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PROFILE OF CD4 COUNT AND TROPONIN I LEVEL IN HIV PATIENT OBTAINING TRIPLE FIXED DOSE COMBINATION (FDC) ANTI-RETROVIRAL THERAPY

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ABSTRACT **Background:** Human immunodeficiency virus (HIV) is the causal agent of Acquired Immunodeficiency Syndrome (AIDS). HIV can attack various organs such as heart, kidney and suppress the immune system. There is cardiovascular manifestation related to HIV as follow: dilated cardiomyopathy, myocarditis, coronary heart disease, and pericardial effusion. Troponin I has bigger sensitivity and specificity than CKMB, and it can detect the presence of new myocardial infarction for up to 2 weeks. **Meth:** This research was conducted in the inpatient and outpatient installation of RSUP dr. Wahidin Sudirohusodo and Laboratory of Clinical Pathology of dr.Wahidin Sudirohusodo Hospital Makasar in October 2018 to December 2018 until the sample was qualified. **Results:** The average of CD4 was found higher in troponin subject of I >= 0,01 (378,7) than troponin subject of I <0,01 (312,2), but it was not significant (p>0,05) statistically. Troponin of I <0,01 was obtained 35 people, whereas Troponin I > 0,01 was detected to have three people with p-value 0.566. Thus, it was not significant statistically. **Doscussion:** This research was obtained statistically and non-statistically because the researched subject of a patient with HIV was stable without complicating factor such as cardiac abnormalities in inpatient and outpatient at RS Wahidin Sudirohusodo. Respondents aged 38-39 years had inflammation in the group who were infected HIV for the risk of cardiovascular atherosclerosis on average at 69 years of age. In another word, troponin I was most detected in old age. Cardiovascular disease is the leading cause of morbidity and mortality in an individual with HIV infection.

KEYWORDS Human Immunodeficiency Virus, Acquired Immunodeficiency Syndrome, Troponin I, Cluster of Differentiation 4.

Introduction

Human immunodeficiency virus (HIV) is the causal agent of Acquired Immunodeficiency Syndrome (AIDS). This disease was first discovered in 1981 in the United States among homosexuals people. The virus of HIV-2 was discovered in 1986, with the majority of infection in West Africa. [1][2] In 2015, the United Nations estimated 36.7 million people worldwide were living with human immunodeficiency virus (HIV), and 2.1 million people were infected. [1] In Indonesia, in 2014 32.711 new HIV cases were reported, so until December 2014, 160.138 people were infected with HIV, although many infected people had died.[3]

HIV can attack various organs such as heart, kidney and sup-

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press immunity system. There is cardiovascular manifestation related to HIV as follow: dilated cardiomyopathy, myocarditis, coronary heart disease, and pericardial effusion. [4]Biomarker of damage to the myocardium is troponin. Troponin I has higher sensitivity and specificity than CKMB, and it can detect new myocardial infarction for up to 2 weeks, but troponin I am limited to patients with heart, kidney or muscle disorders. [5] The causes of increased Troponin I are numerous, including conditions of heart failure, tachycardia, myocarditis, sepsis, anaemia, pulmonary embolism, intracranial bleeding, stroke, drug toxicity, and kidney failure. [6] Kidney manifestations such as Acute Kidney Injury (AKI), HIV-associated nephropathy (HIVAN), Chronic Kidney Disease (CKD) and renal toxicity is associated with therapy. [7][8] HIV suppresses the immune system. One of the most important examinations in assessing immune status and therapeutic response in HIV-infected patients is an examination of CD4 levels. [3] Low immune status in HIV patients marked with CD4 related to independent factors of myocardial damage or the risk of myocardial infarction, which is characterised by an increase in cardiac biomarkers, troponin I. [9]

Troponin I and Troponin T are in cardiac and skeletal muscle, but it is different from gene coding. Tests that are based on high-affinity antibodies, specific to troponin T and Troponin I. Cardiac troponin (cTn) has been widely used as a sensitive and specific marker for detection of lesions in the myocardium.[10] Increased troponin can occur without the acute coronary syndrome. The underlying mechanisms include an imbalance in supply and oxygen demand, disorders of the autonomic nervous system, inflammation, trauma, cardiotoxic agents, or stretch of the heart wall. Without knowing the mechanism of troponin release into the blood from myocytes, an increase in troponin almost always has implications for a poor prognosis.[11]

The cardiovascular complication is often obtained in infected HIV patient. Based on various publications, the prevalence of myocardial abnormalities among AIDS patients is 25% -75%. Possible abnormalities in HIV positive patients are systolic dysfunction, pericardial effusion, infective endocarditis, myocarditis, ischemic heart disease, pulmonary hypertension, and malignancies involving the heart such as Kaposi sarcoma or lymphoma. [12] [13] [14] [15]

