ORIGINAL ARTICLE

SURVIVAL AND PREDICTORS OF THE SURVIVAL OF HIV-INFECTED ADULT PATIENTS TAKING HAART AT HAWASSA UNIVERSITY REFERRAL HOSPITAL

Asressie M, Yigzaw K, Telake A

ABSTRACT

Introduction*: The discovery of the combined antiretroviral therapy was a turning point which changed the outlook about AIDS from a virtually death sentence to a manageable chronic disease. Although the field of HIV medicine is rapidly changing, there is lack of recent knowledge about the survival and the predictors of the survival of HIV-infected patients taking HAART in the study area.*

Objective*: To assess the predictors of the survival of patients living with HIV/AIDS who are taking highly active antiretroviral therapy.*

Methods*: Retrospective three-year follow up (cohort) study was employed for randomly selected 436 HIV infected adult patients who were HAART initiated at Hawassa University Referral Hospital. Data was collected from the patients' records by trained BSc. nurses who used a pretested and structured checklist. The Kaplan-Meier and the Cox proportional hazards model were used to estimate survival after HAART initiation and to identify predictors, respectively. Descriptive summary statistics, bivariate, and multivariate regression analyses were used for significance tests.*

Result: *Two hundred fifty-seven (58.9%) study subjects were females and the median age of patients was 31years (IQR=27-39). Three hundred and twelve (71.5%) of the subjects were below 10^{th} grade in educational status with 199 (45.6%) ambulatory and bedridden in functional status, 413 (94.7%) in stages III & IV at the initiation of ART. Two hundred eighty-five (65.4%) of the patients had a CD_4 cell count of less than 200cells/µl, and there were a total of 52 deaths during the follow up period of which 32 (61.5%) & 42 (80.8%) died within the first three and six months of initiation of therapy, respectively. The cumulative probabilities of survival of these patients were 90%, 88%, 87.5% and 87% at 6, 12, 24 and 36 months, respectively. Male sex (HR=1.961, P-value=0.038), bedridden (HR=6.023, P-value<0.001) functional status, CD_4 count below 50cells/µl (HR=3.388, P-value=0.012), not using Cotrimoxazole chemoprophylaxis (HR=2.883, P-value= 0.018) and hemoglobin level below 10mg/dl (HR=6.393, P-value<0.001) were statistically significant predictors of survival, indicating that being male, bedridden, CD_4 count of less than 50cells/µl, not using chemoprophylaxis, and hemoglobin level <10mg/dl increase the risk of death of HIV infected patients who are taking ART with respective hazard ratios.*

Conclusion: *Delayed initiation of ART and not using chemoprophylaxis are poor prognostic factors of survival for HIV/AIDS patients.*

Key words: *survival, predictors, HAART*

INTRODUCTION

Following the first case in 1981, there have been tremendous increases in the understanding of the cause (etiology), mode of transmission, pathogenesis and development of HIV/AIDS (1-3). This knowledge led to the development of the first antiretroviral drug in 1986 and several others since then. So, the advancement of antiretroviral medication evolved from no therapy, monotherapy to combination therapy (4).

Because monotherapy could not suppress the HIV virus efficiently and rather led to the development of resistance, HAART (a combination of three antiretroviral drugs) was recommended in 1996. It was a turning point at which the outlook about AIDS changed from a virtual death sentence to a manageable chronic disease. It was also the year in which optimism & hope was felt at a palpable level (1-5).

The primary goal of effective HAART is to prolong life, reduce HIV related mortality and morbidity in people living with HIV/AIDS (6, 7). To achieve this in the current era, HIV physicians used the slogan

.

"Hit HIV Hard, only when necessary" (8). The main question now is when to start for a better outcome because the times of initiation of ART differ, particularly between developed and developing countries while evidences show that earlier initiation of ART results in longer survival. But many resource limited settings use more conservative criteria for initiating ART than developed countries for different reasons (6).

Ethiopia launched the fee-based and free ART in 2003 and 2005, respectively (7). In February 2010 there were 532 health institutions providing ART (9).

With the fast changing field of HIV medicine, continuous evaluation of the outcomes of intervention is a cornerstone. But there is lack of recent evidence showing the survival time and predictors of the survival after the initiation of ART in Ethiopia in general and Hawassa Referral Hospital in particular. The aim of this research is to assess the predictors of the survival of patients who are taking a highly active antiretroviral therapy at Hawassa University Referral Hospital, SNNPR, Ethiopia.

METHODS

STUDY DESIGN: A retrospective three year follow up (cohort) study using patient records was employed on HIV infected adult patients who were initiated on HAART at Hawassa University Referral Hospital from July 4, 1998- July 3,1999E.C. The reason behind the selection of this period as the initial time for the study was that it was the first time the hospital started the ART service.

