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The Difference of PT, aPTT, Fibrinogen & D-Dimer Activities in HIV Patients with CD4 Count of ≤ 200/µL and ≥ 200/µL

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Abstract

Introduction: HIV is a developing disease that has been a global problem. The progress of HIV infection is characterized by decreased CD4 count. Hemostasis disorder is often found in patients with HIV, where the formed virus-antibody complex can activate the coagulation system, beginning from the activation of the Hageman factor (Factor XII) into the active form (Factor XIIa). This factor will activate the fibrinolysis process. Fibrin polymer is broken down into fragments X and Y. Fragment Y is further broken down into Fragment D and E, which is known as D-dimer.

Objective: To determine the difference of PT, aPTT, Fibrinogen, and D-Dimer in HIV patients with a CD4 lymphocyte count of < 200/µL and > 200/µL in H. Adam Malik General Hospital Medan.

Hypothesis: There is a difference of PT and aPTT activities in HIV patients with a CD4 count of < 200 cells/µL and ≥ 200 cells/µL and a difference of D-dimer and fibrinogen levels in HIV patients with a CD4 count of < 200/µL and > 200/µL in H. Adam Malik General Hospital Medan.

Methods: This study was conducted in the Clinical Pathology Laboratory, Department of Internal Medicine, H. Adam Malik General Hospital. Samples were collected with a consecutive sampling method which included patients diagnosed with HIV in H. Adam Malik General Hospital Medan from September 2019 to July 2020 who fulfilled the inclusion and exclusion criteria. Thirty-eight patients were divided into two groups, i.e., HIV patients with a CD4 count of < 200/µL and HIV patients with a CD4 lymphocyte count of > 200/ µL.

Results: Mann-Whitney test was used to assess the comparison of PT and aPTT values between HIV patients with a CD4 count of < 200 cells/µL and ≥ 200 cells/µL. The result was significant with a p-value = 0.002, which means that there is a significant difference in PT and aPTT values between HIV patients with a CD4 count of < 200 cells/µL and ≥ 200 cells/µL. An Independent T-test was used to assess the difference in fibrinogen level between HIV patients with a CD4 count of < 200/µL and > 200/µL, which resulted in p-value = 0.032. This means that there is a significant difference in fibrinogen levels between HIV patients with a CD4 count of < 200/µL and > 200/µL. Mann-Whitney test was used to determine the comparison in D-dimer level between HIV patients with a CD4 count of < 200/µL and > 200/µL, which showed a p-value = 0.002. This indicated a significant difference in D-dimer level between HIV patients with a CD4 count of < 200/µL and > 200/µL.

Conclusion: The lower the CD4 lymphocyte count, the higher the activities of PT, aPTT, fibrinogen, and D-dimer in HIV patients.

Keywords: HIV, PT, aPTT, D-Dimer, Fibrinogen, Hemostasis

Introduction

HIV (Human Immunodeficiency Virus) is a continuously developing disease that affects globally. In 2021, WHO found 2.3 million cases of HIV and 1.6 million people died of AIDS (Acquired Immunodeficiency Syndrome). Among them, 210,000 people were under 15 years old (WHO, 2017).

HIV/AIDS patients in Indonesia keep increasing each year. In 2013, there were 29,037 new HIV cases and 11,493 new AIDS cases. In 2014, the number of new cases increased to 32,711 new HIV cases and 7,875

new AIDS cases. In 2015, new cases finding declined to 30,935 new HIV cases and 6,081 new AIDS cases. The national prevalence of HIV/AIDS in 2015 was 32.95% (Kemenkes RI, 2014).

HIV/AIDS can affect all age groups. Most new AIDS cases in Indonesia were within the 20-29 age group, which was 31.8%. The incubation period from HIV infection to AIDS is 5-1 years. Most HIV patients are infected when they were between 15-19 years old or in their teenage years. Based on the data from Ditjen P2P, from 1987 to March 2016, there were 1,778 students with AIDS (Kemenkes RI, 2011).

