SURVIVAL RATE AND SOCIO-DEMOGRAPHIC DETERMINANTS OF MORTALITY IN ADULT HIV/AIDS PATIENTS ON ANTI-RETROVIAL THERAPY (ART) IN MYANMAR: A REGISTRY BASED RETROSPECTIVE COHORT STUDY 2005-2015

Aung Tin Kyaw*, Yothin Sawangdee, Pojjana Hunchangsith, Umaporn Pattaravanich

Institute for Population and Social Research, Mahidol University, Phuttamonthon, Nakhonpathom, 73170, Thailand

ABSTRACT:

Background: With increasing coverage of anti-retroviral therapy (ART) among people living with HIV/AIDS, their survival has been improved in recent years. However, the country is still facing a substantial number of AIDS related deaths. In response to this problem, this study assesses the survival rate of adult HIV-infected patients receiving ART and identifies the determinants of their mortality including socio-demographic factors to identify areas for improvements.

Methods: A registry-based retrospective cohort study was applied by reviewing records of patients receiving ART between June 1, 2005 and May 31, 2015 at the HIV-specialist hospital in Yangon, Myanmar. Time to death was the main outcome measure in the study and the outcome date was December 31, 2015. Life Table Analysis, the Kaplan- Meier method and the Cox proportional hazards model were used to estimate survival and to identify determinants of mortality. A total of 7995 patients were included in the analysis.

Results: The mean follow-up time of the sample was 34.57 (SD ± 30.14) months and the median survival time of the sample was longer than 127 months. Mortality rate was 3.95 deaths per 100-person-year of follow up period. The cumulative probabilities of survival at 6 months, 1 year, 5 years and 10 years of receiving ART were 0.91, 0.90, 0.86 and 0.83 respectively. Among the six socio-demographic characteristics, age and sex of the HIV-infected patients on ART are associated with their mortality, i.e. age at the start of ART of ≥35 years (Adjusted Hazard Ratio =1.28) and male (Adjusted Hazard Ratio =1.24). No OI prophylaxis (Adjusted Hazard Ratio =4.63), <95% ART adherence (Adjusted Hazard Ratio =14.78), not changing ART regimen during the course (Adjusted Hazard Ratio =2.31), WHO clinical staging 3 and 4 (Adjusted Hazard Ratio =1.39), bedridden functional status (Adjusted Hazard Ratio =2.18) and baseline CD_4 count of <200/mm^3 (Adjusted Hazard Ratio =1.66) were treatment and clinical factors associated with HIV mortality after adjusting other covariates.

Conclusion: The findings indicate that priority should be given to patients who have a high risk of mortality within six months after initiation of ART. The study provides information to policy makers and HIV/AIDS program implementers to plan and implement appropriate interventions for the improvement of survival of HIV/AIDS patients in Myanmar.

Keywords: Adult mortality; HIV/AIDS patients on ART; Socio-demographic factors; Survival rate; Myanmar

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INTRODUCTION

Acquired Immunodeficiency Syndrome (AIDS) caused by human immunodeficiency virus (HIV) is

* *Correspondence to: Aung Tin Kyaw*
E-mail: aungtinkyaw1313@gmail.com

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still a serious health problem and a leading cause of death globally [1]. According to the World Health Organization (WHO), in 2014, there were 36.9 million people living with HIV and 2 million people died from AIDS-related causes worldwide. In Asia and the Pacific, 240,000 people died of AIDS-related causes during 2014. Between 2000 and 2014, the number of AIDS-related deaths in the region increased by 11% [2].

In South and Southeast Asia, the rate of new HIV infections has decreased. However, the total number of people living with HIV continues to rise [1]. It is clearly known that antiretroviral therapy (ART) has improved the survival of patients with HIV/AIDS. The goal of ART is to achieve maximal and sustained suppression of viral replication, to restore immune function, to reduce HIV associated morbidity and mortality, to increase the quality of life and to improve survival [3]. The ART has been shown to significantly change the HIV disease progression. ART has prevented 2.5 million deaths in low- and middle-income countries globally since 1995 [4].