STUDY AREA: Hawassa University Referral Hospital founded in 1998 E.C., is located in Hawassa city, capital of SNNPR. The hospital is providing services by four major departments with a capacity of 350 beds. In addition, it provides services in the departments of Ophthalmology, Dentistry, Psychiatry, VCT, and ART. Its ART Clinic has been giving a comprehensive HIV/AIDS care and treatment services for pre-ART and ART patients since 1998 E.C. by trained BSc. nurses and physician supported data clerks.

SOURCE POPULATION: All adult patients (2,195) taking HAART at Hawassa University Referral Hospital.

STUDY POPULATION: All adult patients (630) initiated on a highly active antiretroviral therapy from July 4, 1998 – July 3, 1999 E.C., with complete initial recordings.

INCLUSION CRITERIA: All adult patients aged > 15years were included, patients who were on HAART from June 1998 to June1999 E.C. at Hawassa University Referral Hospital.

EXCLUSION CRITERIA: A total of fifteen patient recordings with incomplete initial clinical values were excluded before sampling.

SAMPLE SIZE DETERMINATION & SAMPLING TECHNIQUE: Sample size was determined by using the EPI-INFO sample size calculation formula for cohort/comparative cross-sectional design. By taking Power = 85 Confidence level = 95%, Ratio (number in exposed: non-exposed) = 1:1, proportion of exposed (Stage IV)= 15.7% and proportion of unexposed (Stage I, II, III)= 6.3% (from Arbaminch's study). The final estimated sample size from this formula, **436**, was used as a minimum sample size of the study.

SAMPLING TECHNIQUE: The study subjects were selected by simple random sampling using computer-generated random numbers and taking the pre-coded patient registrations as a sampling frame.

DATA COLLECTION TECHNIQUE: Data were collected from patient registration books or charts by trained and experienced degree graduate nurses working in the ART clinic of the hospital. They worked under a close supervision using a pretested and structured check list from August 30 to September 28, 2010.

DATA PROCESSING AND ANALYSIS: Data were entered by EP-Info version 3.5.1, 2008 and analyzed using the SPSS version 16 software package. Descriptive and summary statistics was done for all variables. The Cox proportional hazards model was used to identify the predictors of survival. The bivariate Cox regression model was fitted and variables with a p-value of < 0.2 were entered in to the multivariate model. In multiple cox-regressions model, a p-value of < 0.05 was used for the cut point for identifying the significant predictors of survival. The stepwise regression method was employed in multiple Cox-regression models to control multicolinearity. The Kaplan-Meier model was used to estimate survival after HAART initiation and log rank tests to compare survival across categories. The proportional hazards assumption was checked by a scaled schoenfeld residual plot.

DATA QUALITY ASSURANCE: The data collection checklist was pretested with 10% of the subjects and questionnaire re-structuring was done prior to the actual data collection. Data collectors were trained and closely supervised by the principal investigator.

The completeness of the checklist was inspected by supervisors at sites.

Ethical clearance was obtained from the Ethical/ Institutional Review Boards of the School of Public Health, College of Medicine and Health Sciences, the University of Gondar, and Hawassa University. Oral permission was asked from the ART Coordinator of the hospital. Confidentiality was insured by engaging nurses working in the ART Clinic of the hospital, excluding patient names and unique ART numbers from the data collection checklist, and by not describing individuals in the results of the study.

RESULTS

BASELINE SOCIO-DEMOGRAPHIC CHARACTERISTICS OF THE STUDY SUBJECTS: A total of 436 patient records were reviewed for baseline/ initial characteristics and outcomes after the follow up periods. The median age of patients was 31years (IQR=27-39) with the majority 330 (75.7%) patients in the age group of 15-39 years at the start of the antiretroviral therapy.

Of the total study subjects, the majority, 212(48.6%), were unemployed, and 227 (52.1%) were married. Concerning educational status, 37.8% of the study participants were at the level 9^{th} &10^{th} grade . (Table 1describes the socio-demographic characteristics of patients). The median weight at initiation of the antiretroviral therapy was 50kg (IQR= 44-56), with the minimum and maximum weights of 25 & 99 kg, respectively.

CLINICAL CHARACTERISTICS OF PATIENTS AT ART INITIATION: Two hundred and ninety-nine (68.6%) of the patients had opportunistic infections. Of these, 96 (22%), had more than one opportunistic infections at the time of initiation of the antiretroviral therapy. A quarter of these patients had tuberculosis followed by recurrent pneumonia. Three-fourths of the patients disclosed their HIV status, and about 301 (69%) were eligible by both the CD_4 count and clinically. At the initiation of the antiretroviral treatment all of the patients included in the study started their treatment with first line antiretroviral therapy. Nearly half, 196 (45%), of the patients were taking drug type 1a (Stavudine, lamivudine, nevirapine), followed by 92 (21.1%) taking drug type 1c (Stavudine, lamivudine, nevirapine). Cotrimexazole chemoprophylaxis was the only chemoprophylaxis given to 412 (94.5%) of the patients at the initiation of the antiretroviral therapy. Of the total patients who started taking the antiretroviral therapy, the majority, 237 (54.4%), were working in their functional status at the initiation of the therapy. The minimum and maximum CD_4 count was 3 & 902cells/µl, respectively, with a median of 156 cells/ µl (IQR= 82.25-244.75). The minimum & maximum hemoglobin level at the initiation of the antiretroviral therapy was 4 mg/dl and 17 mg/dl with a median of 13 mg/dl (IQR=11-14 mg/dl) (Table 2).

