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Statistical Modeling of Survival of Tuberculosis Infected HIV Patients Treated with Antiretroviral Treatment: A Case of Felege Hiwot Referral Hospital, Bahir Dar, Ethiopia

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Abstract

Objectives: This study focused on modeling of the survival of tuberculosis infected HIV patients treated with antiretroviral treatment in Felege Hiwot referral hospital.

Methods: Human Immunodeficiency Virus/tuberculosis (HIV/TB) co-infected patients aged 15 years and above were selected using simple random sampling and included in the study. The sample size for this study was 314 patients. Kaplan-Meier survival curves and Log-Rank test were used to compare the survival experience of different category of patients, and proportional hazards Cox proportional hazards model was employed to identify independent predictors of survival of HIV/TB patients.

Results: Of the total samples 66 (21.0%) were died and 248 (79.0%) were censored. The results of single covariate analysis show that the variables: sex, age, marital status, literacy status, employment status, family size number of living rooms, CD4 count, baseline body weight, WHO stage, regimen type, knowledge about ART, condom use, drug use, alcohol intake, tuberclosis category and regimen change were found to be factors that significantly influence the survival of HIV/TB co-infected patients at 25% significance level. From the Cox regression analysis, the independent factors CD4 count, tuberculosis category, number of living rooms, employment status, alcohol and tobacco use were significant. The odds of being at risk of death for patients who does not smoke tobacco is 47.5% less than those who use tobacco.

Conclusions: In conclusion, baseline CD4 count, tuberculosis category, number of living rooms, employment status, alcohol and tobacco use were the main factors significantly influencing the survival time of HIV/TB co-infected patients. We recommend that, there should be a careful monitoring of patients with low CD4 count, less than two numbers of rooms, disseminated and extra-pulmonary TB, having risk behaviors like drinking alcohol and not being employed is necessary to improve survival of HIV/TB co-infected patients.

Keywords: HIV/TB Co-infection • Survival Analysis • Antiretroviral Treatment • Cox proportional hazards model

Introduction

Background

The dual infections of HIV and Tuberculosis remain serious health issues in the world. Globally, the incidence of opportunistic infections among AIDS patients has declined after ART introduction. However, tuberculosis, among other infectious diseases remains a major cause of morbidity in developing countries. Without treatment, as with other opportunistic infections, HIV and TB can work together to shorten the life of the person infected [1]. The world health organization recommends that all HIV infected persons should be screened for TB and HIV infected persons without active TB disease be evaluated for treatment of latent TB infection. The impact of HIV/AIDS on TB is significant. With 24% of all TB deaths being associated with HIV, 13% of new TB cases are related to HIV/AIDS at the global [2].

The world health organization (WHO) estimates that 11.1 million people are co-infected with TB and HIV, over 90% of these dually infected individuals reside in developing nations. In 2011, 430,000 people are estimated to have died of TB and HIV co-infection [3, 4]. In the same year, Seventy-nine percent of the HIV positive TB cases were in the African region. The burden of disease through HIV/TB co-infection is particularly high in sub-Saharan African [4]. ART alone somewhat reduces the risk of TB disease; however, even after ART is started, the risk of TB still remains many times higher than the general population, especially during the first few years of ART. Even among those who have already had TB in the past and been cured, they are still extremely susceptible to recurrent TB disease. Ethiopia was among the first few African countries to introduce ART in 2003, in selected health facilities following the issuance of the National Antiretroviral Drugs (ARVs) Supply and Use Policy in 2002. The Ethiopian free ART scheme was launched in 2005 [5].

TB is the most common opportunistic infection among HIV infected individuals including those who are taking ART and co-infected individuals are at high risk of death. TB may occur at any stage of HIV disease and is frequently the first recognized presentation of underlying HIV infection. As compared to people without HIV, people living with HIV have a 20-fold higher risk of developing TB and the risk continues to increase as CD4 cell counts progressively decline [6].

In Ethiopia, TB is the leading cause of morbidity, one of the three major causes for hospital admission, and the second killer next to malaria [7]. TB and HIV co-infection are associated with special diagnostic and therapeutic challenges and constitute an immense burden on healthcare systems of heavily infected countries like Ethiopia [7, 8]. The TB-HIV co-infection rate in Ethiopia is 41% [3]. This rate is still high; consequently, it needs further study to identify factors related to high rates of HIV/TB co-infection and low survival times of these patients.

