Survival Predictors of People Living with HIV/ AIDS in Wamena, Papua

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ABSTRACT

Background: Quality of life (QoL) is an important component in the evaluation of the well-being of people living with HIV and AIDS (PLWHA), especially with the appreciable rise in longevity of PLWHA. The analysis of the quality of life is essential for the healthcare policies and services directed toward PLWHA, since this indicator values the perception of people about their own life and health. However, little is known about the determinant of QoL in PLWHA in Papua. The aim of this study was to analyze survival predictors of people living with HIV/ AIDS in Wamena, Papua, Indonesia.

Subjects and Method: This was a retrospective cohort study conducted in Wamena Hospital, Papua, from December 2017 to February 2018. A cohort of 304 PLWHA was selected for this study from the medical record at Wamena Hospital. The dependent variable was survival. The independent variables were adherence to ART, nutritional status, age, and coinfection. The data were collected from medical record and questionnaire. The data were analyzed by Cox regression model.

Results: The risk of dying of PLWHA if adherent to take the ART was lower than not adherent to take the ART (HR= 0.45; 95% CI= 0.06 to 0.33; p= 0.002). The risk of dying of PLWHA with poor nutritional status was higher than good nutritional status (HR= 12.78; 95% CI= 6.81 to 23.98; p< 0.001). The risk of dying of PLWHA aged ≥35 years was slightly higher than <35 years (HR= 1.47; 95% CI= 1.00 to 2.17; p= 0.050). The risk of dying of PLWHA with coinfected was higher than without coinfected (HR= 1.59; 95% CI= 1.15 to 2.23; p= 0.006).

Conclusion: The risk of dying of PLWHA decreases if adherent to take the ART, but increases with poor nutritional status, age ≥35 years, and coinfection.

Keywords: survival, adherence to treatment, people living with HIV/ AIDS.

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ion of the virus in the early stages. Even if they can survive, people living with HIV/AIDS (PLWHA) may not live well or feel satisfied. Quality of life becomes important to identify the condition of PLWHA in living its life. (Hasanah et al., 2011; Arjun et al., 2015).

HIV/AIDS prevention program in Indonesia leading to the paradigm of zero new infection, zero AIDS-related death, and zero discrimination. These Paradigm were trying to be realized in four pillars, namely (1) Prevention of HIV transmission. (2) Care, support, and treatment (PDP). (3) Mitigation of impacts of psychosocial-economic support. (4) Creation of a conducive environment.

The second pillar of Care, Support, and Treatment (CST) efforts include strengthening and developing health services, preventing and treating opportunistic infections, antiretroviral treatment, support education, and training for PLW.

The program aims to reduce morbidity and hospitalization rates, AIDS-related mortality rates, and improve the quality of life of HIV-infected persons at various stages. (Kementerian Kesehatan Republik Indonesia - Direktorat Jenderal Pengendalian Penyakit dan Penyehatan Lingkungan, 2011).

The aim of this study was to analyze survival predictors of people living with HIV/AIDS in Wamena, Papua, Indonesia.

**SUBJECTS AND METHOD**
This was a retrospective cohort study conducted in Wamena Hospital, Papua, from December 2017 to February 2018.

A cohort of 304 PLWHA was selected for this study from the medical record at Wamena Hospital. The dependent variable was survival. The independent variables were adherence to ART, nutritional status, age, and coinfection.

Survival was defined as the length of time required by the patient since the diagnosis of PLWHA to death.

Survival assessment for surviving patients is the length of the patient suffering from AIDS until the study is completed with a permanent status of life.

Co-infection is a coexisting disease experienced after a patient has AIDS, in other words, is a disease that arises as a result of AIDS include tuberculosis, sexually transmitted diseases, non-sexual infectious diseases, diarrhea, and other chronic diseases.

The data were collected from medical record and questionnaire. The data were analyzed by Cox regression model.

**RESULTS**
The risk of dying of PLWHA if adherent to take the ART was lower than not adherent to take the ART (HR=0.45; 95% CI= 0.06 to 0.33; p= 0.002).

The risk of dying of PLWHA with poor nutritional status was higher than good nutritional status (HR= 12.78; 95% CI= 6.81 to 23.98; p< 0.001).