Table 1: Socio-demographic characteristics of HIV/ AIDS patients at initiation of ART at Hawassa University Referral Hospital, Oct, 2010.

Variables	Numbers	Percentage
Sex		
Female	257	58.9
Male	179	41.1
Age		
15-24	58	13.3
25-34	206	47.2
35-44	117	26.8
45-54	40	9.2
55-64	13	3.0
65^{+}	2	0.5
Marital status		
Married	227	52.1
Single	89	20.4
Widowed	60	13.8
Divorced	47	10.8
Separated	13	3
Educational status		
Unable to read & write	97	22.2
Primary (1-8)	147	33.7
Secondary (9-10)	165	37.8
Preparatory	1	0.2
Higher education	26	6
Occupational status		
Unemployed	212	48.6
Daily laborer	140	32.1
Employed	28	6.4
Driver	27	6.2
Merchant	25	5.7
Farmer	4	0.9

Table 2: The clinical characteristics of HIV/AIDS patients at the initiation of antiretroviral therapy at Hawassa University referral hospital Oct, 2010.

Characteristics	Number	percent
Eligibility criteria		
clinical	76	17.4
Immunological	59	13.5
Both clinical and immunological	301	69
Opportunistic infection		
yes	299	68.6
No	177	31.4
Cotrimexazole chemoprophylaxis use		
yes	412	94.5
No	24	5.5
Functional status		
Working	237	54.4
Ambulatory	165	37.8
Bedridden	34	7.8
CD_4 count		
< 200 cell/µl	285	65.4
≥ 200 cell/µl	151	34.6
Hemoglobin level		
<10mg/dl	46	10.5
≥10mg/dl	390	89.4

According to WHO clinical staging, the majority, 277(63.5%) and 136 (31.2%), of the patients were in clinical stages III and IV, respectively, at the initiation of the antiretroviral therapy.

FOLLOW UP RESULTS: All patients were followed for complete 36 months (three years), but for a variety of reasons study participants were retained in the cohort for different lengths of time: they stayed for a minimum of one month, a maximum of thirty-six, and a median of thirty-six months. Pertaining to the outcomes of patients at the end of the follow up period, 256 (58.7%) were alive and 52 (11.9%) dead. The other 75 (17.2%), 44 (10.1%), and 9 (2.1%) patients dropped, transferred out and stopped their treatment respectively. Regarding the time of death of HIV infected patients who were taking HAART, 13 (25%), 32 (61.5%), 42 (80.8%) and 48 (92.3%) of the deaths were within the first one, three, six and twelve months from the start of antiretroviral treatment, respectively. The majority, 36 (69.2%), of the patients who died during the follow up period disclosed their HIV status while the rest didn't.

Out of the 52 deceased patients, 71.2% had opportunistic infections at the initiation of the antiretroviral therapy. All of the patients who died during the follow up period were using the first line regimen drugs. Out of the total HIV infected patients who died, 16 (30.8%) had a CD_4 cell count of less than 50cells/µl, 29 (55.8%) between 50-200cells/µl, and 7 (13.4%) greater than or equal to 200cells/µl. The initial hemoglobin level was less than 10mg/dl for 23 (44.2%) of the total patients who died during the follow up period (see Table 3 for socio-demographic characteristics).

SURVIVAL: As indicated above, the study participants stayed in the cohort for different lengths of time which made the general population at risk of death 10,589 person month or 883 person years. The total death within the three years was 52 persons. This made the risk of death after the initiation of the antiretroviral therapy 52/883 = 6 persons per 100 persons years. Based on the analysis of the data from all patients who were antiretroviral therapy initiated, the cumulative probability of 6, 12, 24 and 36 months of survival from the antiretroviral therapy initiation was 90%, 88%, 87% and 86%, respectively (see Figure 1, Kaplan Meier). The median survival time for the cohort was not reached within this three-year follow up period.

Table 3: The outcome status of study subjects at the end of follow up with respect to their initial socio-demographic and clinical characteristics at HU Referral Hospital, Oct, 2010.