There are many studies that showed the survival analysis and determinants factors on HIV/AIDS patients who taking ART. In a cross-sectional study from Cambodia which was conducted with patients who had been receiving ART for 24 ± 2 months, the outcomes of patients as alive, dead, transferred out, loss to follow up were 84.1%, 12.7%, 1.4% , 1.7% respectively and the estimate of 2 years survival was 85.5% [5]. There are studies which have been investigated the biochemical parameters and WHO clinical staging of patients which have high impacts on the success of HIV treatment [6]. The WHO clinical staging 3 & 4, low haemoglobin level [7], tuberculosis (TB) co-infection and other co-infections [4], low CD_4 count, low lymphocyte count, high viral load of patients [3] were identified as risk factors for mortality of the HIV-patients on ART. Moreover, the risk for death was higher in patients with late AIDS stage, low CD_4 count, anemia, under nutrition, and co-infection with tuberculosis [8]. Like clinical and biological factors, socio-demographic factors are also crucial for the disease outcomes. A prospective cohort study in southern region of Thailand showed that the incident rate was 2.23 per 1,000 person/ month while the median survival time was 257.03 months [1]. This study demonstrated that demographic factors such as sex, race, marital status, occupation, resident area are significantly affected mortality among HIV/AIDS patients like other important factors such as risk of infection, sexual behavior, type of patient, and complimentary care [1].

Socio-demographic characteristics of individuals and its correlates such as gender, migration and housing status, ethnicity, race, income, literacy status, employment, access to information, availability and affordability to treatment and care are found to be associated with morbidity and mortality of HIV/AIDS in most developing countries [9]. Some studies showed that the socio-demographic situation of a person had an impact on the likelihood of affecting by the virus and developing AIDS. For example, Damtew, et al. [8] found that single marital status, being illiterate, bedridden functional status, low ART adherence, co-infection with tuberculosis and irregularity of follow-up status were associated with higher risk of adult HIV/AIDS mortality ($p< 0.05$). From above statements, it is clear that ART is one of the important factors that can be delay mortality. On the other hand, the adult HIV/AIDS patients who have different socio-demographic and different clinical background may have different survival time and mortality status. Although there are many studies regarding the impact of clinical factors on HIV/AIDS patients on ART, the scientific evidence on the socio-demographic impact on people and communities was comparatively deficient in many developing countries.

Myanmar, as a low-income country, had no exception in the HIV/AIDS epidemic. Myanmar is one of the countries hardest hit by the HIV epidemic in Asia. According to the latest estimation by the Asian Epidemic Model, the HIV prevalence among the adult population (15-49) in Myanmar is 0.54% in 2014. According to epidemiological modeling, the adult population aged 15 years and older was around 212,000 PLHIV and 34% of them were females. Estimated 9,000 new infections occurred in 2014 [10]. It was illustrated in Health in Myanmar, the latest national report published by the Ministry of Health, that according to hospital statistics in 2012, the first single leading cause of death was HIV/AIDS and it accounted for 6.6% of all causes of death [11].

During the last years, the coverage of ART among people living with HIV/AIDS in Myanmar has improved. As a consequence, mortality rates have declined significantly in Myanmar [10]. However, HIV/AIDS is still become the first leading cause of death in the country with over 10,000

deaths in 2014 [10, 11]. This study was undertaken with the objectives to estimate the survival rates of AIDS patients on ART and to identify factors including socio-demographic factors that have impact on the mortality of HIV AIDS patients with the hope that the results would contribute to existing knowledge.

MATERIALS AND METHODS

This study was a registry-based retrospective cohort study using secondary data from Mingalardon Specialist Hospital, Yangon, Myanmar. The cohort in this study is HIV-infected individuals of both male and female of age between 13 to 78 years who had started ART treatment in Mingaladon Specialist Hospital from 1st June 2005 to 31st May 2015. Time to death was the main outcome measure in the study and the outcome date was December 31, 2015. The Mingalardon Specialist Hospital is the main hospital and tertiary centre for all HIV/AIDS patients all over Myanmar. Total 8,038 adult patients have been registered during the ten years period but only 7995 patients were included in the analysis because the incompleteness of outcome dates of 43 patients.