Most of the studies in Ethiopia focused on the prevention and factors that increase the chance of contracting the disease. It can be said that, less attention was given on the survival of HIV positive patients infected with tuberculosis taking ART. The extent of relevance of socio-demographic, clinical and risk behavior factors for survival of HIV/TB in Ethiopia setting is not yet well described by previous studies. This study motivates to identify the major factors affecting survival time of HIV/TB co-infected patients under ART and to predict the survival probability of these individuals. Thus the main objective of this study is to model the survival time of people living with HIV under anti-retroviral therapy who had screened positive for tuberculosis.

Methods and Matreials

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The study area

This study was conducted at Felege Hiwot referral hospital, which is located in Bahir Dar city. The city is located approximately 565 km northwest from the capital city of Ethiopia, Addis Ababa. Based on the 2007 census conducted by the Central Statistics Agency of Ethiopia, Bahir Dar city has a total population of 221,991, of whom 108,456(48.8%) are men and 113,535(51.14%) women. Felege Hiwot Referral Hospital provides general outpatient and inpatient services, including surgical and obstetric emergency care. Infectious diseases account for most of the inpatient and outpatient visits. It has been providing voluntary counseling and testing (VCT) services. In 2003, the ART clinic of the Referral Hospital started its activity; after the Ethiopia government launches free ART in 2005, the Referral Hospital started to provide free service to patients.

The data

This study is a retrospective cohort study. The study reviews patient's pre-ART charts, intake forms and follow up charts of HIV/TB co-infected patients in Bahir Dar Felege Hiwot Referral hospital. Each patient has one medical file containing all TB and HIV notes, which includes the patient intake forms and HIV care and follow-up card, prepared by Federal ministry of health (FMOH). Thus, in this study secondary data, which collected from patients follow up records, are used. From this record of the patients, the variables, which are important for the study, are selected by using the patient's identification number or the laboratory code without any direct contact with the patients. Instead, it is done by communicating with the nurses and counselors to get the medical record and other information important for the study. By the time we collect the data, 15,150 patients have visited the ART clinic. Of these 10441 are on ART since the start of ART and currently active ART patients are 6074. The total number of patients in the target population is 806, with a sample size of 325.

Sampling design and sampling methods

The target populations for this study are patients under the follow up of ART at Felege Hiwot referral hospital from October 2007 to September 2012 co-infected with tuberculosis. To sample those TB tested HIV patients from the population of HIV patients obtained from Felege Hiwot Referral hospital ART clinic data by using their charts and then select HIV/TB co-infected patients by simple random sampling technique. Our analysis was restricted to HIV patients under ART who are positively screened for tuberculosis, whose age is ≥15 years. The study include an HIV infected patients >=15 years of age under ART and diagnosed for TB and receive TB treatment. However the study exclude those patients on ART with age less than 15 years, those patients who are not initiated for antiretroviral treatment, those who are tuberculosis negative, those with unknown TB status, whose diagnosis time was missing and those patients whose death month was missing by looking the patient's record. Then, for each patient satisfying eligibility criteria the medical file is traced to have explanatory information.

Variables included in the study

Dependent variable

The dependent variable used in this analysis is survival time of HIV-TB co-infected patients. It was measured in months starting from date of ART initiation to death or censored time. Patient Status were coded as '1' if the death time is observed and '0' if censored.

Independent variables

Variables included in the study were selected based on some past studies and those that are expected to be determinant factors of the survival of HIV patients infected with tuberculosis. This study considers several predictors to examine the major factors of survival of HIV/TB co-infected patients. The variables considered in this study were: Age, Gender, Residence of patient, Marital status, Literacy status, Religion, Base line body weight, CD4 count at the start of ART, Regimen type at start of ART, Knowledge about ART, Employment status, Number of living rooms at start, Number of people in the household (family size) at start, WHO clinical stage at start of ART, Alcohol intake, Tuberculosis category, Tobacco use, Drug use, Condom use during sexual intercourse, and Regimen change during TB diagnosis.