The teenager is a large age group in the world. Based on the data from WHO, teenagers aged 10-19 years reached 1.2 billion in the world or 18% of the world's population. In Indonesia, the population of teenagers in 2010 reached 43.5 million, or 18% of the Indonesian population. Almost a fifth of the world and Indonesian population are teenagers (Sumantri R, 2009).

Hemostasis disorder often occurs in HIV patients. HIV-related thrombocytopenia (Tr-HIV) is the most common hemostasis disorder with high morbidity and affects patients from all risk groups independently based on age, gender, or stage of infection. Two mechanisms are responsible for Tr-HIV, namely bone marrow failure and immunological disorder, which is an immune complex circulation sored in platelet membrane and autoantibody production aims at the platelets (Kiefer E, 2014).

Other than that, there are several abnormalities during the coagulation cascade phase which can cause bleeding or thrombosis in HIV patients. The most common is prolonged aPTT test, production of lupus anticoagulant and anticardiolipin antibody, and some naturally occurring anticoagulant disorders. Thrombotic thrombocytopenic purpura, which is recently associated with HIV, has a clinical presentation and therapy alternative similar to the classic disease. Knowledge on hemostasis disorders in HIV seropositive patients allows for a more rational treatment in HIV patients (Kuller LH, 2008).

Several coagulation disorders have been reported in patients infected with HIV. A severe thrombocytopenia case was first observed in a contaminated homosexual male patient, and prolonged aPTT because of the lupus-like anticoagulant with a frequency of 8-70% of patients studied. Lupus anticoagulant has been proven to occur often during an acute opportunistic infection such as *Pneumocystis carinii*. Recently, there is an increase in the prevalence of protein S and heparin cofactor II deficiency, two physiological coagulation inhibitors that often declines in patients infected with HIV. The same occurs in fibrin polymerization defect related to hypoalbuminemia that induces prolongation of thrombin and coagulation time. Fibrinolytic system abnormality is also reported, such as an increase of the level of tissue plasminogen activator and type 1 plasminogen activator inhibitor. The acute-phase response can have a key role. The pathogenesis of this hemostasis disorder is not understood completely. Furthermore, D-dimer level is found to increase in patients infected with HIV. This gives the impression that HIV infection may be related to a prethrombotic condition that may lead to clinical thrombosis in several patients infected with HIV (Justice AC, 2012).

Several authors reported hemostasis disorder during HIV infection, including Choi *et al*. in Korea that reported a prevalence of 2.4% of HIV patients with thrombocytopenia, Mannuci and Gringeri in Italia who reported 5-15% of HIV patients with platelet decrease lower than those reported by Talom in a study in Mali in 2005. Toulon in 1998 reported hyperfibrinogenaemia during HIV infection, while Omoregie *et al*. in Nigeria reported low prothrombin time (PT) and prolonged activated partial thromboplastin time (aPTT) in HIV-infected patients, and further prove that low PT is related to a very low CD4 count. This disorder can cause hemostasis disorders such as bleeding or thrombosis during HIV infection (Boulware DR, 2011, Duprez DA, 2012).

The progress of HIV infection is characterized by decreased CD4+ T lymphocytes, most of the HIV target cells in humans. The speed of CD4 decrease has been known to be used as a guide for the development of AIDS. CD4 count declines gradually during the disease. The speed of decrease is 100 cells/year on average (Teitelman AM, 2016). WHO, 2005 stated that looking at the CD4 cell count in patients infected with HIV can determine the stadium of HIV. The stadium of HIV based on CD4 count can be divided into several categories, ie., a CD4 count of > 500/µL is considered normal, while < 200/µL is considered severe (WHO, 2005).