Anti-RetroViral(ART) mechanism toward heart blood vessel effects include: the enhancement of oxidative stress, the increase of endothelial permeability, increased molecular cell adhesion, increased lipid accumulation in blood vessel walls, impaired response to vascular damage, endothelial dysfunction, and persistent inflammation and immune activation. [16] The causes of inflammation associated with HIV patients include: increased monocyte activation, increased T cell activation, increased endothelial adhesion, and hypercoagulation, which causes cardiovascular, bone, renal, liver, neurological, and malignant comorbidities. [17]

HIV can be the cause of myocarditis. It is expected that HIV in the myocardial system causes cell damage through immunological response provocation. [18]. Mesa et al. reported that a one-year survival rate of 51% of patients is positive HIV with PAH. [14] [19]

The medicine which can cause cardiotoxic is Amphotericin B, which can cause side effects such as stiffness, fever, myalgia, headache, renal dysfunction, and heart disorders such as bradycardia and other cardiac arrhythmias.[20]. The effect of antiviral therapy on the incidence and prevalence of cardiovascular-related HIV haven't been clear yet. Investigating the Data Collection on the Adverse Event of Anti-HIV Drugs Study, a prospective observational study of 23,468 HIV positive patients, found that the incidence of myocardial infarction increase by an average of 26% per year from therapy with combination antiretroviral agents. Further analysis of data from the same population indicates that there are a higher incidence and risk of cardiac and cerebrovascular events. [14]Several studies have shown that an increased incidence of cardiovascular disease in HIV patients is associated with traditional risk factors for cardiovascular disease, antiviral treatment, low HDL levels, and the inflammatory status caused by HIV. [21]

Table 1 Characteristic of Subject Based on Variable Category

Variable		n	%
Gender	Male	29	76,3
	Female	9	23,7
age	<40 years	22	57,9
	≥ 40 years	16	42,1
CD4 Category	<200	9	23,7
	200-349	12	31,6
	350-499	11	28,9
	≥ 500	6	15,8
Troponin I	<0,01	35	92,1
	≥ 0,01	3	7,9

Materials and methods

This research used analytical descriptive with the cross-sectional method. The study was conducted in the inpatient and outpatient installation at RSUP dr. Wahidin Sudirohusodo and Laboratory of Clinical Pathology of Dr Wahidin Sudirohusodo Makassar from October 2018 to December 2018. It had been approved by the ethics committee of the Faculty of Medicine with reference number: 1092 / H4.8.4.5.31 / PP 36-KOMETIK/2018.

A. Population

Subject who was diagnosed with HIV/AIDS were aged over 18 years and under 45 years. Patients who were getting a Triple Fixed Dose Combination (FDC), willing to take part in the research and signed a letter of approval, while the exclusion criteria were: Age> 45 years.

B. Method and Collecting the Data

The subjects were all inpatient and outpatient diagnosed HIV and obtaining Triple Adult Fix Dose Combination (FDC)Anti-RetroViral therapy. Subjects were checked CD4 and Troponin I at the same time. Descriptive analysis was carried out to assess CD4 court profile and Troponin I toward patients with HIV.

C. Statistic Analysis

It used SPSS program version 22. It is conducted descriptive statistical calculations, frequency distribution, Fisher Exact statistical test, Independent-t and Chi-Square test. The test results were significant if the value was p <0.05.

Table 2 Distribution of Troponin I Based on CD4 Category

CD4 Category		Troponin I		Total	p
		<0,01	≥ 0,01		
<350	n	12	2	21	
	%	90,5%	9,5%	100,0%	
≥ 350	n	16	1	17	
	%	94,1%	5,9%	100,0%	1,000
Total	n	35	3	38	
	%	92,1%	7,9%	100,0%	

Table 3 Analysis of CD4 Level and Troponin I Level

The Average of CD4 Based on Troponin I				
Troponin I	n	Mean	SD	p
<0,01	35	312,2	186,5	0,566
≥ 0,01	3	378,7	252,4	

Result

Most observed subjects were male (76,3%), aged <40 years (57,9%), whereas aged <40 of 16 people or 42.1%. The results of laboratory tests showed that the majority of subjects had CD4 200-349 (31.6%) and at least> = 500 (15.8%), while troponin I was only detected in 3 subjects (7.9%). (Table.1). Based on the number of subjects with Troponin I detected, t subjects had CD4 <350 and one subjects had CD4> = 350. It was not statistically significant (p> 0.05). (Table.2). Analysis of CD4 levels and oponin I levels, the average of CD4 was fou to be higher in subjects with troponin I> = 0.01 (378 than in subjects with troponin I <0.01 (312.2), but it was not statistically significant (p> 0.05). (Table.3)

Discussion

The previous study had been proved that there was an increased incidence cardiovascular disease in HIV patients related to traditional risk factors for cardiovascular disease, antiviral treatment, low HDL levels, and the ammatory status caused by HIV. Traditional cardiovascular risk factors in this population of patients did not have a predictive cardiovascular risk. [21]