Data Analysis

Descriptive methods for survival data

An initial step in the analysis of a set of survival data is to present numerical or graphical summaries of the survival times for individuals in a particular group. This includes survival distribution and Kaplan Meier survival function estimation that are used for the estimation of the distribution of survival time from all of the observations available. In addition, we can make comparisons of the life experience of two or more groups of subjects differing for a given characteristic. Now a day is the Kaplan Meier method for estimating survival curves and the Log Rank test for comparing two-estimated survival curves are most frequently used statistical tools in medical reports on survival data [9].

Semi-parametric models for survival data

The statistical approach to be used in this study is the analysis of time to event data, which is survival data analysis. Survival analysis is an important statistical technique used to describe and model time–to–event data. The most popular of the semi-parametric models is the Proportional hazards model, which has the property that ratio of the hazards of two individuals at time t can depend on the values of their explanatory variables, say $\beta \ni x = \beta_1 x_1 + \beta_2 x_2 + \ldots + \beta_p x_p$, but does not depend on time t [10].

Since no particular form of probability distribution is assumed for the survival times, proportional hazards model is referred to as a semi-parametric or distribution free model. The Cox proportional hazards model is given by:

h(t;X) = exp^(β^' X) h0(t)

where $h(t;\boldsymbol{X})$ represents the hazard function for the i^{th} patient; $h_0(t)$ is the baseline hazard function at time t; $\beta = (\beta_1, \beta_2, \ldots, \beta_p)$ is a vector of unknown parameters that are assumed to be the same for all individuals in the study and $\boldsymbol{X} = (x_{1i}, x_{2i}, \ldots, x_{ki})$ for $i=1,2,\ldots,n$ is a vector of explanatory variables for the i^{th} individual at time t. Consequently, from the proportional hazard function, we can obtain the estimated survivor function, which is given by:

S^_i (t)= S^0 (t)exp (β ^,X)

Where, $\hat{S}_0(t)$ is the baseline survival function. Fitting a proportional hazards model to an observed set of survival data involves estimating the unknown parameters = $(\beta_1, \beta_2, \ldots, \beta_p)$ in the model.

The goal of Cox regression is to explore the association between the survival of patient and many covariates (independent variables or predictors). To accomplish this goal, we need to create a model that includes all variables that are useful in predicting the dependent variable. First, consider the model that will include all the predictors that had a p-value of less than 0.25 in the univariate analyses. That means any variable whose univariate test has a p-value < 0.25 should be considered as a candidate for multivariate analysis.

Results and Discussion

Univariate analysis

The data comprised a sample of 314 patients who are enrolled in Felege Hiwot Referral hospital ART clinic with TB. Out of 314 patients considered in the analysis, 66 (21.0%) were dead and 248 (79.0%) were censored. The distribution of patient's death status based on the socio-demographic and the clinical and risk behavior characteristics are summarized in respectively (Table 1). As can be seen, 237 (75.5%) of the patients live in town, whereas 72 (22.9 %) and 5 (1.6%) live near town and rural areas respectively; and 148 (47.1%) and 166(52.9%) are female and male patients, respectively. Among different categories of marital status, widowed patients have small proportion of deaths (1.9%) with respect to total population. Patient who are not able to work due to illness have high proportion of death than the working and unemployed groups. Patients who have less than two family numbers accounted a larger proportion in the sample (about 54.5%) compared to patients with more than two family numbers (45.5%). Similarly, patients with less than two living rooms accounted a larger proportion in the sample (about 57.0%) compared to patients who have more than two living rooms (43.0%).

It can be observed from that, patients who are in WHO clinical stage III and stage IV have high proportion in HIV/TB deaths with respect to total population.

Table-1. The distribution of HIV/TB co-infected patient's death status with respect to different socio-demographic variables of the patients.