After data cleaning, descriptive and summary statistics were carried out. In lines with its objective of this study, survival rate (cumulative survival rate) analysis using life table method and Kaplan Meier method to identify the survival rate of adult HIV/AIDS patients. Additionally, bivariate analysis and multivariate Cox proportional hazards model were applied to investigate the factors determining the adult mortality among HIV/AIDS patients.

The dependent variable for survival rate analysis was death and its time of occurrence measured by ratio scale. It is defined as all of the deaths occurring after ART initiation, but before the end of study period. For hazard ratio analysis, the dependent variable was presented by two outcome categories, coded by 0 = patients was still alive or lost to follow-up or transferred out during the studied period, and 1 = patients died during the study period after starting ART treatment.

There were 16 independent variables in this study. They are: 6 socio-demographic factors (age, sex, marital status, literacy status, employment status, residence); one behavioural risk factor (alcohol consumption); 4 treatment factors (delayed seeking care for HIV/AIDS, Cotrimoxazole for OI prophylaxis, ART adherence, ART regimen change); and 5 clinical factors (WHO clinical staging, CD_4 cell count, Hemoglobin level, HIV/TB co-infection, baseline functional status).

In this study, a life table presents the proportion surviving, the cumulative hazard function, and the hazard rates of a large group of subjects followed over time. The Kaplan- Meier method is also used to estimate the probability of surviving for a specified length of time. It provides medium survival time (cumulative survival proportion to 0.5), five year survival rate (cumulative survival proportion to at 60 months) and average hazard rate (compare two survival experiences, computed by dividing the number of subjects who do not survive by the sum of observed survival times).

Cox-proportional hazards model was used for examining the determinants of mortality. Enter method was used to select variables for the final. Hazard ratio with its 95% confidence interval and p value <0.05 was used to measure strength of association and identify statistical significant result.

Ethical considerations

Ethical clearance was taken from the Institutional Review Board of Institute for Population and Social Research (IPSR-IRB), Mahidol University with the approval letter of COA.No 2016/08-072 dated on August 25, 2016. Permission letter for using the secondary data was obtained from the Medical Superintendent of the Mingalardon Specialist Hospital after receiving permission letter from the Director General of Department of Medical Care, Ministry of Health and Sports. Ethical problem was kept to minimum. Names and unique ART numbers of patients were not included in the analysis.

RESULTS

The study cohort included 7995 patients with a mean age of 35.84 years (SD±8.8) and the median (IQR) age of 35 years (30-41). Out of the total study population, 57.1% were males. Among them, 61.1% were married and 84.9% answered that they come from urban area for seeking care for HIV/AIDS. For literacy and employment status, 11.7 % were illiterate and 34.4% were unemployed at the time of ART initiation. Concentrating on alcohol consumption, 18.7 % were alcoholics and 9.1% had <95% of ART adherence. About three-fourth of the study population had delayed seeking care for HIV/AIDS. At the time of ART initiation, 65.6% were in WHO clinical stage III & IV and 11.8% had bedridden functional status. Among the study participants, 48.0% developed active TB infection

Table 1 Yearly enrolment, alive, dead, lost to follow-up and transfer out status of HIV-infected adults for ART

