Survival of HIV/AIDS patients with antiretroviral therapy in association with first-line regimens from 2007 – 2010 in Haji AdamMalik general hospital Medan

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Abstract. The mortality related to AIDS have decreased dramatically among HIV infected patients taking HAART. HAART is the combination of at least 3 antiretroviral drugs based on the recommendation of WHO. The recent guideline for 1st line therapy recommended by the Indonesian Ministry of Health was Zidovudine/Lamivudine/Nevirapine (ZDV+3TC+NVP), Zidovudine/Lamivudine/Efavirenz (ZDV+3TC+EFV), Stavudine/Lamivudine/Nevirapine (d4T+3TC+NVP), Stavudine/Lamivudine/Efavirenz (d4T+3TC+EFV). Due to a side effect of Stavudine, Ministry of Health plan to pass out Stavudin from the regimens for 1st line therapy. We wanted to evaluate the survival of HIV/AIDS patients with first-line regimens in HAM general hospital Medan. A cohort retrospective study was conducted to evaluate the survival of HIV/AIDS patients taking a combination of 1st line antiretroviral therapy between January 2007 and December 2010. From 2007-2010, among 609 HIV/AIDS patients with first-line ARV medication, 77.5% were male, and 22.5% were female. The most common risk infection was heterosexual. The majority of the patients were in 25-34 years old group. Most of the patients with CD4 1-50 cell/mm3. 2 years survival rate in HIV/AIDS patients taking ZDV+3TC+NVP, ZDV+3TC+EFV, d4T+3TC+NVP, d4T+3TC+EFV were 61.5%, 61.2%, 57.5% and 59.3% respectively. There were no significant differences of 24 months survival in both regimen with or without d4T, 61.8% vs 63.6%.

1. Introduction
Acquired Immune Deficiency Syndrome (AIDS) is a set of symptoms or diseases caused by Human Immunodeficiency Virus (HIV) weakens the immune system. AIDS is the final step of HIV infection,[1] Recently, HIV and AIDS cases become more apparent as health issues in Indonesia and have changed from low epidemic to concentrated epidemic. Surveys done on certain sub-population show HIV prevalence in several provinces reaches over than 5% consistently. Indonesian Ministry of Health estimated there are 350k people with HIV and AIDS in 2011. WHO reported there are 34.2 million people with HIV in 2011, where 8 million of them already got ARV (Antiretroviral) medication, which is 20% higher than in 2010.[2]
Since the using of Highly Active Antiretroviral Therapy (HAART), the mortal rate of HIV/AIDS patients dramatically decreases. The composition of HAART is the combination of at least three medicines as suggested by WHO, where one treatment is at least from Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI) type, and the other two are at least from Nucleoside Reverse Transcriptase Inhibitor(NRTI).[3] According to Indonesian Ministry of Health guidance, the first line
of HAART should consist of zidovudin+lamivudine+nevirapin, zidovudin+lamivudine+efavirenz, stavudine + lamivudine + nevirapine, stavudine + lamivudine + efavirenz. [4] We know that HIV/AIDS patients will consume ARV for the rest of their lives because it can suppress virus replication. But there is bad implication caused by ARV since it has a toxic effect both short and long-term which can affect patients’ survival. [5] Bendavid and friends studied the benefit, costs, and survival rate of patients who use stavudine + lamivudine + nevirapine regimen worse than zidovudine + lamivudine + nevirapine regimen. [6] Currently, Indonesian Ministry of Health plans to pass stavudine out from the first line of regimen since it has a bad side effect. Thus, we plan to study the survival of HIV/AIDS patients who use the first line of the regimen in H. Adam Malik Medan General Hospital.

2. Methods
This study is using cohort retrospective method to assess the survival of HIV/AIDS patients who get the first line of ARV from January 2007 to December 2010 in H. Adam Malik Medan General Hospital. Subjects’ characteristic with their demography were obtained through interviews. The correlation between regimen and survival is presented by using Kaplan Meier test. Collected data were pooled and then analyzed by using SPSS 12 with a significant level of p<0.05 (95% confidence interval).

3. Results
This study was by using cohort data of patients who got antiretroviral (ARV) drug between 2007 and 2010 in H. Adam Malik Medan General Hospital. A total of 609 patients were studied which consist of 472 (77.5%) male and 143 (22.3%) female with an average age of 32 years. Based on their age, these patients can be divided into five groups: Group a15-24 years old (12.8%), Group b25-34 years old (55.7%), Group c35-44 years old (25.1%), Group d45-54 years old (5.1%), and Group e> 55 years old (1.3%).