Explanatory variables	Codes	Number of Censored (%)	Number of Death (%)	Total (%)
Gender	Female Male	117(37.3%) 130(41.4%)	31(9.9%) 36(11.5%)	148(47.1%) 166(52.9%)
Residence of patients	Town Near town Rural	186(59.2%) 59(18.8%) 3(1.0%)	51(16.2%) 13(4.5%) 2(0.6%)	237(75.5%) 72(22.9%) 5(1.6%)
Marital status	Never married Married Separate Divorced Widow	45(14.3%) 110(35.0%) 38(12.1%) 40(12.7%) 14(4.5%)	9(2.9%) 32(10.2%) 6(1.9%) 13(4.1%) 6(1.9%)	54(17.2%) 142(45.2% 44(14.0%) 53(16.9%) 20(6.4%)
Literacy status	Illiterate Primary Secondary Tertiary	61(19.4%) 54(17.2%) 90(28.7%) 43(13.7%)	15(4.8%) 20(6.4%) 18(5.7%) 13(4.1%)	76(24.2%) 74(23.6%) 108(34.4%) 56(17.8%)
Religion	Orthodox Muslim Others (protestant, catholic, etc)	228(72.6%) 15(4.8%) 5(1.6%)	60(19.1%) 5(1.6%) 1(0.3%)	288(91.7%) 21(6.4%) 6(1.9%)
Employment status	Unemployed Employed Not working due to illness	53(16.9%) 31(9.9%) 164(52.2%)	15(4.8%) 22(7.0%) 29(9.2%)	68(21.7%) 53(16.9%) 193(61.5%)
Number of living rooms	<2 >=2	137(43.6%) 111 (35.4%)	42(13.4%) 24(7.6%)	179(57.0%) 135(43.0%)
Family size	<2 >=2	128(40.8%) 120(38.2%)	43(13.7%) 23(7.3%)	171(54.5%) 143(45.5%)

Similarly, the data indicate that there are a very high proportion of deaths among HIV/TB co-infected individuals, who experience risk behaviors like not using condom during sexual intercourse, drinking alcohol, smoking tobacco and using soft/hard drugs. Most of the study subjects 150 (47.8%) had extra-pulmonary Tuberculosis, 143(45.5%) had pulmonary (both smear negative and smear positive) and 21 (6.7%) had disseminated tuberculosis. Patients who are already on ART, when TB treatment begun the ART regimen must be modified at least the completion of TB therapy. In this study 130 (41.4%) patients change their original regimen type during TB diagnosis, of these 26 (8.3%) are died (Table 2).

It indicates the descriptive measures of age, CD4 count and baseline body weight of patients in the study. From this table we can see that, the mean age of individual is 32.42 with standard deviation 9.032. The average CD4 count at the start of ART treatment was 114.18, and the average baseline body weight at start of ART was 46.86.

displays the details of the log rank test for the different categorical variables. Statistical test using log-rank test in shows that there is significant difference between the survival time of male and female patients. Among different employment categories, patients who have no work due to illness had the lowest survival time ($p<0.000$). With increasing number of living rooms, the survival time increases. On the other hand, when family size decreases, survival time decreases. The log-rank test for survival difference of these two variables were all highly significance ($p<0.000$). The other categorical variables in the study are age and marital status of the patients. As the result shows, both are not statistically significant at 5% significant level (Table 3).

Table 2. The distribution of HIV/TB co-infected patient's death status with respect to different clinical and risk behavior characteristics of patients.

	N	Minimum	Maximum	Mean	Std. Deviation
Age of patients	314	15	68	32.4	9.032
CD4 count at the start of art treatment	314	3	396	11.18	85.535
Baseline body weight for a patient	314	24	69	46.86	7.607

Table 3. Descriptive results of patients for continuous variables.