Year	Alive	Dead	Lost to follow-up	Transfer out	Total yearly Enrolment
	Frequency (%)	Frequency (%)	Frequency (%)	Frequency (%)	
2005	47 (78.3)	4(6.7)	2(3.3)	7(11.7)	60
2006	216(67.5)	52(16.3)	28(8.8)	24(7.5)	320
2007	172(61.4)	52(18.6)	34(12.1)	22(7.9)	280
2008	246(67.6)	64(17.6)	38(10.4)	16(4.4)	364
2009	243(60.1)	84(20.8)	53(13.1)	24(5.9)	404
2010	507(71.7)	97(13.7)	83(11.7)	20(2.8)	707
2011	853(73.8)	131(11.3)	146(12.6)	26(2.2)	1156
2012	555(71.6)	109(14.1)	97(12.5)	14(1.8)	775
2013	916(76.1)	94(7.8)	162(13.5)	31(2.6)	1203
2014	1455(76.5)	148(7.8)	231(12.1)	69(3.6)	1903
2015	640(77.8)	74(9.0)	77(9.4)	32(3.9)	823
Total	5850(73.2)	909(11.4)	951(11.9)	285(3.5)	7995

Table 2 Survival analysis of HIV positive adult on ART by actuarial life table method

Surviving time interval (Months)	Number entering	Number exposed to risk	Number of terminal events	Proportion surviving	Cumulative proportion surviving at end of interval	Hazard rate
0 - 5	7995	7699.500	610	.9208	.9208	.0137
6 - 11	6794	6380.000	91	.9857	.9076	.0024
12 - 17	5875	5390.000	59	.9891	.8977	.0018
18 - 23	4846	4529.500	31	.9932	.8916	.0011
24 - 29	4182	3893.500	19	.9951	.8872	.0008
30 - 35	3586	3368.000	22	.9935	.8814	.0011
36 - 41	3128	2947.000	14	.9952	.8772	.0008
42 - 47	2752	2624.000	12	.9954	.8732	.0008
48 - 53	2484	2357.000	11	.9953	.8691	.0008
54 - 59	2219	1895.500	15	.9921	.8623	.0013
60 - 65	1557	1323.000	4	.9970	.8597	.0005
66 - 71	1085	1052.500	5	.9952	.8556	.0008
72 - 77	1015	920.500	3	.9967	.8528	.0005
78 - 83	823	786.000	4	.9949	.8484	.0009
84 - 89	745	657.000	2	.9970	.8459	.0005
90 - 95	567	513.500	2	.9961	.8426	.0007
96 - 101	458	418.500	1	.9976	.8406	.0004
102 - 107	378	325.500	3	.9908	.8328	.0015
108 - 113	270	201.500	1	.9950	.8287	.0008
114 - 119	132	90.000	0	1.0000	.8287	.0000
120 - 125	48	31.500	0	1.0000	.8287	.0000
126 - 127	15	7.500	0	1.0000	.8287	.0000

during the course of treatment. With regard to chemoprophylaxis, the majority, 88.9% were given co-trimoxazole for OI prophylaxis. During the course of ART treatment, 39.6% had been changed ART regimen including second line ART. The median (IQR) CD_4 count and hemoglobin of the cohort were 105 cells /μL (34-229 cells /μL) and 11.6 g/dL (9.7-12 cells /μL) respectively.

A total of 909 (11.4%) patients died during the ten year follow-up period (Table 1), with majority of deaths 610 (67.1%) occurring in the first six months (HR: 0.0137) (Table 2). Two hundred eighty five (3.5%) patients were transferred to other facilities and 951 (11.9%) were lost-to follow up. The remaining 5850 (73.2%) were active until the last censoring date (Table 1).

The overall mortality rate in the cohort during the 23,036.55 person-years of follow up period was 3.95 /100 person year of follow up period. The six months, one year, five years and 10 years survival rate of the HIV-infected adults on ART were 90.76%, 89.77%, 85.97% and 82.87% respectively (Table 2).