Variables	Patient outcome at end of follow up				
	Alive	Died	DO	TO	Stop
Sex					
Male	95(37%)	29(56%)	33(44%)	17(39%)	5(56%)
Female	161(63%)	23(44%)	42(56%)	27(61%)	4(44%)
Marital status					
Single	47(18%)	11(21%)	19(25%)	10(23%)	2(22%)
Married	135(53%)	27(52%)	35(47%)	26(59%)	4(45%)
Others	74(29%)	14(27%)	21(28%)	8(18%)	3(33%)
Educational status					
Can't read & write	50(20%)	12(23%)	27(36%)	4(9%)	4(45%)
Primary	94(37%)	18(35%)	17(23%)	15(34%)	3(33%)
Secondary & above	112(43%)	22(42%)	31(41%)	25(57%)	2(22%)
Occupational status					
Employed	20(8%)	2(4%)	4(6%)	1(2%)	1(11%)
Unemployed	129(50%)	23(44%)	37(49%)	21(48%)	2(22%)
Daily laborer	81(32%)	17(33%)	22(29%)	15(34%)	5(56%)
Others	26(10%)	10(19%)	12(16%)	7(16%)	1(11%)
Functional status					
Working	165(64%)	12(23%)	32(43%)	21(48%)	7(78%)
Ambulatory & Bed ridden	91(36%)	40(77%)	43(57%)	23(52%)	2(22%)
WHO clinical staging at initiation of ART					
II & III	181(71%)	29(56%)	47(63%)	35(80%)	8(89%)
IV	75(29%)	23(44%)	28(37%)	9(20%)	1(11%)

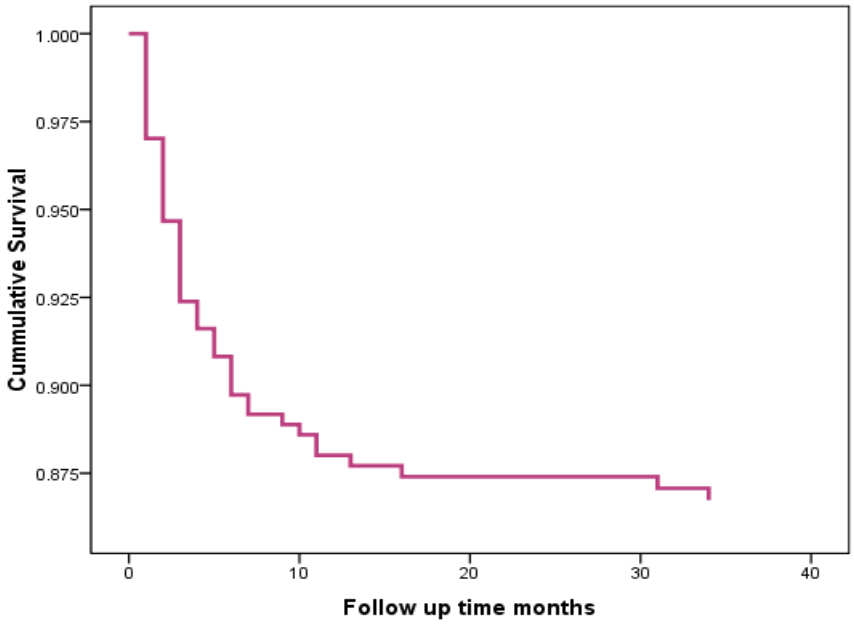

Figure 1: *The survival plot (Kaplan Meier) showing probability of survival of HIV infected patients taking antiretroviral therapy at Hawassa University Referral Hospital Oct, 2010*

PREDICTORS: Regarding the predictors of survival of HIV infected patients taking antiretroviral therapy, in the bivariate analysis, male sex had a lower risk of survival or higher risk of death (HR= 1.955, 95% CI=1.131-3.380) than female sex with a statistically significant difference between its categories (female Vs male) (log rank test, P-value= 0.014) (Figure 2).

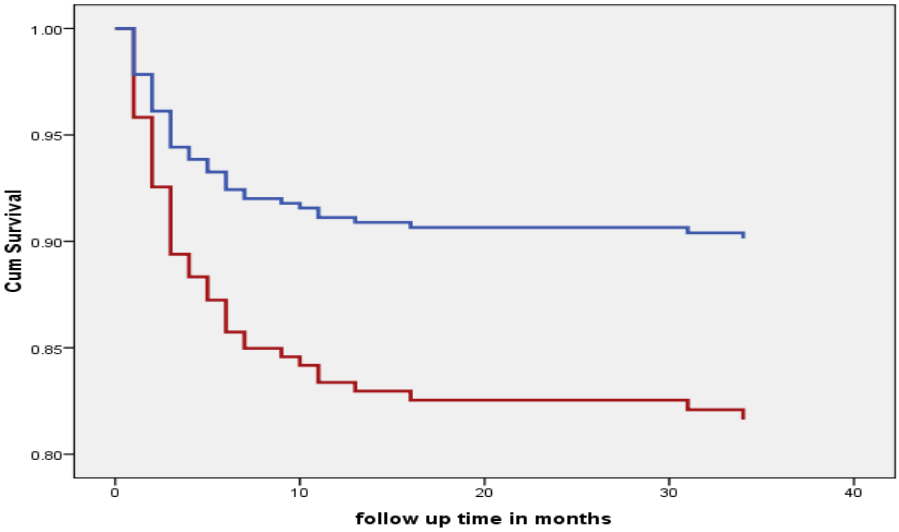

Figure 2: *The survival plot of male and female HIV infected adult patients who were taking antiretroviral treatment at Hawassa University referral hospital, Oct, 2010*