The recent research was conducted to 38 subjects of a patient with HIV who obtained Anti-Retroviral Triple Adult (FDC) Therapy. All subject required inclusion criteria who were hospitalized and outpatient at Wahidin Sudirohusodo Hospital in October-December 2018. From the results of th study, it found more male than women with subjects aged 18-45 years, with an average of 38.2 ± 5.7 years, with an average of 38.5 years. In this research, there were more male genders, 29 people (76.3%), compared to 9 women (23.7%), while according to the age of <40 years, there were 22 people, 40 years of 16 people, or 42.1%. CD4 category <200 found 9 people (23.7%), CD4 200-349 of 12 people (31.6%), CD4 350-499 of 11 people (28.9%), while> 500 of 6 people (15 , 8%). The value of Troponin I <0.01 found 35 people (92.1%) while troponin I 0.01 was only detected three people (7.9%). (see Table.1). Based on Dau et al., males who were infected HIV had more risk actors of traditional Coronary Arter Disease (CAD) than control who were not infected with HIV. Left ventricular dysfunction, dilated card myopathy and myocarditis, the frequency is more pronounced in AIDS patients. In a pre-ART study, global hypokinetic LV was found in 14.5% of patients and was associated with a low CD4 count, while Coronary Heart Disease (CHF) was acquired in 2% of patients. [22]

The research revealed that patient with HIV had a higher risk of Car vascular Disease (CVD). Other researches also mentioned that 17% of men and 12% of women .with HIV had a ten-year risk of developing coronary he t disease (CHD) with a prediction of more than 25%. Twenty subjects had modifiable CHD risk factors such as smoking (up to 40%), more than 40% of male and 60% of female met the overweight criteria with 25 or more Basal Metabolic Rate (BMR). HAART therapy could be responsible for increased cardiovascular risk. [23] Side effects of antiretroviral therapy were considered to play a role in creasing cardiovascular risk. PIs had been associated with hepatotoxicity. NNRTIs were known to cause skin rashes, and NRTIs had been related to hepatotoxicity, lactic acidosis, lipodystrophy, and skin rashes. [24]

According to Zhang et al. in 2008, he stated that participant in this analysis, if they were aged 40 years or more while conducting the vey, they were reported at least had one of these conditions: coronary heart disease, angina, or heart attack. Furthermore, the age of 40 years or more was enchmark for cardiovascular risk. [25] According to Korff S et al. In symptomatic patients with suspected Acute Coronary Syndrome (ACS), accompanied by an increase in troponin I, often cause lesions that were significantly undetectable by coronary angiography, the cause of thrombus that contained many platelets causes ruptured plaque to dissolve spontaneously or after thrombolytic administration or which have been released, causing atherosclerotic lesions that were not significant at the time of angiography. However, an increase in troponin implied a higher risk of causing death or acute myocardial infarction so that in other words, it can be said heart risk factors associated with Troponin I. [26]

The distribution of Troponin I based on CD4 category, there was CD4 <350 of 21 people and CD4 >350 of 17 people. It was obtained more CD4<350 in this research than CD4>350. In this research, it was taking a CD4 value of less than 350 because the condition was considered AIDS. [27] (see Table. 2).In the analysis of CD4 ass iation with Troponin I, the average of CD4 was found higher i subjects with troponin I> = 0.01 with an average (378.7) than in subjects with troponin I <0.01 (312.2), but it was statistically not significant (p> 0.05). In which Troponin I <0.01 was obtained of 35 people, while Troponin I> 0.01 detected only of 3 people, with a value of p 0.566. Thus, it was not statistically significant. (See Table. 3). The factors that influenced this were because the subjects observed were from stable HIV patients without complicating factors such as the presence of cardiac abnormalities in both inpatients and outpatients at RS Wahidin Hospital Sudirohusodo. The respondents who were studied on average were 38 -39 years, in contrast to research conducted by Subramanian et al. The occurrence of inflammation in groups infected with HIV for the risk of average cardiovascular atherosclerosis at age 69 years. [28] In other words, troponin I was detected more frequently in old age.

In this research, observed subjects were stable patients with HIV without previous cardiovascular complications, so that the increase in troponin I did not affect myocardial damage. Based

research by Mansoor et al., HIV infection was associated with left ventricular hypertrophy and LVMI (Left Ventricular Mass Index), the underlying mechanism had not been yet clear, it was considered to involve several factors [29]. Research conducted by Cipta H et al. stated that groups with cardiac abnormalities had lower CD4 counts compared to groups without cardiac abnormalities. Besides, there was a relationship between the two, in which the more significant the CD4 count, the less likely it was to find a cardiac abnormality, with a value of p = 0.034. [30]

Conclusion

The proportion of CD4 count of observed Patient with HIV is the majority in an advanced stage. There is no increase in the population of troponin I proportion.

Conflict of Interest

The author declares that there is no conflict of interest in this research.

Funding

All fund of this research is met personal funds of the author. All patient has signed informed consent sheet before taking the data sample, and the result of patients' laboratory is confidential.

Ethics Committee

The ethical committee has approved on Faculty of Medicine with reference number: 1092/H4.8.4.5.31/PP 36-KOMETIK/2018.

List of Abbreviations:

HIV: Human immunodeficiency virus
AIDS: Acquired Immunodeficiency Syndrome
CD4: Cluster of Differentiation 4

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