Larissa *et al*. found that hyperfibrinogenaemia is observed in 28.8% of HIV patients. This study also confirmed hyperfibrinogenaemia condition and an increase of C reactive protein (CRP) during HIV infection. This can be explained by the occurrence of inflammatory reactions induced by cytokine synthesized during HIV infection. Inflammatory markers such as fibrinogen are thought by many authors as a risk factor of cardiovascular disease, both in HIV-infected people and non-HIV-infected people (Ford ES, 2010).

The hemostasis system is maintained by the interaction between endothelial cells, coagulation protein, and platelet as the primary components to maintain blood fluidity in a normal condition. In an injury, all three components work together in a coagulation system. Endothelial cells provide a non-thrombogenic layer in blood vessels. The functions of endothelial cells in the hemostasis system include synthesizing tissue factor (TF), storing von Willebrand factor, and acting in the fibrinolysis system by producing plasminogen activator inhibitor (PAI-I), and containing thrombomodulin receptor (Leftkowitz JB, 2008).

PAI-I binds to thrombin and activates thrombin activatable fibrinolytic inhibitor (TAFI) that acts in the anticoagulant system by producing tissue factor pathway inhibitor (TFPI), tissue plasminogen activator (tPA), prostacyclin (PGI2) and activate protein C. The surface of endothelial cells contains heparin-like material, which is an antithrombin cofactor (Verhamme P, 2006).

Platelet is a very important cell in the coagulation process. Platelets interact with extracellular matrix components during injury to form a platelet plug to cover blood vessel lesions. Activated platelets can also produce various platelet agonists that mediate smooth muscle contraction resulting in vasoconstriction (Verhamme P, 2006).

The coagulation cascade model through the intrinsic and extrinsic pathways gives the impression that both pathways work separately. However, clinical manifestation denies this concept. Around fifteen years ago, a new hypothesis emerged to understand the hemostasis process. A cell-based model of coagulation stated that coagulation occurs in overlapping stages, which are initiation, amplification, and propagation (Smith SA, 2009).

The initiation stage begins in cells that can express tissue factor (TF) which forms a complex with factor VIIa and activates factor IXa and Xa. Factor Xa binds with factor Va on the cell surface and produces small amounts of thrombin. Factor Xa is immediately inhibited so that it cannot move to other cells. The amplification stage started after an injury, in which platelets come out from blood vessels and attach to thrombin produced during the initiation stage. Thrombin activates platelet so that there is a surface change, and a release of mostly active factor V. Thrombin also activates cofactor V and VIII and activates factor XI to factor Xia (Itoh S, 2013).

The propagation stage occurs on the activated platelet surface. In this stage, FIXa binds with VIIIa. The amount of FIXa increases from the result of platelets binding with FXIa. The FIXa/VIIIa complex activates FXa in the platelets and immediately binds with FVa to convert prothrombin into thrombin. Subsequently, the formation of thrombin converts fibrinogen into fibrin (Verhamme P, 2006).

After the fibrin clot is formed, there should be a mechanism to limit the amount of fibrin clot and clot release when the injury heals. There are three mechanisms to control the formation of fibrin clots, i.e., TFPI, antithrombin-heparin mechanism, and protein C anticoagulant pathway. Meanwhile, those responsible for the release and degradation of a fibrin clot are the fibrinolysis system. Plasmin plays an important role in fibrinolysis and is catalyzed by tPA or urokinase-type plasminogen activator (uPA). The inhibitors in the fibrinolysis system are PAI-1 and antiplasmin (Verhamme P, 2006).

The formed antibody-virus complex can activate the coagulation system, starting from the activation of the Hageman factor (factor XII) into the active form (factor XIIa). Subsequently, this factor XIIa will activate other coagulation factors sequentially following a cascade to finally form fibrin. Aside from activating the coagulation system, factor XIIa will also activate the fibrinolysis system by converting plasminogen into plasmin through the enzymatic process. Plasmin has proteolytic properties with a special target, which is fibrin. Fibrin polymers are broken down into fragments X and Y. Fragment Y is further broken down into fragment D and fragment E, which is known as D-dimer. These fibrin degradation products (FDP) have anticoagulant properties. Thus, a high amount can inhibit hemostasis. Prolonged activation of the coagulation and fibrinolysis system resulted in a decrease of various coagulation factors, such as factor II, V, VII, VIII, IX, and X and plasminogen. This aggravates bleeding in HIV patients.

