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**Sex and Functional Status As A Predictor Of Death Of People Living With HIV/AIDS On ARV
Therapy In Buleleng Hospital**

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Abstrak

Kasus kematian dalam HIV/AIDS masih menjadi tolak ukur keberhasilan pengobatan. Kajian tentang prediktor kematian pada Odha di populasi umum masih sangat terbatas. Metode yang di gunakan Longitudinal analitik dengan pendekatan retrospektif menggunakan data kohort pasien yang menerima ARV (antiretroviral) di RSUD Buleleng dalam periode waktu 2006-2015. Analisa menggunakan regresi logistic dengan SPSS versi 17. Hasil menunjukkan dari total 1204 bahwa insiden rate kematian total sebesar 3 per 100 person years. Kasus kematian 50% terjadi pada 0.14 tahun pengamatan. Laki-laki dan status fungsional kerja terbukti sebagai prediktor kematian pada odha. Laki-laki memiliki risiko kematian 2.12 kali lebih tinggi dibandingkan perempuan (aOR 2.12 (p 0.01 CI 1.28-3.51). Status fungsional baring meningkatkan risiko kematian aOR 2.14 (CI 1.39-3.29 p 0.01). Kesimpulannya yaitu laki-laki memiliki risiko kematian yang lebih besar dibandingkan perempuan. Sebaiknya evaluasi keberhasilan terapi ARV mempertimbangkan kajian dan perbedaan kebutuhan antara perempuan dan laki-laki. Status fungsional baring menunjukkan kondisi klinis yang buruk sehingga meningkatkan risiko kematian pada Odha. Evaluasi terhadap keteraturan pengobatan dan kejadian kematian berbasis gender sebaiknya dilakukan lebih intensif.

Kata kunci: sex, HIV/AIDS, status fungsional

Abstract

Cases of death in HIV / AIDS are still a benchmark for the success of treatment. Studies of predictors of death in people with HIV in the general population are still very limited. Longitudinal analytic with a retrospective approach using cohort data of patients receiving antiretroviral drugs at Buleleng General Hospital in the period 2006-2015. The analysis uses logistic regression with SPSS version 17. Results show a total of 1204 that the incidence of total mortality rate is 3 per 100 person-years. 50% of deaths occurred at 0.14 years of observation. Men and the general functional status of employment were predictors of death in PLHAs. Men have a risk of death 2.12 times higher than that of women (aOR 2.12 (p 0.01 CI 1.28-3.51). The functional status of beds increases the risk of death aOR 2.14 (CI 1.39-3.29 p 0.01). Men have a risk of death evaluation of the success of antiretroviral therapy considers studies and differences in needs between women and men. The functional status of beds shows a poor clinical condition that increases the risk of death in people with HIV. Evaluation of regularity of treatment and the incidence of gender-based deaths should be done more intensively.

Keyword: sex, human immunodeficiency virus/ acquired immuno deficiency syndrome, functional status

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INTRODUCTION

The HIV / AIDS epidemic is still a global issue that continues to receive special attention. Various programs have been developed to achieve the goal of reducing the risk of transmission. The four pillars of HIV / AIDS prevention in Indonesia all lead to the paradigm of zero new infection, zero AIDS-related death and zero discrimination including prevention, care, support and treatment, impact mitigation, and conducive environmental preparation(1,2).

The death of HIV / AIDS patients after receiving therapy in Bali is the seventh-highest percentage of deaths in Indonesia. This figure is still below the national death rate (18.04%), but it is still far from the target of zero AIDS-related death. Likewise, the cumulative loss to follow up (LTFU) incidence trend in Indonesia has increased, as of June 2013 by 15.74% to 17.95% as of June 2014. Bali Province ranks fifth in Indonesia in terms of the number of HIV / AIDS cases. In the second quarter of 2014 in Bali Province, there were 5802 PLHIV who had received ARV therapy with 3598 still on ARV therapy, 1063 LTFU, 664 died, 459 referred out and 18 stopped ARV therapy (1). Buleleng Regency is the second-largest area in Bali Province with the second-highest number of HIV cases with 593 cases (13.92%)(1).

