

CHAPTER I

INTRODUCTION

1.1 Background of Study

Since its discovery in 1981, Human Immunodeficiency Virus (HIV) infection has become a major global problem. According to Joint United Nation Program for HIV/AIDS (UNAID), in 2012, HIV/AIDS was estimated infecting 35.3 million people worldwide.^{1,2}

The incidence of HIV infection in Indonesia was 127,427 people and the incidence of AIDS was 52,348 people in the period of October-December 2013, which were increased from 118,787 HIV-infected patients and 45,650 patients with AIDS in the period of July-September 2013. In Central Java, the incidence of HIV infection was also increased from 5,406 patients in the third trimester of 2013 to 5,661 patients in the fourth trimester of 2013.³

The development of anti retroviral therapy (ART) has reduced mortality among HIV/AIDS patients. Coincident with these advances, was described a lipodystrophy syndrome occurring in patients taking ART. The syndrome is characterized by body fat redistribution and metabolic abnormalities. The metabolic disturbances reported are elevated triglyceride, cholesterol and fasting blood glucose level. A study taken in Uganda showed that prolonged exposure to ART in children contributes to metabolic changes thus increasing the cardiovascular risk of adulthood. It is proven that there is a direct connection between plasma cholesterol level and the arteriosclerotic process, especially the

correlation between aortic fatty streaks in young persons with elevated serum cholesterol level.⁴⁻⁶

Stavudine, a Nucleoside Reverse Transcriptase Inhibitor (NRTI), has the highest propensity for causing mitochondrial dysfunction, yet it is relatively inexpensive and often has better availability in the developing world. According to 2013 WHO Antiretroviral Guidelines, stavudine administration should be discontinued due to its metabolic toxicities on mitochondria. A drug like stavudine has high capacity of inhibiting mtDNA γ -polymerase, which will cause mtDNA depletion and lipodystrophy as a further effect. A study in Western India showed that the prevalence of lipodystrophy was 46.1% and lipoatrophy was significantly associated with stavudine administration. A study in Tanzania resulted that 73% patients taking antiretroviral therapy suffered from dyslipidemia which was worse in patients who took stavudine.⁷⁻¹¹

In Dr. Kariadi Hospital Semarang, there is little data known about the association between stavudine administration to lipodystrophy and dyslipidemia in Dr. Kariadi Hospital Semarang. The aim of this study is to determine the association between stavudine administration with lipodystrophy and dyslipidemia among HIV infected patients in Dr. Kariadi Hospital Semarang and also their associated routine demographic informations.

1.2 Research Question

What is the association between stavudine administration with lipodystrophy and dyslipidemia among HIV-infected patients in Dr. Kariadi Hospital Semarang?

1.3 Research Purposes

1. To determine the association between stavudine administration with lipodystrophy among HIV-infected patients in Dr. Kariadi Hospital Semarang.
2. To determine the association between stavudine administration with dyslipidemia among HIV-infected patients in Dr. Kariadi Hospital Semarang.
3. To determine the association between lipodystrophy with routine demographic informations (age, gender, CD4 count, and duration of treatment) among HIV-infected patients with stavudine administration in Dr. Kariadi Hospital Semarang.
4. To determine the association between dyslipidemia and routine demographic informations (age, gender, CD4 count, and duration of treatment) among HIV-infected patients with stavudine administration in Dr. Kariadi Hospital Semarang.

1.4 Research Benefits

1. Determining the association between stavudine administration with lipodystrophy and dyslipidemia among HIV-infected patients in Dr. Kariadi Hospital Semarang.
2. Collecting data of the prevalence of lipodystrophy and dyslipidemia among HIV-infected patients with stavudine administration in Dr. Kariadi Hospital Semarang to support the substitution of stavudine therapy with other less toxic ART.
3. Collecting data of the prevalence of lipodystrophy and dyslipidemia among HIV-infected patients with stavudine administration in Dr. Kariadi Hospital Semarang to support the advanced studies of ART side effects.

1.5. Research Originality

Table 1. Research Originality

Researchers	Articles	Year	Methods	Subjects	Results
Pujari, Sanjay N., et al. ¹⁰	Lipodystrophy and Dyslipidemia Among Patients Taking First Line, World Health Organization-Recommended Highly Active Antiretroviral Therapy Regimens in Western India.	2005	Observational study, Cross-Sectional Method.	306 ART naive patients and patients who have been treated with ZDV/3TC/ NVP and d4T/3TC/ NVP for > 1 year.	The prevalence of lipodystrophy was 46.1 % and lipoatrophy was significantly higher in patients with d4T use.
V, Joly, et al. ⁴	Increased risk of lipoatrophy under Stavudine in HIV-1-infected patients: results of a substudy from a comparative trial.	2002	Experimental study, Randomized Control Trial	170 patients pretreated with ZDV, DDI, or ddC for >6 months but naive for 3TC, d4T, and PIs.	The incidence of lipoatrophy was increased in the d4T v.s the AZT arms as followed: facial atrophy 48% vs. 22% buttock atrophy 47% vs. 20%, lower limb atrophy 49% vs. 22%, venomegaly 57% vs. 24%.
Liu, Enju, et al. ¹¹	First-line Antiretroviral Therapy and Changes in Lipid Levels Over 3 Years Among HIV-Infected Adults in Tanzania.	2013	Observational Study, Prospective Cohort Method	6385 HIV-infected adults receiving first-line ART regimens included the combinati	The prevalence of dyslipidemia increased to 73% after a 3-year follow up. Patients who received AZT had a greater reduction in

				on of 2 NRTIs, either d4T or ZDV along with 3TC and 1 NNRTI.	TG levels and a lower increase at 3 years compared with d4T group.
Ceccato, M.G.B., et al. ¹²	Antiretroviral Therapy-Associated Dyslipidemia in Patients from a Reference Center in Brazil.	2011	Observational study, cross-sectional method.	620 patients who confirmed HIV infection and had received ART	Dyslipidemia was associated with older age, the use of d4T, and longer exposure of ART. There was no correlation between dyslipidemia and gender.

. The study will be an observational study using cross-sectional study design. The study will be focused on the association between stavudine administrations with lipodystrophy and dyslipidemia among HIV-infected patients in Dr. Kariadi Hospital. This study will also determine the association between patients' age, sex, current CD4 count, and duration of treatment with the incidence of lipodystrophy and dyslipidemia in patients with stavudine administration.