The kinin and complement systems are also activated by factor XIIa. This factor activates pre-kallikrein to kallikrein, which is also a proteolytic enzyme. Kallikrein will convert kinin to bradykinin, a substance that acts in specific processes, including the inflammatory process that causes dilation and increased permeability of the blood vessels. The complement system is one of the basic mediators in the inflammatory process and holds an important role in the body's immune system against infection. Complements are a group of inactive proteins that can be activated by factor XIIa. The result of this activation is cell lysis. On the other hand, there is also the formation of toxins that increases the permeability of blood vessels.

Screening for coagulation factors routinely performed in the laboratory includes prothrombin time (PT), activated partial thromboplastin (aPTT), and thrombin (TT). CD4 is expressed on the surface of the mature lymphocyte subset. Most CD4 is expressed on the surface of Th cells (a very small amount might be found on the surface of T-cytotoxic cells) that interacts with MHC class II (Kresno, 2013). There are two types of interaction between CD4 and MHC class II, which is a direct interaction that is important for ontogeny and CD4 function in the peripheral blood. The second interaction includes CD4 working as a receptor for the entry of antigen into lymphocytes, especially HIV through gp120 contained in the surface of HIV (Kresno, 2013). CD4 lymphocyte count is an important substitute marker for the development of HIV. CD4 lymphocyte count is acknowledged as one of the most important predictors of HIV (Deuffic-Burban *et al*., 2007). The liver is affected by HIV infection. The liver is the primary organ responsible to synthesize coagulation factors. Liver infection by HIV can cause coagulation factor disorders. CD4+ count is used to measure immune status and HIV progression (R *et al*., 2009).

Methods

This is an analytical study with a cross-sectional design conducted in the Clinical Pathology Department of USU Faculty of Medicine/H. Adam Malik General Hospital Medan in cooperation with the Department of Internal Medicine, Tropical Disease and Infection Division of USU Faculty of Medicine/ H. Adam Malik General Hospital Medan from September 2019-November 2019. The population of this study was HIV patients who visited the Polyclinic and Inpatient Installation of the Department of Internal Medicine of H. Adam Malik General Hospital Medan from September 2019-November 2019. The samples were HIV/AIDS patients treated in the HIV treatment room and outpatient special care unit whose CD4 count was checked. Samples were collected consecutively on all populations that fulfilled the criteria. The inclusion criteria include a minimum age of 18 years old, newly diagnosed with HIV using strategy III method, new patients whose CD4 count was checked, with a CD4 count of < 200 cells/μL and ≥ 200 cells/μL and willing to participate in the study. Meanwhile, the exclusion criteria include recently consumed aspirin or drugs that affect hemostasis.

The sample size was predetermined at 38 people, which were divided into 2 groups. The obtained data were analyzed using the SPSS (Statistical Package for Social Sciences, Chicago, IL, USA) software for Windows. The characteristics of the subjects were presented in tabulation and described. Independent T-test is used if the data were normally distributed, otherwise Mann-Whitney test is used. All statistical tests with a p-value < 0.05 were considered significant.

Results

This study involved 29 male patients (76.3%), and 9 female patients (23.7%). The study also found that the mean age of all patients was 33.79 years old with a standard deviation of 10.08. The age range in this study was 18-55 years old with a median of 32 years. The most age group in this study was between 25-30 years old and 31-35 years old, which is presented in Table 1.