The success of ARV therapy requires adherence to therapy for HIV / AIDS patients so patient compliance must always be monitored and evaluated regularly at each visit. Failure of antiretroviral therapy is often caused by non-compliance with patients taking ARVs (2-5). Gender is a variable that greatly determines the pattern of adherence in antiretroviral therapy.

The risk of death in men tends to be higher (RR 1.19, aSHR 1.7) compared to women (6,7). The beginning of treatment is also a consideration of the success of the therapy given. Clinical conditions often related to the incidence of death in PLHAs are bodyweight, CD4 cell count, clinical stage and functional status. Studies on predictors of PLHIV death by ARV therapy in Bali Province, in particular, are still limited. This study aims to analyze the predictors of death in people with HIV in ARV therapy in Buleleng District Hospital

MATERIALS AND METHODS

This study is a longitudinal analytic study with a retrospective approach using cohort data of patients receiving antiretroviral drugs in Buleleng Regional Hospital in the 2006-2015 time period and taking them cross-sectional. Analysis using logistic regression with SPSS version 17. The study was conducted at the Edelweis VCT Polyclinic of Buleleng District Hospital during the study period, November-December 2018. Data were collected using data collection forms that are still in the form of hard copies made into soft copies (in the form of Microsoft Excel) for easy analysis. Data collected in the form of secondary data from medical records and patient cohort registers. The number of samples in this study was 1204 people with a period of observation from 2005-2014. The research instrument used was the medical record observation sheet. Data were analyzed using multivariate logistic regression analysis using the backward method, the existence of a confounding variable determined by a significance of 5% and a change in survival/hazard rate of 10% or more in the main variable with the SPSS 17 software program.