The risk of dying of PLWHA aged ≥35 years was slightly higher than <35 years (HR= 1.47; 95% CI= 1.00 to 2.17; p= 0.050). The risk of dying of PLWHA with coinfected was higher than without coinfected (HR= 1.59; 95% CI= 1.15 to 2.23; p= 0.006).

Table 1. The results cox regression analysis of survival predictor of PLWHA

| Independent Variables         | HR  | 95% CI | p     |
|------------------------------|-----|--------|-------|
| Adherent to take the ART     | 0.45| 0.06   | 0.33  | 0.002 |
| Poor nutritional status      | 12.78| 6.81  | 23.98 | <0.001|
| Aged ≥35 years               | 1.47| 1.00   | 2.17  | 0.050 |
| Coinfected                   | 1.59| 1.15   | 2.23  | 0.006 |

N observation = 184
Log likelihood = -84.53
p<0.001
DISCUSSIONS
1. Adherent to ART
The development of antiretroviral drugs has significantly altered the perception of HIV / AIDS from a very potentially fatal illness to be chronic and potentially treatable, and the availability the administration of antiretroviral therapy (ART) has significantly reduced HIV and AIDS-related mortality and morbidity. (Oguntibeju, 2012)

This situation makes the World Health Organization (WHO) strive to achieve the 90% coverage target of care for all HIV patients as well as 90% virological success in treated patients and requires a minimum achievement of adherence approximately 95% (UNAIDS, 2015; Paterson et al., 2000).

According to (Iacob and Jugulete, 2017) here are 4 main factors that can affect ART adherence: (1) Selective antiretroviral drugs, which can cause various side effects. (2) Doctors' devotions include lack of time dedicated to counseling and building trust relationships. (3) Patients have not been able to receive the benefits and disadvantages of ART. (4) social and family backgrounds can not persuade patients to continue ART.

Effective antiretroviral therapy can decrease morbidity and mortality for people with a CD4 cell count of 200-350 cells / mm3. Various data indicate that decreased risk of mortality and complication related
AIDS or non-AIDS in PLWHA who started ART when CD4 cell counts, 350 cells / μL. (Schey, et al 2016).

In 2010, HIV-1 treatment guidelines in the United States and the EU recommended three fully active antiretroviral drugs when CD4 + cell in peripheral blood decreased to 350 cells / mm3, a stage where viral rates could often reach 10,000-100,000 copies per mL. (Arts and Hazuda, 2012; Lodi et al., 2011)

The Kaplan-Meier survival estimated of patients who adherent to antiretroviral therapy is much higher than non-adherent patients.

ART provides an effective treatment for patients with 6 classes of pharmacological drugs including: (1) Nucleoside reverse transcriptase inhibitors (NRTIs). (2) Non-nucleoside reverse transcriptase inhibitors (NNRTIs). (3) Protease inhibitors (PIs). (4) Integrase inhibitor (INSTIs). (5) Fusion Inhibitor (FI). (6) Chemokine receptor antagonist (CCR5 antagonist). (7) Inhibitor entry (post-mounted inhibitor directed to CD4). (Rathbun, 2017).

Each class targets different steps in the viral life cycle and its use in clinical practice was largely determined by ease or complexity of use, side effects, clinical efficacy, practice guidance, and physician preferences. Non-compliance causes a failure of therapy and the occurrence of resistance mechanisms.

NRTIs were managed as prodrugs requiring host cell entry and phosphorylation by cellular kinase before providing antiviral effects. NRTIs prevent the formation of 30-50-phosphodiester bonds resulting in termination of growth and termination of viral DNA chains. (Boyer et al., 2001; Rigourd et al., 2002).

Resistance to NRTIs was mediated by two mechanisms: ATP-dependent pyrophosphorolysis which is the removal of NRTIs from the 30 ends of the newborn chains and increased discrimination between the deoxyribonucleotide substrate and the inhibitor. (Naeger., et al 2002).

NNRTI inhibits HIV-1 by binding and promoting the formation of proximal hydrophobic pockets. NNRTI binding to the virus may reduce polymerase activity. (Sluis-Cremer., et al 2004).