Explanatory variables	Codes	Number of censored (%)	Number of death (%)	Total (%)
Who stage at start	Stage I	14(4.5%)	1(0.3%)	15(4.8%)
	Stage II	43(13.7%)	7(2.2%)	50(15.9%)
	Stage III	141(44.9%)	31(9.9%)	172(54.8%)
	Stage IV	50(15.9%)	27(8.6%)	77(24.5%)
Tuberculosis category	Pulmonary	122(38.9%)	21(6.7%)	143(45.5%)
	Extra-pulmonary	118(37.6%)	32(10.2%)	150(47.8%)
	Disseminated	8(2.5%)	13(4.1%)	21(6.7%)
Regimen type at start	1A	81(25.8%)	24(7.6%)	105(33.4%)
	1B	48(15.3%)	10(3.2%)	58(18.5%)
	1C	80(25.5%)	19(6.1%)	99(31.5%)
	1D	39(12.4%)	13(4.1%)	52(16.6%)
Regimen change during TB diagnosis	No	144(45.9%)	40(12.7%)	184(58.6%)
	Yes	104(33.1%)	26(8.3%)	130(41.4%)
Knowledge about ART	No	43(13.7%)	24(7.6%)	67(21.3%)
	Yes	205(65.3%)	42(13.4%)	247(78.7%)
Alcohol use	No	203(64.3%)	41(13.4%)	244(77.7%)
	Yes	45(14.3%)	25(8.0%)	70(22.3%)
Tobacco use	No	216(68.8%)	49(15.6%)	265(84.4%)
	Yes	32(1.2%)	17(5.4%)	49(15.6%)
Drug use	No	187(59.6%)	41(13.1%)	228(72.6%)
	Yes	61(19.4%)	25(8.0%)	86(27.4%)
Condom use during sexual intercourse	Never	193(61.5%)	56(17.8%)	249(79.3%)
	Sometimes	34(10.8%)	5(1.6%)	39(12.4%)
	Rarely	9(2.9%)	4(1.3%)	13(4.1%)
	Always	12(3.8%)	1(0.3%)	13(4.1%)

Single covariate analysis

The single covariate analysis based on the Wald statistics for each explanatory variable provides a preliminary insight into the relationship between each covariates and survival time of HIV/TB co-infected patients. The results are presented. A modest level of significance 25% was used to select potential covariates included in multiple covariate Cox regression analysis. Based on the Wald test results, 17 covariates with p-values less than 0.25 are selected for inclusion in the multiple Cox regression analyses. These are sex, age, marital status, education level, employment status, number of living rooms, family size, CD4 count, baseline body weight, WHO stage, knowledge about ART, alcohol intake, tobacco use, drug abuse, tuberculosis category and regimen change. Condom use has p-value greater than 25% significance level. Since, it prevents HIV transmission; it is included in the final model purposefully (Table 4).

Table 4. Comparison of Survival Experience on HIV/TB Co-infected Patients Using Different Predictors.

Variables		Mean survival time	Chi-square	Log rank p-value
Sex	Female	32.397	5.029	0.025**
	Male	40.431		
Age	15-24	30.577	3.809	0.283
	25-34	40.077		
	35-44	37.589		
	45 and above	28.459		
Residence	Town	37.708	2.533	0.282
	Near town	40.047		
	Rural	23.800		
Marital status	Never married	34.113	4.008	0.405
	Married	38.630		
	Separate	39.443		
	Divorced	35.067		
	Widow	32.778		
Literacy status	Illiterate	30.269	5.849	0.119
	Primary	34.016		
	Secondary	37.917		
	Tertiary	40.892		
Religion	Orthodox	39.083	0.196	0.907
	Muslim	23.518		
	Others	27.000		
Baseline body weight	<40	32.955	11.448	0.009**
	40-50	37.619		
	50-60	37.275		
	Above 60	41.381		
Baseline CD4 count	<50	32.556	28.871	0.000**
	51-200	37.599		
	>=200	44.969		
Regimen type	1A	38.742	0.932	0.817
	1B	29.765		
	1C	38.643		
	1D	36.068		
Knowledge about ART	No	28.245	28.828	0.000**
	Yes	40.867		
Employment status	Unemployed	32.807	54.338	0.000**
	Not working due to illness	19.666		
	Employed	42.072		
Number of living room	<2	35.542	10.226	0.001**
	>=2	41.311		
Number of person in house	<2	36.308	14.138	0.000**
	>=2	40.397		
WHO clinical stage	Stage I	40.000	26.143	0.000**
	Stage II	43.403		
	Stage III	38.115		
	Stage IV	31.956		
Drug abuse	No	40.848	22.019	0.000**
	Yes	26.578		

Alcohol	No	40.907	26.373	0.000**
	Yes	28.950		
Tobacco use	No	40.354	22.343	0.000**
	Yes	21.341		
TB category	Pulmonary	42.114	39.469	0.000**
	Extra- Pulmonary	35.449		
	Disseminated	24.599		
Condom use	Never	32.272	3.674	0.298
	Sometimes	42.653		
	Rarely	36.200		
	Always	12.000		
Regimen change	No	35.669	4.549	0.033**
	Yes	40.692		

Table 5. Single Covariate Analysis of Cox Proportional Hazards on the Time to Death of HIV/TB Co-infected Patients.