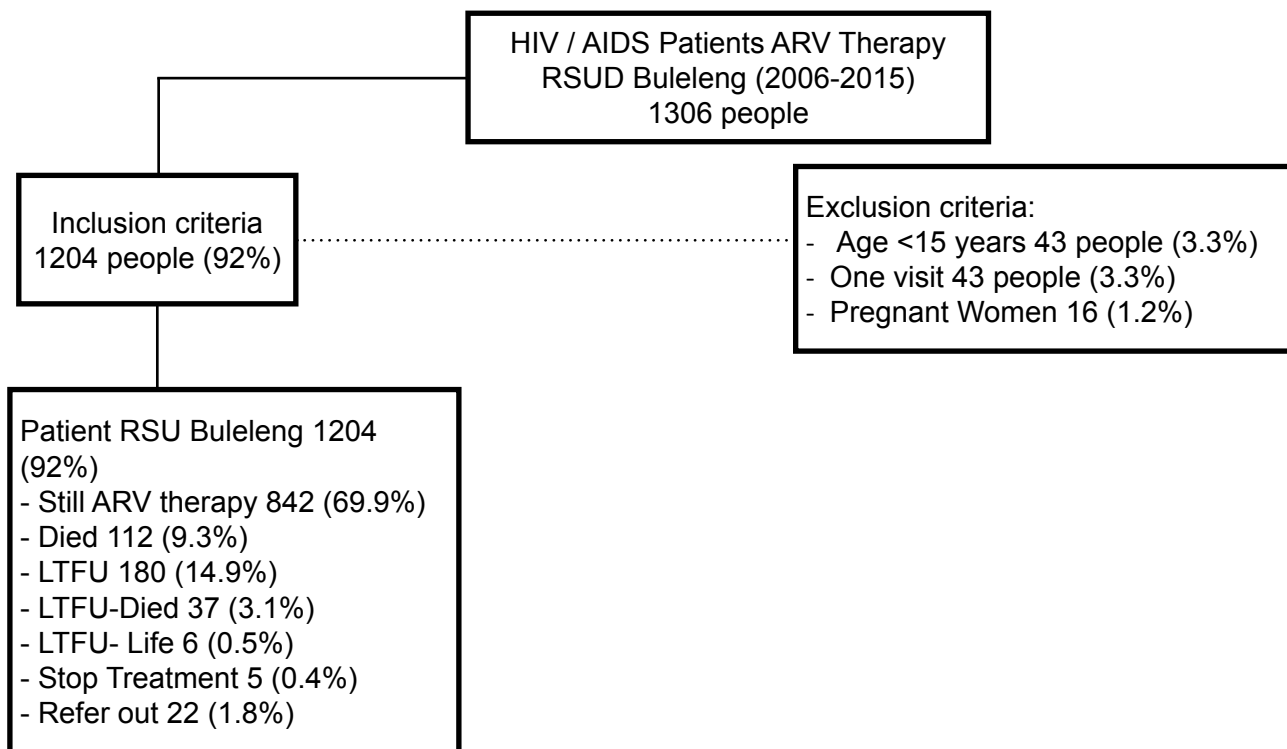
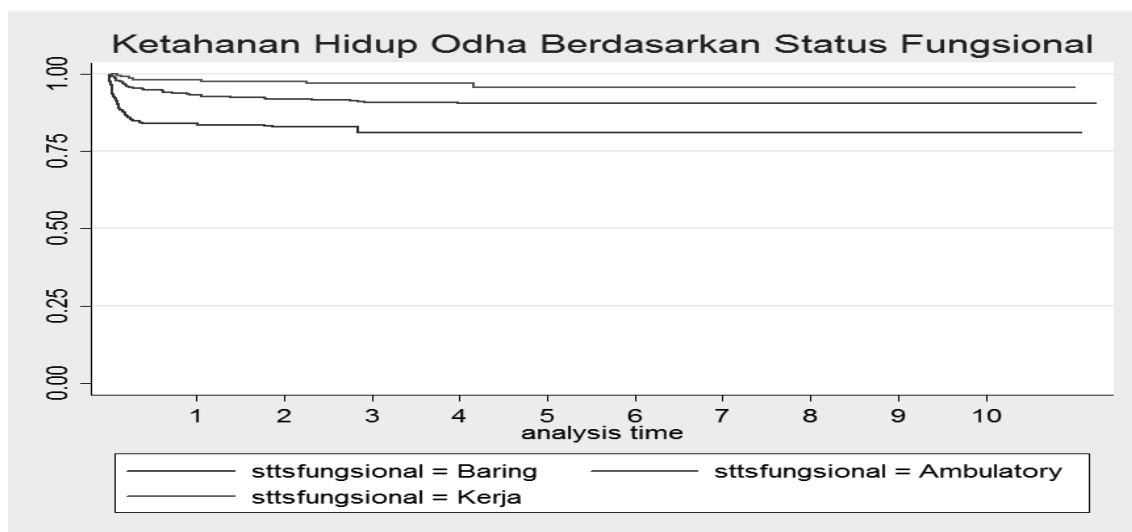


Figure 1. Sample Research Selection Procedure



Graph 1. Survival of People with HIV Based on Functional Status

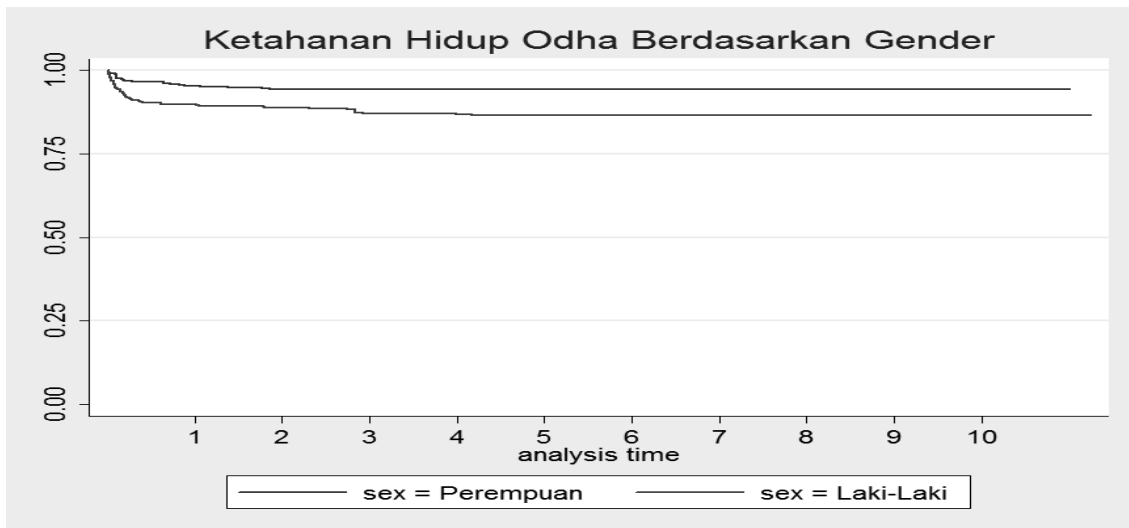
The sample research selection procedure is illustrated in Figure 1.