The other predictor variable which was statistically significant at (P-value= 0.072) was the antiretroviral therapy eligibility criteria. Patients started on HAART based on clinical eligibility alone had a better survival than on eligibility by both clinical and immunological (CD_4) criteria with (HR=0.268, 95% CI= 0.084-0.868), meaning that making patients eligible by clinical criteria alone had a low risk of death than by both immunological and clinical criteria.

Patient initial weight at the start of ART is another predictor variable of survival with HR =0.961 (95% CI=0.931-0.992) which implies that a 1kg increase in patient weight will decrease the hazard of death by 3.9%. The other statistically significant predictor is the functional status of patients at the initiation of ART. It is significant at p-value of <0.001 with (log-rank, P-value<0.001). Being bedridden at the time of ART initiation has an HR of 13.986 (95% CI=6.589-29.685) and being ambulatory has a HR of 3.251 (95%CI=1.63-6.50) from working the functional status. This shows that a decreased functional status at ART initiation has a higher risk of death.

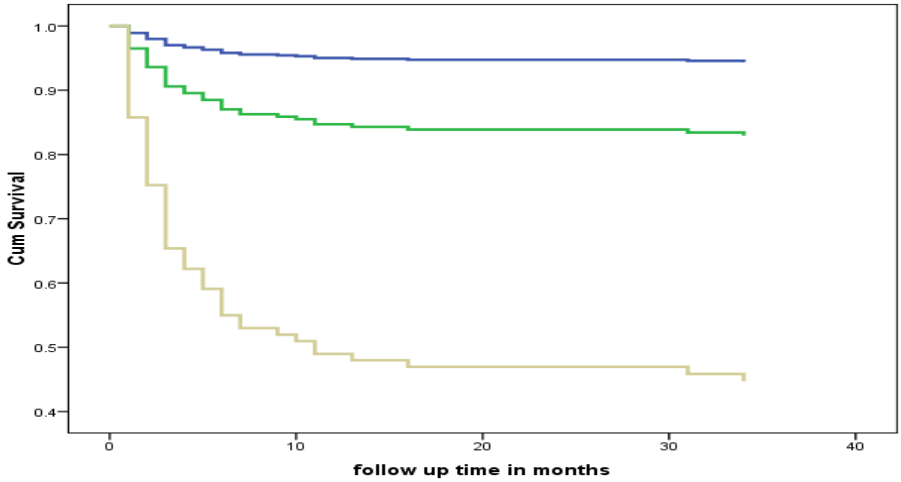

Figure 3: *The survival plot with respect to functional status of HIV infected patients taking ART at Hawassa University referral hospital, Oct, 2010*

Cotrimexazole chemoprophylaxis use is the other significant predictor of survival of HIV infected adult patients who are taking ART in bivariate analysis with HR=0.227 (95% CI=0.111-0.467) with a log rang test of P<0.001 (i.e. cotrimexazole use reduce hazard of death by 77.3% than not using it).

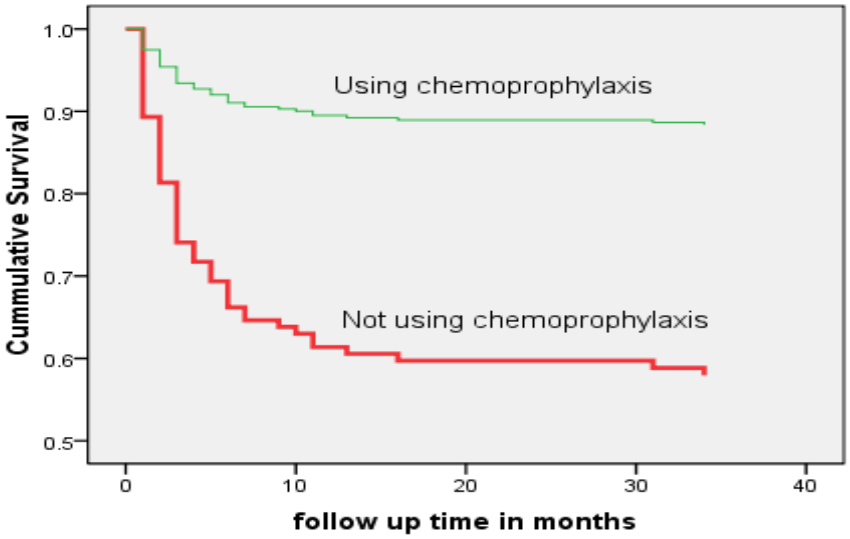

Figure 4: *The survival plot of HIV patients taking ART with respect to their chemoprophylaxis use at Hawassa University referral hospital. Oct, 2010*