Variables	$\hat{\beta}$	s.e	Wald	df	Sig.	$exp(\hat{\beta})$	95% CI for $exp(\hat{\beta})$	
							Lower	Upper
Sex	-0.579	0.262	4.897	1	0.027*	0.560	0.335	0.936
Age	0.234	0.152	2.383	1	0.123**	1.262	0.939	1.702
Location	0.038	0.266	0.021	1	0.884	1.040	0.617	1.753
Religion	-0.062	0.335	0.034	1	0.852	0.940	0.487	1.813
Marital status	0.129	0.103	1.574	1	0.209**	1.138	0.930	1.394
Literacy status	-0.186	0.117	2.541	1	0.112**	0.830	0.659	1.044
Employment status	-0.492	0.137	12.991	1	0.000*	0.611	0.468	0.799
Family size	-0.969	0.267	13.206	1	0.000*	0.379	0.225	0.640
Number of living rooms	-0.825	0.265	9.717	1	0.002*	0.438	0.261	0.736
CD4 count	-1.013	0.194	27.169	1	0.000*	0.363	0.248	0.532
Baseline body weight	-0.302	0.154	3.855	1	0.049*	0.740	0.547	0.999
WHO stage	0.832	0.173	23.139	1	0.000*	2.300	1.638	3.229
Regimen type	0.164	0.110	2.214	1	0.137**	1.178	0.949	1.461
Knowledge about ART	-1.266	0.264	23.005	1	0.000*	0.264	0.157	0.445
Condom use	-0.197	0.197	1.001	1	0.316	0.821	0.558	1.208
Drug use	1.185	0.266	19.874	1	0.000*	3.271	1.943	5.508
Tobacco use	1.280	0.288	19.760	1	0.000*	3.597	2.046	6.326
Alcohol use	1.250	0.258	23.395	1	0.000*	3.493	2.104	5.798
TB category	0.983	0.184	28.569	1	0.000*	2.675	1.865	3.837
Regimen change	-0.568	0.268	4.489	1	0.034*	0.567	0.335	0.958

Multiple covariate analysis

Multiple-covariate analysis is done using the significant variables in the single covariate analysis. A stepwise selection method was carried out to select the most important covariates among the 17 covariates provided from the univariate analyses. As a result, six of the variables were found to be significant using the stepwise likelihood ratio test of Cox regression procedure at significance level of 0.05 (Table 5).

The variables that are found to be significant in the final model are TB category, CD4 count, number of living rooms, employment status, alcohol intake and tobacco use. The values of the Wald statistic for individual β coefficients support that the estimated values $\hat{a}_i$'s are significantly different from zero at α=5% level of significance for all the above six covariates. The remaining variables, which were used in the single covariate analysis, are found to be non-significant at α=5% level. The estimated parameters $\hat{a}_i$, their standard error, and the hazard ratio corresponding to each estimated coefficient is given in the Table. As can be seen from this, survival of the co-infected patients is significantly related with TB category, baseline CD4 count, number of living rooms, employment status, alcohol intake and tobacco use.

Finally, we take into account the possible interactions among covariates that are significant in multivariable analysis (i.e., by taking one covariate at a time to the model). The Wald statistic is employed for the same task and the result verifies that none of the interaction terms were significant at 5% level.

As can be seen in the martingale residual plot shows that, there is no indication of a lack of fit of the model to individual observations.

Interpretation and discussion of the results

As we have seen from, the variables TB category, baseline CD4 count, alcohol intake, tobacco use, number of living rooms and employment status remain in multi-covariate model as the factors affecting survival status of HIV/TB co-infected patients. We can now interpret the effect of these covariates by using their estimated Hazard ratio given in above.

The first factor, which affects the survival of HIV patients with TB, is the category of TB. Poor survival of HIV patients with TB correlates with the anatomical site of TB. The odds ratio indicates that the risk of death in patients with both pulmonary and extra-pulmonary TB is 29.0% and 44.7% less than the patients with disseminated TB category respectively. Similar findings were also reported in earlier study conducted by [11].