The median survival time is longer than the

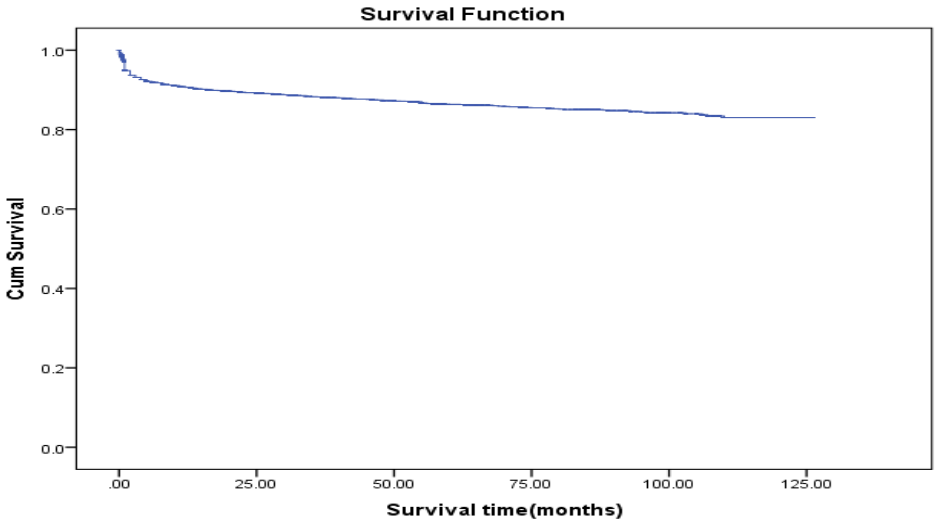

Figure 1 Survival curve of HIV-infected patients on ART from Mingaladon Specialist

Table 3 Adjusted hazard ratios for outcome of death by different characteristics

Characteristics	Exp (B) (95% CI)	Wald ϰ2	*p* value
Age at the start of ART			
<35 years (ref-)	1		
≥35 years	1.28 (1.12-1.46)	14.22	<0.001
Sex			
Female (ref-)	1		
Male	1.24 (1.07-1.42)	9.14	0.003
Co-trimoxazole for OI prophylaxis			
Yes (ref-)	1		
No	4.63 (3.97-5.39)	382.54	<0.001
ART adherence			
≥95% (ref-)	1		
<95%	14.78 (12.77-17.12)	1301.58	<0.001
ART regimen change			
Changed (ref-)	1		
Not changed	2.31 (1.96-2.71)	101.83	<0.001
WHO clinical staging			
Stage 1 & 2(ref-)	1		
Stage 3 & 4	1.39 (1.15-1.67)	11.63	0.001
Baseline functional status			
Working (ref-)	1		
Bed ridden	2.18 (1.87-2.54)	88.60	<0.001
CD4 level			
≥200 / mm3 (ref-)	1		
<200 / mm3	1.66 (1.35-2.04)	21.31	<0.001

total follow-up period (i.e. more than 127 months) because the survival probability at the latest follow-up time was still more than 0.5 (Figure 1).

In bivariate Cox regression analysis, among the sixteen independent variables, thirteen variables such as age at the time of ART initiation, sex, marital status, alcohol consumption, delayed seeking care for HIV/AIDS, co-trimoxazole prophylaxis, ART adherence, ART regimen change, baseline functional status, WHO clinical stage, CD4 count, haemoglobin level and HIV-TB co-infection were associated with mortality ($p < 0.05$). Residence and employment status also had association with mortality at $p < 0.1$ level.

In the multivariate Cox regression analysis, the independent, significant predictors of mortality

in patients on ART at Mingaladon specialist hospital were age of older than 35 years at the time of ART initiation (AHR: 1.28; 95%CI: 1.12- 1.46), male sex (AHR: 1.24; 95%CI: 1.07- 1.42), no Cotrimoxazole for OI prophylaxis (AHR: 4.63; 95%CI: 3.97- 5.40), not changing ART regimen (AHR: 2.31; 95%CI: 1.97-2.72), < 95% ART adherence (AHR: 14.79; 95%CI: 12.77-17.12), WHO stage 2 & 3 (AHR:1.39; 95%CI: 1.15-1.68) CD4 count < 200 cells/mL (AHR: 1.66; 95%CI: 1.36-2.04) and bedridden functional status (AHR: 2.18; 95%CI: 1.87- 2.54) (Table 3).