An initial CD_4 cell count of less than 50 cells/µl (HR=6.799, P-value<0.001) and a CD_4 cell count of 50-200cells/µl (HR=2.968, P-value=0.010) are significant predictors of death than a CD_4 cell count of ≥ 200cells/µl for HIV infected patients taking ART. This indicates that patients initiated ART with a CD_4 count of < 200 cells/µl have a higher hazard of death than those who initiated ART with > 200 cells/µl CD_4 cell count (Figure 5). The categories are statistically different at a log rank test of P<0.001.

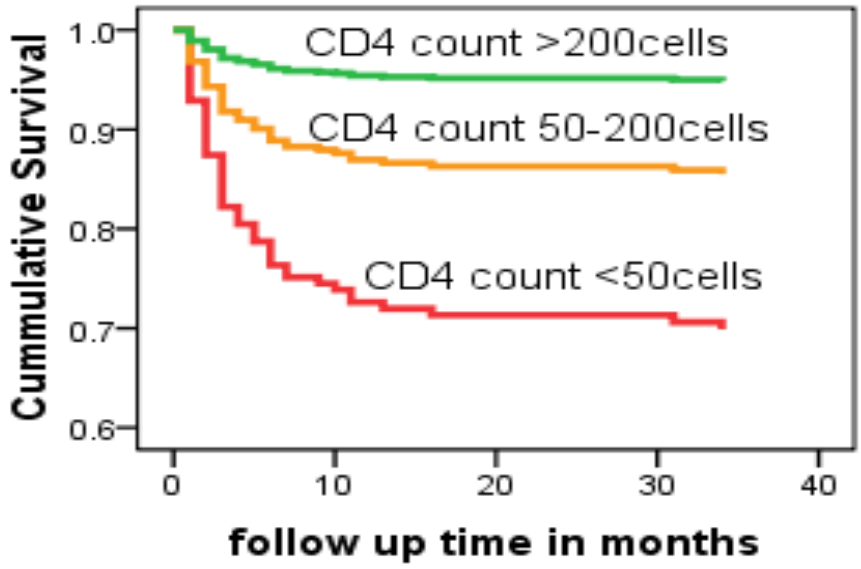

Figure 5: *The survival plot of HIV patients taking ART with respect to their CD_4 count at Hawassa University referral hospital. Oct, 2010*

WHO clinical stages II &III (HR=0.551, P-value=0.033) show a lower hazard of death than stage IV and hemoglobin level of < 10mg/dl (HR=9.555, P-value<0.001) had a higher hazard of death than a hemoglobin level of ≥ 10mg/dl.

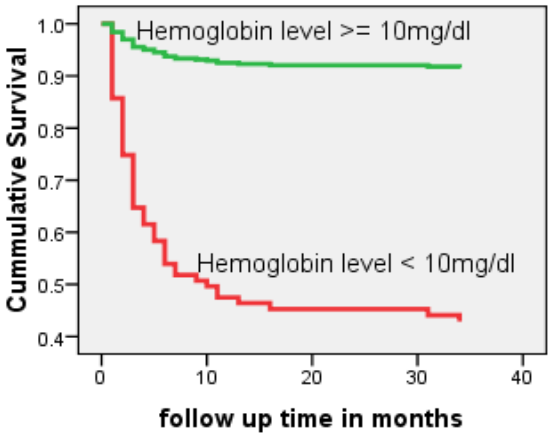

Figure 6: *The survival plot of HIV patients taking ART with respect to their initial hemoglobin level at Hawassa University referral hospital. Oct. 2010*

In the multivariate analysis, male sex (P-value=0.038), functional status (P-value<0.001), use of chemoprophylaxis (P-value=0.018), hemoglobin level (P-value<0.001) and CD_4 cell count (0.010) remain in the final model as a statistically significant predictor of survival for HIV infected patients who are taking ART. The following table summarizes the bivariate and multivariate analysis results.