Observations made during VCT practice by looking at cohort register studies that the incidence of death in people with HIV is still high. Besides, the level of patient adherence to therapy is still low as evidenced by the high percentage of LTFU and mortality in people with HIV in Buleleng Hospital. It is hoped that the results of this study will provide an overview of the clinical

and demographic conditions of PLHAs who have received ARV therapy for the past 10 years.

RESULTS AND DISCUSSION

The results of the study of 1204 PLHA patients data that met the inclusion criteria that the percentage of death cases was 9.30%. The proportion of deaths in men is 79.46% and women are 20.54%. The mortality rate is 3 per 100 person-years with a median time of death



Graph 2. Survival of PLHIV Based on Gender

at 0.14 years (1.7 months) of observation. This condition shows that of the 112 deaths in PLHAs who received ARV therapy 50% of deaths occurred at 5.25 years after therapy. Based on functional and gender status conditions, survival rates for PLHAs are illustrated in the graph below:

Based on table 1 shows that the percentage of deaths of HIV-positive people mostly occurred in men (79.46%), access to health facilities more than 5 kilometers (86.61%), functional status (54.29%), clinical stages 3 and 4 (90.91%), body weight less than 50 kilograms (73.91%), CD4 levels less than 200 cells / mm³ (94.59%), zidovudine type therapy (75.70%) and nevirapine type regimens (81.83%). After the proportion test was performed, there was a statistically significant difference in the proportion of cases of death of HIV-positive people based on sex (p 0.01), functional status (0.01), clinical-stage (0.01), weight (0.04), CD4 level (0.01) and NRTI regimen (p 0.01). In multivariate analysis, not all of the variables to enter because two-variable have missing data more than 50 % were weight and CD4.

Multivariate analysis shows that two variables are predictors of death in people with HIV, namely sex and functional status. HIV-positive men with gender are 2.12 times more

Tabel 1. Condition of Death in People with HIV Based on Clinical and Demographic Characteristics

Characteristics	Death PLWH			
	n	%	p	
	1	2	3	4
Sex				0.01*
Female		23	20.54	
Male		89	79.46	
Distance from Health Facilities				0.54
≤ 5 km		15	13.39	
> 5 km		97	86.61	
Functional Status				0.01*
Baring		57	54.29	
Ambulatory		41	39.05	
Kerja		7	6.67	
Stadium Klinis				0.01*
Stadium 1 dan 2		9	9.09	
Stadium 3 dan 4		90	90.91	
Weight				0.04*
>50 kg		6	26.09	
≤ 50 kg		17	73.91	
CD4				0.02*
>200cell/mm ³		2	5.41	
≤ 200cell/mm ³		35	94.59	
NRTI				0.01*
Tenofovir		9	8.41	
Stavudine		17	15.89	
Zidovudine		81	75.70	
NNRTI				0.16
Evapirine		20	18.69	
Nevirapine		87	81.83	

at risk of dying than women, while functional status conditions, which are lying, also have a risk of 2.14 times death compared to working and ambulatory conditions.

Table 2. Multivariate Predictors of Death of People with HIV in ARV Therapy in Buleleng Hospital.