DISCUSSION

There were a total of 7995 HIV-infected adult on ART were included in the analysis. During the study period of ten years, 909 (11.36%) patients had died after initiation of ART. The mortality percentage in this study was found to be lower than the studies from neighboring countries. This percentage was reported to be 13.2% among Thai HIV-infected adults on ART during 2000 and 2007 [12] and 27.4% among Vietnamese HIV-infected adults on ART during 2007 to 2010 [13].

There are 23,036.55 person years of follow-up and the mortality rate is 3.95 per 100 person year. This finding is comparable to those reported in other articles from resource-limited settings and the mortality rate is found to be lower than some other studies. The mortality rate among Cambodian HIV-infected patients on ART in 2004-2005 was 9.1 per 100 person year [14]. Similarly, the mortality rate among Vietnamese HIV-infected patients on ART in 2007- 2010 was 7.4/100 person year [13]. One of the two studies from rural area China during 2007 and 2008 showed that the mortality rate was 9.9/100 person year [15] but another study done in Henan province of China during 2005 to 2014 showed that the mortality rate was 3.2/100 person year [16].

In this study, the percentage of HIV-infected adults who had survived up to one year was 89.77%. From Thailand's ART program scale-up and patient's outcome study conducted between 2000 and 2007 showed that overall 1 year survival was 89% [12]. A cross-sectional survey conducted during 2004 and 2005 in Cambodia stated that the estimate of two years survival was 85.5% [5]. A randomized control trial done during 2007 and 2010 in Vietnam described that the survival probability was 91% after one year [13]. Another study in China during 2004 to 2015 showed that the one year cumulative survival rate of was 93.7% [16].

Out of a total of 909 deaths over 10 years period, 610 (73%) died within six months after initiation of ART and 701 (77.1%) died within one year after initiation of ART. The death rate was higher than other studies, such as, 74.1% of the deaths occurred in the first year after treatment in one Ethiopian study, and even that 74.1% was found to be higher than other studies [17]. Therefore, special attention should be paid to investigate thorough assessment of OIs before initiating ART and intensive follow-up visits should be arranged during the first six months of ART initiation. Among the 610 deaths which were occurred within six months after initiation of ART, 36 (5.9%) were the youths (13- 24 years) and 466 (76.4%) were young adults of 25- 44 years age group.

There were eight independent variables that are significantly associated with mortality in multivariate cox regression analysis. These eight independent variables are age at the start of ART, sex, Co-trimoxazole for OI prophylaxis, adherence for ART, ART regimen change during the course of ART treatment, WHO clinical staging, baseline functional status and baseline CD4 cell count.

In this study, patients of age 35 years or over 35 years of age at the initiation of ART are 1.3 times higher risk to death compare with less than 35 years of age at the initiation of ART (HR 1.3; 95% CI 1.13 - 1.48). Similar relationship between age and mortality were also found in many studies, such as the Vietnamese study (AHR 2.8;CI 1.5 - 5.2) [13], China study (AHR 1.2;CI 1.16 - 1.24) [16], Cambodian study (AHR 2.5;CI 0.9 - 6.6) [5]. The higher risk among older patients can be explained by the facts that older age is associated with delayed seeking for HIV/AIDS (51.8% Vs 48.2%), bedridden functional status (50.9% Vs 49.1%), advanced WHO staging 3 & 4 (51.8% Vs 48.2%) and lower CD4 count (52.1% Vs 47.9%).

Male patients are 1.2 times higher risk to death compare with female patients (HR 1.2; 95% CI 1.03 - 1.39). Similar relationship between sex and mortality were also found in many studies. In Thai study, the adjusted hazard rate for male sex was 1.96 (CI; 1.86 to 2.07) [12]. In Cambodian study, the adjusted hazard rate for male sex was 1.75 (CI; 1.04 to 3.0) [14]. In China study, the adjusted hazard rate for male sex was 1.28 (CI; 1.20 to 1.37) [16]. The reasons behind that male sex has more significant association with mortality might be explained that male is associated with delayed seeking for HIV/AIDS (61.6% Vs 38.9%), bedridden functional

status (61.8% Vs 38.2%), advanced WHO staging 3 & 4 (62.5% Vs 37.5%), lower CD4 count (61% Vs 39%) lower ART adherence (64.6% Vs 35.4%) and more alcohol consumption (94% Vs 6%).