Table 4: The bivariate and multivariate analysis of statistically significant predictors of survival of HIV infected patients who were taking ART at Hawassa University Referral Hospital, Oct. 2010

variable	Number of death	[11]CHR	P-value	Log-rank	[12]AHR	95% CI
Sex						
Male	29	1.955	0.016	0.014	1.961	1.04-3.71
Female	23	1			1	
Eligibility			0.072			
Both	43	1				
Clinical	3	0.268	0.028	0.049		
CD_4	6	0.689	0.393			
Functional status			<0.001	<0.001	*P-value <0.001	
Working	12	1			1	
Ambulatory	24	3.251	0.001		1.512	0.70-3.25
Bed ridden	16	13.99	<0.001		6.023	2.63-13.81
Prophylaxis						
use	9	1		<0.001	1	
Not use	43	4.41	<0.001		2.883	1.20-6.91
Stage						
IV	23	1		0.029		
II & III	29	0.551	0.033			
CD_4 count			<0.001		*P-value=0.010	
≥200	7	1			1	
50-200	29	2.968	0.010	<0.001	1.401	0.57-3.42
< 50	16	6.799	<0.001		3.388	1.31-8.75
Weight	52	0.961	0.015			
Hemoglobin						
>=10mg/dl	29	1		<0.001	1	
<10mg/dl	23	9.555	<0.001		6.393	3.46-11.80

** - over all p-values for variables having greater than two categories*

DISCUSSION

In this study, about 75% of the patients were in the age group of 15-40 years, and the middle 50% of them were in the age group of 27-39 years showing the affected groups of individuals are in the main productive and reproductive age. About two-thirds (68%) of the patients had opportunistic infections of whom a quarter (25.7%) had tuberculosis, and tuberculosis was the second main reason for drug change of patients after starting ART, indicating that tuberculosis is the main opportunistic infection for both ART and pre-ART patients. The majority, (65%) of the patients, had a CD_4 count of below 200cells/µl at ART initiation that complicates patient outcome and may have an effect on the survival of patients after the initiation of treatment. Moreover, around 62% and 81% of the patients died during the first three and six months of ART initiation, respectively; 45 (86.54%) of the individuals who died had aCD_4.cell count of below 200 cell/µl. Delayed presentation and initiation of ART, Immune Reconstitution Inflammatory Syndrome or drug side effect could be the possible explanations for these early deaths.

The 6th month cumulative probability of survival of these patients was 0.90 (90%), which is a little higher than Botswana's (87.8%), and exactly the same as Haiti's (90%) (12, 13). The 12th month cumulative probability of survival of patients in this study was 0.88 (88%) which is comparable with lower and middle income countries (0.74-0.94) and the Brazilian (88%) but higher than Malawi's (81%), and Botswana's (82.7%) results. This might be due to the differences in the settings and the time of follow up because Botswana's study was national and that of Malawi was in a district setting, while this study was in an urban setting (12-15). The 24th month cumulative probability of survival was 87% in this study, which is similar with the Brazilian (86%), but higher than Malawi's (72%) (15, 16). Eighty-six percent of the patients survived at the end of 3 years in this study, but 79.3% in Botswana's study (12). When we see the overall survival of patients in this study, it is similar and comparable with many of the studies cited.

Regarding the predictors of survival, being male has 1.961 times higher risk of death than being female, which is consistent with studies in Brazil, Malawi and Botswana (12, 15, 16). This might be due to delayed presentation, use of substance, risky sexual behavior, or poor adherence of men to ART.

In this study, being bedridden at the initiation of ART has 6.023 times higher hazard/risk of death than working functional status. This indicates bed ridden patients at the time of ART initiation have a shorter survival time than working patients. This might be due to late presentation of patients or delayed initiation of ART that affect the clinical and immunological improvement.

Not using cotrimexazole chemoprophylaxis has 2.883 times more hazard of death than using it which is consistent with the Croatian finding (17). This may be due to the fact that Cotrimoxazole chemoprophylaxis prevents the development of very serious opportunistic infections, thereby reducing the clinical deterioration of HIV infected patients.

The hazard of death in patients with <50cells/µl CD_4 cell is 3.388 times higher than those with $\geq$200 cells/µl at HAART initiation, implying that patients who start HAART at CD_4 cell >200 cells/µl have a 70% reduction in risk of death than those with lower CD_4. This is consistent with studies in low and middle income countries, Croatia and Serbia/Montenegro, Botswana, Malawi, Haiti and South Africa (12-14, 16-19).

Hemoglobin level <10mg/dl has 6,393 times higher risk of death than >10mg/dl in patients on ART initiation. This shows that anemic patients at ART initiation have a lower survival than non/mildly anemic patients. This is consistent with Botswana's, South African, and Tanzanian studies (12, 17, 20). Anemia at the start of ART may be complicated with the use of ARVs, presence of opportunistic infections or nutritional deficiency.

This study is limited in terms of the duration of follow up and by being a retrospective and non-informative censoring.

CONCLUSION

The six, twelve, twenty four and thirty-six months of survival of these patients is comparable with those of many of the studies done in different parts of the world. This study shows the highest probability of death in the first six months and decreases there after. Bed ridden functional status, male sex, not using Cotrimoxazole chemoprophylaxis, low CD_4 count, and low hemoglobin level are predictors of poor survival, indicating delayed presentation, being male and not using chemoprophylaxis play an important role for the survival of patients after HAART initiation.

