=10%, B=9%, A1B=3%, A2B=1%, Asian A1=27%, A2=rarely, B=25%, A1B=5%, A2B=rarely and African

A1=19%, A2=8%, B=20%, A1B=3%, A2B=1%. O blood type is found in most wide populations.<sup>11</sup> A recent study found that phenotypic factors were associated with a high risk of venous thrombosis.<sup>15</sup> This study did not obtain the AB blood type samples. It may be caused from rare population of individuals with AB blood type, similar to the a previous study of Preston & Barr.<sup>7</sup>

Factor VIII activity and non-O blood type are independent risk factors for venous thromboembolism. Allegedly, A1 allele gene also plays a role in the occurrence of thromboembolic. Several previous studies found that factor VIII contributes to the occurrence of thrombosis, according to Kraaijenhagen *et al.* and Kyrle *et al.*<sup>4</sup>

The high activity of factor VIII is related to prothrombotic hyperactivity in arterial and venous systems. According to Vormittag, factor VIII activity of >232% is an independent risk factor for the incidence of thromboembolic complications. Kamphuisen stated that only 4% of factor VIII activity >123% may cause the incidence of arterial thrombosis.<sup>13</sup> High factor-VIII activity is the risk factor of thrombosis, with a greater impact on venous thrombosis than arterial thrombosis.<sup>15</sup> In this study, factor VIII activity between O and non-O blood types was not significantly different.

Limitation of this study were that age, sex and diagnosis of disease were not consider. The samples were studied only in A, B and O blood types with normal APTT and PPT values. Previous studies found that factor VIII activity was not affected by age, gender and diagnosis of disease. Some studies also suggested

that high factor VIII activity was affected by pregnancy, surgical intervention, the use of birth control pills, diabetes mellitus, renal failure and malignant disease.<sup>5</sup> The mechanism of genetic and environmental factors, that leads to a high factor VIII activity, as the cause of thrombosis, is not yet fully known.<sup>13-15</sup>

## CONCLUSION AND SUGGESTION

No significant differences were present in factor VIII activity between A, B and O blood types. Further research is needed with a larger number of samples and including AB blood type.

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