Table 1. Characteristics of Patients

Variable	N	%	Mean ± SD	Median (Min-Max)
Age (year)	38		33.79(10.08)	32(18-55)
Age Interval				
16-20 years	3	7.9		
21-25 years	5	13.2		
25-30 years	8	21.1		
31-35 years	8	21.1		
36-40 years	6	15.8		
41-45 years	1	2.6		
46-50 years	3	7.9		
51-55 years	4	10.5		
Gender				

Men	29	76.3		
Women	9	23.7		

Mann-Whitney was used to determine the comparison in PT value between HIV patients with a CD4 count of < 200 cells/μL and ≥ 200 cells/μL and the result was p-value = 0.002. This shows that there is a significant difference in PT value between HIV patients with a CD4 lymphocyte count of < 200 cells/μL and ≥ 200 cells/μL, which is presented in Table 2.

Table 2. PT values between HIV patients with a CD4 lymphocyte count of < 200 cells/μL and HIV patients with a CD4 lymphocyte count of ≥ 200 cells/μL.

Variable	HIV Patient		P-Value
	CD4 <200 (n=19)	CD4 ≥200 (n=19)	
	Median (Min-Max)	Median (Min-Max)	
PT value (seconds)	17.20 (11.60-36.50)	13.40 (10.60-29.50)	0.026*

*Mann-Whitney test

The Mann-Whitney test used to determine the comparison in aPTT value between HIV patients with a CD4 count of < 200 cells/μL and HIV patients with a CD4 count of ≥ 200 cells/μL resulted in a p-value of 0.002. This shows that there is a significant difference in aPTT values between HIV patients with a CD4 lymphocyte count of < 200 cells/μL and ≥ 200 cells/μL which is shown in Table 3.

Table 3. Comparison in aPTT values between HIV patients with a CD4 lymphocyte count of < 200 cells/μL and HIV patients with a CD4 lymphocyte count of ≥ 200 cells/μL.

Variable	HIV Patient		P-Value
	CD4 <200 (n=19)	CD4 ≥200 (n=19)	
	Median (Min-Max)	Median (Min-Max)	
aPTT value (seconds)	48.50(32.50-118.50)	34.20(28.80-56.80)	0.002*

*Mann-Whitney test

This study took blood samples to assess hemostasis physiology and other parameters, including platelet count. The mean platelet count was 81.33 (32.97) x 10^3/μL and a median of 79.20 (18.00-161.00) x 10^3/μL. A CD4 lymphocyte count showed a mean level of 201.81 (170.01) /μL with a median of 6192.50 (5.0-576.00) /μL. Fibrinogen level examination showed a mean value of 345.42 (90.65) mg/dL with a median of 348.00 (142.00-558.00) mg/dL. D-dimer test showed a mean value of 756.78 (1520.60) mg/dL with a median of 201.00 (5.00-6556.00) mg/dL.

Independent T-test was used to determine the comparison in fibrinogen level between HIV patients with a CD4 lymphocyte count of < 200 cells/μL and > 200 cells/μL and resulted in a p-value = 0.032. This showed that there is a significant difference in fibrinogen level between HIV patients with a CD4 lymphocyte count of < 200 cells/μL and > 200 cells/μL, which is presented in Table 4

Table 4. Comparison of fibrinogen level between HIV patients with a CD4 lymphocyte count of < 200 cells/μL and HIV patients with a CD4 lymphocyte count of ≥ 200 cells/μL.

Variable	HIV Patient		P-Value
	CD4<200 (n=19)	CD4>200 (n=19)	
	Mean (SD)	Mean (SD)	
Fibrinogen level (mg/dL)	376.52(107.48)	314.31(310.00)	0.032*

*Independent T-test

The Mann-Whitney test to compare D-dimer level between HIV patients with a CD4 lymphocyte count of < 200 cells/μL and > 200 cells/μL resulted in a p-value = 0.002. This showed that there is a significant

difference in D-dimer level between HIV patients with a CD4 count of < 200 cells/µL and > 200 cells/µL, which is presented in Table 5.

Table 5. Comparison of D-dimer level between HIV patients with a CD4 lymphocyte count of < 200 cells/µL and HIV patients with a CD4 lymphocyte count of ≥ 200 cells/µL.