NNRTI resistance was generated from substitutions of amino acids such as L100, K101, K103, E138, V179, Y181, and Y188 in NNRTI binding sacs. (Bacheler et al., 2000; Dykes et al., 2001).

The HIV-1 Protease is an enzyme responsible for the cleavage of viral gags and polyprotein precursor gags during virion maturation. However, protease genes have great plasticity, with polymorphism observed in 49 of 99 codons, and many more than 20 substitutions known to be associated with resistance (Shafer et al., 2007).

The HIV-1 entry exploits some host proteins for a set of complicated events leading to the fusion membrane and the release of the viral nucleus into the cytoplasm. Fusion Inhibitor is a crystalline structure of ectodomain gp41 and from ectodomain partnered with peptide inhibitors (C34). The fusion inhibitor peptide was designed based on the discovery that two homologous domains in the gp41 virus protein must interact, one of these domains by heterologous proteins can bind and interfere with intramolecular interactions of viral proteins and have significant antiviral activity against HIV-1 (Lalezari et al., 2003; Wilen., et al 2012).

The CCR5 antagonist is a small molecule bonded to the hydrophobic pouch inside the CCR5 helical transmembrane that has been shown to inhibit viral replication in the macaque model and to prevent vaginal transmission. So far, three
antagonists (VCV, MVC, and Aplaviroc) have been shown to inhibit human replication virus. (Dorr et al., 2005; Veazey et al., 2005).

2. Nutritional status
According to WHO, nutritional support should be fundamental for a comprehensive response to HIV and AIDS. Malnutrition status in PLWHA were associated with chronic complication, increased morbidity, and reduced survival, even when ART is available (Who and Searo, 2008; Arjun et al., 2015).

A study in the United States found that micronutrient supplements significantly increased CD4 cell counts, and studies among HIV-infected adults in Haiti, Kenya, Malawi, and Zambia have shown significant positive effects of micronutrient supplementation. Increased intake of either macro or micronutrient food can optimize health outcomes for people living with HIV. (Kaiser et al., 2006).

A previous study from (Venter., et al 2009) showed the correlation between CD4 cell count, body weight, and body mass index (BMI). when CD4 number decrease by 100 cells / μl was associated with a 1.9 kg decrease in body weight of HIV-infected adults.

Diarrhea and fever were clinical complications associated with chronic malnutrition and weight loss. The impact of HIV/AIDS can decline dramatically if individuals take care of their health, plan for the future for their families and prevent further spread of infection. Patients need to get educational nutrition on topics such as diet diversity, food safety principles and recommendations set for the community including food aid targeted. (Kirkcaldy et al., 2006; Hendricks et al., 2010).

Health workers should provide education and build nutrition support groups for PLWHA.

3. Co-infection
Co-infection is a major factor that promotes increased morbidity and mortality in PLWHA. The World Health Organization (WHO) reported that more or less a quarter of the 1.5 million deaths of HIV-infected patients were associated with tuberculosis and others co-infection (Lewandowski, 2015).

Based on the status of immune suppression in PLWHA, other co-infections can present with a variety of clinical syndromes with atypical manifestations that pose challenges in diagnosis and clinical management..

Chronic HIV co-infection is more than other infectious diseases, as the HIV virus immobilizes the immune system and allows reactivation of the active pathogens or increases susceptibility to exogenous pathogens. Although in the current era of morbidity and mortality the opportunistic diseases have declined, infections such as Cytomegalovirus (CMV), tuberculosis, hepatitis C and B, Human Papillomavirus (HPV) remain a major health problem in chronically chronic HIV-infected individuals (Zanoni and Gandhi, 2014).

The role of co-infection in increasing morbidity and mortality remains a major problem today. In a study of HIV-infected populations in South Africa, showed that patients with active TB infection had elevated levels of soluble inflammatory biomarkers associated with monocyte activation, as well as T-cell activation surface markers (Sullivan et al., 2015).

Patients with active TB infection had lower CD4 T-cells. this explains that Co-Infection plays a fundamental role in immune activation in all stages of coinfected HIV infection may increase the risk of higher cardiovascular disease (Boulougoura and Sereti, 2016).
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