The odds of death risk, for those with CD4 count <50 is 7.703 times higher than those with CD4 count >=200. The odds of death risk with CD4 count between 51 and 200 is 5.928 times higher than those with CD4 count >=200 adjusting

Table 6. The Parameter estimates, Standard errors and the Hazard Ratios of the Variables in Final Cox proportional Hazards Model.

Variables	$\hat{\beta}$	S.E.	Wald	Df	Sig.	$exp(\hat{\beta})$	95% CI $for\ exp(\hat{\beta})$
CD4 count(ref.= >=200)							
CD4 count (<=50)	1.951	0.587	11.034	1	0.000***	7.703	(2.225,22.231)
CD4 count (51-200)	1.779	0.550	10.441	1	0.001***	5.928	(3.014,17.449)
Employment status(ref=Employed)							
Unemployed	0.794	0.347	5.222	1	0.022***	2.214	(1.120,4.376)
Not working due to illness	1.642	0.354	21.508	1	0.000***	5.168	(2.581,10.346)
Number of living room(ref=>2)							
Number of living room (<2)	0.588	0.278	4.488	1	0.031***	1.801	(1.045,3.105)
Tobacco use(ref=No)							
Tobacco use(Yes)	-0.644	0.314	4.213	1	0.040***	0.525	(0.284,0.971)
Alcohol(ref=No)							
Alcohol(Yes)	-1.024	0.288	12.601	1	0.000***	0.359	(0.204,0.632)
Tuberculosis category (ref=Disseminated)							
Plumonary	-1.219	0.407	8.975	1	0.002***	0.290	(0.130,0.645)
Extra- Pulmonary	-0.805	0.354	5.172	1	0.023***	0.447	(0.223,0.895)

for other covariates in the study. Thus, higher baseline CD4 count is associated with reduced risk of death of HIV patients with TB. In line with our findings, studies by provided evidence that low baseline CD4 cell count was a strong risk factor for early mortality (Table 4).

It is an undeniable fact that employment status of a patient is a major factor in maintaining his/her income levels and living conditions. The results from our study show that employment status also has significant influence on HIV/TB co-infected patients. The odds ratio estimate shows that the hazard of death for patients not working due to illness is 5.168 times higher than those on the job. This result agrees with the results of similarly, patients living in more than two rooms are more likely to survive than those living in less than two rooms (odds ratio = 1.801). Number of living rooms can be used as an indicator economic status of patients. Patients with better economic status have better chances of survival under ART.

The other covariate that has negative impact on survival of HIV/TB co-infected patients is drinking alcohol. The outcome of this study shows that the hazard rate of the non-alcoholic patients is about 36% lower than for patients who drink alcohol. Tobacco use has also significant effect on the survival of HIV/TB co-infected patients. Smokers are more likely to be infected with TB and to progress to active TB disease. If tobacco smoking increases the impact of TB in HIV-negative individuals, its effect in HIV-positive individuals may be significantly greater. Data from this study supports the association of tobacco smoking and HIV/TB co-infected individuals. The odds of being at risk of death for patients who does not smoke tobacco is less by 47.5% than those who use tobacco (Table 5, 6).

Conclusion and Recommendations

The objective of the present study was to examine the survival probability of HIV/TB co-infected patients and to identify major factors that affect the survival of patients under ART. To achieve this end, Cox regression analysis was conducted, and the result shows that TB category, CD4 count, employment status, number of living rooms, alcohol and tobacco use were found to be significant factors.

Although, TB is a preventable and curable disease in almost any socio-economic circumstances especially with the implementation of DOTs, it is associated with high mortality in HIV infection. Effective TB treatment and ART reduces mortality among HIV/TB co-infected patients, but in this study survival of patients co-infected with HIV and TB remains low. So, from this result we recommend the following.

Early admission of the patients is recommended. Physicians are expected to work hard to bring about behavioral changes. Moreover, systematic screening and close follow up of patients for signs and symptoms of TB after starting ART should be given attention. In addition, the limited availability of more sensitive diagnostic tests for TB in HIV/AIDS patients under ART must be addressed. Furthermore, further research is recommended to deal with how to increase the survival probability of HIV/TB co-infected patients treated with ART.

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