However some studies from Africa proved that female sex was more vulnerable to get mortality outcomes due to the socioeconomic inequalities. For example, in the study of Chapoto and Jayne, young single women in rural Zambian sample during 2001 to 2004 were 2 to 5 times more likely to die of HIV/AIDS related diseases [18].

The WHO had recommended prescribing co-trimoxazole to all symptomatic patients with WHO stage 2, 3 and 4. However, 92% of patients with stage 2, 3 & 4 had taken Cotrimoxazole for OI prophylaxis at the time of ART initiation in this study whereas 76% of asymptomatic patients with stage 1 had taken Cotrimoxazole for OI prophylaxis. The study found that those patients who were not on co-trimoxazole at the time of ART initiation were 4.64 times higher risk to death compare with those patients on co-trimoxazole (HR 4.64; 95% CI 3.98 - 5.40). The other studies proved that Cotrimoxazole for OI prophylaxis reduces the mortality rate about 46% [19] and 63% [20], 44% [21] and 21% [22]. But the significant association between co-trimoxazole for OI prophylaxis and mortality was not found in some studies [8, 13, 17].

Concerning with ART regime change during the course of treatment, 39.6% patients has been changed ART regimen during the study period including second line drugs. The patients who have not changed ART regime during the course of treatment are 2.3 times higher risk to death compare with those patients who have changed ART regime during the course of treatment (HR 2.30; 95% CI 1.95 - 2.71). Similar relationship between ART regime change during the course of treatment and mortality were also found in many studies. A study from Vietnam reported that patients who have changed initial ART regimen were 77% decrease in the risk of mortality compared to those patients who have not changed initial regimen [13].

The patients with WHO clinical stage 3 and 4 are 1.4 times higher risk to death compare with those patients WHO clinical stage 1 and 2 (HR 2.30; 95% CI 1.15 - 1.68). This finding is the same as those reported in other articles from resource-limited settings. One of the studies done in Thailand stated that AIDS patients are 1.75 times higher risk to death compare with asymptomatic HIV patients (HR 1.75; 95% CI 1.61 - 1.90) [12]. Another study in Vietnam illustrated that patients with WHO clinical stage 3 and 4 are 3.3 times higher risk to death compare with those patients WHO clinical stage 1 and 2 (HR 3.3; 95% CI 1.4 – 8.2) [13].

The patients with bedridden functional status are 2.17 times higher risk to death compare to those patients with working functional status (HR 2.17; 95% CI 1.86 - 2.53). This finding is also consistent with studies conducted in different parts of the world. A study from Ethiopia identified that patients with bedridden functional status are 4.09 times higher risk to death compare to those patients with working functional status (HR 4.09; 95% CI 2.12 - 7.90) [17]. Another study in Vietnam clarified that patients with bedridden functional status are three folds in the risk of mortality compare to those who were in working functional status (HR 2.9; 95% CI 1.33 - 6.32) [13].

The patients with CD_4 count of less than 200/mm^3 are 1.65 times higher risk to death compare to those patients with CD_4 count of more than or equal to 200/ mm^3 (HR 1.65; 95% CI 1.34 - 2.03). This finding is supported by other research findings. In Thailand study, patients with CD_4 count of less than 50/mm^3 are 2.43 times higher risk to death compare with patients with CD_4 count of more than or equal to 200/mm^3 (HR 2.43; 95% CI 2.09 - 2.83) [12]. Another study in Vietnam explained that patients with patients with CD_4 count of less than 100/mm^3 are 2.6 folds in the risk of mortality compare to those whose CD_4 count was more than or equal to 100/mm^3 (HR 2.6; 95% CI 1.2 – 5.9) [13].