Variable	HIV Patient		P-Value
	CD4<200 (n=19)	CD4>200 (n=19)	
	Median (Min-Max)	Median (Min-Max)	
D-Dimer level (mg/dL)	410.00(5.00-6556)	165.00(12.00-824.00)	0.010*

*Mann-Whitney test

Discussion

This study is a cross-sectional study to determine the hemostasis levels between HIV patients with a CD4 count of < 200 cells/µL and >200 cells/µL in H. Adam Malik General Hospital Medan. This study was conducted in the Department of Clinical Pathology and the Department of Internal Medicine of H. Adam Malik General Hospital with a consecutive sampling method on HIV patients from September 2019 to July 2020.

Out of 38 HIV patient samples, 76.3% were men and 23.7% were women. This was in line with the data from *Direktorat Jenderal Pencegahan dan Penanggulangan Penyakit* (Ditjen P2P) in 2017 sourced from HIV-AIDS and STD (Sexually Transmitted Disease) Information System (SIHA) which reported that between October-December 2017 (4^{th} quarter), 62% of HIV cases that were reported involved men (Kementerian Kesehatan RI, 2018). However, this was in contrast with the data from WHO in 2019 that from all HIV patients in the world, women were more (19.2 million souls) compared to men (17 million souls) (WHO, 2019). This study found that the mean age of HIV patients was 33.79 years old with a median of 32 years old. This was in line with the data from Kemenkes RI, where the most age of HIV patients was within the range of 25-49 years old compared to other age groups (Kementerian Kesehatan RI, 2018).

CD4 count is used to measure immunity status and the disease progression and a cut-off of < 200/µL made the patients are vulnerable to opportunistic infection and other conditions, including AIDS (Oguntibeju, Van Den Heever, and Van Schalkwyk, 2006). AIDS patients were reported to have declined platelet production, while early HIV-infected patients are more prone to experience an increase of platelet peripheral damage by antiplatelet antibodies (Najean and Rain, 1994). Both mechanisms are responsible for the low platelet count in HIV patients with a CD4 count of < 200 cells/µL and > 200 cells/µL.

HIV infection is associated with endothelial damage which can cause the activation of the coagulation system and the consumption of blood coagulation factors. Along with the development of HIV, characterized by reduced CD4 count, endothelial activation and a possibility of liver damage can increase because of consumption of blood coagulation factor and/or abnormal production of the coagulation factors that depends on the liver. Other than that, lupus anticoagulant (LA), anticardiolipin antibody (aCL), and liver damage can be seen in patients infected by HIV. All these factors (endothelial damage, LA, aCL, and liver damage) can affect PT and aPTT and can explain high PT and aPTT levels observed in the HIV patients in this study (Najean and Rain, 1994; Karpatkin, Nardi, and Green, 2002; Leticia *et al*., 2014).

This study found a significant difference in fibrinogen level between HIV patients with a CD4 lymphocyte count of < 200 cells/µL and > 200 cells/µL ($p = 0.032$). This result was in line with a study on HIV patients in Iran by Abdollahi *et al*., 2013, which found a decrease in fibrinogen level in HIV patients with a CD4 count of < 200 cells/µL. However, Leticia *et al*., 2014, who conducted a study on HIV patients in Nigeria, did not find a significant difference in fibrinogen level between HIV patients with a CD4 lymphocyte count of < 200 cells/µL and > 200 cells/µL. This might be caused by different methods and the antiretroviral drugs used.

HIV infection causes coagulation activation which can increase the risk of atherosclerosis and vein thromboembolic disease. Thrombin is the key enzyme in blood coagulation and is known for its various functions, such as the formation of fibrin, platelet aggregation, tissue repair, and other aspects of the disease pathogenesis. A subprocess that leads to the formation of thrombin can be operationally described as the initiation, propagation, and termination stages. The exposure/expression of tissue factor (for example, in

vascular endothelium or damaged monocytes) combines with factor (F) VIIa to begin a series of procoagulant activation (for example, FX, FIX, and FV) that produces thrombin which facilitates fibrinogen break down. This will cause a decrease in fibrinogen level, especially in patients with a CD4 lymphocyte count of < 200 cells/µL, which is more prone to infection (Baker *et al*., 2013).