RECOMMENDATION

Provision of chemoprophylaxis, earlier ART initiation (>200cells/µl count and working functional status), close follow up of HIV infected adult patients taking ART, particularly in the first six months of ART initiation, investigating and intervening for possible causes of anemia are the possible solutions for improving the survival of patients taking HAART.

REFERENCE

1. Bill F. A Brief History of HIV: The body positive: The complete HIV/AIDS resource. New York, NY 10107: Body Health Resources Corporation; September/October 2007.
2. Ministry of Health & Family Welfare, Government of India. Antiretroviral Therapy Guidelines for HIV-Infected Adults and Adolescents Including Post-exposure Prophylaxis in India. New Delhi: National AIDS control organization; May 2007.
3. Marshal J. History of the HIV epidemic. Cornell University AIDS education and training center; March 2006.
4. Michael S, Raymond A. HIV Treatments: A History of Scientific Advance. The body positive: The complete HIV/AIDS resource. New York, NY 10107: Body Health Resources Corporation; July 2001.
5. Panos Global AIDS Program. Antiretroviral drugs for all: Obstacles to access to HIV/AIDS treatment: Lessons from Ethiopia, Haiti, India, Nepal and Zambia. May 2006. Accessed from www.panosaids.org on 18/05/2010.
6. Michael A, Heidi S, Nancy R. Antiretroviral Treatment. In; HIV Curriculum for the health professional. Houston, Texas, U.S.A: Baylor International Pediatric AIDS Initiative Baylor College of medicine; 2010.
7. Department of Disease Prevention and Control Team. Guideline for implementation of antiretroviral therapy in Ethiopia. Addis Ababa, Ethiopia: Ministry of Health; January 2007.
8. Christian H, Jürgen K. R, Bernd Sebastian K. HIV Medicine. Paris: Flying Publisher; 2006. Accessed from htt:\\ www.HIVMedicine.com on 18/05/2010.
9. MOH- FHAPCO. Monthly HIV Care and ART Update. Addis Ababa: FHAPCO February 2010.accessed from htt:\\www.HAPCO.GOV.et on 18/05/2010.
10. Degu J, Aschalew E, Yewubnesh H, Bernt L. Predictors of early death in a cohort of Ethiopian patients treated with HAART. BMC Infectious Diseases, BioMed Central, 01 September 2006; 6(136).
11. Abiyou K. Health outcome of patients on antiretroviral treatment at Zewditu memorial hospital. February 2009. Unpublished paper.
12. Bussmann H, Wester CW, Ndwapi N, et al. Five -year outcomes of initial patients treated in Botswana's National Antiretroviral Treatment Program. Global Health Sciences Literature Digest May 11, 2009. Accessed from htt:// www.ncbi.nih.gov/pubmed/ on 15/01/2010.
13. Patrice S, Paul L,Macarthur C, et al. Antiretroviral Therapy in a Thousand Patients with AIDS in Haiti. The New England journal of medicine December 1 2005; 353 (22):2325-2334 accessed from www.nejm.org on April 30, 2010
14. Dr Peter White, Survival of HIV-infected patients on antiretroviral therapy (ART) in lower and middle-income countries (LINCs): a systematic review. In; improving parameter estimation, projection methods, uncertainty estimation, and epidemic classification: Report of a meeting of the UNAIDS Reference Group on Estimates, Modeling and Projections held in Prague, Czech Republic, November 29th – December 1st 2006. London: UNAIDS; March 2007. Accessed from http://www.epidem.org on 28/04/2010.
15. Ladjane S, Wolmer de M, Heloisa R. Survival of AIDS Patients and Characteristics of Those Who Died Over Eight Years of Highly Active Antiretroviral Therapy, at a Referral Center in Northeast Brazil. The Brazilian Journal of Infectious Diseases 2008; 12(4):269-277.
16. Laurent F, Arnaud J, Loretxu P,et al. Scaling up of highly active antiretroviral therapy in a rural district of Malawi: an effectiveness assessment. Lancet April 22, 2006; 367: 1335–1342.
17. Josip B, Miroslav L, Davorka L, et al. Marked Improvement in Survival among Adult Croatian AIDS Patients after the Introduction of Highly Active Antiretroviral treatment. Coll. Antropol 2006; 30 (1): 175–179.
18. Jevtovic D, Salemovic D, Ranin J, et al. Long-term survival of HIV-infected patients treated with highly active antiretroviral therapy in Serbia and Montenegro. British HIV Association HIV Medicine 2007; 8: 75–79.
19. Bisola O, Hui Z, Rochelle P, et al. Predictors of mortality in patients initiating antiretroviral therapy Durban, South Africa. South African medical journal March 2008: 98 (3): 204-208.

20. Asgeir J, Ezra N, Bernard J, et al. Predictors of mortality in HIV-infected patients starting anti-retroviral therapy in a rural hospital in Tanzania. BMC Infectious Diseases, BioMed Central 2008; 8(52).