Characteristics	Odds Ratio (95 % CI)		p
	1	2	
Sex			
Female		1.00 (ref)	
Male		2.12 (1.28-3.50)	0.01*
Functional Status			
Baring		1.00 (ref)	
Ambulatory		0.33 (0.15-0.75)	0.03*
Kerja		2.14 (1.39-3.29)	0.01*
Distance from Health Facilities			
≤ 5 km		1.00 (ref)	
> 5 km		2.23 (0.28-17.49)	0.44
Stadium Klinis			
Stadium 1 dan 2		1.00 (ref)	
Stadium 3 dan 4		2.07 (0.54-7.84)	0.28
NRTI			
Tenofovir		1.00 (ref)	
Stavudine		2.23 (0.28-17.49)	0.44
Zidovudine		2.20 (0.25-15.50)	0.54
NNRTI			
Evapirine		1.00 (ref)	
Nevirapine		4.56 (0.28-15.49)	0.78

* p-value < 0,05 untuk multivariate

The incidence in this study is lower when compared to TAHOD TREAT (Asia HIV Observational Database) data which includes 18 sites in the Asia Pacific region, which is 21.4 per 100 PY, but is higher when compared to countries in Southeast Asia such as India (7.1 per 100 PY) and Vietnam (8.9 per 100 PY) (7–9). Likewise, if compared with developed countries, it tends to have a lower incidence such as France (4.3 per 100 person-years) and Europe (3,272 per 100 person-years)(6).

Deaths to PLHAs are an important measure of the success of ARV therapy. The clinical condition is an important study before starting therapy. People with HIV who start therapy in poor clinical conditions have a higher risk of death (7,8).

Men with HIV have a 2.1 times risk of dying compared to women. This is very possible because the behavior and compliance of men are lower than women. Men are more at risk of

death because they tend to come to the service when sick and are less willing to provide detailed information.⁶ Men have variations in mobility and a high risk of drug abuse that can interfere with adherence to antiretroviral therapy so that they are more likely to experience death.⁷ Most men with drug addiction experience higher toxicity due to interactions with ARV drugs that lead to discontinuation of therapy.⁸ The conditions are different for women who are more likely to come to health care facilities than men for reproductive services and child health services.⁹ Women may seek immediate care because they are the primary caregivers in the family and feel they have a greater responsibility to stay healthy.¹⁰ Men are more likely to experience death if they have advanced disease, this shows that death in men is likely to occur due to a disease that gets worse or death.⁹

Functional status in the lying category is a predictor of death in people with HIV with aOR 2.14 (CI 1.39-3.29 p 0.01). The condition of lying in PLHAs receiving ARV therapy is closely related to poor clinical status. Functional status assessment is based on observations and interviews conducted following its categorization criteria. Functional status in PLHAs can be divided into three namely work status, ambulatory and lying. Working status is categorized if PLHAs are still able to work normally, patients who are unable to work normally and <50% lying down are categorized as having an ambulatory status, while patients who are continuously (or> 50%) lying in bed are categorized as lying (11). The main purpose of ART is to provide opportunities for people to be productive in their work and daily life. Therefore, productivity measures that are functional status can be used as an indicator of the success of ART programs (12). Patients with poor clinical conditions are easily seen from the functional status indicated. Most of those who come with bedridden conditions have worse clinical conditions so that the chance of death

is also greater (11-14). Functional status is ambulatory also increases the risk of LTFU with an adjusted sHR of 1.25 (95% CI: 1.01 to 1.54) (13). Other studies have shown that ambulatory functional status is a protective factor against mortality in people with HIV (aHR 0.4 95% CI 0.3-0.6 p = 0.001) (13).

The results of this study indicate that gender and functional status can be important studies to consider before starting ARV therapy. HIV pre and posttest counseling should be done more intensively to avoid non-compliance with therapies that can result in death.

CONCLUSION AND RECOMMENDATION

The incidence of death in PLHAs on ARV therapy in the last 10 years reached 3 per 100 person-years with a median time of death at 0.14 years (1.7 months) observation. Sex classification is that men have a risk of death 2 times greater than women. Lying functional status increases the risk of death by 2.1 times. It is recommended that the evaluation of the success of ARV therapy considers the study and differences in needs between women and men without ignoring their functional status. Evaluation of the regularity of treatment and gender-based death events should be done more intensively.

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