More than 90% of the HIV-infected patients on ART in this study had good adherence for ART at the last follow-up visits. In this study, ART adherence has significant association with mortality in both bivariate and multivariate analysis controlling other covariates. The patients with poor ART adherence are 14.87 times higher risk to death compare with those patients with good ART adherence (HR 14.87; 95% CI 12.7 - 17.4). ART adherence is the most important predictors in this study because it has the largest hazard ratio and the statistically significant associations among residence, employment status, marital status and HIV/TB co-infection status were changed if ART adherence was added into the model. This means that some socio-demographic variables and HIV/TB co-infection status have no association with mortality in the absence of good ART adherence. Therefore, ART adherence is very important for policy implication.

Residence, baseline haemoglobin level, alcohol and HIV/TB co-infection did not show significant associations with mortality in this study. According to the previous literature, alcohol acts through behavioural and physiological pathways to impact on the acquisition, further transmission and then progression of HIV disease [23]. However, alcohol consumption has no significant association with mortality although the patients who drink alcohol are more likely to die compared with those who do not (14.4% vs 10.7% respectively). Contrasting with the finding from this study, most of the previous studies that identified predictors of mortality among HIV-infected patients on ART suggested that HIV/TB co-infection was one of the most important predictors. On the other hand, some of the studies did not find the significant association between HIV/TB co-infection and mortality among HIV-infected patients on ART, for example, a study conducted in Vietnam did not find the relationship among HIV/TB co-infected HIV-infected patients on ART and mortality [13].

LIMITATIONS OF THE STUDY

There were some limitations on using secondary data. There was no information about ethnicity, race, income, migration and housing status, access to information, availability and affordability to treatment and care. The patients did not disclose their definite mode of transmission and sexual risk behaviour, it was inaccurate to analyze in this study. Moreover, only literacy status was known instead of education level. Another limitation was related to the patients of loss to follow-up. Those patients could not confirm whether they were alive or dead according to the data set and they were censored. On the other hand, the exact cause of deaths could not be determined (AIDS related, injury, accidents, homicide, suicide, etc,…) in this study, therefore, attributing all of them to be AIDS related deaths could over estimate AIDS related mortality. Other limitations include incomplete data on literacy status, employment status, alcohol consumption, WHO clinical staging, baseline functional status, delayed seeking care for HIV/AIDS, Hb level and CD_4 count. Long duration of the study period could also affect the survival of patients in this study. For example, the situations in 2005 and 2015 were different such as the eligible criteria for enrolment of ART (geographical criteria and immunological criteria) and ART regimen were changed according to the National Treatment Guideline. As the data for this study was from only one hospital, it could not represent all HIV patients on ART in Myanmar. Nevertheless, the findings demonstrate the outcomes of HIV treatment in a large government sponsored program for a long period.

CONCLUSION AND RECOMMENDATION

In this study, male, older age, WHO clinical stage 3 or 4, not changing ART regimen, bedridden functional status and low CD_4 count were the risk factors for AIDS-related deaths. These indicators should be used to identify patients at higher risk of early mortality in the ART treatment programs. Importantly, co-trimoxazole should be prescribed strictly according to National AIDS Treatment Guideline because not taking co-trimoxazole is one of the risk factors associated with AIDS-related death. The highest hazard rate was found among patients during the first six months of ART initiation. This finding suggested paying special attention to the HIV-infected patients through assessment of OIs and intensive follow-up during the first six months of ART initiation. The finding indicates ART adherence as a very important predictor for AIDS-related deaths. Thus, ways and means should be explored through qualitative researches and share that information to the health care providers to get perfect ART adherence and in turn to prevent the development of drug resistance. These findings are important information for policy makers and HIV/AIDS program implementers to plan and implement appropriate interventions for the improvement of survival of HIV/AIDS patients in Myanmar.

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