Among these patients, 302 people (60.9%) have 1-50 cell/mm³ CD4 level, 171 people (34.5%) have 51-200 cell/mm³ CD4 level, and 23 people (4.6%) have >200 cell/mm³ CD4 level. Most patients are in clinical stage 3 (68.1%) of WHO classification system. The most risk factor is heterosexual (88.8%) with the most used regimen is ZDV+3TC+NVP (52.9%). The complete characteristics can be in Table 1 below.

Table 1. Patient characteristics.

| Variables      | n  | %   |
|----------------|----|-----|
| Age            |    |     |
| 15-24 years old| 78 | 12.8|
| 25-34 years old| 339| 55.7|
| 35-44 years old| 153| 25.1|
| 45-54 years old| 31 | 5.1 |
| >55 years old  | 8  | 1.3 |
| Gender         |    |     |
| Female         | 137| 22.5|
| Male           | 472| 77.5|
| Risk Factor    |    |     |
| Hetero         | 541| 88.8|
| Homo           | 3  | 0.5 |
| IDU            | 64 | 10.7|
| Regimen        |    |     |
| D4T+3TC+EFV    | 113| 18.5|
| D4T+3TC+NVP    | 40 | 6.6 |
| ZDV+3TC+EFV    | 134| 22.0|
| ZDV+3TC+NVP    | 322| 52.9|
| CD4            |    |     |
Based on Graph 1 below, there is no significant difference in survival among four regimens used in RSUP H. Adam Malik Medan General Hospital within 24 months. The survival of ZDV+3TC+NVP, ZDV+3TC+EFV, d4T+3TC+NVP and d4T+3TC+EFV are 63.8%, 63.2%, 60.5% and 62.3% respectively (Figure 1).

Figure 1. Survival function based on first regimen medication.

There is also no significant difference between regimen with d4T and without d4T in 24 month period where their survival values are 61.8% and 63.6% respectively (Figure 2).

Figure 2. Survival function based on stavudin/non-stavudin regimen.
4. Discussion

The highest risk factor is heterosexual which means there are more male since the male has higher mobility than female and male has a higher probability of IDU. There is the same case in the Indonesian Ministry of Health that the number of HIV male patients (23702 patients) is greater than the female (12338 patients).

Most patients have very low CD4 level (79% CD4<200 cell/mm³). The first regimen used in this study contained zidovudine/stavudin+lamivudine+nevirapin/efavirenz and based on Kaplan Meyer analysis, there is no significant difference of survival value within 24 months. The survival of AZT+3TC+NEV, AZT+3TC+EFV, d4T+3TC+NEV and d4T+3TC+EFV are 63.8%, 63.2%, 60.5% and 62.3% respectively. There is a fact by Berenguer and colleagues that the medication result by using regimen ARV with ddi/3TC/EFV is almost the same with using regimen with ZDV/3TC/EFV. Medication that used regimen with ZDV is needed to be stopped due to hematology side effect.[7]

Bendavid and colleagues reported that the life expectancy of patients who use regimen ARV with ZDV/3TC/NVP, ZDV/3TC/EFV, and d4T/3TC/NVP was not significantly different. The important insight of this report is that regimen with d4T is more expensive since it minimizes the side effect.[6] In 2006 WHO recommended that d4T should be avoided due to its toxic effect and in 2009 d4T was removed from the first line of regimen and TDF was started to be used in the regimen.[8] TDF was used only in the second line of regimen and in Indonesia, ARV is very limited in availability. The study in Lesotho reports that 30% of patients needed to change from using d4T based regimen to non-d4T based regimen.[9] Innes and colleagues report that lowering down the d4T dose into 2x20 milligram will suppress virus at the same level of 2x30 milligram with lower toxic risk if combined with 3TC and EFV.[10] This study showed the same result that there is no significant difference in survival between patients who use d4T and non-d4T. Cohort data showed that more patients with ZDV experienced switch therapy than patients with d4T due to anemia side effect.

5. Conclusion

No significant survival improvement of HIV-AIDS patients who get first line regimen. No specific survival rate between patients who use d4T and non-d4T. Regimen with d4T can be used when there is no proper medicine available.

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