This study found a significant result in D-dimer level between HIV patients with a CD4 lymphocyte count of < 200 cells/µL and > 200 cells/µL ($p = 0.032$). The mean level of D-dimer in all cases in this study was also higher than normal (756.78 mg/dL). This was in line with the results found in a study on HIV patients in the United States by Borges *et al*., 2014 who found a negative correlation between CD4 lymphocyte level and D-dimer level in HIV patients. Chronic inflammation and an activated coagulation system are general characteristics of HIV infection. A complex interaction of various factors that cause inflammation, endothelial dysfunction, and active coagulation in patients with HIV. Increased D-dimer level does not necessarily determine by HIV infection, only reflect the presence of unmeasured comorbidities or cofounders truly associated with an activated coagulant (Fichtenbaum, 2011; Borges *et al*., 2014).

CD4 count is used to measure immunity status and the disease progression and a cut-off of < 200/µL made the patients are vulnerable to opportunistic infection and other conditions, including AIDS (Oguntibeju, Van Den Heever, and Van Schalkwyk, 2006). AIDS patients were reported to have declined platelet production, while early HIV-infected patients are more prone to experience an increase of platelet peripheral damage by antiplatelet antibodies (Najean and Rain, 1994). Both mechanisms are responsible for the low platelet count in HIV patients with a CD4 count of < 200 cells/µL and > 200 cells/µL.

Laboratory test results found a significant difference in PT value between HIV patients with a CD4 lymphocyte count of < 200 cells/µL and ≥ 200 cells/µL ($p = 0.002$). the aPTT value between HIV patients with a CD4 count of < 200 cells/µL and ≥ 200 cells/µL also showed a significant difference ($p = 0.002$). This was in line with a study conducted in HIV patients in Nigeria, where the difference in PT and aPTT value between HIV patients with a CD4 lymphocyte count of < 200 cells/µL and ≥ 200 cells/µL was significant ($p < 0.005$) (Omoregie *et al*., 2009). A different result was found in a study by Thulasi Raman *et al*., 2016 who conducted a study on coagulation parameters in Indian HIV patients. The study did not find a significant difference in PT value between HIV patients with a CD4 lymphocyte count of < 200 cells/µL and ≥ 200 cells/µL ($p = 0.125$). However, there was a significant difference in aPTT value between HIV patients with a CD4 count of < 200 cells/µL and HIV patients with a CD4 lymphocyte count of ≥ 200 cells/µL ($p = 0.0006$).

Conclusion

Based on the analysis obtained in this study, we conclude that there is a significant difference in the activity of PT (prolonged PT in HIV patients with a CD4 count of < 200 cells/µL compared to HIV patients with a CD4 count of ≥ 200 cells/µL) in H. Adam Malik General Hospital Medan. There is also a significant difference in aPTT activity (prolonged aPTT in HIV patients with a CD4 count of < 200 cells/µL compared to HIV patients with a CD4 count of ≥ 200 cells/µL) in H. Adam Malik General Hospital Medan. There is a significant difference in fibrinogen (increased fibrinogen in HIV patients with a CD4 count of < 200 cells/µL compared to HIV patients with a CD4 count of ≥ 200 cells/µL) in H. Adam Malik General Hospital Medan. There is a significant difference in D-dimer (increased D-dimer in HIV patients with a CD4 count of < 200 cells/µL compared to HIV patients with a CD4 count of ≥ 200 cells/µL) in H. Adam Malik General Hospital Medan. There is also a decrease of CD4 count in HIV patients in H. Adam Malik General Hospital Medan.